

**Excerpts From the Director's Report  
*to the***

**National Advisory Council on Drug Abuse**

**Women, Sex/Gender Differences and  
Drug Abuse**



**2005 - 2008**

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# National Institute on Drug Abuse

## Director's Report to Council

The National Advisory Council on Drug Abuse is an advisory body established to provide advice, consultation, and recommendations on the policies and activities of the National Institute on Drug Abuse (NIDA). A critical function of the Council is its role in the dual review process of grant applications which occurs three times each year. Following evaluation of applications for scientific and technical merit by an Initial Review Group composed primarily of non-federal scientific experts in the subject area, a second level of review is provided by the Council so as to ensure a comprehensive and unbiased evaluation of each application.

For the Council to fulfill its full range of responsibilities, it must be kept abreast of NIDA's activities, including the results of NIDA's research. To keep Council informed, the NIDA Director presents a report on NIDA activities entitled, *Director's Report to the National Advisory Council on Drug Abuses*, at each meeting. These full reports are available at <http://www.nida.nih.gov/about/welcome/volkowpage.html#DirectorsReports>.

The present document contains research findings on the topic of women and sex/gender differences that appeared in the issues of the *Director's Report to the National Advisory Council on Drug Abuse* during the years 2005-2008. These reports and future reports can be accessed at <http://www.nida.nih.gov/WHGD/WHGDDirRep.html>.

NIDA supports research on women and sex/gender differences in all areas of drug abuse, from preclinical research to research on interventions and services. For information about this research program, please visit <http://www.nida.nih.gov/WHGD/WHGDHome.html> or contact Cora Lee Wetherington, Ph.D., Program Coordinator, [wetherington@nih.gov](mailto:wetherington@nih.gov), 301-435-1319, or Samia Noursi, Ph.D., Deputy Program Coordinator, [snoursi@mail.nih.gov](mailto:snoursi@mail.nih.gov), 301-594-5622.

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# DIRECTOR'S REPORT TO COUNCIL

February 2005

## **BASIC NEUROSCIENCES RESEARCH**

### Cannabinoids and Pregnancy

Ectopic pregnancy is a major reproductive health issue. Although other underlying causes remain largely unknown, one cause of ectopic pregnancy is embryo retention in the fallopian tube. In a recent study, Dr. Haibin Wang and his associates, Vanderbilt University of Medical Center, Nashville, TN, show that genetic or pharmacologic silencing of cannabinoid receptor CB1 causes retention of a large number of embryos in the mouse oviduct, eventually leading to pregnancy failure. This was reversed by isoproterenol, a beta-adrenergic receptor agonist. Impaired oviductal embryo transport is also observed in wild-type mice treated with methanandamide. Collectively, their results suggest that aberrant cannabinoid signaling impedes coordinated oviductal smooth muscle contraction and relaxation crucial to normal oviductal embryo transport. Colocalization of CB1 and beta2-adrenergic receptors in the oviduct muscularis implies that a basal endocannabinoid tone in collaboration with adrenergic receptor coordinates oviductal motility for normal journey of embryos into the uterus. Besides uncovering a new regulatory mechanism, this study could be clinically relevant to ectopic pregnancy. Wang, H., Guo, Y., Wang, D., Kingsley, P.J., Marnett, L.J., Das, S.K., DuBois, R.N. and Dey, S.K. *Nature Medicine*, 10, pp. 1074-1080, 2004.

### Differences in Maternal Styles of Rearing May Predispose to or Protect Individuals from the Development of Addiction

While many people experiment with drugs, relatively few individuals develop a true addiction. Dr. Michael Meaney and his colleagues hypothesized that, in rats, such individual differences in the actions of addictive drugs might be determined by postnatal rearing conditions. To test this idea, they investigated whether stimulant- and stress-induced activation of nucleus accumbens dopamine transmission and dopamine-dependent behaviors might differ among adult rats that had been either repeatedly subjected to prolonged maternal separation or a brief handling procedure or left undisturbed (non-handled) during the first 14 days of life. They found that, in comparison with their handled counterparts, maternally separated and non-handled animals are hyperactive when placed in a novel setting, display a dose-dependent higher sensitivity to cocaine-induced locomotor activity and respond to a mild stressor (tail-pinch) with significantly greater increases in nucleus accumbens dopamine levels. In addition, maternally separated animals were found to sensitize to the locomotor stimulant action of amphetamine when repeatedly stressed under conditions that failed to sensitize handled and non-handled animals. Finally, quantitative receptor autoradiography revealed a lower density of nucleus accumbens-core and striatal dopamine transporter sites in maternally separated animals. They also found greatly reduced D3 dopamine receptor binding and mRNA levels in the nucleus accumbens-shell of handled animals. Together, these findings provide compelling evidence that disruptions in early postnatal rearing conditions can lead to profound and lasting changes in the responsiveness of mesocorticolimbic dopamine neurons to stress and psychostimulants, and suggest a neurobiological basis for individual differences in vulnerability to compulsive drug taking. Brake, W.G., Zhang, T.Y., Diorio, J., Meaney, M.J. and Gratton, A. *Influence of Early Postnatal Rearing Conditions on Mesocorticolimbic Dopamine and Behavioural Responses to Psychostimulants and Stressors in Adult Rats*. *European Journal of Neuroscience*, 19, pp. 1863-1874, 2004.

## **BASIC BEHAVIORAL RESEARCH**

### Sex Differences in the Escalation of Intravenous Cocaine following Long- or Short-access to Self-administration

Drs. Megan Roth and Marilyn Carroll from University of Minnesota examined sex differences in the escalation of cocaine self-administration using a procedure similar to that previously reported with male rats (Ahmed and Koob, 1998; 1999). This procedure is regarded as an animal model of the transition from drug use to addiction. Initially, rats were given access to cocaine either 6 hours/day (Long Access or LgA) or 1 hour/day (Short Access or Sh) for 21 days. This differential access phase was followed by a post-differential access phase in which all rats had 3 hours/day access to cocaine. As shown previously with male rats, Drs. Roth and Carroll found that for both sexes, in the differential access phase the LgA group self-administered more cocaine infusions than the ShA group. Moreover, they found that LgA females self-administered significantly more cocaine infusions than LgA males. In the post-differential-access phase in which all rats had 3 hours/day access to cocaine, and escalation from use to abuse was measured, LgA females self-administered more cocaine infusions than either LgA males, ShA males or ShA females. This study suggests that given opportunity, females will self-administer more than males and females are more sensitive than males to factors that contribute to the escalation of cocaine intake. Roth, M.E. and Carroll, M.E. Sex Differences in the Escalation of Intravenous Cocaine Intake Following Long- or Short-access to Cocaine Self-administration. *Pharmacology, Biochemistry and Behavior*, 78, pp. 199-207, 2004.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Interpersonal Maladjustment as Predictor of Mother's Response to Relational Parenting Intervention

This research team previously demonstrated that a Relational Psychotherapy Mothers' Group (RPMG) was more effective in improving parenting than standard drug counseling (DC) for mothers enrolled in methadone maintenance. The research team recently examined whether mother's interpersonal maladjustment predicted a differential response to RPMG in a sample of 52 mothers and 24 children ages 7 and 16 who had completed baseline, post-treatment, and 6-month follow-up assessments. Results indicated an interaction effect; as maternal interpersonal maladjustment increased, parenting problems improved for mothers in the RPMG group, but remained the same or worsened for DC mothers. Mothers' and children's reports of child maltreatment risk were in or near the normal range for RPMG mothers but in or near clinical range for DC mothers at post-treatment and follow-up. RPMG mothers reported improved affective interactions and the DC group reported no such improvements, regardless of mothers' level of interpersonal maladjustment. These findings highlight the importance of including parenting interventions in substance abuse treatment and the value of interpersonally oriented interventions for substance-abusing mothers and their children. Suchman, N.E., McMahon, T.J., and Luthar, S.S. *Journal of Substance Abuse Treatment*, 27, pp. 135-143, 2004.

### Prenatal Cocaine: Quantity of Exposure and Gender Influences on School-Age Behavior

Investigators at Wayne State University have reported that both level of prenatal cocaine exposure and gender were significantly associated with school-age behavioral outcomes. Prenatal cocaine exposure was defined in two ways: dichotomous and ordinal. The dichotomous measure consisted of no exposure or any pregnancy exposure. The ordinal measure had three levels (none, some, persistent), with persistent prenatal exposure defined as continued cocaine use up until delivery as evidenced by positive maternal and/or infant urine testing at delivery. Data analyses were based on a total of 473 children, 204 of whom were prenatally exposed to cocaine; 24 of the cocaine-exposed children were classified as having persistent exposure. Behavior at 6 years of age was assessed using a teacher-report scale involving fourteen problem behavior areas. Boys with any prenatal cocaine exposure scored significantly higher (more problem behaviors) than non-exposed boys on the hyperactivity item. No similar cocaine effect was observed for girls. Boys, but

not girls, with persistent exposure had more problems in central processing, motor skills, handling abstract concepts, and passivity to the environment. Covariates controlled for include prenatal exposure to alcohol and other illicit drugs, and postnatal drug use in the home. Delaney-Black, V., Covington, C., Nordstrom, B., et al. Prenatal Cocaine: Quantity of Exposure and Gender Moderation. *Developmental and Behavioral Pediatrics*, 25(4), pp. 254-263, 2004.

### Prenatal Cocaine Exposure and Language Development

Recently-published results from two separate projects provide new information regarding associations between prenatal cocaine exposure and aspects of language development. From the University of Miami, Vogel and colleagues report that when the children in their study were 3 years old (424 children, 226 cocaine-exposed, 198 non-cocaine-exposed), there was a decrease in expressive language score with increasing level of prenatal cocaine exposure. Receptive language was more modestly, and not significantly, related to prenatal cocaine exposure. Using the same language assessment scale, the Clinical Evaluation of Language Fundamentals - Preschool (CELF-P), Lewis and co-investigators at Case Western Reserve University report that for their sample of 4-year-olds (189 cocaine-exposed and 185 non-cocaine-exposed), children exposed to cocaine in utero had poorer expressive and total language scores, and had more mild receptive language delays than nonexposed children. In both studies, the analyses took into account several key variables (e.g., prenatal exposures to alcohol, tobacco, and marijuana). Morrow, C.E., Vogel, A.L., Anthony, J.C., et al. Expressive and Receptive Language Functioning in Preschool Children with Prenatal Cocaine Exposure. *Journal of Pediatric Psychology*, 29(7), pp. 543-554, 2004; Lewis, B.A., Singer, L.T., Short, E.J., et al. Four-Year Language Outcomes of Children Exposed to Cocaine in Utero. *Neurotoxicology and Teratology*, 26(5), pp. 617-627, 2004.

### In Utero Marijuana Exposure Associated with Abnormal Amygdala Dopamine D2 Gene Expression in the Human Fetus

Dr. Yasmin Hurd and her colleagues, using in situ hybridization histochemistry, have published the first description of neurobiological effects of in utero exposure to cannabis in the human fetus. Their results demonstrate that cannabis exposure during prenatal development causes a decrease in dopamine D2 mRNA expression in the amygdala and that the magnitude of this decrease was positively correlated with the level of exposure. Importantly, this decrease in D2 mRNA was gender-specific, occurring in males but not in females. This alteration in the mesocorticolimbic dopaminergic brain circuitry during development may contribute to the emotional and cognitive deficits that have been reported in children prenatally exposed to cannabis. Wang, X., Dow-Edwards, D., Anderson, V., Minkoff, H., Hurd, Y.L. *Biological Psychiatry* 56, pp. 909-915, 2004.

### Sensation Seeking and Symptoms of Disruptive Disorder: Association with Nicotine, Alcohol, and Marijuana Use in Early and Mid-Adolescence

This cross-sectional study examined the association of Sensation Seeking (SS) and symptoms of Disruptive Disorders and investigated the associations of each with the risk of nicotine, alcohol, and marijuana use in a sample of 127 boys and 81 girls aged 11-14 years recruited from child psychiatry, pediatric adolescent, and pediatric family clinics. Results indicated that sensation seeking was correlated with Conduct Disorder (CD) and Oppositional Defiant Disorder (ODD), however, when analyzed by gender, there was a significant correlation between SS and CD for boys, but no significant correlations between Sensation Seeking and any of the Disruptive Disorders for girls. Sensation seeking was associated with nicotine, alcohol, and marijuana use; ODD was associated with nicotine use; and Conduct Disorder was associated with alcohol and marijuana use for boys and girls, and smokeless tobacco use for boys. Results from a series of gender specific regression analyses found that SS and ODD predicted nicotine use by girls and SS and CD predicted alcohol and marijuana use by boys. For all other analyses of cigarette, alcohol, and marijuana use, SS was the only significant predictor. Measurement of Sensation Seeking and symptoms of

Disruptive Disorder in clinic setting can help identify and characterize youth who are at increased risk for drug use during early and mid-adolescence. Martin, C.A., Kelly, T.H., Rayens, M.K., Brogli, B., Himelreich, K., Brenzel, A., Bingcang, C.M., and Omar, H. *Psychological Reports*, 84, pp. 1075-1082, 2004.

### Depression, Negative Self-Image, and Suicidal Attempts as Effects of Substance Use and Substance Dependence

This study examined the degree to which cocaine/crack, marijuana, and alcohol use and dependence from 26.5 to 37 years of age predicted depression, negative self-image, negative personal outlook, and suicidal attempts by age 37 in an inner-city sample of 277 African American men and women. Results from this sample, derived from the National Collaborative Perinatal Project (NCPP), found that substance use and dependence predicted mental health outcomes, controlling for prior depression, psychiatric treatment, and suicide attempts and that these predictions differed by gender. Overall, measures of substance use and dependence demonstrated relatively more predictions of suicide attempts for the men and negative self-image and negative personal outlook for the women. For the female sample, making a suicide attempt was predicted by cocaine/crack use and substance dependence, number of suicide attempts was predicted by cocaine/crack use, and depression was predicted by marijuana use. Negative self-image was predicted by substance use, illicit drug use, and substance dependence, and negative personal outlook was predicted by cocaine/crack use, substance use, and illicit drug use. For the male sample, making a suicide attempt was predicted by illicit drug use and substance use, number of suicide attempts was predicted by cocaine/crack use, illicit drug use, substance use, and substance dependence, and depression was predicted by illicit drug use. Negative personal outlook was predicted by cocaine/crack use, substance use, and substance dependence. There were no significant predictors of negative self-image for males. This study highlights gender differences in the important role of substance use in mental health outcomes. Friedman, A.S., Terras, A., Zhu, W. and McCallum, J. *Journal of Addictive Diseases*, 23(4), pp. 55-71, 2004.

## **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

### Cigarette Access for Minors Has Been Declining, but Remains High

Investigators from the Monitoring the Future Study examined trends in middle and high school students' perceived ease, methods, and locations of access to cigarettes, and assessed differences related to their sociodemographic characteristics and smoking status. Annual data from nationally representative samples of 8th-, 10th-, and 12th-grade students were analyzed for the 1997–2002 period. Analyses revealed that perceived ease of access decreased significantly among never and past smokers. Decreased individual purchasing in retail outlets, as well as decreased purchasing from vending machines, were reported by 8th- and 10th-grade students. All grades reported decreased purchasing from self-service placements of cigarettes. Decreases in access were not reported across all retailer types, and no significant increases were seen in the percent of underage purchasers who reported being asked to show identification. Both gender and ethnicity were significantly related to where and how underage youth reported obtaining cigarettes. Findings show that: (1) cigarette access for minors has been declining, but remains high; (2) perceived access to cigarettes clearly increases with level of smoking; and (3) policies to reduce such access may be having an impact as evidenced by decreased retail and vending machine purchases and self-service purchases. The authors conclude that states should continue to strengthen efforts to reduce youth cigarette access, especially in the areas of confirming buyer age via identification checks, and should make efforts to decrease access across all retailer types. Johnston, L.D., O'Malley, P.M., and Terry-McElrath, Y.M. *Methods, Locations, and Ease of Cigarette Access for American Youth, 1997–2002*. *American Journal of Preventive Medicine*, 27, pp. 267–276, 2004.

### Parenting Practices: A Test of Gender Differences and Four Theoretical Perspectives

The authors tested how adverse childhood experiences (child maltreatment and parent alcohol- and drug-related problems) and adult polydrug use (as a mediator) predict poor parenting in a community sample (237 mothers and 81 fathers). These relationships were framed within several theoretical perspectives, including observational learning, impaired functioning, self-medication, and parentification-pseudomaturity. Structural models revealed that child maltreatment predicted poor parenting practices among mothers. Parent alcohol- and drug-related problems had an indirect detrimental influence on mothers' parenting practices through self-drug problems. Among fathers, emotional neglect experienced as a child predicted lack of parental warmth and more parental neglect, and sexual abuse experienced as a child predicted a rejecting style of parenting. Locke, T.F. and Newcomb, M.D. Child Maltreatment, Parent Alcohol- and Drug-related Problems, Polydrug Problems, and Parenting Practices: A Test of Gender Differences and Four Theoretical Perspectives. *Journal of Family Psychology*, 18, pp. 120-134, 2004.

### Child Maltreatment, Parent Alcohol- and Drug-related Problems, Polydrug Problems, and Parenting Practices: A Test of Gender Differences and Four Theoretical Perspectives

The authors tested how adverse childhood experiences (child maltreatment and parent alcohol- and drug-related problems) and adult polydrug use (as a mediator) predict poor parenting in a community sample (237 mothers and 81 fathers). These relationships were framed within several theoretical perspectives, including observational learning, impaired functioning, self-medication, and parentification-pseudomaturity. Structural models revealed that child maltreatment predicted poor parenting practices among mothers. Parent alcohol- and drug-related problems had an indirect detrimental influence on mothers' parenting practices through self-drug problems. Among fathers, emotional neglect experienced as a child predicted lack of parental warmth and more parental neglect, and sexual abuse experienced as a child predicted a rejecting style of parenting. Locke, T.F. and Newcomb, M.D. Child Maltreatment, Parent Alcohol- and Drug-related Problems, Polydrug Problems, and Parenting Practices: A Test of Gender Differences and Four Theoretical Perspectives. *Journal of Family Psychology*, 18, pp. 120-134, 2004.

### Psychosocial Antecedents of Injection Risk Reduction

This study is based on a collaboration with the Integrated Substance Abuse Program at UCLA. In this study, the authors used the AIDS Risk Reduction Model (ARRM) to test a mediated stage-based longitudinal structural equation model analyzing the impact of intention to change injection risk behaviors on 6-month outcomes in a sample of 294 HIV-negative opiate addicted individuals currently in treatment. The ARRM predicts less occurrence of AIDS risk behaviors through a three-stage process: (1) perceiving one's behavior as risky and recognizing one's skills to reduce the behavior, (2) forming an intention to change behavior, and (3) acting on that intention. Stage 1 ARRM constructs of AIDS knowledge, susceptibility, fear of AIDS and Peer Norms were hypothesized to predict Stage 1 end points of perceived risk, response efficacy, and self-efficacy as well as baseline risk behavior. These constructs predicted Stage 2 (intended risk reduction) which, in turn, predicted the Stage 3 outcome of injection risk behaviors. Prior behavior, continuous participation in treatment, and the effect of gender were also included in the model. Intended risk reduction and continuous participation in treatment significantly predicted less injection risk behavior at Stage 3. Stage 1 constructs of greater self-efficacy, less baseline risk behavior, less susceptibility and greater fear of AIDS predicted intentions to reduce risk as did female gender. Leverage points for change in this highly vulnerable population are discussed in the article. Longshore, D., Stein, J.A. and Conner, B.T. Psychosocial Antecedents of Injection Risk Reduction: A Multivariate Analysis. *AIDS Education and Prevention* 16, pp. 53-66, 2004.

### Mate Similarity for Substance Dependence and Antisocial Personality Disorder

Substance dependence (SD) and antisocial personality disorder (ASPD) are highly comorbid and aggregate in families. Mating assortment may be an important process contributing to this familial aggregation. Authors hypothesized that symptom counts of substance dependence, antisocial personality disorder, and retrospectively assessed conduct disorder (CD) would be correlated significantly among parents of youth in treatment for substance use and conduct problems and, separately, among parents of community controls. Authors examined SD, ASPD, and CD among 151 pairs of parents of adolescents in treatment for substance use and conduct problems, and in 206 pairs of parents of control subjects. For average dependence symptoms (ADS) (the sum of across-drug substance dependence symptoms divided by the number of substance categories meeting minimum threshold use) mother-father correlations were 0.40 for patients and 0.28 for controls. Mother-father correlations for ASPD symptom count were 0.33 for patients and 0.26 for controls and for CD symptom count were 0.31 for patients and 0.10 for controls. Spousal correlations for ADS and ASPD, suggest substantial non-random mating. Results support gender differences in homogamy for SD. Behavior genetic studies of these disorders need to account for assortment to avoid biases in estimates of genetic and environmental effects. Sakai, J.T., Stallings, M.C., Mikulich-Gilbertson, S.K., Corley, R.P., Young, S.E., Hopfer, C.J. and Crowley T.J. *Drug and Alcohol Dependence*, 16, pp. 165-175, 2004.

### Defining Nicotine Dependence for Genetic Research: Evidence from Australian Twins

The authors used items of the DSM-IV and of the Heaviness of Smoking Index to characterize the nicotine dependence phenotype and to identify salient symptoms in a genetically informative community sample of Australian young adult female and male twins. Phenotypic and genetic factor analyses were performed on nine dependence symptoms (the seven DSM-IV substance dependence criteria and the two Heaviness of Smoking Index (HSI) items derived from the Fagerstrom Tolerance Questionnaire, time to first cigarette in the morning and number of cigarettes smoked per day). Phenotypic and genetic analyses were restricted to ever smokers. Results showed that phenotypic nicotine dependence symptom covariation was best captured by two factors with a similar pattern of factor loadings for women and men. In genetic factor analysis item covariation was best captured by two genetic but one shared environmental factor for both women and men; however, item factor loadings differed by gender. All nicotine dependence symptoms were substantially heritable, except for the DSM-IV criterion of 'giving up or reducing important activities in order to smoke', which was weakly familial. The findings suggest that the salient behavioral indices of nicotine dependence are similar for women and men. DSM-IV criteria of tolerance, withdrawal, and experiencing difficulty quitting and HSI items time to first cigarette in the morning and number of cigarettes smoked per day may represent the most highly heritable symptoms of nicotine dependence for both women and men. Lessov, C.N., Martin, N.G., Statham, D.J., Todorov, A.A., Slutske, W.S., Bucholz, K.K., Heath, A.C., and Madden, P.A. *Psychological Medicine*, 34, pp. 865-879, 2004.

### Epidemiology of Inhalant Use, Abuse, and Dependence among Youth

Secondary analysis of data on adolescents aged 12-17 from 2000 and 2001 National Household Surveys on Drug Abuse found that inhalant use was common. Results showed that 0.4% of adolescents met DSM-IV inhalant abuse or dependence criteria in the past year. Inhalant abuse and dependence affected adolescents regardless of gender, age, race/ethnicity, and family income. The progression from inhalant use to abuse or dependence was related to early first use, use of multiple inhalants, and weekly inhalant use. Adolescents with inhalant use disorders reported coexisting multiple drug abuse and dependence, mental health treatment, and delinquent behaviors. Adolescents with an inhalant use disorder may represent a subgroup of highly troubled youth with multiple vulnerabilities. Because early use is associated with progression to abuse and dependence, prevention programs should target elementary school-age children. Wu, L.T., Pilowsky, D.J., and Schlenger, W.E. *Inhalant Abuse and Dependence among Adolescents in the United States*. *J Am Acad Child Adolesc Psychiatry*, 43, pp. 1206-1214, 2004.



### Pathways from Physical Childhood Abuse To Partner Violence In Young Adulthood

Analyses investigated several competing hypotheses about developmental pathways from childhood physical abuse and early aggression to intimate partner violence (IPV) for young adult males and females at age 24. Potential intervening variables included: adolescent violence (age 15 to 18), negative emotionality at age 21, and quality of one's relationship with an intimate partner at age 24. At the bivariate level, nearly all variables were associated in the expected directions. However, tests of possible intervening variables revealed only a few significant results. For males, a strong direct effect of abuse on later partner violence was maintained in each model. For females, the quality of one's relationship with an intimate partner did appear to mediate the effect of childhood abuse on later violence to a partner, raising the possibility of gender differences in developmental pathways linking abuse to IPV. Herrenkohl, T.I., Mason, W.A., Kosterman, R., Lengua, L.J., Hawkins, J.D. and Abbott R.D. *Violence and Victims*, 19, pp. 123-136, 2004.

### Religious Activity and Risk Behavior among African American Adolescents

This study examines how religious activity is associated with risk behaviors, concurrently and developmentally among urban African American adolescents. Seven hundred and five African American youths were interviewed annually during high school. Retention rates for the study exceeded 90%. Frequency of religious activity, sexual intercourse, and alcohol, cigarette, and marijuana use were assessed at each wave. Growth curve analyses found negative concurrent associations between religious activity and each of the four risk behaviors. The developmental effects of religious activity varied by gender. Higher levels of religious activity in 9th grade predicted smaller increases in marijuana use among males and cigarette use among females. In addition, larger decreases in religious activity during high school were associated with greater increases in alcohol use among males and sexual intercourse among females. During high school, religious activity limits the development of certain types of risk behavior among African American youth, even after controlling for reciprocal effects. Steinman, K.J., and Zimmerman M.A. *Religious Activity and Risk Behavior among African American Adolescents: Concurrent and Developmental Effects*. *Am J Community Psychol.*, 33, pp. 151-161, 2004.

### An HIV Prevalence-Based Model for Estimating Urban Risk Populations of IDUs and MSM

Issues of cost and complexity have limited the study of the population size of men who have sex with men (MSM) and injection drug users (IDUs), two groups at clearly increased risk for human immunodeficiency virus (HIV) and other acute and chronic diseases. In this study, researchers developed a prototypical, easily applied estimation model for these populations and applied it to Miami, Florida. This model combined HIV prevalence estimates, HIV seroprevalence rates, and census data to make plausible estimates of the number and proportion of MSM and IDUs under a number of assumptions. Sensitivity analyses were conducted to test the robustness of the model. The model suggests that approximately 9.5% (plausible range 7.7%–11.3%) of Miami males aged 18 years or older are MSM (point estimate, N = 76,500), and 1.4% (plausible range 0.9%–1.9%) of the total population aged 18 years or older are IDUs (point estimate, N= 23,700). Males may be about 2.5 times more likely than females to be IDUs. The estimates were reasonably robust to biases. The model was used to develop MSM and IDU population estimates in selected urban areas across Florida and should be replicable in other medium-to-large urban areas. Such estimates could be useful for behavioral surveillance and resource allocation, including enhanced targeting of community-based interventions for primary and secondary HIV prevention. Lieb, S., Friedman, S., Zeni, M., Chitwood, D., Liberti, T., Gates, G., Metsch, L., Maddox, L., and Kuper, T. *An HIV Prevalence-Based Model for Estimating Urban Risk Populations of IDUs and MSM*. *J Urban Health*, 81, pp. 401-415, 2004.

### The Association of Sexual Dysfunction and Substance Use among a Community Epidemiological Sample

This study examines the prevalence of DSM-III sexual dysfunctions and their association with comorbid drug and alcohol use in a community epidemiologic sample. The data for these analyses are based on the Epidemiological Catchment Area Project, a multistage probability study of the incidence and prevalence of psychiatric disorders in the general population conducted in 1981-83. Only the sample of 3,004 adult community residents in the St. Louis area was queried on DSM-III sexual dysfunctions of inhibited orgasm, functional dyspareunia (painful sex), inhibited sexual excitement (i.e., lack of erection/arousal), and inhibited sexual desire. There was a prevalence rate of 11% for inhibited orgasm, 13% for painful sex, 5% for inhibited sexual excitement, 7% for inhibited sexual desire, and 26% for any of these sexual dysfunctions (14% for men and 33% for women). The prevalence of qualifying lifetime substance use among the population was 37%, with males meeting more drug and alcohol use criteria than females. After controlling for demographics, health status variables, and psychiatric comorbidity (depression disorder, generalized anxiety disorder, antisocial personality disorder, and residual disorders), inhibited orgasm was associated with marijuana and alcohol use. Painful sex was associated with illicit drug use and marijuana use. Inhibited sexual excitement was more likely among illicit drug users. Inhibited sexual desire was not associated with drug or alcohol use. Johnson, S.D., Phelps, D.L. and Cottler, L.B. Archives of Sexual Behavior, 33, pp. 55-63, 2004.

### Males at Greater Risk for Violence, Females Higher Risk of PTSD

This study estimated the cumulative occurrence of traumatic events and posttraumatic stress disorder (PTSD), using fourth edition (DSM-IV) criteria, in a high-risk sample of young people in urban United States. The epidemiological sample (n = 2,311) was recruited in 1985-1986 at entry into first grade of a public school system of a large mid-Atlantic city. Participants were interviewed about history of trauma and PTSD in 2000-2002 when their mean age was 21 years (n = 1,698). The authors found that the lifetime occurrence of assaultive violence was 62.6% in males and 33.7% in females. The risk of assaultive violence in males (but not females) varied by childhood area of residence within the city; the occurrence of other traumas did not vary by area of childhood residence. Females had a higher risk of PTSD than males following assaultive violence (odds ratio = 4.0, 95% confidence interval 2.0-8.3), but not following other traumas. A comparison of the results from this largely inner-city sample with the results from a recent study of a largely suburban sample in another region of the United States in which the same criteria and measures of trauma and PTSD were used suggested the possibility that males' risk for assaultive violence and females' risk for PTSD following exposure to assaultive violence might vary by characteristics of the social environment. Breslau, N., Wilcox, H.C., Storr, C.L., Lucia, V.C., and Anthony, J.C. Trauma Exposure and Posttraumatic Stress Disorder: A Study of Youths in Urban America. J Urban Health, 81, pp. 530-544, 2004.

### Life Transitions Predict Depression and Alcohol Use

This study examined longitudinally the relationship between depressive symptoms and alcohol use in a sample of black youth. Participants were 458 black males and females interviewed annually during the high school years and then for 3 years during the transition to adulthood. The relationship was examined using growth curves with Hierarchical Linear Modeling. The results suggest that depressive symptoms decrease over time, whereas the use of alcohol increases. The findings also suggest that youths use alcohol as a way to cope with depressive symptoms and that males are more likely to use alcohol as self-medication. The results also indicate that changes in alcohol use do not predict depressive symptoms, but that life changes associated with the transition to adulthood, such as attending college, predict changes in depressive symptoms and alcohol use. Findings highlight the role of depressive symptoms for predicting alcohol use among black youth and the role of significant life transitions in altering the pattern of alcohol use presented previously by these youths. Repetto, P.B., Zimmerman, M.A., and Caldwell, C.H. A Longitudinal Study of the Relationship between Depressive Symptoms and Alcohol Use in a Sample of

Inner-city Black Youth. *J Stud Alcohol*, 65, pp. 169-178, 2004.

#### Greater Opportunity to Buy Illegal Drugs in Disadvantaged Neighborhoods

This study investigated whether subgroups of people living in disadvantaged neighborhoods may be more likely to come into contact with drug dealers as compared with persons living in more advantaged areas, with due attention to male-female and race-ethnicity differences. The study used standardized survey data collected using stratified, multistage area probability sampling with a nationally representative sample of household residents age 12 or older (n = 25,500). Evidence supports an inference that women are less likely to be approached by someone selling illegal drugs. The study found no more than modest and generally null racial and ethnicity differences, even for residents living within socially disadvantaged neighborhoods, where chances to buy illegal drugs are found to be more common. Limitations of survey data always merit attention, but this study evidence lends support to the inference that physical and social characteristics of neighborhoods can set the stage for opportunities to become involved with drugs. Storr, C.L., Chen, C.Y., and Anthony, J.C. "Unequal Opportunity": Neighborhood Disadvantage and the Chance to Buy Illegal Drugs. *J Epidemiol Community Health*, 58, pp. 231-237, 2004.

#### Course and Psychosocial Correlates of Personality Disorder Symptoms in Adolescence

Personality disorder symptoms were investigated in a community sample of young people (n=714) to assess their relationship over time with well-being during adolescence and the emergence of intimacy in early adulthood. Drawing on Erikson's theory of psychosocial development, changes in adolescent well-being were conceptualized as indirect indicators of identity consolidation. Cluster B personality disorder symptoms (borderline, histrionic, and narcissistic symptoms) were conceptualized to represent "identity diffusion" – i.e., maladaptive personality traits that usually resolve during the identity crisis of adolescence. Latent growth models were used in two age cohorts to assess (1) interrelationships between Cluster B symptoms, well-being, and intimacy at mean ages 13.8 and 18.6 years; and (2) associations between their developmental trajectories over the next 6 years. As expected, higher personality disorder symptoms were associated with lower well-being during adolescence, and declines in personality disorder symptoms over time were associated with corresponding gains in well-being. Consistent with Erikson's developmental theory, there was an inverse relationship between Cluster B symptoms and intimacy that increased in strength as young people entered adulthood. As an indicator of successful identity consolidation, well-being was significantly associated with intimacy in female adolescents and young adults. Crawford, T.N., Cohen, P., Johnson, J.G., Sneed, J.R., and Brook, J.S. The Course and Psychosocial Correlates of Personality Disorder Symptoms in Adolescence: Erikson's Developmental Theory Revisited. *Journal of Youth and Adolescence*, 33, pp. 373-387, 2004.

#### Risk and Protective Factors related to Physical Violence against Impoverished Women

Violence represents a significant threat to the health of impoverished women. Few studies have examined what characteristics might be associated with increased risk of violence or protection from physical violence directed at such women, although this information is important in informing violence prevention and intervention efforts. According to the authors, this is the first study that has prospectively examined, in representative probability samples of impoverished women, multiple risk and protective factors to understand their relative importance to physical victimization. Study participants were 810 women in Los Angeles County, 402 in shelters and 408 in Section 8 low-income housing, who completed structured interviews at baseline and 6-month follow-up. Significant ( $p < .05$ ) multivariate predictors of physical violence experienced during the 6 months prior to follow-up interview were physical or sexual violence experienced as a child, physical violence experienced during the 6 months prior to baseline interview, having multiple sexual partners, psychological distress, and poor social support. Results of this study highlight the persistence of physical violence in the lives of impoverished women and plausible, prospective risk factors for this violence. Findings also highlight opportunities to reduce women's risk of

experiencing violence through enhancing women's social support and mental health. Wenzel, S.L., Tucker, J.S., Elliott, M.N., Marshall, G.N., and Williamson, S.L. Physical Violence against Impoverished Women: A Longitudinal Analysis of Risk and Protective Factors. *Women's Health Issues*, 14, pp. 44-54, 2004.

### The Co-occurrence of Violence, Substance Use and Disorder, and HIV-Risk Behavior among Sheltered and Low-income Housed Women in Los Angeles County

Violence against women, substance use and disorder, and HIV represent three significant threats to the health of women, yet little is known about the extent of these epidemics among indigent women. This study investigates and documents differences in the prevalence and co-occurrence of physical and sexual violence, substance use and disorder, and HIV risk behavior in sizable probability samples of sheltered homeless and low-income housed women. Retrospective self-reports were obtained through structured interviews with stratified random samples of women residing in shelters (N = 460) and low-income housing (N = 438) in Los Angeles County, California. Results indicated that sheltered women were more likely than housed women to report experiencing physical and sexual violence, substance use and disorder, HIV risk behavior, and co-occurrence of these problems in the past year. Differences remained when propensity weights were used to equate the groups on demographic and background characteristics. Findings suggest remarkable need for services among communities of indigent women. Higher rates of problems among women in shelters highlight the importance of differentiating among subgroups of indigent women in community-based prevention and intervention activities and tentatively suggest a protective influence of housing. Wenzel, S.L., Tucker, J.S., Elliott, M.N., Hambarsoomians, K., Perlman, J., Becker, K., Kollross, C., Golinelli, D. Prevalence and Co-occurrence of Violence, Substance Use and Disorder, and HIV Risk Behavior: A Comparison of Sheltered and Low-income Housed Women in Los Angeles County. *Prev Med.*, 39, pp. 617-624, 2004.

### Child Sexual Abuse and HIV: An Integrative Risk Reduction Approach

In recent years, researchers have noted a significant association between child sexual abuse (CSA) and HIV. This association has important implications for HIV prevention and intervention. First, the fact that women who contract HIV are more likely to have been sexually abused as children suggests a continuum of victimization, such that early victimization may confer greater sexual risk-taking and likelihood of revictimization, resulting in HIV infection. Thus, the possible pathways between CSA and HIV need to be elucidated in order to prevent further negative outcomes. Second, the implications for HIV research and intervention are significant. Sexual abuse during childhood is associated with disturbances in the self that pervade an individual's development, and these disturbances are likely to maintain HIV risk behaviors unless ameliorated. Therefore, individuals who are HIV-positive and have a history of child sexual abuse may face "double jeopardy" for negative outcomes, including additional risks for reinfection, sexual revictimization, physical impairment, and non-adherence to HIV treatment that are beyond those associated with HIV infection. Intervention approaches for HIV-positive women with sexual abuse histories need to consider pathways of risk, ameliorate the disruptions in development that result from CSA, and address the additional additive and interactive influences of HIV and CSA on health outcomes. This chapter presents a brief overview of the consequences of CSA that may lead to higher risk for HIV, offers a critique of early intervention paradigms, and presents an integrative risk-reduction approach for HIV-positive women with CSA histories, currently in clinical trial, that addresses the link between CSA and HIV in a developmental and cultural context. Finally, preliminary findings from the intervention and implications for future directions are discussed. Chin, D., Wyatt, G., Carmona, J. V., Loeb, T.B., and Myers, H. Child Sexual Abuse and HIV: An Integrative Risk Reduction Approach. In L. Koenig, A. O'Leary, L. Doll, and Pecquegnat, (Eds.), *From Child Sexual Abuse to Adult Sexual Risk: Trauma, Revictimization, and Intervention*, pp. 233-250. Washington D.C.: American Psychological Association, 2004.

### Adolescent Predictors of Young Adult and Adult Alcohol Involvement and Dysphoria in a Prospective Community Sample of Women

The adolescent predictors of later alcohol involvement (AI), dysphoria (D), and their shared association (AD) among women have not been adequately established. Three waves of data from an ethnically diverse community sample of women, assessed over 16 years are used to study how various psychosocial factors in adolescence influenced later drinking, depression, and their shared association. Structural equation models revealed that several adolescent ecodevelopmental and social development model variables influenced their later outcome in young adulthood and adulthood. The strongest relation was between adolescent Social Conformity and adult AD ( $\beta = -.46$ ) over a 16-year period, emphasizing the impact of this construct. Numerous other relations were revealed. For instance, less satisfaction with school during adolescence predicted adult AI. Having a good bond to the family in adolescence predicted a lower quantity of alcohol consumed during adulthood. Lower satisfaction with "what you want to be" during adolescence predicted young adult D. Higher levels of adolescent relationship satisfaction and school satisfaction predicted less suicidal ideation as an adult. Prevention interventions focusing on increasing socially conforming attitudes and on strengthening relationships both in and out of the home during adolescence are likely to be effective in reducing aspects of AI, D, and AD for women in the general community. Locke, T. F., and Newcomb, M.D. Adolescent Predictors of Young Adult and Adult Alcohol Involvement and Dysphoria in a Prospective Community Sample of Women. *Prevention Science*, 5, pp. 151-168, 2004.

### Tobacco Smoking and Depressive Symptomatology

Whereas an association between cigarette smoking and depression has been established in Anglo populations, replication of tobacco-depression associations in countries where smoking is growing may provide important new insights. The objectives of this study were to estimate the association of depressive symptomatology with tobacco smoking, number of cigarettes smoked daily, and smoking cessation in a representative sample of the Mexican population. The data come from the Third National Addictions Survey (1998) conducted by the Mexican Ministry of Health, representative of Mexico's civilian population residing in cities and towns with 2500+ inhabitants, aged 18-64. Part of a multi-stage, stratified, probability sample, 1935 men and women answered a version of the survey that also included the CES-D depression scale. Analyses addressed the survey's complex design and controlled for income and educational level. The results showed that, among women only, current smokers had twice the odds of elevated depressive symptomatology than never smokers (OR 2.1, 95% CI 1.3-3.5,  $p = 0.002$ ). For men, only those smoking a pack or more a day had greater odds of depressive symptomatology (OR 5.9, 95% CI 1.6-21.9,  $p = 0.008$ ). Overall, former smokers who ceased smoking within 6 months had lower odds of depressive symptomatology than current smokers (OR 0.4, 95% CI 0.1-1.0,  $p = 0.042$ ). These findings add to the accumulating evidence for the association between smoking and depression in different cultures and populations. Benjet, C., Wagner, F.A., Borges, G.G., and Medina-Mora, M.E. The Relationship of Tobacco Smoking with Depressive Symptomatology in the Third Mexican National Addictions Survey. *Psychol Med*, 34, pp. 881-888, 2004.

### Age at First Use and Psychopathology as Risk Factors for Substance Use Disorder

This paper explores the issue of early drug use as a risk factor for adolescent substance use disorder (SUD), and the possible role of comorbid conduct problems in explaining this association. Sophisticated statistical tests were applied to longitudinal data from a large population-based sample, the Great Smoky Mountains Study, assessed annually between ages 9 and 16. Of note, drug use before age 13 was a strong predictor of transition to SUD, and early use remained a risk factor even in the absence of conduct disorder. Boys with a history of depression were at increased risk for SUD, and girls with anxiety experienced an increased risk at age 16. Findings from such large population-based studies can help target populations at higher risk for drug abuse for appropriate preventive interventions. Sung, M., Erkanli, A., Angold, A., and Costello, E.J.

Effects of Age at First Substance Use and Psychiatric Comorbidity on the Development of Substance Use Disorders. *Drug and Alcohol Dependence*, 75, pp. 287-299, 2004.

### Neurobehavior Disinhibition in Childhood Predicts Suicide Potential and Substance Use Disorder by Young Adulthood

The objectives of this study were to (1) determine whether two factors that are established components of the risk for substance use disorder (SUD) also impact on the risk for suicide; and (2) evaluate whether SUD manifest by early adulthood predicts suicide propensity. Neurobehavior disinhibition assessed in 227 boys at ages 10–12 and 16 and parental history of SUD were prospectively evaluated to determine their association with the risk for SUD and suicide propensity between ages 16 and 19. The results indicated that neurobehavior disinhibition at age 16 predicts suicide propensity between ages 16 and 19 ( $p = .04$ ). A trend was observed ( $p = .08$ ) for SUD manifest between ages 16 and 19 to predict suicide propensity during the same period. Maternal SUD is directly associated with son's SUD risk but not suicide propensity. Paternal SUD predicts son's neurobehavior disinhibition that, in turn, predisposes to SUD. A direct relation between paternal SUD and son's suicide propensity was not observed. These findings suggest that neurobehavior disinhibition, a component of the liability of SUD, is also associated with suicide risk. These results are discussed within a neurobehavioral framework in which prefrontal cortex dysfunction is hypothesized to underlie the risk for these two outcomes. Tarter, R.E., Kirisci, L., Reynolds, M., and Mezzich, A. Relation between cognitive distortions and neurobehavior disinhibition on the development of substance use during adolescence and substance use disorder by young adulthood: a prospective study. *Drug and Alcohol Dependence* 76(2), pp. 125-133, 2004.

## **PREVENTION RESEARCH**

### Preventing Substance Use and Disordered Eating

This article assesses the efficacy of a school-based, sport team-centered program to prevent young female high school athletes' disordered eating and body-shaping drug abuse. The ATHENA (Athletes Targeting Healthy Exercise and Nutrition Alternative) curriculum's 8 weekly 45-minute sessions were incorporated into a team's usual practice activities. Content was gender-specific, peer-led, and explicitly scripted. Experimental athletes reported significantly less ongoing and new use of diet pills and less new use of athletic-enhancing substances (amphetamines, anabolic steroids, and sport supplements). Other health-harming actions were also reduced (e.g., riding with an alcohol-consuming driver, failure to use seat belts, and new sexual activity). ATHENA athletes had positive changes in strength-training, self-efficacy and healthy eating behaviors. Thus, sport teams are effective natural vehicles for gender-specific, peer-led curricula to promote healthy lifestyles and to deter disordered eating, athletic-enhancing substance use, and other health-harming behaviors. Elliot, D.L., Goldberg, L., Moe, E.L., DeFrancesco, C.A., Durham, M.B., and Hix-Small, H. Preventing Substance Use and Disordered Eating: Initial Outcomes of the ATHENA (Athletes Targeting Health Exercise and Nutrition Alternatives) Program. *Archives of Pediatric Adolescent Medicine*, 158, pp. 1043-1049, 2004.

### Predicting Marijuana Use Cessation 5 years after Continuation High School

Cessation from marijuana use five years after completion of continuation high school was predicted by social, attitude, intrapersonal, violence-related, drug use, and demographic baseline measures from 339 high risk teenage marijuana users. Young adult social roles were included as additional predictors. Quitting was defined as no use of marijuana in the last 30 days (42% of the sample at follow-up). Results indicate that baseline level of marijuana use, male gender, young adult marital status, and friends' marijuana use (marginal) remained significant direct predictors of quitting. These results suggest the need to reduce psychological dependence on marijuana and increase social unacceptability of marijuana use across genders to increase prevalence of quit attempts. Sussman, S. and Dent, C.W. Five-Year Prospective

Prediction of Marijuana Use Cessation of Youth at Continuation High Schools. *Addictive Behaviors*, 29(6), pp. 1237-1243, 2004.

#### Adolescent Depression and Suicide Risk Are Associated with Sex and Drug Use Behavior

Although both depression and suicide in adolescents have been associated with drug use and early sexual intercourse, the relationship has not been systematically studied in a nationally representative sample. Sixteen patterns of combined sex and drug use behaviors were obtained through analysis of responses to Wave I of the National Longitudinal Study of Adolescent Health conducted from September 1994 through December 1995. Analyses tested correlations between behavior patterns and current depression, serious suicidal ideation, and previous suicide attempt, controlling for gender, race/ethnicity, family structure, and parent education. Compared to youth who abstain from risk behaviors, involvement in any drinking, smoking, and/or sexual activity was associated with significantly increased chances of depression, suicidal ideation, and suicide attempts. These problems were highest among youth who engaged in illegal drug use. There were few differences between boys and girls who abstain from sex and drug behaviors. Girls were less likely than boys to engage in high-risk behaviors, but those who did tended to be more vulnerable to depression, suicidal ideation, and suicide attempt. Hallfors, D.D., Waller, M.W., Ford, C.A., Halpern, C.T., Brodish, P.H., and Iritani, B. Adolescent Depression and Suicide Risk - Association with Sex and Drug Behavior. *Am J of Preventive Med.*, 27(3), pp. 224-231, 2004.

#### Self-esteem and Alcohol Use

Prior studies have found inconsistent relationships between measures of self-concept and adolescent alcohol use. This study explored whether the link between various measures of self-concept and alcohol use depends on gender and whether negative rather than positive self-esteem (i.e., self-derogation) might be more useful in predicting alcohol use. Students (N = 1459) attending 22 middle and junior high schools in New York City completed surveys that included measures of efficacy, self-derogation, and alcohol use. Participants completed surveys at baseline, 1-year follow-up, and 2-year follow-up. Findings indicate that lower efficacy was related to greater self-derogation a year later across gender. Increased self-derogation predicted higher alcohol use for girls but not boys. These findings are congruent with a literature highlighting the importance of negative thoughts about the self in drinking behavior for women but not men. Epstein, J.A., Griffin, K.W. and Botvin, G.J. Efficacy, Self-derogation, and Alcohol Use among Inner-city Adolescents: Gender Matters. *Journal of Youth & Adolescence*, 33, pp. 159-166, 2004.

#### Influence of Parents on Child Anti-social Behavior

This study examined the unique influence of mothers and fathers on their children's antisocial behavior using a sample of 325 families with sixth grade children. Multiple-group comparisons were conducted to identify differences in the relationships for mothers and fathers with daughters versus sons. Results suggested that, while the relationships were often similar for both parents and for both daughters and sons, mothers and fathers uniquely influenced their child's antisocial behavior depending on the child's gender. Overall, cross-gender influence appeared to be particularly important for fathers' control of their daughters' antisocial behavior. Kosterman, R., Haggerty, K.P., Spoth, R. and Redmond, C. Unique Influence of Mothers and Fathers on their Children's Antisocial Behavior: A Social Development Perspective. *Journal of Marriage and Family*, 66(3), pp. 762-778, 2004.

#### Early Intervention Reduces Marijuana Use and Psychopathology in Recent Rape Victims

Nearly 700,000 adult women are raped annually although only one in seven reports the assault to police and receive forensic exams and other professional services. The forensic exam, nevertheless, provides a unique opportunity for a preventive intervention to aid women to cope with potential stress related to the rape-exam procedures and address potential post-rape psychopathology. The intervention implemented

with 205 adolescent and adult (15 years and older) female rape victims involved a 17-minute videotape that both explains the forensic exam procedures and uses a cognitive-behavioral approach to reduce anxiety and subsequent PTSD versus standard post-rape treatment control. Sixty percent of the women provided 6-week follow up data. Results indicate that at 6-weeks post exam marijuana use was significantly lower in the video intervention group but that there were no significant differences in rates of abusing alcohol or other drugs. The data also found that the video intervention helped women with a prior assault more than those with no prior assault. Resnick, H., Acierno, R., Kilpatrick, D.G. and Holmes, M. Description of an Early Intervention to Prevent Substance Abuse and Psychopathology in Recent Rape Victims. *Behavior Modification*, 29(1), pp. 1-33, 2005.

#### Infusion-LST Compared to LST as Usual

Findings from the first two years of a study to compare a standard Life Skills Training (LST) program with an infused (I-LST) approach was conducted in 9 small, rural school districts that were randomly assigned to LST, I-LST, or control conditions. Male and female subjects were in grade seven. The LST program significantly reduced alcohol use, binge drinking, marijuana use, and inhalant use after one year for females, and the I-LST program significantly reduced smoking, binge drinking, and marijuana use for females. At the end of the second year the I-LST program continued to impact female smoking, but all other results were non-significant. There were no effects on males at either time point. Smith, E.A. Evaluation of Life Skills Training and Infused-Life Skills Training in a Rural Setting: Outcomes at Two Years. *Journal of Alcohol & Drug Education*, 48(1), pp. 51-70, 2004.

#### Cost Comparison of LST and Infusion-LST

A cost-effectiveness comparison of the Life Skills Training (LST) to a LST curriculum infusion approach (I-LST) was conducted. Male and female seventh graders from nine rural schools (2 intervention conditions and control) were followed for two years. After one year, significant effects were observed only for females on alcohol, marijuana, and inhalant use in LST condition and for tobacco, alcohol, and marijuana use for I-LST females. After year two, only the I-LST program affected female smoking. Cost calculations for the two programs included expenditures for training and materials and estimates of teachers' salaries for the project period. Both programs were almost equally effective after one year, but LST was more cost-effective. I-LST cost more to implement, but sustained effects into year two and was therefore more cost-effective overall. Swisher, J. D. A Cost-Effectiveness Comparison of Two Approaches to Life Skills Training. *Journal of Alcohol & Drug Education*, 48(1) pp. 71-78, 2004.

#### Two Prevention Programs Reduce High Risk Behaviors among African American Boys

This study was designed to test the efficacy of two programs to reduce high-risk behaviors, including drug use, delinquency, and high risk sexual behavior, among inner-city African-American youth. Students in grades 5 through 8 and their parents and teachers in twelve metropolitan Chicago schools were involved in a cluster randomized trial. The preventive interventions being tested were 1) a social development curriculum, focusing on social competence skills, and 2) a school/community intervention, consisting of the social development curriculum plus a school-wide climate and parent/community intervention. The control group received an attention-placebo. For boys, both programs significantly reduced violent behavior, provoking behavior, school delinquency, drug use, and recent sexual intercourse. The rate of condom use was increased among boys as well. The school/community intervention was significantly more effective than the curriculum-only intervention in reducing risk based on examination of a combined behavioral measure. There were no significant effects for girls. Flay, B.R., Gramlich, S., Segawa, E., Burns, J.L., and Holliday, M.Y. Effects of Two Prevention Programs on High Risk Behaviors among African American Youth. *Archives of Pediatric and Adolescent Medicine*, 158, pp. 377-384, 2004.



## **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

### Suicidal Behavior, Drug Use, and Depressive Symptoms

This 2-year prospective study of 470 patients following inpatient detoxification, examined factors associated with drug-related suicidal behavior using multivariable regression analyses. Suicidal behavior included suicidal ideation (SI) and suicide attempt (SA). Lifetime prevalence for SI was 28.5%, and for SA, 21.9%. During the 2-year follow-up, 19.9% of the sample endorsed suicidal ideation, and 6.9% reported a suicide attempt. Correlates of lifetime suicidal behavior included younger age, female, Hispanic, greater depressive symptoms, past sexual abuse, and problem sedative or alcohol use. Factors associated with suicidal behavior at follow-up included past suicidal behavior, more depressive symptoms, and more frequent benzodiazepine and alcohol abuse. These findings highlight the importance of addressing the recurrent suicide risk of patients with substance related disorder and frequent monitoring for changes in depressive symptoms and drug use. Wines, J.D., Saitz, R., Horton, N. J., Lloyd-Travaglini, C. and Samet, J. H. Suicidal behavior, drug use and depressive symptoms after detoxification: a 2-year prospective study. *Drug and Alcohol Dependence*, 76S, S21-S29, 2004.

### Motivational Enhancement Therapy for Nicotine Dependence in Methadone-Maintained Pregnant Women

In this study, Dr. Haug and colleagues compared motivational enhancement therapy (MET) to standard-care practitioner advice for reducing smoking during pregnancy in a 2-group randomized design. Participants were 63 pregnant opioid-dependent smokers seeking substance abuse treatment, methadone maintenance, and prenatal care. At a 10-week follow-up, self-report and biological measures indicated no differences in smoking between the MET and standard-care groups. However, MET participants were more likely to have moved forward on the stage of change continuum than those in standard care. Intensive treatment for nicotine dependence, environmental interventions, and innovative harm reduction strategies are recommended to address the barriers to quitting observed in this population of pregnant women. Haug, N.A., Svikis, D.S. and Diclemente, C., *Psychol Addict Behav.* 18, pp. 289-292, 2004.

### Correlates of Motivation to Quit Smoking in Methadone-Maintained Smokers Enrolled in a Smoking Cessation Trial

Investigators examined factors that may be associated with motivation to quit smoking in methadone-maintained persons. A sample of 255 smokers, enrolled in a smoking cessation research protocol, completed measures of their smoking motivation, smoking habit, quitting history, and intent to quit in the future. Analyses indicated that only number of cigarettes smoked per day and expectancies for success with smoking cessation were associated significantly with motivation to quit smoking. These results have implications for understanding motivational processes among methadone-maintained smokers and may help in the design of interventions that will assist this population with quitting smoking. Shadel, W.G., Stein, M.D., Anderson, B.J., Herman, D.S., Bishop, S., Lessor, J.A., Weinstock, M., Anthony, J.L. and Niaura, R. *Addictive Behaviors*, 20, pp. 295-300, 2005.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

### Sex Influences Responses to Disulfiram Treatment in Cocaine-dependent Individuals

Sex and gender influences many physiological and behavioral responses to treatments. Investigators from Yale University and VA Connecticut Health Care System aimed to examine the differential response to disulfiram treatment of cocaine dependence by sex. Sex by treatment interactions from two pooled randomized clinical trials involving 191 cocaine-dependent subjects (36% female) were evaluated. Primary outcomes were days of abstinence and percentage of drug-free urine specimens. Men treated with

disulfiram had better outcomes than those who were not. Women had an intermediate outcome regardless of whether they received disulfiram. Sex differences in response to disulfiram treatment may have important clinical and theoretical implications. Reasons for this apparent difference in sex-based response are not clear, but possible mechanisms worthy of greater study include differences in alcohol use by sex as well as differences in dopamine-mediated responses to cocaine and disulfiram. Nich, C., McCance-Katz, E.F., Petrakis, I.L., Cubells, J.F., Rounsaville, B.J. and Carroll, K.M. Sex Differences in Cocaine-dependent Individuals' Response to Disulfiram Treatment. *Addictive Behaviors*, 29(6), pp. 1123-1128, 2004.

### Therapeutic Vaccines for Substance Dependence

Immunotherapies are under development as a new approach to the treatment of substance dependence. The drugs of abuse currently being tested using this new approach are nicotine, cocaine, phencyclidine and methamphetamine. In laboratory animal models, a range of immunotherapies, including vaccines, monoclonal antibodies and catalytic antibodies, have been shown to reduce drug seeking. In human clinical trials, cocaine and nicotine vaccines have been shown to induce antibody titers while producing few side effects. Studies in humans determining how these vaccines interact in combination with their target drug are underway. Overall, immunotherapy offers a range of potential treatment options: drug treatment, as well as the treatment of overdose, prevention of brain or cardiac toxicity and fetal protection in pregnant drug abusers. Haney, M. and Kosten, T.R. Therapeutic Vaccines for Substance Dependence. *Expert. Rev. Vaccines*. 3, pp. 11-18, 2004.

## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE**

### The Efficacy of an Integrated Risk Reduction Intervention for HIV-positive Women with Child Sexual Abuse Histories

Child sexual abuse (CSA) is associated with HIV risk behaviors<sup>1</sup> and more prevalent among women living with HIV than in the general population. This randomized Stage II clinical trial tested the impact of a culturally congruent psychoeducational intervention designed to reduce sexual risks and increase HIV medication adherence for HIV-positive women with CSA histories. An ethnically diverse sample of 147 women were randomized to two conditions: an 11-session Enhanced Sexual Health Intervention (ESHI) or an attention control. Results based on “intent to treat” analyses of pre-post changes are reported in the article. Additional analyses explored whether the observed effects might depend on “intervention dose,” i.e., number of sessions attended. Women in the ESHI condition reported greater sexual risk reduction than women in the control condition. Although there were no differences between women in the ESHI and control groups on medication adherence, women in the ESHI condition who attended 8 or more sessions reported greater medication adherence at post-test than control women. The findings provide initial support for this culturally- and gender-congruent psychoeducational intervention for HIV-positive women with CSA, and highlight the importance of addressing the effects of CSA on sexual risk reduction and medication adherence in preventive interventions for women. Wyatt, G.E., Longshore, D., Chin, D., Carmona, J.V., Loeb, T.B., Myers, H.F., Warda, N., Liu, H., and Rivkin, I. The Efficacy of an Integrated Risk Reduction Intervention for HIV-positive Women with Child Sexual Abuse Histories. *AIDS and Behavior*, 8, pp. 453-462, 2004.

### Gender Differences in Triazolam Pharmacokinetics

Sixty-one healthy men and women, aged 20 to 75 years, received single 0.25-mg doses of triazolam, a cytochrome P450 (CYP) 3A substrate benzodiazepine, and placebo in a double-blind crossover study. Among women, age had no significant effect on area under the triazolam plasma concentration curve (AUC) (Spearman  $r=0.14$ ,  $P=.44$ ) or clearance ( $r=-0.09$ ,  $P=.62$ ). Among men, AUC increased ( $r=0.43$ ,  $P\leq .02$ ) and clearance declined ( $r=-0.42$ ,  $P\leq .02$ ) with increasing age. Gender differences in triazolam kinetics

were not apparent. Compared with placebo, triazolam impaired digit-symbol substitution test performance, increased observer-rated sedation, impaired delayed recall of information learned at 1.5 hours after dosing, and increased electroencephalographic beta amplitude. Among men, mean values of relative digit-symbol substitution test decrement ( $P \leq .002$ ) and observer-rated sedation ( $P \leq .05$ ) were significantly greater in elderly subjects compared with young subjects. Age-dependent differences among women reached significance for observer-rated sedation ( $P \leq .02$ ). A combination of higher plasma levels and increased intrinsic sensitivity explained the greater pharmacodynamic effects of triazolam in elderly subjects. Although the findings are consistent with reduced clearance of triazolam in elderly men, individual variability was large and was not explained by identifiable demographic or environmental factors. Greenblatt, D.J., Harmatz, J.S., von Moltke, L.L., Wright, C.E. and Shader, R.I. Age and Gender Effects on the Pharmacokinetics and Pharmacodynamics of Triazolam, A Cytochrome P450 3A Substrate. *Clin Pharmacol Ther.*, 76(5), pp. 467-479, 2004.

#### Effect of Hard-Drug Use on CD4 Cell Percentage, HIV RNA Level, and Progression to AIDS-Defining Class C Events among HIV-Infected Women

In vitro and animal studies suggest that cocaine and heroin increase HIV replication and suppress immune function, whereas epidemiologic studies are inconclusive regarding their effect on HIV infection progression. The authors prospectively examined the association between illicit-drug use and 4 outcome measures (CD4 cell percentage, HIV RNA level, survival to class C diagnosis of HIV infection, and death) in a national cohort of HIV-infected women. Women enrolled between 1989 and 1995 were followed for 5 years and repeatedly interviewed about illicit (“hard”)–drug use. Up to 3 periodic urine screens validated self-reported use. Outcomes were compared between hard-drug users (women using cocaine, heroin, methadone, or injecting drugs) and nonusers, adjusting for age, antiretroviral therapy, number of pregnancies, smoking, and baseline CD4 cell percentage. Of 1148 women, 40% reported baseline hard-drug use during pregnancy. In multivariate analyses, hard-drug use was not associated with change in CD4 cell percentage ( $P = 0.84$ ), HIV RNA level ( $P = 0.48$ ), or all-cause mortality (relative hazard = 1.10; 95% confidence interval, 0.61-1.98). Hard-drug users did, however, exhibit a higher risk of developing class C diagnoses (relative hazard = 1.65; 95% confidence interval, 1.00-2.72), especially herpes, pulmonary tuberculosis, and recurrent pneumonia. Hard-drug-using women may have a higher risk for nonfatal opportunistic infections. Thorpe, L.E., Frederick, M., Pitt, J., Cheng, I., Watts, D.H., Buschur, S., Green, K., Zorrilla, C., Landesman, S.H. and Hershov, R.C. Effect of Hard-Drug Use on CD4 Cell Percentage, HIV RNA Level, and Progression to AIDS-Defining Class C Events Among HIV-Infected Women. *J Acquir Immune Defic Syndr.* 37(3), pp. 1423-1430, 2004.

#### Drug Use and Disease Progression among HIV-Infected Women

Investigators from the Women and Infants HIV Transmission Study (WITS) have examined the relationship between drug use and four outcome measures: two markers of HIV disease progression (CD4 cell percentage, and HIV RNA level), and two clinical outcomes (progression to a first AIDS-defining class C event, and mortality). WITS is a multi-site longitudinal study of the health of HIV-infected mothers and their children, as well as mother-to-child HIV transmission. It is jointly supported by NIAID, NICHD, and NIDA. A woman was categorized as a ‘hard drug’ user if she reported use of cocaine, crack, heroin, or other opiates (including methadone), if she reported engaging in injection drug use, or if her urine was positive for any of these drugs. Three time periods were examined for hard drug use (once during pregnancy, and two later points). Each woman was followed for up to five years. Outcomes were compared between hard drug users and nonusers, adjusting for age, antiretroviral therapy, number of pregnancies, smoking, and baseline CD4 cell percentage. Of 1148 women, 40% reported baseline hard drug use during pregnancy. In multivariate analyses, hard drug use was not associated with change in CD4 cell percentage, HIV RNA level, or all-cause mortality. Hard drug users did exhibit a higher risk of developing class C diagnoses, especially herpes, pulmonary tuberculosis, and recurrent pneumonia, leading to a conclusion that HIV-infected women who use hard drugs may be at higher risk for nonfatal

opportunistic infections. The investigators consider a number of reasons why a relationship was not found between hard-drug use and CD4 cell percentage or HIV RNA level, given findings of relationships of cocaine and heroin to HIV replication and immune function in animal and in vitro studies, but they also point out that their findings are consistent with most prior epidemiologic evidence. Thorpe, L.E., Frederick, M., Pitt, J., et al. Effect of Hard-Drug Use on CD4 Cell Percentage, HIV RNA Level, and Progression to AIDS-Defining Class C Events among HIV-Infected Women. *JAIDS*, 37(3), pp. 1423-1430, 2004.

### Adult Trauma and HIV Status among Latinas

Latinas have unique cultural factors that can contribute to their health. Recent immigration, documentation status, and language barriers can impact their lives in various ways. Additional stressors and experiencing traumatic events can impact psychological adjustment and substance use. This study tests the differential contribution of adult trauma and other life stressors to psychological adjustment and substance use among Latinas who differ in their HIV status and level of acculturation. A community sample of 121 (87 HIV-positive and 34 HIV-negative) 18 to 50 year old Latinas participated in this study using baseline and one-year follow-up data. Path analyses examined the influence of acculturation, HIV status, and adult trauma, including intimate partner violence (IPV) and sexual assault, on subsequent changes in psychological adjustment (depression) and substance use one year later. Demographic variables of age, education, and relationship status were controlled and further analyses examined the interactive influence of HIV status and acculturation and trauma on the outcomes. Findings indicate that both acculturation and HIV status were related to the outcome variables, but did not influence these over time, emphasizing the developmental stability of these processes. Education was the most prominent variable in protecting these women from HIV, depression, and intimate partner violence (IPV), but placed them at greater risk for illicit drug use. The primary predictors of change in the outcome variables were domestic and sexual trauma that were exacerbated by HIV positive status. Newcomb, M.D., and Carmona, J.V. Adult Trauma and HIV Status among Latinas: Effects upon Psychological Adjustment and Substance Use. *AIDS and Behavior*, 8, pp. 417-428, 2004.

## **SERVICES RESEARCH**

### Gender Differences in Older Adult Treatment Outcomes For Alcohol Dependence

This study examined clinical characteristics and treatment outcomes of older alcohol-dependent men and women in a mixed-age private outpatient chemical dependency program. The sample comprised 92 patients aged 55 to 77 (63 men and 29 women). The measures consisted of demographic characteristics, alcohol and drug use and dependence, drinking history, health status, psychiatric symptoms, length of stay in treatment, use of Alcoholics Anonymous and 6-month treatment outcomes. Results showed that women reported later initiation of heavy drinking (5+ drinks per occasion) than the men, but had similar drinking levels at the treatment intake interview. At the 6-month follow-up, 79.3% of women reported abstinence from alcohol and drugs in the prior 30 days versus 54.0% of men ( $p = .02$ ). Greater length of stay in treatment predicted abstinence at 6 months. Among those who were not abstinent, none of the women reported heavy drinking in the 30 days prior to follow-up, whereas non-abstinent men reported a mean (SD) of 4.0 (9.2) heavy drinking days ( $p = .025$ ). The results suggest that older women may have better drinking outcomes compared with older men, following treatment for alcohol dependence. Satre, D.D., Mertens, J.R., and Weisner, C. Gender Differences in Older Adult Treatment Outcomes for Alcohol Dependence. *Journal of Studies on Alcohol*, 65(5), pp. 638-642, 2004.

### Five-Year Treatment Outcomes Favorable to Older Adults

This study compared 5-year treatment outcomes of older adults to those of middle-aged and younger adults in a large managed care chemical dependency program. Investigators examined age group differences in individual, treatment and extra-treatment factors, which may influence long-term outcome. Seventy-seven per cent of original study participants completed a telephone interview 5 years after outpatient chemical dependency treatment at Kaiser Permanente. This sample (N = 925) included 65 patients aged 55-77, 296 patients aged 40-54 and 564 patients aged 18-39 (age at baseline). Measures at follow-up included alcohol and drug use, Addiction Severity Index (ASI), Alcoholics Anonymous Affiliation Scale, social resource and self-reported health questions. Mortality data were obtained from contact with family members of patients as well as automated health plan records. Older adults were less likely to be drug-dependent at baseline than younger and middle-aged adults, and had longer retention in treatment than younger adults. At 5 years, older adults were less likely than younger adults to have close family or friends who encouraged alcohol or drug use. Fifty-two per cent of older adults reported total abstinence from alcohol and drugs in the previous 30 days versus 40% of younger adults. Older women had higher 30-day abstinence than older men or younger women. Among participants dependent only on alcohol, there were no significant age differences in 30-day abstinence. In logistic regression analysis, age group was not significant. Variables associated with greater age that independently predicted 30-day abstinence in the logistic regression model included longer retention in treatment and having no close family or friends who encouraged alcohol or drug use at 5 years; female gender was also significant. Results indicate that older adults have favorable long-term outcome following treatment relative to younger adults, but these differences may be accounted for by variables associated with age such as type of substance dependence, treatment retention, social networks and gender. Age differences in these characteristics inform intervention strategies to support long-term recovery of older adults and provide direction for investigation of how age affects outcome. Satre, D.D., Mertens, J.R., Arean, P.A and Weisner, C. Five-year Alcohol and Drug Treatment Outcomes of Older Adults Versus Middle-aged and Younger Adults in a Managed Care Program. *Addiction*, 99(10), pp. 1286-1297, 2004.

### An HIV Prevalence-based Model for Estimating Urban Risk Populations of Injection Drug Users and Men Who Have Sex with Men

Issues of cost and complexity have limited the study of the population sizes of men who have sex with men (MSM) and injection drug users (IDUs), two groups at clearly increased risk for human immunodeficiency virus (HIV) and other acute and chronic diseases. Authors developed a prototypical, easily applied estimation model for these populations and applied it to Miami, Florida. This model combined HIV prevalence estimates, HIV seroprevalence rates, and census data to make plausible estimates of the number and proportion of MSM and IDUs under a number of assumptions. Sensitivity analyses were conducted to test the robustness of the model. The model suggests that approximately 9.5% (plausible range 7.7%–11.3%) of Miami males aged 18 years or older are MSM (point estimate, N=76,500), and 1.4% (plausible range 0.9%–1.9%) of the total population aged 18 years or older are IDUs (point estimate, N=23,700). Males may be about 2.5 times more likely than females to be IDUs. The estimates were reasonably robust to biases. The model was used to develop MSM and IDU population estimates in selected urban areas across Florida and should be replicable in other medium-to-large urban areas. Such estimates could be useful for behavioral surveillance and resource allocation, including enhanced targeting of community-based interventions for primary and secondary HIV prevention. Lieb, S., Friedman, S.R., Zeni, M.B., Chitwood, D.D., Liberti, T.M., Gates, G.J., Metsch, L.R., Maddox, L.M., and Kuper, T. Comprehensive Model of Substance Abuse Treatment Processes Introduced. *Journal of Urban Health: Bulletin of the New York Academy of Medicine*, 81(3), pp. 401-415, 2004.

### Mixed Results for Step Down Continuing Care in the Treatment of Substance Abuse

This study examined the predictors of participation in step down continuing care (i.e., contiguous episode of care at a lower level of intensity) in publicly funded substance abuse treatment programs, and the relation between participation in step down care and alcohol and crack cocaine use outcomes over a 36-month follow-up. The sample included patients in residential/inpatient programs (IP; N = 134) and intensive outpatient programs (IOP; AT = 370). About one-third of IP patients received step down continuing care; fewer than 25% of IOP patients received step down continuing care. Patients who received step down continuing care following IP had greater social support at intake and were more likely to be female and White than those who did not receive continuing care. Patients who received continuing care following IOP were more likely than those who did not to be female and employed, and were older, had higher self-efficacy, and shorter lengths of stay in IOP. Participation in step down care was not associated with other factors assessed at intake. In the IP sample, receiving step down continuing care was not associated with better alcohol or crack cocaine use outcomes over the 36-month follow-up. In the IOP sample, there were no main effects favoring continuing care for either alcohol or crack cocaine use outcomes. However, patients who received continuing care had less crack cocaine use in the first six months of the follow-up. These findings suggest that new models of continuing care are needed that are more acceptable to patients, produce better outcomes, and are cost-effective. McKay, J.R., Foltz, C., Leahy, P., Stephens, R., Orwin, R.G., and Crowley, E.M. Step Down Continuing Care in the Treatment of Substance Abuse: Correlates of Participation and Outcome Effects. *Evaluation and Program Planning*, 27(3), pp. 321-331, 2004.

### To What Extent Are Key Services Offered in Treatment Programs for Special Populations?

Many substance abuse treatment (SAT) facilities offer programs tailored for special populations such as women, adolescents, gays/lesbians and others. Previous research shows that there are specific services that are integral to the successful treatment of these populations (e.g., family therapy for adolescents, childcare and transportation assistance for women, and HIV testing and counseling for gays/lesbians). This study examines whether facilities that report having programs for special populations actually offer the recommended services. The data come from the 2000 National Survey of Substance Abuse Treatment Services, which contains information on service offerings, special programs and other characteristics for all SAT facilities in the USA. The results indicate that facilities with special programs are more likely to offer the recommended key services. However, often less than half of these facilities provide the key services. There are consistent differences by ownership status, with for-profit facilities less likely to offer many of the key services. To What Extent are Key Services Offered in Treatment Programs for Special Populations? Olmstead, T. and Sindelar, J.L. *Journal of Substance Abuse Treatment*, 27(1), pp. 9-15, 2004.

## **INTRAMURAL RESEARCH**

### **CHEMISTRY AND DRUG METABOLISM SECTION CLINICAL PHARMACOLOGY AND THERAPEUTICS RESEARCH BRANCH**

#### Neonatal Abstinence Syndrome in Methadone-exposed Infants is Altered by Level of Prenatal Tobacco Exposure

Maternal tobacco consumption during pregnancy has been associated with lower birth weight infants, preterm births, intrauterine growth retardation, smaller head circumference and increase in morbidity, yet few studies have examined the role tobacco has on the opiate neonatal abstinence syndrome (NAS). This study examined the effect of prenatal tobacco exposure on NAS for infants born to mothers maintained on methadone during gestation. Twenty-nine pregnant women and their newborn infants participated in this study. Tobacco exposure was based on maternal self-report with 16 women reporting cigarette

consumption of 10 or less per day and 13 reporting smoking 20 cigarettes or more a day. The onset, peak, and duration of NAS were examined. Results showed that infants born to mothers who reported smoking 20 or more cigarettes per day had significantly higher NAS peak scores of 9.8 versus 4.8, and took longer to peak (113.0 h versus 37.8 h), than light smokers of 10 or fewer cigarettes per day. Investigators concluded that tobacco use in conjunction with methadone plays an important role in the timing and severity of NAS in prenatally exposed infants. Choo, R.E., Huestis, M.A., Schroeder, J.R., Shin, A.S. and Jones, H.E. *Drug and Alcohol Dependence*, 75, pp. 253-260, 2004.

#### Methamphetamine and Amphetamine Concentrations in Meconium of Neonates of Women Enrolled in the IDEAL Study of In Utero Methamphetamine Exposure

The Infant Development, Environment, and Lifestyle (IDEAL) study is a multi-center, longitudinal investigation of the effects of prenatal methamphetamine exposure. Meconium, a useful matrix for identifying in utero drug exposure, was employed to identify gestational drug use. Of the 13,808 mothers screened, 1631 were consented and 176 enrolled. MA exposed mothers (n=84) were identified by self-report of gestational MA use and/or GC/MS confirmation of MA, AMP, and/or MDMA in infant meconium. Comparison participants (n=92) were matched by race, birth weight, maternal education and type of insurance, denied amphetamines use and had negative meconium results. Among the 1631 mothers, self-reported use rates were 5.2% (amphetamines), 25% (tobacco) and 5.9% (cannabis). Positive meconium screening rates were 3.6% for any amphetamine, 20% cotinine and 11.2% cannabis. For specimens that screened positive, 40.7% of amphetamines and 20.2% of cannabis specimens were confirmed. On average, 68% of the meconium from neonates whose mothers reported 3rd trimester use had detectable MA, while detection rates were  $\leq 10\%$  for self-reported use during the 1st and/or 2nd trimesters. Mean  $\pm$  SD, median and range of MA concentrations were  $3674 \pm 3406$ , 2623, 479 to 13,431 ng/g meconium and AMP  $569 \pm 543$ , 403, 30 to 2000 ng/g meconium in infants whose mothers reported 3rd trimester use. However, the highest MA (19,376 and 16,976 ng/g) and AMP (2765 ng/g) concentrations were found in offspring born to women who reported MA use only in the 1st or 1st and 2nd trimesters, raising questions about the self-report. The log transformed meconium MA concentrations significantly correlated with the frequency of MA use in the 3rd trimester ( $r=0.645$ ,  $P=0.004$ ), although variability prevents prediction of frequency of use for an individual mother. AMP was always detected in MA positive meconium. In 55% of the GCMS positive samples, the ratios of amphetamine to MA were 0.1 to 0.2; 14% were less than 0.1 and 18% were 0.2 to 0.3. Meconium analysis for MA is a useful adjunct to self-report for identification of MA exposure; however, the greatest sensitivity was achieved with specimens collected from offspring of women who reported use in the 3rd trimester. Further research is needed to determine if there are additional MA metabolites in meconium that could improve the identification of MA-exposed infants. Zhao, Z., Liu, J., LaGasse, L.L., Derauf, C., Grant, P., Shah, R., Arria, A., Haning, W., Smith, L.M., Lester, B. and Huestis, M.A., Poster, 2004. Joint Meeting of the Society of Forensic Toxicologists and The International Association of Forensic Toxicologists, Washington, DC, August 28-September 3, 2004.

# DIRECTOR'S REPORT TO COUNCIL

May 2005

## **BASIC NEUROSCIENCE RESEARCH**

### Morphine and Stress Response in Adult Female Offspring

It has been shown that adult female rats react to stressors more intensely than adult male rats and that opioids have an inhibitory effect on the stress response. Furthermore, the response of the hypothalamic pituitary adrenal (HPA) axis to stress is known to be gender specific. In a recent paper, Dr. Ilona Vathy and her associates report that prenatal morphine exposure alters the HPA axis-regulated stress response and the sensitivity of negative feedback that are affected by the fluctuation of ovarian hormones. This study examined the effects of prenatal morphine exposure on ACTH and CORT plasma concentrations before and after restraint stress in proestrus (high estrogen level) and diestrus (low estrogen level) female rats. Prenatal morphine exposure differentially altered the ACTH and CORT responses to stress and the sensitivity of negative feedback of glucocorticoid (GR) probably by affecting the characteristics of GR receptors, and thereby altering the HP axis-controlled stress response. Slamberova, R., Rimanoczy, A., Riley, M.A., and Vathy, I. Hypothalamo-Pituitary-Adrenal Axis-Regulated Stress Response and Negative Feedback Sensitivity is Altered by Prenatal Morphine Exposure in Adult Female Rats. *Neuroendocrinology*, 80, pp. 192-200, 2004.

## **BASIC BEHAVIORAL RESEARCH**

### Analogous Changes in Striatal Gene Expression Follow Sexual Experience or Exposure to Drugs of Abuse

It has been suggested that drugs of abuse “hijack” neural systems that evolved to support natural motivated behaviors. Thus, an understanding of the neural control of natural behaviors can help us understand the specific pathology of drug abuse. Motivated behaviors that exhibit properties such as sensitization – an increase in behavioral response with repeated exposures to motivating stimuli – are of particular interest in this regard. Repeated sexual experiences, like repeated drug use, produce long-term changes including sensitization of dopamine release in the nucleus accumbens and dorsal striatum. Previously, Drs. Katherine Bradley and Robert Meisel showed that amphetamine-stimulated locomotor activity was sensitized by previous sexual experience in female Syrian hamsters. They are now collaborating with Dr. Paul Mermelstein to investigate the molecular mechanisms underlying neuroadaptations produced by sexual experience. In this study, they used DNA microarray techniques to identify genes differentially expressed within the nucleus accumbens and dorsal striatum between sexually experienced and sexually naïve female hamsters. For these experiments, female hamsters were ovariectomized and hormonally primed. Half of them were then exposed to a stimulus male once a week for six weeks, while the other half remained naïve. On week seven, the two groups were subdivided, with one half of each exposed to a stimulus male. In comparison with sexually naïve animals, sexually experienced hamsters that received a stimulus male on week seven exhibited an increase in a large number of genes. Conversely, sexually experienced females that did not receive a stimulus male on week seven exhibited a reduction in the expression of many genes compared to naïve animals. The data for the nucleus accumbens and dorsal striatum were similar in terms of directional changes and the categories of genes regulated by the experimental conditions. However, the specific genes exhibiting changes in expression differed between these two brain areas. The investigators also observed that many of the gene classes and specific genes regulated by sexual experience overlapped with those previously reported to be regulated by chronic administration of drugs of abuse, and that many of these genes are involved in forms of neuronal plasticity such as changes in excitability or dendritic growth. These experiments are among the first to profile genes regulated by sexual behaviors in brain areas



(the mesolimbic and nigrostriatal dopamine pathways) involved in long term neuroadaptive changes underlying addiction. And, importantly, studies like this may help us understand why, unlike drug use, natural motivated behaviors do not, in general, progress to an uncontrolled, compulsive state. Bradley, K.C., Boulware, M.B., Jiang, H., Doerge, R.W., Meisel, R.L. and Mermelstein, P.M. Sexual Experience Generates Distinct Patterns of Gene Expression Within the Nucleus Accumbens and Dorsal Striatum of Female Syrian Hamsters. *Genes, Brain and Behavior*, 4, pp. 31-44, 2005.

#### Early Life Stress Enhances Relapse in an Animal Model

Observations from clinical studies on cocaine abusers show that both psychological and physical stress elicit drug craving. Moreover, risk for drug use has been associated with adverse life events and chronic stress. Thus, stress may contribute to the vulnerability for drug abuse behavior and to the propensity to maintain this behavior or to relapse. A vast preclinical literature has modeled deleterious effects of physical and social stressors on acquisition, maintenance and reinstatement of drug seeking. Animal models of early life stress employ neonatal isolation procedures that involve prolonged separation from the mother for one hour per day over post-natal days 2 through 12. Neonatal stress has previously been shown to enhance vulnerability for acquisition of cocaine self-administration, but subsequent effects on relapse after self-administration has been extinguished are unknown. In the present study, the investigators compared male and female rats that were subjected to neonatal isolation with controls that were only handled and returned to the litter. All animals were trained for cocaine i.v. self-administration at 90 days of age, under a fixed ratio 1 schedule of reinforcement. They were then subjected to seven consecutive sessions of a 24-hr discrete trial procedure that provides extended access to drug and has been used to develop excessive, uncontrollable intake. This was followed by 10 days of extinction during which time animals did not receive drug infusion for operant responses in the chamber. After the tenth session, rats were tested in a single one-hour reinstatement session in the presence of cues previously paired with i.v. drug delivery. Group comparisons revealed that during acquisition, female rats took more cocaine than males, replicating findings of many prior preclinical studies on gender differences in cocaine intake. During extinction responding, females also tended to respond at higher levels during initial extinction sessions than males, and isolated rats responded at much higher levels than handled controls. Similarly, neonatally isolated rats responded at much higher levels during cue-induced reinstatement testing – making approximately 48% more responses in the presence of drug-associated cues. The findings of this study indicate that early stress may enhance the vulnerability for relapse to cocaine-seeking behavior in adulthood, when cues previously associated with drug reinforcement are encountered. Lynch, W.J., Mangini, L.D., and Taylor, J.R. Neonatal Isolation Stress Potentiates Cocaine-Seeking Behavior in Adult Male and Female Rats. *Neuropsychopharmacology*, 30, pp. 322-329, 2005.

#### Sucrose Intake Enhances Behavioral Sensitization Produced by Cocaine

Prior research has revealed interactions between an animal's history with sweet solutions and psychostimulant drug self-administration. For example, access to a sweet solution can prevent acquisition, and decrease the continued maintenance of cocaine self-administration. Dr. Blake Gosnell from the Neuropsychiatric Research Institute has now shown that experience with sucrose can sensitize animals to the locomotor-activating effects of cocaine. For 38 days, three groups of rats had daily 1-hr access either to sucrose, ground rat chow, or alternating daily access to either chow or sucrose. On the following two days, respectively, rats were given an i.p cocaine injection and an i.p saline injection. In response to the cocaine injection, rats pre-exposed to sucrose exhibited an elevated, although non-significant, locomotor response compared to the other two groups. Next, for five days, rats were given an injection of cocaine and immediately returned to their home cage. Then one and 15 days after the final cocaine injection they were tested for their locomotor response to cocaine. On the first day, all rats exhibited a sensitized locomotor response to cocaine with the sucrose group exhibiting the greatest sensitization. When tested 15 days after the last cocaine injection, sensitization was still present and was greater in the previously exposed sucrose group than the other two. These outcomes indicate that repeated, intermittent intake of a palatable food can

potentiate the effect of cocaine on locomotor behavior, and are consistent with other studies showing that food reward and drug reward are subserved by overlapping neural circuits. This area of investigation may contribute to understanding high rates of comorbidity between eating disorders and substance abuse, especially in females. Gosnell, B.A. Sucrose Intake Enhances Behavioral Sensitization Produced by Cocaine. *Brain Research*, 1031, pp. 194-201, 2005.

#### Pharmacokinetics of Intravenous Cocaine Across the Menstrual Cycle in Rhesus Monkeys

Numerous rodent studies have demonstrated that cocaine sensitivity is greater in females than in males and that this sensitivity varies with the estrus cycle. Laboratory-based studies in humans have also documented sex differences and menstrual cycle differences in the subjective effects of cocaine thus raising questions about possible fluctuations in cocaine pharmacokinetics during the menstrual cycle. Drs. Suzette Evans and Richard Foltin addressed this issue by studying the rhesus monkey, which has a menstrual cycle similar in length and hormonal fluctuations to that in humans. They examined cocaine pharmacokinetics in five female rhesus monkeys given acute i.v. doses of 0, 0.25, 0.50 and 1.0 mg/kg cocaine during four phases of the menstrual cycle: menses, midfollicular, periovulatory and midluteal. Plasma levels of cocaine and cocaine metabolites benzoylecgonine (BZE) and ecgonine methyl ester (EME) were measured at multiple time points during 90 min following each cocaine injection. The researchers found that peak plasma levels of cocaine increased as a function of dose, but did not vary with the menstrual cycle. There were also no menstrual cycle differences in either the time to achieve peak plasma levels of cocaine or the half-life of cocaine. On the other hand, levels of cocaine metabolites did vary with the menstrual cycle. Plasma levels of BZE and EME were greatest during the luteal phase particularly following the highest cocaine dose. In an analysis of their data from a prior study in which plasma cocaine metabolite levels were collected in women who received repeated doses of 12 mg smoked cocaine during the follicular and luteal phases (Evans et al., 2002), Drs. Evans and Foltin also found that BZE plasma levels were higher in the luteal phase than in the follicular. The present findings, along with the similarity of the menstrual cycle in rhesus monkey and in humans, point to the feasibility of the rhesus monkey model to further our understanding of the role of the menstrual cycle in acute and chronic effects of cocaine. Evans, S.M., and Foltin, R.W. Pharmacokinetics of Intravenous Cocaine across the Menstrual Cycle in Rhesus Monkeys. *Neuropsychopharmacology*, 29, pp. 1889-1900, 2004.

#### Impulsivity (Delay Discounting) as a Predictor of Acquisition of IV Cocaine Self-Administration

Studies in humans have shown a relationship between drug abuse and impulsivity as measured by delayed discounting. Cigarette smokers, crack/cocaine abusers, and opioid dependent individuals, for example, discount delayed rewards more than non-drug users, although it is not clear whether the impulsivity precedes the development of drug abuse or is a consequence. This question was addressed by researchers at the University of Minnesota and University of Wisconsin-Eau Claire using an animal model in which they compared acquisition of cocaine self-administration in female rats that differed in baseline level of impulsivity, as measured by choice for an immediate small reinforcer (one 45 mg food pellet) over a delayed larger reinforcer (three 45 mg food pellets). The researchers found that acquisition of cocaine self-administration occurred in a greater percentage of the rats that exhibited high levels of baseline impulsivity compared to those that exhibited low levels of baseline impulsivity. These data are consistent with and extend prior research showing that rats that exhibited high impulsive choices consumed more ethanol than those that exhibited medium or low impulsive choices (Poulos et al., 1995) and therefore point to impulsivity as a factor that may predispose one to drug abuse. The authors caution, however, that the relationship between impulsivity and drug use may not be unidirectional, citing findings from an earlier study (Richards et al., 1999) in which rats receiving chronic methamphetamine showed increased delay discounting. Perry, J.L., Larson, E.B., German, J.P., Madden, G.J., and Carroll, M.E. Impulsivity (Delay Discounting) as a Predictor of Acquisition of IV Cocaine Self-Administration in Female Rats. *Psychopharmacology*, 178, pp. 193-201, 2005.

## Repeated Maternal Separation in Mice: Sex Differences in Cocaine-Induced Behavioral Sensitization in Adulthood

Experimental protocols in rats have documented that repeated maternal separation (MS) of the neonate can produce changes in the dopamine system and in the hypothalamic-pituitary-adrenal axis (HPA axis), including enhancement of cocaine-induced increases in ventral striatal dopamine levels and elevated basal levels of circulating glucocorticoids and glucocorticoid response to mild stress. Dr. Klaus Miczek and colleagues now report the effects of MS on cocaine-induced sensitization, on glucocorticoid receptors in the hippocampus, and on the dopamine transporter in the nucleus accumbens in male and female neonatal mice. MS occurred for 1 hour per day on postnatal days (PD)1-13. Induction of sensitization occurred during PD 50-59 with mice receiving daily i.p. injections of 10-mg/kg cocaine. The development of locomotor sensitization was assessed on PD 50, 54, and 59. Expression of sensitization was assessed on PD 69 or 71 and on PD 99 by measuring the locomotor response to 7.5 mg/kg i.p. cocaine injections. On PD 50, the locomotor response to cocaine was greater in MS females than in non-MS females, MS males, and non-MS males. On PD 54 and 59, all MS mice exhibited enhancement of cocaine-induced locomotion. Assessment of the expression of cocaine locomotor sensitization on PD 69 or 71 and on PD 99 indicated an enhancement of sensitization in MS males, but not in females. This study is the first to report a relationship between MS and cocaine reactivity in mice. Whereas prior studies of MS rats have shown down-regulation of hippocampal glucocorticoid receptor expression and increased accumbal dopamine transporter binding, in the present study neither of these measures were affected by MS; however, but both measures were greater in females than males. Possible explanations for these discrepancies between MS rats and MS mice include differences in maternal care in rats and mice and differences in the daily length of MS used in this study and prior studies with rats. Kikusui, T., Faccidomo, S., and Miczek, K.A. Repeated Maternal Separation: Differences in Cocaine-Induced Behavioral Sensitization in Adult Male and Female Mice. *Psychopharmacology*, 178, pp. 202-210, 2005.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Motor Development During the First 18 Months of Life in Children with Prenatal Cocaine Exposure

In a recent report from the multi-site Maternal Lifestyle Study, Miller-Loncar and colleagues examined patterns of motor development during the first 18 months of life in children with in utero exposure to cocaine. Motor development was examined at 1, 4, 12, and 18 months of age. The children were divided into two groups: 392 cocaine-exposed and 776 comparison. Exposure status was determined by meconium assay and maternal self-report. Relationships between level of exposure and motor development were also analyzed. Motor skills were assessed at 1 month using the NICU Network Neurobehavioral Scale (NNNS), at 4 months using the posture and fine motor assessment of infants (PFMAI), at 12 months using the Bayley Scales of Infant Development-Second Edition (BSID-II), and at 18 months using the Peabody Developmental Motor Scales (PDMS). Hierarchical linear modeling (HLM) was used to analyze change in motor skills from 1 to 18 months of age. Children with prenatal cocaine exposure showed low motor skills at their initial status of 1 month but displayed significant increases over time. Both higher and lower levels of tobacco use related to poorer motor performance on average. Heavy cocaine use related to poorer motor performance as compared to no use, but there were no effects of level of cocaine use on change in motor skills. Miller-Loncar, C., Lester, B.M., Seifer, R., et al. Predictors of Motor Development in Children Prenatally Exposed to Cocaine. *Neurotoxicology and Teratology*, 27(2), pp. 213-220, 2005.

### Gender and Alcohol Exposure Influence Prenatal Cocaine Effects on Child Behavior at 7 Years of Age

A Wayne State University study research team has reported findings from analyses intended to provide new information on how gender and prenatal exposure to alcohol affect relationships between prenatal cocaine exposure and behavior problems at school age. This report is based on assessments conducted when the children were 7 years of age (a total of 499 children, 214 of which were exposed prenatally to cocaine).

Analyses of teacher-reported child externalizing behavior problems data were stratified by gender and prenatal alcohol exposure status, and controlled for significant pre- and postnatal confounders. Results indicated that among boys with prenatal alcohol exposure, those with persistent cocaine exposure throughout pregnancy had significantly higher levels of delinquent behavior compared to boys with no cocaine exposure. Boys with any prenatal cocaine exposure were twice as likely as unexposed boys to have clinically significant externalizing behavior scores. However, no association was found between prenatal cocaine exposure and scores on externalizing behavior and specific syndromes for boys with no prenatal alcohol exposure. Among girls with no prenatal alcohol exposure, those with persistent cocaine exposure had significantly higher levels of externalizing behaviors and aggressive behaviors compared to girls with no prenatal cocaine exposure, and were almost five times as likely to have clinically significant externalizing behavior scores. However, for girls with prenatal alcohol exposure, no association between prenatal cocaine exposure and scores on externalizing behavior and specific syndromes was found after control for confounding. The investigators state that the current findings support gender- and alcohol-moderated effects of prenatal cocaine exposure on school-age teacher-reported child behavior problems. They also note that these findings are similar to what they have reported for independent parent-reported behaviors. Nordstrom Bailey, B., Sood, B.G., Sokol, R.J., et al. Gender and Alcohol Moderate Prenatal Cocaine Effects on Teacher-report of Child Behavior. *Neurotoxicology and Teratology*, 27(2), pp. 181-189, 2005.

#### Attentional Functioning and Impulse Control in 10-Year-Old Children Exposed to Cocaine in Utero

University of Pennsylvania investigators examined the question of whether children with gestational cocaine exposure may be at risk for difficulties in attentional functioning and impulse control. They administered the Gordon Diagnostic System (GDS) and subtests of the Halstead-Reitan Battery to inner-city children with and without gestational cocaine exposure at age 10 years. The GDS involves a visual computerized task battery that measures impulsivity and sustained attention through three tasks of increasing stress arousal. The subtests of the Halstead-Reitan Battery used were the Trail Making Test (a measure of visual attention) and the Seashore Rhythm Test (a measure of auditory attention). These assessments involved 40 exposed and 40 non-exposed children, a subset of the original study cohort. Subtle differences were found between the prenatally cocaine-exposed children and those not exposed to cocaine during gestation (on the GDS Delay and Distractibility Tasks). With these two exceptions, children had similar performance, with both groups performing poorly. Attentional functioning and impulse control were also assessed in school. Teachers did not distinguish between exposed and non-exposed children, although both groups presented behavioral problems. The researchers concluded that gestational cocaine exposure may be associated with subtle problems in attention and impulse control, putting exposed children at higher risk of developing significant behavioral problems as cognitive demands increase. They also noted that these analyses involved a small sample, and that there is need for continued investigation of the interplay between school performance and attentional regulation and impulse control in order to more fully develop knowledge of long-term effects of gestational cocaine exposure. Savage, J., Brodsky, N.L., Malmud, E., et al. Attentional Functioning and Impulse Control in Cocaine-Exposed and Control Children at Age Ten Years. *Developmental and Behavioral Pediatrics*, 26(1), pp. 42-47, 2005.

#### Youth Tobacco and Marijuana Use Relative to Prenatal Cigarette and Marijuana Exposure

As part of their long-term follow-up of prenatal marijuana and tobacco exposure, researchers at Carleton University have examined whether maternal cigarette smoking and marijuana use during pregnancy were associated with an increased risk of initiation and daily/regular use of tobacco and marijuana among one hundred fifty-two 16- to 21-year-old adolescent offspring. The participants were from a low risk, predominately middle-class sample participating in an ongoing, longitudinal study. Findings indicated that offspring whose mothers reported smoking cigarettes during their pregnancy were more than twice as likely to have initiated cigarette smoking during adolescence than offspring of mothers who reported no smoking while pregnant. Offspring of mothers who reported using marijuana during pregnancy were at increased

risk for both subsequent initiation of cigarette smoking (OR=2.58) and marijuana use (OR=2.76), as well as daily cigarette smoking (OR=2.36), as compared to offspring of whose mothers did not report using marijuana while pregnant. There was also evidence indicating that dose-response relationships existed between prenatal exposure to marijuana and offspring use of cigarettes and marijuana. These associations were found to be more pronounced for males than females, and remained after consideration of potential confounding variables. The authors note that these results suggest that maternal cigarette smoking and marijuana use during pregnancy are risk factors for later smoking and marijuana use among adolescent offspring, and add to the weight of evidence supporting the importance of programs aimed at drug use prevention and cessation among women during pregnancy. Porath, A.J. and Fried, P.A. Effects of Prenatal Cigarette and Marijuana Exposure on Drug Use Among Offspring. *Neurotoxicology and Teratology*, 27(2), pp. 267-277, 2005.

#### Suicidal Behavior, Drug Use and Depressive Symptoms after Detoxification: a 2-Year Prospective Study

Individuals with substance-related disorders are at increased risk for suicidal behavior. This study examined factors associated with drug-related suicidal behavior using multivariable regression analyses in a 2-year prospective study of 470 inpatients enrolled from an unlocked, detoxification unit. Suicidal behavior included suicidal ideation (SI) and suicide attempt (SA). Lifetime prevalence for SI was 28.5%, and for SA, 21.9%. During the 2-year follow-up, 19.9% of the sample endorsed suicidal ideation and 6.9% reported a suicide attempt. Correlates of lifetime suicidal behavior included younger age, female, Hispanic, greater depressive symptoms, past sexual abuse, and problem sedative or alcohol use. Factors associated with suicidal behavior at follow-up included past suicidal behavior, more depressive symptoms, and more frequent benzodiazepine and alcohol use. Cocaine and heroin use did not reach statistical significance. Differences in "suicide potential" may exist between drug categories with CNS depressants increasing the risk. These findings highlight the importance of addressing the recurrent 'suicide risk' of patients with substance-related disorders and regular monitoring for changes in depressive symptoms and drug use. Based on the prevalence and severity of this problem, the role of universal suicide screening of individuals with substance-related disorders merits greater attention. Wines, J.D. Jr., Saitz, R., Horton, N.J., Lloyd-Travaglini, C., and Samet, J.H. *Drug and Alcohol Dependence*, 76, Supplement 1, pp. S21-S29, 2004.

#### Predictors of Infection with Chlamydia or Gonorrhea in Incarcerated Adolescents

This cross-sectional study examined the prevalence, multiple correlates, and gender differences in chlamydia and gonorrhea infections among adolescents, aged 13 to 18, incarcerated in a youth detention center in the southern region of the United States. Rates of undiagnosed chlamydia were 24.7% for incarcerated girls and 8.1% for boys. Gonorrhea was detected in 7.3% of the girls and 1.5% of the boys. Predictors of STD positivity differed for boys and girls. Demographic characteristics (gender, race, and age) account for 52% of the total variance in STD infections; youths' behavior accounts for approximately one third of the total variance, and psychological and family variables account for 8.6% and 7.2% of the total variance, respectively. Sexual activity while under the influence of alcohol was associated with a greater likelihood of testing positive for an STD. Beliefs about alcohol and other drugs regarding loss of control and enhancement of sex were not associated with testing positive. This study demonstrates that an approach that considers psychological and social influences on adolescent sexual behavior is useful for identifying potential risk and protective factors of adolescent STD/HIV risk that are amenable to intervention. Robertson, A.A., Thomas, C.B., St Lawrence, J.S., and Pack, R. *Sexually Transmitted Diseases*, 32(2), pp. 115-122, 2005.

#### Effects of Smoking and Smoking Abstinence on Cognition in Adolescent Tobacco Smokers

There is considerable evidence that exposure to nicotine during early development can have neurotoxic effects. In this study, Dr. Leslie Jacobsen and her colleagues sought to determine whether exposure to nicotine during adolescence had demonstrable cognitive effects. Behavioral data from 41 adolescent

smokers and 32 non-users were obtained on a number of cognitive tasks. Abstinence from smoking, for both male and female adolescent nicotine users, significantly decreased their performance on a test of verbal learning. In a memory task, smokers performed less accurately than non-smokers; this difference was greater when the smokers were abstinent. Whether abstinent or not, the magnitude of the performance difference between smokers and non-smokers was positively correlated with smoking history (number of pack-years). In tests of visual and auditory attention, smokers were found to perform as accurately as non-smokers, but their reaction times were slower. Finally, in terms of gender effects, male smokers were found to perform less accurately than female smokers. Male smokers, however, tended to have smoked longer than female smokers and to have started smoking earlier, which may account for at least part of the difference. These findings strongly suggest that nicotine exposure during adolescence has deleterious effects. Jacobsen, L.K., Krystal, J.H., Mencl, W.E., Westerveld, M., Frost, S.J., and Pugh, K.R. *Biol. Psychiatry*, pp. 56-66, 2005.

## **CLINICAL NEUROSCIENCE RESEARCH**

### Neurotoxic Effects of Prenatal Methamphetamine (METH) Exposure on the Developing Brain and on Cognition

Dr. Linda Chang and associates at the University of Hawaii examined Meth-exposed children (n=13) and unexposed controls (n=15) with MRI in a pilot study to examine neurotoxic effects of prenatal METH exposure. Global brain volumes and regional brain structures were quantified. Ten METH-exposed and nine unexposed children also completed neurocognitive assessments. METH-exposed children scored lower on measures of visual motor integration, attention, verbal memory and long-term spatial memory. There were no differences among the groups in motor skills, short delay spatial memory or measures of non-verbal intelligence. Despite comparable whole brain volumes in each group, the METH-exposed children had smaller putamen bilaterally (-17.7%), smaller globus pallidus (left: -27%, right: 30%), smaller hippocampus volumes (left: -19%, right: -20%) and a trend for a smaller caudate bilaterally (-13%). The reduction in these brain structures correlated with poorer performance on sustained attention and delayed verbal memory. No group differences in volumes were noted in the thalamus, midbrain or the cerebellum. In summary, compared with the control group, children prenatally exposed to METH exhibit smaller subcortical volumes and associated neurocognitive deficits. These preliminary findings suggest that prenatal METH exposure may be neurotoxic to the developing brain. Chang, L., Smith, L.M., LoPresti, C., Yonekura, M.L., Kuo J., Walot, I. and Ernst, T. *Psychiatry Research*, 132, pp. 95-106, 2004.

### New Measures of Corpus Callosum Size Are Related To Drug Abuse and To Childhood Neglect and Abuse

While many neuroimaging studies focus on deficits in cortical gray matter in patients with drug abuse or with cognitive deficits, Dr. Moeller and associates at the University of Texas Health Science Center, Houston, have used recent technology in Diffusion Tensor Imaging (DTI) and found reduced white matter integrity in areas of the corpus callosum in cocaine-dependent subjects. In addition, tests of impulsivity showed significant (negative) correlations with callosal integrity. It should be noted, however, that not the entire callosum showed a difference between cocaine-dependent subjects and controls; differences were found only in the genu and rostral body and are likely related to cross-connecting areas in the prefrontal cortex. Moeller, F.G., Hasan, K.M., Steinberg, J.L., Kramer L.A., Dougherty, D.M., Santos, R.M., Valdes, I., Swann, A.C., Barratt, E.S. and Narayan, P.A. *Neuropsychopharmacology*, 30, pp. 610-617, 2005.

### Childhood Neglect Is Associated With Reduced Corpus Callosum Area

Dr. Teicher and colleagues at McLean Hospital reported reduced corpus callosum area in children who were neglected or abused. This is important because early physical or sexual abuse is likely associated with later drug abuse. However, the affected areas were posterior to those found by Moeller and associates. Nevertheless, these data may help understand the effect of early events in brain development and their

impact on drug abuse liability. Teicher, M.H., Dumont, N.L., Ito, Y., Vaituzis, C., Giedd, J.N and Anderson, S.L. *Biological Psychiatry*, 56, pp. 80-85, 2004.

### Specific Brain Regions Are Activated Following Script-Induced Emotions In Cocaine Users and in Non-Using Individuals

Dr. Sinha at Yale University has found limbic and other brain structures to be activated as measured by fMRI in cocaine users and in non-using subjects as they listen to personalized scripts designed to induce heightened emotions. In non-using subjects, increases were observed in limbic and midbrain regions such as the striatum, and thalamic regions, caudate, putamen, hippocampus, parahippocampus and posterior cingulate. In some of these areas, left activation was greater. In cocaine users, stress tended to activate temporal areas in addition to medial and superior frontal gyri and anterior cingulate. Of most interest, women seemed to have the greater activation. Sinha, R., Lacadie, C., Skudlarski, P. and Wexler, B.E., *Annals of the New York Academy of Science*, 1032, pp. 254-257, 2004; Li, C-S.R., Koston, T.R. and Sinha, R. *Biological Psychiatry*, 57, pp. 487-494, 2005.

## **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

### Caregiver Factors Buffer Effects of Violence Exposure on Adjustment Problems

This short-term, longitudinal interview study used an ecological framework to explore protective factors within the child, the caregiver, the caregiver-child relationship, and the community that might moderate relations between community violence exposure and subsequent internalizing and externalizing adjustment problems and the different patterns of protection they might confer. Participants included 101 pairs of African American female caregivers and one of their children (56% male, M = 11.15 yrs, SD = 1.28) living in high-violence areas of a mid-sized southeastern city. Child emotion regulation skill, felt acceptance from caregiver, observed quality of caregiver-child interaction, and caregiver regulation of emotion each were protective, but the pattern of protection differed across level of the child's ecology and form of adjustment. Kliwer, W., Cunningham, J.N., Diehl, R., Parrish, K.A., Walker, J.M, Atiyeh, C., Neace, B., Duncan, L., Taylor, K. and Mejia, R. *Violence Exposure and Adjustment in Inner-city Youth: Child and Caregiver Emotion Regulation Skill, Caregiver-child Relationship Quality, and Neighborhood Cohesion as Protective Factor*. *J Clin Child Adolesc Psychol*. 33(3), pp. 477-487, 2004.

### Effects of Parent and Peer Support on Adolescent Substance Use

This research tested comparative effects of parent and peer support on adolescent substance use (tobacco, alcohol, and marijuana) with data from 2 assessments of a multiethnic sample of 1,826 adolescents, mean age 12.3 years. Multiple regression analyses indicated that parental support was inversely related to substance use and that peer support was positively related to substance use, as a suppression effect. Structural modeling analyses indicated that effects of support were mediated through pathways involving good self-control, poor self-control, and risk-taking tendency, parent and peer support had different patterns of relations to these mediators. The mediators had pathways to substance use through positive and negative recent events and through peer affiliations. Effects for gender and ethnicity were also noted. Mechanisms of operation for parent and peer support are discussed. Wills, T.A., Resko, J.A., Ainette, M.G. and Mendoza, D. *Role of Parent Support and Peer Support in Adolescent Substance Use, A Test of Mediated Effects*. *Psychology of Addictive Behaviors*, 18, pp.122-134, 2004.

### Reliability of Proxy Reports of Parental Smoking

To investigate the accuracy of offspring assessments of parental smoking status, this study assessed 116 parents and 151 adult children (276 parent-child dyads) who provided data on both their own and their parents' smoking status. All currently smoking and all ex-smoking parents were correctly classified as ever-

smokers by their offspring (n=79 and 100, respectively). Of the 97 offspring who reported on never-smoking parents, 88 correctly classified their parents as never-smokers. Thus, sensitivity for detecting ever-smoking in parents was 100%, and specificity, 91%. Because all incorrect classifications involved never-smoking parents, further analyses focused on this group. Too few parents were misclassified to permit testing of parental characteristics. Offspring who misclassified their parents were significantly older than those who did not; neither sex nor smoking status of the offspring was associated with the increased likelihood of misclassification. No significant differences were discovered for dyadic factors (concordance/discordance for sex; parent-offspring age difference). Overall, these results support the utility of proxy reports of parental smoking phenotype by adult informants when self-report is unavailable. Pomerleau, C.S., Snedecor, S., Ninowski, R., Gaulrapp, S., Pomerleau, O.F. and Kardia, S.L. Differences in Accuracy of Offspring Assessment Based on Parental Smoking Status. *Addictive Behaviors* 30, pp. 437-441, 2005.

### Identifying Venues for Purposive Sampling of Hard-to-reach Latino Youth

This study of recruitment venues in a Latino neighborhood was designed with the following objectives: (1) to identify venues where Latino youth at risk for unintended pregnancies and sexually transmitted infections (STIs) could be reached; (2) to describe different youth crowds, and (3) to investigate how and where youth meet their sex partners. Based on neighborhood venues mapped using Map-Info, and ethnographic interviews conducted with 62 youth recruited primarily from street sites, 3 types of “crowds” were identified, including gang related “regulars,” individuals affiliated with street economy, and females. Findings suggest that gang members dominate venues in The Mission and that street sites are important venues to meet sexual partners. This qualitative assessment produced insights into research planning, outreach, and interventions with Latino youth who are at disproportionate risk for unintended pregnancies and STIs. Auerswald, C.L., Greene, K., Minnis, A., Doherty, I., Ellen, J. and Padian, N. Qualitative Assessment of Venues for Purposive Sampling of Hard-to-reach Youth. *Sexually Transmitted Diseases*, 31, pp. 133-138, 2004.

### School-level Clustering of Youthful Drug Involvement in Seven Latin American Countries

This study estimated the occurrence and school-level clustering of drug involvement among school-attending adolescent youths in each of seven countries in Latin America. During 1999-2000, anonymous self-administered questionnaires on drug involvement and related behaviors were administered to a cross-sectional, nationally representative sample that included a total of 12,797 students in the following seven countries, Costa Rica (n = 1,702), the Dominican Republic (n = 2,023), El Salvador (n = 1,628), Guatemala (n = 2,530), Honduras (n = 1,752), Nicaragua (n = 1,419), and Panama (n = 1,743). (The PACARDO name concatenates PA for Panama, CA for Centroamerica, and RDO for Republica Dominicana). Estimates for exposure opportunity and actual use of alcohol, tobacco, inhalants, marijuana, cocaine (crack/coca paste), amphetamines and methamphetamines, tranquilizers, ecstasy, and heroin were assessed via responses about questions on age of first chance to try each drug, and first use. Cumulative occurrence estimates for alcohol, tobacco, inhalants, marijuana, and illegal drug use for the overall sample were, respectively, 52%, 29%, 5%, 4%, and 5%. In comparison to females, males were more likely to use alcohol, tobacco, inhalants, marijuana, and illegal drugs, the odds ratio estimates were 1.3, 2.1, 1.6, 4.1, and 3.2, respectively. School-level clustering was noted in all countries for alcohol and tobacco use. It was also noted in Costa Rica, El Salvador, Guatemala, and Panama for illegal drug use. This report sheds new light on adolescent drug experiences in Panama, the five Spanish-heritage countries of Central America, and the Dominican Republic, and presents the first estimates of school-level clustering of youthful drug involvement in these seven countries. Placed in relation to school survey findings from North America and Europe, these estimates indicate lower levels of drug involvement in these seven countries of the Americas. For example, in the United States of America 70% of surveyed youths had tried alcohol and 59% had smoked tobacco. By comparison, in these seven countries, only 51% have tried alcohol and only 29% have smoked tobacco. Future research will help to clarify explanations for the observed variations across different countries of the



world. In the meantime, strengthening of school-based and other prevention efforts in the seven-country PACARDO area may help these countries slow the spread of youthful drug involvement, reduce school-level clustering, and avoid the periodic epidemics of illegal drug use that have been experienced in North America. Dormitzer, C.M., Gonzalez, G.B., Penna, M., Bejarano, J., Obando, P., Sanchez, M., Vittetoe, K., Gutierrez, U., Alfaro, J., Meneses, G., Diaz, J.B., Herrera, M., Hasbun, J., Chisman, A., Caris, L., Chen, C.Y. and Anthony, J.C. The PACARDO Research Project, Youthful Drug Involvement in Central America and the Dominican Republic. *Pan American Journal of Public Health*, 15, pp. 400-416, 2004.

#### Difference between Ever- and Never-Smokers

This study examined whether 52 same-sex sibling pairs discordant for ever-smoking differed on psychiatric cofactors, alcohol and caffeine use, and responses to initial exposure to smoking. Ever-smokers scored significantly higher on measures of novelty seeking, depression, and childhood ADHD, and on alcohol dependence, alcohol intake, and caffeine intake. They reported significantly more pleasurable experiences, dizziness, "buzz," and relaxation upon initial exposure to smoking and significantly fewer displeasurable sensations, nausea, and cough than did nicotine-exposed, never-smoking siblings. Ever-smokers had significantly fewer years of education than their never-smoking siblings, suggesting that the concentration of smokers in lower socioeconomic strata may be partly due to downward mobility among smokers, possibly because of the observed elevation in psychiatric cofactors, which may interfere with academic performance. These findings are consistent with differences previously identified in unrelated ever- and never-smokers. Because same-sex siblings typically share a large set of common environments during childhood, the findings could be due either to genetic differences among siblings and/or (excepting educational level and responses to early exposure) to differences in adult environments. Pomerleau, C.S., Pomerleau, O.F., Snedecor, S.M., Gaulrapp, S. and Kardia, S.L.R. Heterogeneity in Phenotypes Based on Smoking Status in the Great Lakes Smoker Sibling Registry. *Addictive Behaviors* 29, pp. 1851-1855, 2004.

#### HPA-axis Dysregulation among Female Smokers with and without Depression

To determine whether smokers with a history of depression are differentially susceptible to smoking withdrawal, depressed mood induction and/or hypothalamic-pituitary-adrenal (HPA) axis dysregulation during smoking abstinence, 24 women smokers with and without such a history were studied. During one 5-day interval, participants smoked ad libitum, during a second they abstained. On day 4, the participants were exposed to the Velten mood induction procedure (VMIP). Participants were then instructed to take 1 mg dexamethasone at 11 pm. At 4 pm on day 5, blood samples were withdrawn to determine the cortisol and ACTH response. Despite lower baseline cotinine levels, history-positive participants displayed more pronounced overall withdrawal distress than did history-negative participants, regardless of condition. The VMIP increased depression as well as negative responses on other profile of mood states subscales. Despite many overall group differences, no significant main effects for smoking condition nor interaction effects emerged. All participants evinced cortisol suppression in response to dexamethasone during both conditions, but the degree of suppression did not differ as a function of either abstinence or depression history. In history-positive smokers, however, ACTH levels trended toward overall elevation and showed almost no suppression during abstinence, thus exacerbation of HPA dysregulation in history-positive smokers during smoking abstinence cannot be ruled out. Pomerleau, O.F., Pomerleau, C.S., Snedecor, S.M., Gaulrapp, S., Brouwer, R.N. and Cameron, O.G. Depression, Smoking Abstinence and HPA Function in Women Smokers. *Human Psychopharmacology-Clinical and Experimental*, 19, pp. 467-476, 2004.

#### Impact of September 11 Attacks on Young Adult Drug Abuse

The authors took advantage of their ongoing longitudinal study to assess the impact of the September 11 attacks on psychopathology in young adults who lived far from New York City. During that year, 730 rural

19-21 year olds were re-assessed, one third after the attacks. Findings differed by gender and by level of prior stress. Although men showed slightly more tendency to have one or more symptoms of posttraumatic stress disorder, their rates of substance use disorder after September 11 were lower, regardless of prior use history. Women showed increased rates of substance use and abuse after the attacks. The attacks also proved a greater stressor for those under low to moderate levels of stress than for those already under significant stress. No other psychiatric disorders showed an increase after September 11 in this sample. This “natural experiment” suggests that, if confirmed in other studies, even those who are geographically removed from a traumatic event may be vulnerable, and that interventions for those at greater risk may be indicated to prevent further costs in event of such an attack. Costello, E.J, Erkanli, A., Keeler, G., and Angold, A. Distant Trauma: A Prospective Study of the Effects of September 11th on Young Adults in North Carolina. *Applied Developmental Science*, 8, pp. 211-220, 2004.

## **PREVENTION RESEARCH**

### Predicting Early Adolescent Gang Involvement from Middle School Adaptation

This study examined the role of adaptation in the first year of middle school (Grade 6, age 11) to affiliation with gangs by the last year of middle school (Grade 8, age 13). The sample consisted of 714 European American (EA) and African American (AA) boys and girls. Specifically, academic grades, reports of antisocial behavior and peer relations in 6th grade were used to predict gang involvement by 8th grade, measured through self-, peer, teacher, and counselor reports. Unexpectedly, self-report measures of gang involvement did not correlate highly with peer and school staff reports. The results, however, were similar for other and self-report measures of gang involvement. Analysis of means revealed statistically reliable differences in 8th-grade gang involvement as a function of the youth gender and ethnicity. Structural equation prediction models revealed that peer nominations of rejection, acceptance, academic failure, and antisocial behavior were predictive of gang involvement for most youth. These findings suggest that the youth level of problem behavior and the school ecology (e.g., peer rejection, school failure) require attention in the design of interventions to prevent the formation of gangs among high-risk young adolescents. Dishion, T.J., Nelson, S.E. and Yasui, M. *Journal of Clinical Child and Adolescent Psychology* 34(1), pp. 62-73, 2005.

### Maternal Stress and Distress Increase Disruptive Behavior Problems in Boys

This study examined how self-reported maternal stress and distress are associated with child disruptive behaviors, based on mother and teacher ratings of child disruptive behavior problems (attention problems, aggression, and delinquency) collected for 215 boys between 9 and 12 years of age. Participating mothers also provided self-report data on socioeconomic status (SES), parenting stress, and distress (depression and anxiety/somatization). Low SES was significantly associated with both mother- and teacher-reported child disruptive behavior problems. In addition, the relation between parenting stress and mother-reported child disruptive behavior problems was found when SES was controlled. A significant relation between maternal distress and mother-reported child disruptive behavior problems (particularly attention problems), also was observed when both SES and parenting stress were controlled. Maternal stress and distress were not significantly related to teacher-reported child disruptive behavior problems. Although the lack of an association between teacher-reported behavior problems and maternal stress and distress might be interpreted as a rater bias by these mothers, it may be that the mothers' symptoms are associated with a stressful home environment, thus exacerbating child disruptive behavior problems and eventually leading to a reciprocal relation between symptomatology in mothers and children. Barry, T.D., Dunlap, S.T., Cotton, S.J., Lochman, J.E. and Wells, K.C. *The Influence of Maternal Stress and Distress on Disruptive Behavior Problems in Boys. Journal of the American Academy of Child and Adolescent Psychiatry*, 44(3), pp. 265-273, 2005.

### Tobacco and Alcohol Use as an Explanation for the Association between Externalizing Behavior and Illicit Drug Use among Delinquent Adolescents

Substance use among adolescents is frequently comorbid with other psychiatric disorders. Most studies of these comorbidities use samples of middle or high school students or draw from inpatient settings. Less is known about substance use and psychiatric comorbidity among delinquent adolescents. The present study examined data from two cohorts of juvenile offenders collected over a 2-year period (n=245, n=299). Participants reported frequency of cigarette, alcohol, marijuana, and other substance use. Participants' parents completed a measure of behavior problems. Path analyses suggested that parental reports of externalizing problems were significantly related to self-reported substance use while parental reports of internalizing problems were not. These findings suggest that smoking and alcohol use act as mediators between externalizing problems and marijuana and other drug use. Although there were some mean differences by gender, the pattern of relationships among the variables did not differ by gender. Helstrom, A., Bryan, A., Hutchison, K.E., Riggs, P.D. and Blechman, E.A. Tobacco and Alcohol Use as an Explanation for the Association between Externalizing Behavior and Illicit Drug Use among Delinquent Adolescents. *Prevention Science*, 5(4), pp. 267-277, 2004.

### Vulnerability of Children of Incarcerated Addict Mothers: Implications for Preventive Intervention

This preliminary report examined the characteristics, experiences, and behavior of 88 primarily African-American adolescents with incarcerated addict mothers. The age, gender, and risk factor profiles with the children's adjustment status, based on self-reported questionnaire information and selected personality/behavioral assessment inventories, indicated that in spite of the incarceration of their substance-abusing mothers, the majority of these children were neither especially deviant nor maladjusted. All but a small percentage had successfully avoided substance abuse and the adoption of a deviant lifestyle at this point in their development. In most cases, mother surrogates (usually a grandmother or other family member) had functioned as primary caregivers of the children for many years prior to the incarceration of their birth mothers, possibly attenuating the negative impact ordinarily associated with a mother's absence from the home. However, there was a general indication of problematic school behavior and vulnerability to deviant peer influences that should be addressed in efforts aimed at preventing the escalation of deviant activity in such children. In almost all cases the child's caregiver needed caseworker support services. Hanlon, T.E., Blatchley, R.J., Bennett-Sears, T., O'Grady, K.E., Rose, M. and Callaman, J.M. Vulnerability of Children of Incarcerated Addict Mothers: Implications for Preventive Intervention. *Children and Youth Services Review*, 27(1), pp. 67-84, 2005.

### Characteristics and Vulnerability of Incarcerated Drug-Abusing Mothers

Although the number of drug-addicted incarcerated mothers has grown substantially in recent years, there is little information on their unique characteristics and vulnerabilities. This study examined data on 167 incarcerated drug-abusing mothers from Baltimore City who had volunteered for a parenting program offered at a Maryland correctional facility. Prior to entering this program, these mothers completed a battery of assessment measures including an extensive interview covering their early developmental and current experiences and standardized tests of psychological adjustment and parenting satisfaction. Analyses of these data focused on the link between risk/protective factors drawn from the early development experiences of these and their current adjustment status. There were significant relationships between higher risk levels and less favorable current adjustment suggesting the need to develop both prevention and clinical intervention efforts targeting both mothers and their children. Hanlon, T.E., O'Grady, K.E., Bennett-Sears, T. and Callaman, J.M. Incarcerated Drug-Abusing Mothers: Their Characteristics and Vulnerability. *American Journal of Drug and Alcohol Abuse*, 31(1), pp. 59-77, 2005.

### Racial and Gender Differences in Patterns of Adolescent Sexual Risk Behaviors

Sexual and substance use behaviors co-vary in adolescence. There also are racial and gender differences in the prevalence of HIV and other sexually transmitted diseases (STDs). These differences in subgroup risk behavior differences have not been systematically investigated with nationally representative data. Using cluster analysis 13,998 non-Hispanic black and white participants in the National Longitudinal Study of Adolescent Health, Wave 1, were grouped according to self-reported substance use and sexual behavior. Multinomial logit analyses examined racial and gender differences by cluster. Among 16 clusters, the two defined by the lowest risk behaviors (sexual abstinence and little or no substance use) comprised 47% of adolescents; fewer than 1% in these groups reported ever having received an STD diagnosis. The next largest cluster—characterized by sexual activity (on average, with one lifetime partner) and infrequent substance use—contained 15% of participants but nearly one-third of adolescent with STDs. Blacks were more likely than whites to be in this group. Black males also were more likely than white males to be in three small clusters characterized by high-risk sexual behaviors (i.e., having had sex with a male or with at least 14 partners, or for drugs or money). Although Black females generally were the least likely to be in high-risk behavior clusters, they were most likely to report STDs. Thus, adolescents' risk behavior patterns vary by race and gender, and do not necessarily correlate with their STD prevalence. Halpern, C.T., Hallfors, D., Bauer, D.J., Iritani, B., Waller, M.W. and Cho, H. Implications of Racial and Gender Differences in Patterns of Adolescent Risk Behavior for HIV and Other Sexually Transmitted Diseases. *Perspectives on Sexual and Reproductive Health*, 36(6), pp. 239-247, 2004.

### Development and Validation of a Gender-Balanced Measure of Aggression-Relevant Social Cognition

This study examined the psychometric properties of the Social-Cognitive Assessment Profile (SCAP), a gender-balanced measure of social information processing (SIP) in a sample of 371 (139 girls, 232 boys) 2nd- to 4th-grade children. The SCAP assesses 4 dimensions of SIP (Inferring Hostile Intent, Constructing Hostile Goals, Generating Aggressive Solutions, and Anticipating Positive Outcomes for Aggression) in the context of peer conflict involving relational and overt provocation. Confirmatory factor analyses indicated that the 4 latent factors provided a good fit to the data for girls and boys and for African American and non-African American children. Regression analyses in which teacher and peer evaluations of aggression and peer evaluations of social competencies were regressed on each of the 4 SCAP scales supported the test's convergent and discriminant validity. These results suggest that the SCAP is an easily administered and brief measure of SIP that is appropriate for racially diverse populations of elementary boys and girls. Hughes, J.N., Meehan, B.T., and Cavell, T.A. *Journal of Clinical Child and Adolescent Psychology*, 33(2), pp. 292-302, 2004.

### Infusion-LST Compared to LST as Usual

Findings from the first two years of a study to compare a standard Life Skills Training (LST) program with an infused (I-LST) approach was conducted in 9 small, rural school districts that were randomly assigned to LST, I-LST, or control conditions. Male and female subjects were in grade seven. The LST program significantly reduced alcohol use, binge drinking, marijuana use, and inhalant use after one year for females, and the I-LST program significantly reduced smoking, binge drinking, and marijuana use for females. At the end of the second year the I-LST program continued to impact female smoking, but all other results were non-significant. There were no effects on males at either time point. Smith, E.A. Evaluation of Life Skills Training and Infused-Life Skills Training in a Rural Setting: Outcomes at Two Years. *Journal of Alcohol & Drug Education*, 48(1), pp. 51-70, 2004.

### Cost Comparison of LST and Infusion-LST

A cost-effectiveness comparison of the Life Skills Training (LST) to a LST curriculum infusion approach (I-LST) was conducted. Male and female seventh graders from nine rural schools (2 intervention

conditions and control) were followed for two years. After one year, significant effects were observed only for females on alcohol, marijuana, and inhalant use in LST condition and for tobacco, alcohol, and marijuana use for I-LST females. After year two, only the I-LST program affected female smoking. Costs for the two programs included actual expenditures for training and materials as well as estimates of teachers' salaries for their project time were calculated. Both programs were almost equally effective after one year, but LST was more cost-effective. I-LST cost more to implement, but sustained effects into year two and was therefore more cost-effective overall. Swisher, J. D. A Cost-Effectiveness Comparison of Two Approaches to Life Skills Training. *Journal of Alcohol & Drug Education*, 48(1) pp. 71-78, 2004.

### Perceived Life Chances and Alcohol Use

The relationship between low perceived chances for success in life and binge drinking was examined in a sample of economically disadvantaged, predominantly black and Hispanic students, urban adolescents (N = 774) from 13 inner-city schools. Subjects completed confidential questionnaires in the 7th, 8th, and 9th grades. Eight items measured students' estimation of achieving certain adaptive life goals. Students who reported that they typically drink five or more drinks per drinking occasion were identified as binge drinkers. Results indicated that rates of binge drinking increased and perceived life chances decreased for both boys and girls from the 7th to 9th grade. Moreover, higher perceived life chances in the 7th grade predicted less binge drinking in the 8th grade, whereas binge drinking in the 8th grade predicted lower perceived life chances in the 9th grade, controlling for change over time in both variables. Griffin, K.W., Botvin, G.J., Nichols, T.R. and Scheier, L.M. Low Perceived Chances for Success in Life and Binge Drinking among Inner-city Minority Youth. *Journal of Adolescent Health*, 34, pp. 501-507, 2004.

### Self-esteem and Alcohol Use

Prior studies have found inconsistent relationships between measures of self-concept and adolescent alcohol use. This study explored whether the link between various measures of self-concept and alcohol use depends on gender and whether negative rather than positive self-esteem (i.e., self-derogation) might be more useful in predicting alcohol use. Students (N = 1459) attending 22 middle and junior high schools in New York City completed surveys that included measures of efficacy, self-derogation, and alcohol use. Participants completed surveys at baseline, 1-year follow-up, and 2-year follow-up. Findings indicate that lower efficacy was related to greater self-derogation a year later across gender. Increased self-derogation predicted higher alcohol use for girls but not boys. These findings are congruent with a literature highlighting the importance of negative thoughts about the self in drinking behavior for women but not men. Epstein, J.A., Griffin, K.W. and Botvin, G.J. Efficacy, Self-derogation, and Alcohol Use among Inner-city Adolescents: Gender Matters. *Journal of Youth & Adolescence* 33, pp. 159-166, 2004.

### Influence of Parents on Child Anti-social Behavior

This study examined the unique influence of mothers and fathers on their children's antisocial behavior using a sample of 325 families with sixth grade children. Multiple-group comparisons were conducted to identify differences in the relationships for mothers and fathers with daughters versus sons. Results suggested that, while the relationships were often similar for both parents and for both daughters and sons, mothers and fathers uniquely influenced their child's antisocial behavior depending on the child's gender. Overall, cross-gender influence appeared to be particularly important for fathers' control of their daughters' antisocial behavior. Kosterman, R., Haggerty, K.P., Spoth, R. and Redmond, C. Unique Influence of Mothers and Fathers on their Children's Antisocial Behavior: A Social Development Perspective. *Journal of Marriage and Family* 66(3), pp. 762-778, 2004.

### Does Perception of Behavior Affect Behavior?

This research examined whether parents' and children's perceptions have reciprocal self-fulfilling prophecy effects on each others' behavior. Mothers, fathers, and their adolescent children completed self-report surveys and engaged in videotaped dyadic interaction tasks. The surveys assessed parents' and children's perceptions of their own and the other's typical hostility and warmth. Observers coded the videotaped interactions to assess the actual hostility and warmth exhibited by mothers, fathers, and children. Data from 658 mother-child dyads were consistent with the conclusion that children had a self-fulfilling effect on their mothers' hostile behavior, but that mothers did not have a reciprocal self-fulfilling effect on their children's hostility. The data did not support the existence of self-fulfilling prophecies among the mother-child dyads with respect to warmth, or among the 576 father-child dyads for either the hostility- or warmth-relevant data. Madon, S., Guyll, M. and Spoth, R. The Self-fulfilling Prophecy as an Intra-family Dynamic, *Journal of Family Psychology* 18(3), pp. 459-469, 2004.

### **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

#### A Pilot Study on Voucher-based Incentives to Promote Abstinence from Cigarette Smoking during Pregnancy and Postpartum

Dr. Higgins and colleagues from the University of Vermont report results from a pilot study examining the use of vouchers redeemable for retail items as incentives for smoking cessation during pregnancy and postpartum. Fifty-eight women who were still smoking upon entering prenatal care were assigned to either contingent or noncontingent voucher conditions. Vouchers were available throughout pregnancy and for 12 weeks postpartum. In the contingent condition, vouchers were earned for biochemically verified smoking abstinence; in the noncontingent condition, vouchers were earned independent of smoking status. Contingent vouchers significantly increased abstinence at the end-of-pregnancy (37% vs. 9%), and 12-week postpartum (33% vs. 0%) assessments. That effect remained significant at the 24-week postpartum assessment (27% vs. 0%), which was 12 weeks after discontinuation of the voucher program. The magnitude of these treatment effects exceeds levels typically observed with pregnant and recently postpartum smokers, and the maintenance of effects through 24 weeks postpartum extends the duration beyond those reported previously. Higgins, S.T., Heil, S.H., Solomon, L.J., Lussier, J.P. and Lynch, M.E. *Nicotine and Tobacco Research*, 6(6), pp. 1015-1020, 2004.

#### Perceived Risks and Benefits of Smoking Cessation: Gender-specific Predictors of Motivation and Treatment Outcome

The primary aim of this study was to examine gender differences in perceived risks and benefits of smoking cessation and their relationship to pretreatment motivation and treatment outcome. A self-report instrument was developed for this purpose. Findings are reported from a subsample of 93 participants out of 573 treatment seeking smokers entering a smoking cessation study. Females indicated greater likelihood ratings of perceived risks and benefits than males. For women and men, perceived benefits were positively associated with motivation, and perceived risks were negatively associated with motivation and treatment outcome. Women evidenced stronger associations between perceived risks and pretreatment motivation, and treatment outcome. Knowledge of perceived risks and benefits associated with smoking cessation is critical for public education campaigns and could inform intervention strategies designed to modify sex-specific beliefs associated with lowered behavioral intentions to quit smoking. McKee, S.A., O'Malley, S.S., Salovey, P., Krishnan-Sarin, S. and Mazure, C.M. *Addictive Behaviors*, 30, pp. 423-435, 2005.

#### Dual and Multiple Diagnosis among Runaway and Homeless Youth

Dr. Natasha Slesnick and Jillian Prestopnik report on the clinical presentations of 226 youth at two homeless shelters participating in a study of family treatment for substance abuse. Regarding substance use

disorders, 81% met criteria for marijuana abuse or dependence, 64% met criteria for alcohol abuse or dependence, and about half (44%) met criteria for two substance use disorders. About 60% of youth met criteria for at least one substance use disorder and at least one psychiatric diagnosis. Of these youth, 60% met criteria for Oppositional Defiant Disorder or Conduct Disorder (ODD/CD); 34% met criteria for an Affective Disorder; and 54% met criteria for an Anxiety Disorder. Youth with ODD/CD were significantly more likely to use marijuana than other youth. Young men were significantly more likely than young women to meet criteria for ODD/CD, while young women were significantly more likely to meet criteria for Affective Disorders and Anxiety Disorders, and to have multiple diagnoses. These results highlight the large overlap between substance use disorders and psychiatric disorders found, and the need for appropriate treatment, among runaway youth. Slesnick, N. and Prestopnik, J.L. *American Journal of Drug and Alcohol Abuse*, 31, pp. 179-201, 2005.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

### Transdermal Nicotine Use in Postmenopausal Women and Hormone Replacement Therapy

Ninety-four postmenopausal female smokers were recruited according to HRT and non-HRT use (self-selecting) then randomized within strata to active nicotine or placebo nicotine patch. After 1 baseline week of smoking, participants quit smoking for 2 weeks. Women received cessation counseling and were monitored for abstinence. Dependent measures were collected during five clinic visits. Two-way analysis of covariance (ANCOVA) were run on change scores for dependent variables, with nicotine patch group (active/placebo) and HRT group (HRT/non-HRT) as independent variables and age as a covariate. No interactions were found between HRT and patch condition, but both showed specific effects. During the first abstinent week, women on active nicotine patch (compared with placebo) experienced less severe withdrawal, greater reductions in cigarette cravings, and lower (more favorable) Factor 1 scores on the Questionnaire of Smoking Urges. During the second abstinent week, women using HRT (compared with the non-HRT group) exhibited better mood (Profile of Mood States scores) and less depression (Beck Depression Inventory scores). These results suggest the following: First, the efficacy of transdermal nicotine replacement is not adversely modified by women's HRT use; second, ovarian hormones might influence women's responses to smoking cessation, and thus should be considered in developing effective strategies for women to quit smoking. Allen, S.S., Hatsukami, D.K., Bade, T. and Center, B. *Transdermal Nicotine Use in Postmenopausal Women: Does the Treatment Efficacy Differ in Women Using and Not Using Hormone Replacement Therapy?* *Nicotine Tob. Res.*, 6(5), pp. 777-788, October 2004.

### Re-emergence of Tobacco Smoking Using a Waterpipe

Waterpipes are increasing in popularity, and more must be learned about them so that we can understand their effects on public health, curtail their spread, and help their users quit. Research regarding waterpipe epidemiology and health effects is limited; no published studies address treatment efforts. Waterpipe use is increasing globally, particularly in the Eastern Mediterranean Region, where perceptions regarding health effects and traditional values may facilitate use among women and children. Waterpipe smoke contains harmful constituents and there is preliminary evidence linking waterpipe smoking to a variety of life threatening conditions, including pulmonary disease, coronary heart disease, and pregnancy related complications. More scientific documentation and careful analysis is required before the spread of waterpipe use and its health effects can be understood, and empirically guided treatment and public policy strategies can be implemented. Maziak, W., Ward, K. D., Afifi Soweid, R. A. and Eissenberg, T. *Tobacco Smoking Using a Waterpipe: A Re-emerging Strain in a Global Epidemic.* *Tob. Control*, 13(4), pp. 327-333, 2004.

### Gender Effects of Reported in Utero Tobacco Exposure on Smoking Initiation, Progression and Nicotine Dependence in Adult Offspring

The investigators studied the relationship between self-reported in utero tobacco exposure and gender on smoking initiation, progression of cigarette use (i.e., telescoping), and current levels of nicotine dependence in adult treatment-seeking smokers. Subjects (N = 298) who reported "yes" (28% of the original sample) or "no" (50% of the original sample) to in utero tobacco exposure were included in the analyses. Telescoping was calculated as the difference between the age respondents smoked their "first full cigarette" and the age when they started smoking daily. Females who reported being exposed in utero transitioned from initial to daily cigarette use more rapidly than females not exposed. The opposite effect was found for males, which may be related to our finding that in utero exposure lowered the age of cigarette experimentation in exposed compared with unexposed males. Measures of current cigarette use and dependence (i.e., Fagerstrom Test for Nicotine Dependence, prior withdrawal, number of past year quit attempts) were significantly associated with reported in utero exposure, gender, or interactions of exposure and gender. In utero tobacco exposure may accelerate the progression from experimentation to daily use in girls, result in early tobacco experimentation among boys, and produce higher levels of nicotine dependence among adult smokers. Oncken, C., McKee, S., Krishnan-Sarin, S., O'Malley, S. and Mazure, C. Gender Effects of Reported In Utero Tobacco Exposure on Smoking Initiation, Progression and Nicotine Dependence in Adult Offspring. *Nicotine Tob. Res.*, 6(5), pp. 829-833, October 2004.

### Progesterone Treatment and Cocaine Responses

The investigators examined the interaction between progesterone and cocaine in both male and female cocaine users using subjective, physiological and behavioral outcomes. A total of 10 subjects, 6 male and 4 female cocaine users, had two experimental sessions. Before each session, participants received either two oral doses of 200 mg of progesterone or placebo. Two hours after the second dose of medication treatment, the participants received a 0.3 mg/kg dose of cocaine intravenously and started the self-administration period, in which five optional doses of cocaine were available. Progesterone treatment attenuated the cocaine-induced diastolic blood pressure increases without affecting the systolic blood pressure and heart rate increases. Progesterone treatment also attenuated the subjective ratings of high and feel the effect of last dose in response to cocaine but did not affect cocaine self-administration behavior. These results suggest that progesterone attenuates some of the physiological and subjective effects of cocaine in both male and female participants. Sofuoglu, M., Mitchell, E. and Kosten, T.R. Effects of Progesterone Treatment on Cocaine Responses in Male and Female Cocaine Users. *Pharmacol Biochem Behav.*, 78(4), pp. 699-705, August 2004.

## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE**

### Sexual Risk among Injection Drug Users Recruited from Syringe Exchange Programs in California

The objective of this study was to examine correlates of sexual risk among injection drug users (IDUs). A total of 1445 IDUs were recruited from California syringe exchange programs. Consistent condom use was independently related to being HIV-positive, having multiple sex partners, not having a steady partner, not sharing syringes, and not injecting amphetamines for men; and engaging in sex work, not sharing syringes, and not having a steady partner for women. Having multiple recent sexual partnerships that included a steady partner was related to engaging in sex work, speedball injection, and amphetamine use among men; and younger age, having had a sexually transmitted disease (STD), engaging in sex work, and using alcohol among women. Having heterosexual anal sex was related to having had an STD, having multiple sexual partners, using amphetamines, and syringe-sharing for men; and younger age and amphetamine use for women. Authors conclude that comprehensive prevention interventions addressing multiple sexual and injection risk behaviors are needed for IDUs. Bogart, L.M., Kral, A.H., Scott, A., Anderson, R., Flynn, N.,



Gilbert, M.L. and Bluthenthal, R.N. Sexual Risk Among Injection Drug Users Recruited from Syringe Exchange Programs in California. *Sex Transm Dis.*, 32(1), pp. 27-34, January 2005.

#### Early Puberty in Girls: The Case of Premature Adrenarche

In this article authors examine the issue of early puberty in girls. First, a brief overview of normal pubertal development is provided, including the two endocrine components of puberty: gonadarche and adrenarche. Second, authors critically discuss the controversy regarding whether puberty truly is occurring earlier in girls. Third, they emphasize one type of early puberty, the case of premature adrenarche (PA). PA is used to illustrate the importance of identifying types of early puberty, evaluating the types to determine causality, determining whether follow-up of early puberty is necessary, and showing the potential ramifications of ignoring this variation in pubertal development. Findings from a pilot study comparing PA and on-time puberty children are used to show the importance of determining whether early puberty is normal in all cases. Dorn, L.D. and Rotenstein, D. Early Puberty in Girls: The Case of Premature Adrenarche. *Womens Health Issues*, 14(6), pp. 177-183, November-December 2004.

#### Vitamin D Deficiency and Seasonal Variation in an Adult South Florida Population

Hypovitaminosis D is associated with impaired neuromuscular function, bone loss, and fractures. If a person is not taking a vitamin supplement, sun exposure is often the greatest source of vitamin D. Thus, vitamin D deficiency is not uncommon in the winter, particularly in northern latitudes. The goal of this study was to establish the prevalence of vitamin D deficiency in south Florida (U.S.), a region of year-round sunny weather. At the end of the winter, 212 men and women attending an internal medicine clinic at a local county hospital were enrolled for measurements of 25-hydroxyvitamin D [25(OH)D], 1,25-dihydroxyvitamin D, and PTH; 99 participants returned at the end of summer. The mean (sd) winter 25(OH)D concentration was 24.9 8.7 ng/ml (62.3 21.8 nmol/liter) in men and 22.4 8.2 ng/ml (56.0 20.5 nmol/liter) in women. In winter, the prevalence of hypovitaminosis D, defined as 25(OH)D less than 20 ng/ml (50 nmol/liter), was 38% and 40% in men and women, respectively. In the 99 subjects who returned for the end of summer visit, the mean 25(OH)D concentration was 31.0 11.0 ng/ml (77.5 27.5 nmol/liter) in men and 25.0 9.4 ng/ml (62.5 23.5 nmol/liter) in women. Seasonal variation represented a 14% summer increase in 25(OH)D concentrations in men and a 13% increase in women, both of which were statistically significant. The prevalence of hypovitaminosis D is considerable even in southern latitudes and should be taken into account in the evaluation of postmenopausal and male osteoporosis. Levis, S., Gomez, A., Jimenez, C., Veras, L., Ma, F., Lai, S., Hollis, B. and Roos, B.A. Vitamin D Deficiency and Seasonal Variation in an Adult South Florida Population. *J Clin Endocrinol Metab.*, 90(3), pp. 1557-1562, March 2005.

### **SERVICES RESEARCH**

#### Treatment Outcomes among Women and Men Methamphetamine Abusers In California

A prospective longitudinal study examined treatment outcomes among 1073 methamphetamine-abusing patients (567 women, 506 men) from 32 community-based outpatient and residential programs in 13 California counties. Data were collected at intake and at 3 months and 9 months after admission. With one exception, improvements from baseline to follow-up were observed in all areas measured by the Addiction Severity Index (ASI) for both women and men in either modality. However, compared to men, women demonstrated greater improvement in family relationships and resolution of medical problems, while maintaining the same level of improvement as men in all other areas. These results showed gains for women despite higher unemployment, greater childcare responsibilities, co-habitation with someone who also used alcohol or drugs, relatively more reports of physical or sexual abuse and more psychiatric symptoms. Hser, Y., Evans, E., and Huang, Y. Treatment Outcomes among Women and Men Methamphetamine Abusers in California. *Journal of Substance Abuse Treatment*, 28(1), pp. 77-85, 2005.

### Housing Offers Protective Function For Substance Abuse and Violence in Indigent Women

A study examining retrospective self-reports of stratified random samples of women residing in shelters (N = 460) and low-income housing (N = 438) in Los Angeles County, California found that sheltered women were more likely than housed women to report physical and sexual violence, substance use and disorder, HIV risk behavior, and the co-occurrence of these problems in the past year. Differences remained when propensity weights were used to equate the groups on demographic and background characteristics. Wenzel, S.L., Tucker, J.S., Elliott, M.V., Hambarsoomians, K., Perlman, J., Becker, K., Kollross, C. and Golinelli, D. Prevalence and Co-occurrence of Violence, Substance Use and Disorder, and HIV Risk Behavior: A Comparison of Sheltered and Low-income Housed Women in Los Angeles County. *Preventive Medicine* 39, pp. 617-624, 2004.

### Men and Women Similar In Recovery Rates But Different In Psychosocial Functioning

Gender differences were examined at 36 months following residential or outpatient drug-free treatment among 951 participants in the Chicago Target Cities Project, the majority of whom were female (62%) and African American (93%). There were no differences in the proportion of men and women who reported any alcohol or drug use at the 36-month follow-up, with an overall reduction of 41% from intake. Greater proportions of men were incarcerated or employed, whereas greater proportions of women had returned to treatment, lived with their children, lived with a substance user, or had interpersonal problems. Women, as a group, had greater increases over time in self-help participation, free time spent with family, non-using family/friends, and employment. Although both men and women showed significant improvements following treatment, gender differences persisted in several areas of psychosocial functioning related to recovery. Grella, C.E., Scott, C.K., and Foss, M.A. Gender Differences in Long-term Drug Treatment Outcomes in Chicago PETS. *Journal of Substance Abuse Treatment*, 28, pp. 3-12, 2005.

### Using Client Characteristics to Understand Treatment Process in the Therapeutic Community

Therapeutic communities (TCs) improve post-treatment outcomes for substance abusers, but little is known about the in-treatment experience for clients with different backgrounds, experiences, and needs. This study examined the in-treatment experience of TC participants and examined the relationships between treatment process and client characteristics. Research participants included 447 adults and 148 adolescents receiving treatment in community-based TC programs in New York, California, and Texas. Data related to treatment process were collected using the Therapeutic Community Treatment Process: Dimensions of Change Instrument. Data on demographic characteristics, substance use and treatment history, and client risk factors were extracted from intake interviews and analyzed separately for adolescent and adult residents. Multivariate general linear models were used to examine the effect of client variables on treatment process, after controlling for treatment duration and program effects. Adult clients in the study were on average 36 years old, over half were male, and 57% were African American. The average age of adolescent clients was 17, with 73% being male, and 43 % Hispanic. Adult program participants who were 25 years or older, female, and had prior drug treatment were more positive about their experiences in the TC as indicated in their higher Community Environment scores. Adolescents with one or more arrests within the past 2 years were more negative about both their experiences in the TC and their self-concept as indicated in lower scores on process dimensions of the Community Environment and Personal Development and Change scales. Results from this study indicate how differences in client characteristics affect important treatment process variables including readiness for change and motivation for treatment. Chan, K.S., Wenzel, S., Orlando, M., Montagnet, C., Mandell, W., Becker, K. and Ebener, P. How important are Client Characteristics to Understanding Treatment Process in the Therapeutic Community? *The American Journal of Drug and Alcohol Abuse*, 30(4), pp. 871–891, 2004.

### Women's Perception of Therapeutic Communities

A comprehensive measure of treatment was administered to 447 adults and 148 adolescents receiving treatment at community-based TC programs in New York, California, and Texas. Data on demographic characteristics, substance use and treatment history, and client risk factors were extracted from intake interviews and analyzed separately for adult and adolescent residents. Controlling for treatment duration and program effects, female clients over 25 who had prior drug treatment experience reported more positive perceptions of the therapeutic community environment and expressed more willingness to change in contrast to younger males with no prior treatment experience or with one or more arrests within the past 2 years. Chan, K.S., Wenzel, S., Orlando, M., Montagnet, C., Mandell, W., Becker, K., and Ebener, P. How Important Are Client Characteristics to Understanding Treatment Process in the Therapeutic Community? *The American Journal of Drug and Alcohol Abuse* 30(4), pp. 871-891, 2004.

### Physical Violence against Impoverished Women: Risk and Protective Factors

Violence represents a significant threat to the health of impoverished women. Few studies have attempted to identify risk and protective factors associated with violence directed at these women, although this information might be useful for violence prevention. In a representative probability sample of impoverished women, this study prospectively examined multiple risk and protective factors to understand their relative importance to physical victimization. Study participants included 810 women in Los Angeles County, 402 living in shelters and 408 living in Section 8 low-income housing, who completed structured interviews at baseline and 6-month follow-up. Significant ( $p < .05$ ) multivariate predictors of physical violence experienced during the 6 months prior to the follow-up interview included physical or sexual violence experienced as a child, physical violence experienced during the 6 months prior to baseline interview, having multiple sexual partners, psychological distress, and poor social support. Results highlight the persistence of physical violence in the lives of impoverished women and prospective risk factors for this violence. Findings also highlight opportunities to reduce women's risk of experiencing violence through enhancing social support and mental health. Wenzel, S.L., Tucker, J.S., Elliott, M.N., Marshall, G.N. and Williamson, S.L. Physical Violence against Impoverished Women: A Longitudinal Analysis of Risk and Protective Factors. *Women's Health Issues*, 14(5), pp. 144-154, 2004.

### Gender Differences Found in Comprehensive Services in Substance Abuse Treatment

Utilizing data from the National Treatment Improvement Evaluation Study (NTIES), collected from 1992 to 1997, researchers report noteworthy gender differences. The analytic sample consisted of 3,142 clients (1,123 women and 2,019 men) from 59 treatment facilities. Findings show that greater proportions of women receive services; and when individual, service, and treatment organizational characteristics are controlled for, women show greater reductions in post-treatment substance use. Further, women and men differ in their responsiveness to organizational characteristics. The availability of on-site services and the frequency of counseling significantly predict reduced post-treatment substance use for men, but not for women. Marsh, J.C., Cao, D. and D'Aunno, T.D. Gender Differences in the Impact of Comprehensive Services in Substance Abuse Treatment. *Journal of Substance Abuse Treatment*, 27, pp. 289-300, 2004.

# DIRECTOR'S REPORT TO COUNCIL

September 2005

## **BASIC NEUROSCIENCE RESEARCH**

### Cocaine and Development

Cocaine use during pregnancy is associated with neurobehavioral problems in school-aged children that implicate alterations in attentional processes, potentially due to impairments in the noradrenergic system. In a recent study, NIDA supported researchers report a direct, disruptive effect of cocaine on noradrenergic neurons that may provide a neurobiological basis for changes in attentional function observed, in clinical and pre-clinical investigations, in offspring exposed to cocaine in utero. In this study, rats were administered cocaine in a physiologically relevant dose during critical phases of gestation. The locus coeruleus, a brain region, was analyzed for neurite outgrowth characteristics. Results showed that cocaine inhibited locus coeruleus neurite outgrowth and development and female offspring appeared most vulnerable to such effects. Snow, D.S., Carman, H.M., Smith, J.D., Booze, R.M., Welch, M.A. and Mactutus, C.F. Cocaine-induced Inhibition of Process Outgrowth in Locus Coeruleus Neurons: Role of Gestational Exposure Period and Offspring Sex. *International Journal of Developmental Neuroscience*, 22(5), pp. 297-308, 2004.

## **BASIC BEHAVIORAL RESEARCH**

### Inhibition of Dopaminergic and Serotonergic Reuptake during Gestation Has a Variety of Effects on Maternal Behavior in the Rat

Psychostimulants, antidepressants, anti-anxiety medications, and some antipsychotics all inhibit reuptake of one or more of the catecholamine neurotransmitters. Dr. Josephine Johns previously showed that gestational exposure to cocaine alters several aspects of maternal behavior and oxytocin levels in the rat, but it was not known whether this effect was mediated by cocaine-induced inhibition of catecholamine reuptake, or which neurotransmitters were involved. In this study, she systematically tested specific reuptake blockers of dopamine and serotonin during gestation, alone or in combination, to determine the effect of long-term reuptake inhibition on maternal behavior, postpartum aggression towards an intruder ("maternal aggression"), and oxytocin levels. Rat dams were treated throughout gestation with amfonelic acid, fluoxetine, or a combination of both at various doses, to investigate effects of reuptake inhibition of dopamine and serotonin systems, respectively. The more appetitive aspects of maternal behavior (nesting, licking, touching), and general activity of the dams, were increased by a low dose of amfonelic acid, a high dose of fluoxetine, or the high dose combination, more than other treatments. Maternal aggression was decreased by amfonelic acid and somewhat increased by fluoxetine. The results for crouching behavior were complex, but overall suggested both dopaminergic and serotonergic involvement. Dopamine uptake inhibition had a strong effect on hippocampal oxytocin levels, while receptor dynamics appeared to be more strongly affected by serotonin uptake inhibition. Dr. Johns is continuing her examination of oxytocin levels and receptor expression, which as recent studies suggest, may have a greater role in maternal care in humans than previously thought. Since pregnant women frequently take drugs (e.g. antidepressants, cocaine) that induce long-term reuptake inhibition of dopamine and/or serotonin, it is important to understand the effects of such drugs on behavior and biochemistry. The quantitative measures in this study indicate that long-term reuptake inhibition of dopamine or serotonin, or both, has specific and complex effects on different aspects of maternal behavior. The overall conclusion is that these treatments do not impair maternal behavior per se, but they alter it in a variety of ways that can further our understanding of alterations in human maternal behavior after perinatal exposure to drugs with the same mechanism of

action. Johns, J.M., Joyner, P.W., McMurray, M.S., Elliott, D.L., Hofler, V.E., Middleton, C.L., Knupp, K., Greenhill, K.W., Lomas, L.M. and Walker, C.H. The Effects of Dopaminergic/serotonergic Reuptake Inhibition on Maternal Behavior, Maternal Aggression, and Oxytocin in the Rat. *Pharmacology, Biochemistry and Behavior*, 81, pp. 769-785, 2005.

#### Preclinical “Binge” Model of Inhalant Abuse for Studying Prenatal Exposure Effects

Dr. Scott Bowen at Wayne State University has developed a binge model for exposing animals to abused inhalants. In his static exposure chambers, animals receive high concentrations of solvents over relatively brief exposure periods, mimicking the typical pattern of solvent abuse in humans. Previous exposure paradigms have employed long-term, relatively low levels of inhalant treatment, but with this model, the investigator attempts to produce repeated and rapidly resolved high-peak blood solvent concentrations. Recently he has used this procedure to study the teratogenic impact of toluene exposure during gestational days eight through 20 in the rat. Solvent abuse in adolescent females of childbearing age is a concern because rates of first-time solvent use among young people between 18 and 25 rose 243% during the 1990s and toluene-related embryopathy and malformations have been reported, with high levels of exposure linked to gross morphological teratogenicity. Moreover, follow-up evaluations reveal developmental delays and language impairment, among other neurological pathologies, and retardation in physical growth. In the present study, timed-pregnant females were exposed twice per day for 15 min to either 8000 (L) or 12,000 (H) ppm toluene. There was also an “air-only” control group (C) that was placed in the chambers twice daily for an equal amount of time. Pups were assessed on measures of early neonatal growth, perinatal outcome, and neurobehavioral development. From whole litter assessments of reflex development, strength and motor coordination, the investigators note a greater number of weaker pups in the highest dose group on post-natal (PN) day 16 (i.e., close to half the animals from the H group were at or below the 25<sup>th</sup> percentile of the C group). There were also significant effects of solvent exposure on negative geotaxis, with longer latencies for both concentration groups on PN days 6-8. On PN1, H litters weighed significantly less than the other two groups. However, between PN12-21, H pups gained relatively more weight than control animals, showing “catch up” growth. The authors also observed a dose relationship for gross malformations, external soft tissue malformations, number of pups classified as “runts”, and neonatal mortality: The percentage of litters affected by these three kinds of outcomes was 12.5, 29.4 and 52.9 for the CF, L and H exposure conditions, respectively. These differences were seen with similar maternal weights and maternal weight gains across the three groups. There were also no significant between group differences in total litter size or mean gestational length. It appears that this procedure, using high dose, binge exposure conditions, may better reproduce the key pharmacodynamic features of inhalant abuse in humans and provide a more valid characterization of toluene embryopathy than studies employing longer, lower dose exposure. Bowen, S.E., Batis, J.C., Mohammadi, M.H. and Hannigan, J.H. Abuse Pattern of Gestational Toluene Exposure and Early Postnatal Development in Rats. *Neurotoxicology and Teratology*, 27, pp. 105-116, 2005.

#### Decreased Motivation to Obtain Cocaine Following Extended Access: Effects of Sex and Ovarian Hormones

As described in the September 2004 Director’s Report to Council, Drs. Wendy Lynch and Jane Taylor reported sex differences in cocaine self-administration (1.5 mg/kg/infusion) under a 24-hour access procedure in which rats received four 10-min discrete trials per hour for seven days -- a procedure which produces escalation of cocaine intake in a binge-abstinence pattern. Drs. Lynch and Taylor found that compared to males, females self-administered more cocaine, self-administered for longer periods of time, and exhibited greater disruption in the diurnal control over cocaine intake. In an assessment of long-term changes in cocaine motivation, conducted following a 10-day forced abstinence period, females exhibited an increase in motivation for cocaine as measured by behavior under a progressive ratio schedule, whereas males did not. (Lynch, W.J. and Taylor, J.R. Sex Differences in the Behavioral Effects of 24-hr Access to Cocaine under a Discrete Trial Procedure. *Neuropsychopharmacology*, 29, pp. 943-951, 2004). In a recent

follow-up study, these researchers examined more immediate changes in cocaine motivation by testing 1, 2, and 3 days following the 7-day discrete trial procedure. Whereas males showed no change in cocaine motivation over the three test days, as assessed by progressive ratio performance, females exhibited a marked reduction in motivation. By comparing ovariectomized females with and without estrogen replacement, the researchers found that estrogen modulated the motivation for cocaine. Taken together, these two studies indicate that at 1, 2, 3, and 10 days following seven days of high access to cocaine, males exhibit no change in cocaine motivation, whereas females exhibit a reduction at 1, 2, and 3 days, and an increase at 10 days. These outcomes, along with earlier research using variations of the 24-hr discrete trials procedure with only male rats, illustrate male-female differences in the development and time course of cocaine motivation during and following extended access to cocaine. These data add to a growing body of human and animal literature indicating sex differences in cocaine addiction. Lynch, W.J. and Taylor, J.R. Decreased Motivation Following Cocaine Self-administration Under Extended Access Conditions: Effects of Sex and Ovarian Hormones. *Neuropsychopharmacology*, 30, pp. 927-935, 2005.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Prenatal Tobacco Exposure and Offspring Smoking in Early Adolescence

In this prospective study of a birth cohort of 567 14-year-olds, investigators at the University of Pittsburgh examined relationships among trimester-specific prenatal tobacco exposure (PTE), offspring smoking, and other correlates of adolescent smoking. Average age of the adolescents was 14.8 years (range: 13.9–16.6 years). Approximately half of the sample was female, and about half was African-American. Data on maternal tobacco and other substance use were collected both prenatally and postnatally. Fifty-one percent of the mothers were prenatal smokers and 53% smoked when their children were 14 years old. PTE in the third trimester significantly predicted offspring smoking (ever/never, smoking level, age of onset) when demographic and other prenatal substances were included in the analyses. PTE remained a significant predictor of the level of adolescent smoking when maternal and child psychological characteristics were added to the model. When more proximal measures of the child's smoking were included in the model, including mother's current smoking and friends' smoking, PTE was no longer significant. Significant predictors of adolescent smoking at age 14 were female gender, Caucasian race, child externalizing behavior, maternal anxiety, and child depressive symptoms. The authors conclude that although direct effects of PTE on offspring smoking behavior have previously been reported from this study and by others, by early-adolescence, this association was not significant in this sample after controlling for the more proximal covariates of adolescent smoking such as mother's current smoking and peer smoking. They also note that many of the reports in the literature that indicate a relationship between PTE and offspring smoking have been retrospective or have not included important variables such as other prenatal substance exposures, maternal and child psycho-social characteristics, mother's current smoking, and friends' smoking. Cornelius, M.D., Leech, S.L., Goldschmidt, L. and Day, N.L. Is Prenatal Tobacco Exposure a Risk Factor for Early Adolescent Smoking? *Neurotoxicology and Teratology*, 27, pp. 667-676, 2005.

### School Performance of Children with Gestational Cocaine Exposure

Researchers from the University of Pennsylvania have reported results on school performance in a sample of children exposed to cocaine in utero. At the completion of fourth grade, a total of 135 children (62 with gestational cocaine exposure and 73 without) who were enrolled at birth and followed prospectively, were evaluated using report card data, standardized test results, teacher and parent report, and natal and early childhood data. Successful grade progression was defined as completing grades 1 through 4 without being retained. Cocaine-exposed and control children were similar in school performance (all  $p \geq 0.10$ ): successful grade progression (71% cocaine-exposed vs. 84% control), Grade Point Average ( $2.4 \pm 0.8$  vs.  $2.6 \pm 0.7$ ), reading below grade level (30% vs. 28%), and standardized test scores below average (reading [32% vs. 35%], math [57% vs. 44%], science [39% vs. 36%]). Children with successful progression, regardless of cocaine exposure, had higher Full Scale IQ and better home environments. The researchers conclude that

in this inner-city cohort, cocaine-exposed and control children had similar poor school performance, with better home environment and higher Intelligence Quotient associated with an advantage for successful grade progression, regardless of gestational cocaine exposure. Hurt, H., Brodsky, N.L., Roth, H., et al. School Performance of Children with Gestational Cocaine Exposure. *Neurotoxicology and Teratology*, 27, pp. 23-211, 2005.

#### Prenatal Drug Exposure and Selective Attention in Preschoolers

Based on research conducted at Case Western Reserve University, a recent report focused on selective attention in a large, polysubstance cocaine-exposed cohort of 4-year-olds and their at-risk comparison group. Maternal pregnancy use of cocaine and use of cigarettes were both associated with increased commission errors, interpreted as indicative of inferior selective attention. Severity of maternal use of marijuana during pregnancy was positively correlated with omission errors, suggesting impaired sustained attention. Substance exposure effects were independent of maternal postpartum psychological distress, birth mother cognitive functioning, current caregiver functioning, other substance exposures, and child concurrent verbal IQ. Noland, J.S., Singer, L.T., Short, E.J., et al. Prenatal Drug Exposure and Selective Attention in Preschoolers. *Neurotoxicology and Teratology*, 27, pp. 429-438, 2005.

#### Relative Ability of Biologic Specimens and Interviews to Detect Prenatal Cocaine Exposure

University of Florida researchers recruited women in a labor and delivery service, enrolling all consenting patients with a history of prenatal cocaine use and the next admission with no recorded use. During the immediate postpartum period, private, structured interviews were carried out to obtain details of prenatal cocaine use and to identify a priori exclusion criteria (other illicit drug use, high alcohol use and chronic illnesses and medications). Amniotic fluid, cord blood, infant urine, meconium, and maternal hair were also collected. All specimens were blindly analyzed with respect to exposure, using gas chromatography/mass spectrometry. Of 115 subjects, 46 had one or more biologic specimens positive for cocaine metabolites and five admitted prenatal use, but had negative specimens. Of these 51 identified as users by any method, 38 admitted, 32 were positive for urine, 28 for hair, and 25 for meconium. Of the 38 admitters, 87% had positive specimens. Of the 77 denying use, 17% were positive. Urine was most frequently positive in identified users, 67% overall and 62% of users who denied. Hair was next, positive in 65% of all users and 50% of users who denied. Of the 13 subjects who denied use but were positive on at least one specimen, four were identified solely by urine, two only by hair and one only by meconium. Self-report identified five users with all negative specimens. The authors conclude that although no one method identified all users, the single method that maximally identified users was detailed history taken by experienced interviewers. Eyler, F.D., Behnke, M., Wobie, K., Garvan, C.W. and Tebbett, I. Relative Ability of Biologic Specimens and Interviews to Detect Prenatal Cocaine Use. *Neurotoxicology and Teratology*, 27, pp. 677-687, 2005.

### **CLINICAL NEUROSCIENCE RESEARCH**

#### Enlarged Striatum in Abstinent Methamphetamine Abusers: A Possible Compensatory Response

Since so little is known about structural brain abnormalities associated with methamphetamine (METH) abuse, Dr. Linda Chang and colleagues at University of Hawaii evaluated METH-dependent subjects for possible morphometric changes. They focused on the striatum of recently abstinent METH abusers, to determine whether morphometric changes, if any, were related to cognitive performance, and to evaluate if there might be sex-by-METH interactions on morphometry. Structural MRI was performed in 50 METH and 50 comparison subjects with age range and gender controlled. Quantitative morphometric analyses were performed in the subcortical gray matter, cerebellum and corpus callosum (CC). Neuropsychological tests were also performed in 44 METH and 28 comparison subjects. All METH users, regardless of gender, showed an enlarged putamen and GP when compared to controls. Additionally, female METH

users displayed a larger mid-posterior CC. Although METH users had normal cognitive function, those with smaller striatal structures reported greater cumulative METH usage and had poorer cognitive performance. Since METH subjects with less cumulative METH usage had larger striatal structures and had relatively normal cognitive performance, the enlarged putamen and GP might represent a compensatory response to maintain function. Possible mechanisms for the striatal enlargement include glial activation and inflammatory changes associated with METH-induced injury. Chang, L., Cloak, C., Patterson, K., Grob, C., Miller, E.N. and Ernst, T. *Biol Psychiatry*, 157, pp. 967-974, 2005.

#### Significant Association of the A4 Subunit of the Nicotine Acetylcholine Receptor with Nicotine Dependence

M.D. Li and colleagues studied over 2000 subjects from more than 600 families with three measures of smoking severity (heaviness, quantity, and dependence) and demonstrated association with at least two (of six studied) single nucleotide polymorphisms (SNPs). However, different SNPs were associated in different ethnic groups (African Americans and European Americans). Furthermore, in female African Americans on SNP was significantly associated with all three nicotine dependence measures. The  $\beta 2$  subunit of the nAChR gene was also examined but no association was found. This study is believed to be the first to confirm a genetic role of the CHR4 gene, separately in African and European American samples as well as indicate that such an association may be sex-specific as well. Li, M.D., Beuten, J., Ma, J.Z., Payne, T.J., Lou, X.-Y., Garcia, V., Duenes, A.S., Crews, K.M. and Elston, R.C. *Human Molecular Genetics*, 14, pp. 1211-1219, 2005.

#### Body Mass Predicts Orbitofrontal Activity during Visual Presentations of High-Calorie Foods

Yurgelun-Todd and colleagues at McLean Hospital used BOLD fMRI to investigate the relationship between weight status and reward-related brain activity in normal weight humans. Orbitofrontal and anterior cingulate cortex activity as measured by fMRI in 13 healthy, normal-weight adult women as they viewed images of high-calorie and low-calorie foods, and dining-related utensils. Body mass index correlated negatively with both cingulate and orbitofrontal activity during high-calorie viewing, negatively with orbitofrontal activity during low-calorie viewing, and positively with orbitofrontal activity during presentations of nonedible utensils. With greater body mass, activity was reduced in brain regions important for evaluating and modifying learned stimulus-reward associations, suggesting a relationship between weight status and responsiveness of the orbitofrontal cortex to rewarding food images. Killgore, W.D.S. and Yurgelun-Todd, D.A. *Neuroreport*, 16, pp. 859-863, 2005.

#### Epidemiological Risk Estimates of Cocaine Dependence for the United States, 2000-2001

This paper presents new estimates for the risk of becoming cocaine dependent within 24 months after first use of the drug, and study subgroup variation in this risk. The study estimates are based on the National Household Survey on Drug Abuse conducted during 2000-2001, with a representative sample of U.S. residents aged 12 years and older ( $n = 114,241$ ). A total of 1081 respondents were found to have used cocaine for the first time within 24 months prior to assessment. Between 5 and 6% of these recent-onset users had become cocaine dependent since onset of use. Excess risk of recent cocaine dependence soon after onset of cocaine use was found for female subjects, young adults aged 21-25 years, and non-Hispanic Black/African-Americans. The use of crack-cocaine and taking cocaine by injection was associated with having become cocaine dependent soon after onset of use. These epidemiologic findings help to quantify the continuing public health burden associated with new onsets of cocaine use in the 21st century. O'Brien, M.S. and Anthony, J.C. *Risk of Becoming Cocaine Dependent, Epidemiological Estimates for the United States, 2000-2001*. *Neuropsychopharmacology*, 30, pp. 1006-1018, 2005.



## Early Violent Death among Delinquent Youth

This study compared mortality rates for delinquent youth with those for the general population, controlling for differences in gender, race/ethnicity, and age. This prospective longitudinal study examined mortality rates among 1829 youth (1172 male and 657 female) enrolled in the Northwestern Juvenile Project, a study of health needs and outcomes of delinquent youth. Participants, 10 to 18 years of age, were sampled randomly from intake at the Cook County Juvenile Temporary Detention Center in Chicago, Illinois, between 1995 and 1998. The sample was stratified according to gender, race/ethnicity (African American, non-Hispanic white, Hispanic, or other), age (10-13 or  $\geq 14$  years), and legal status (processed as a juvenile or as an adult), to obtain enough participants for examination of key subgroups. The sample included 1005 African American (54.9%), 296 non-Hispanic white (16.2%), 524 Hispanic (28.17%), and 4 other-race/ethnicity (0.2%) subjects. Data on deaths and causes of death were obtained from family reports or records and were then verified by the local medical examiner or the National Death Index. For comparisons of mortality rates for delinquents and the general population, all data were weighted according to the racial/ethnic, gender, and age characteristics of the detention center, these weighted standardized populations were used to calculate reported percentages and mortality ratios. Mortality ratios were calculated by comparing the sample's mortality rates with those for the general population of Cook County, controlling for differences in gender, race/ethnicity, and age. Results indicated that sixty-five youth died during the follow-up period. All deaths were from external causes. As determined by using the weighted percentages to estimate causes of death, 95.5% of deaths were homicides or legal interventions (90.1% homicides and 5.4% legal interventions), 1.1% of all deaths were suicides, 1.3% were from motor vehicle accidents, 0.5% were from other accidents, and 1.6% were from other external causes. Among homicides, 93.0% were from gunshot wounds. The overall mortality rate was greater than 4 times the general-population rate. The mortality rate among female youth was nearly 8 times the general-population rate. African American male youth had the highest mortality rate (887 deaths per 100 000 person-years). These findings indicate that early violent death among delinquent and general-population youth affects racial/ethnic minorities disproportionately and should be addressed, as are other health disparities. Future studies should identify the most promising modifiable risk factors and preventive interventions, explore the causes of death among delinquent female youth, and examine whether minority youth express suicidal intent by putting themselves at risk for homicide. Teplin, L.A., McClelland, G.M., Abram, K.M., and Mileusnic, D. Early Violent Death among Delinquent Youth: A Prospective Longitudinal Study. *Pediatrics*, 115, pp. 1586-1593, 2005.

## Gender/Racial Differences in "Jock" Identity, Dating, and Adolescent Sexual Risk

Despite recent declines in overall sexual activity, sexual risk-taking remains a substantial danger to US youth. Existing research points to athletic participation as a promising venue for reducing these risks. Linear regressions and multiple analyses of covariance were performed on a longitudinal sample of nearly 600 Western New York adolescents in order to examine gender- and race-specific relationships between "jock" identity and adolescent sexual risk-taking, including age of sexual onset, past-year and lifetime frequency of sexual intercourse, and number of sexual partners. After controlling for age, race, socioeconomic status, and family cohesion, male jocks reported more frequent dating than nonjocks but female jocks did not. For both genders, athletic activity was associated with lower levels of sexual risk-taking, however, jock identity was associated with higher levels of sexual risk-taking, particularly among African American adolescents. Future research should distinguish between subjective and objective dimensions of athletic involvement as factors in adolescent sexual risk. Miller, K.E., Farrell, M.P., Barnes, G.M., Melnick, M.J. and Sabo, D. Gender/racial Differences in Jock Identity, Dating, and Adolescent Sexual Risk. *Journal of Youth and Adolescence*, 34, pp. 123-136, 2005.

### Nicotine Phenotypes based on Withdrawal Discomfort, Response to Smoking, and Ability to Abstain

Smoking is often viewed as a comprehensive phenotype rather than a complex set of traits involving intermediate phenotypes. To explore this issue in a laboratory setting, researchers tested 69 smokers stratified on depression, nicotine dependence, and gender. On the third day of an initial withdrawal period, participants were tested for differences in uncued and cued craving and withdrawal. On the fourth day, participants were exposed to a controlled dose of smoke and assessed for physiological and hedonic effects and reduction of craving and withdrawal. Following resumption of smoking for at least a week, participants were then tested on their ability to abstain for an 11-day interval. During the withdrawal test, high-depressed smokers and men exhibited elevated craving and withdrawal scores overall, whereas no differences emerged for dependence. Cue exposure produced significant increases in craving but not withdrawal. During the smoke-exposure test, men were significantly more likely than women, and high-depressed smokers more likely than low-depressed smokers, to show evidence of experiencing pleasurable "buzzes." High-dependent smokers showed significant increases in diastolic blood pressure, possibly suggestive of greater sensitivity to nicotine. During the quit test, high-dependent smokers had more difficulty abstaining than low-dependent smokers, and women more than men, no differences emerged based on depression. Independently of group membership, inability to abstain was predicted by increased anxiety, depression, and difficulty concentrating in response to cue exposure. These findings provide support for the existence of phenotypes that can be distinguished by withdrawal symptomatology (primarily driven by depression) and ability to remain abstinent (primarily driven by dependence). Pomerleau, O.F., Pomerleau, C.S., Mehlinger, A.M., Snedecor, S.M., Ninowski, R. and Sen, A. Nicotine Dependence, Depression, and Gender: Characterizing Phenotypes Based On Withdrawal Discomfort, Response to Smoking and Ability to Abstain. *Nicotine & Tobacco Research*, 7, pp. 91-102, 2005.

### Timing of Entry into Fatherhood in Young, At-Risk Men

The timing of first fatherhood was examined in a sample of 206 at-risk, predominantly White men, followed prospectively for 17 years. An event history analysis was used to test a model wherein antisocial behavior, the contextual and familial factors that may contribute to the development of antisocial behavior, and common correlates of such behavior, including academic failure, substance use, and early initiation of sexual behaviors, lead both directly and indirectly to an early transition to fatherhood. Having a mother who was younger at first birth, low family socioeconomic status, poor academic skills, failure to use condoms, and being in a cohabitating or marital relationship predicted entry into fatherhood. Pears, K.C., Pierce, S.L., Kim, H.K., Capaldi, D.M. and Owen, L.D. The Timing of Entry into Fatherhood in Young, At-risk Men. *Journal of Marriage and the Family*, 67, pp. 429-447, 2005.

### Personality Factors Contributing to Comorbidity

The authors investigated the role of personality traits in accounting for comorbidity in common psychiatric and substance use disorders. 7588 participants in a population-based twin registry in Virginia were interviewed with the SCID to determine lifetime diagnoses of common psychiatric and substance use disorders, and completed self-report questionnaires to determine dimensions of neuroticism, extraversion, and novelty seeking. Of note, neuroticism accounted for the highest proportion of comorbidity within internalizing (mood and anxiety) disorders (20-45%) and between internalizing and externalizing (antisocial and substance use) disorders (19-88%). Variation in neuroticism and novelty seeking each accounted for a modest proportion (10-12% and 7-14%, respectively) of the comorbidity within externalizing disorders. Extraversion contributed negligibly. Although rates of disorders differed among the genders, the patterns of comorbidity accounted for by personality were similar in males and females. These findings extend previous research on personality and psychiatric disorder by using a population-based sample and by quantifying the proportion of comorbidity explained by personality dimension. Given that comorbidity among psychiatric and substance use disorders is extremely common, these findings can help refine our understanding of those underlying traits that put individuals at risk for multiple later

disorders, regardless of gender, particularly the role of neuroticism. Khan, A.A., Jacobson, K.C., Gardner, C.O., Prescott, C.A. and Kendler, K.S. Personality and Comorbidity of Common Psychiatric Disorders. *British Journal of Psychiatry*, 186, pp. 190-196, 2005.

#### Association of Early Adolescent Problem Behavior with Adult Psychopathology

The authors investigated whether the association between adolescent problem behavior and adult substance use and mental health disorders was general, such that adolescent problem behavior elevates the risk for a variety of adult disorders, or outcome-specific, such that each problem behavior is associated specifically with an increased risk for disorders clinically linked to that behavior (e.g., early alcohol use with adult alcohol abuse). A population-based group of 578 male and 674 female twins reported whether they had ever engaged in, and the age of initiation of, five adolescent problem behaviors: smoking, alcohol use, illicit drug use, police trouble, and sexual intercourse. Participants also completed a structured clinical interview at both ages 17 and 20 covering substance use disorders, major depressive disorder, and antisocial personality disorder. Each problem behavior was significantly related with each clinical diagnosis. The association was especially marked for those who had engaged in multiple problem behaviors before age 15. Among those with four or more problem behaviors before age 15, the lifetime rates of substance use disorders, antisocial personality disorder, and major depressive disorder exceeded 90%, 90%, and 30% in males and 60%, 35%, and 55% in females, respectively. The association between the clinical diagnoses and adolescent problem behavior was largely accounted for by two highly correlated factors. This study suggests that early adolescent problem behavior identifies a subset of youth who are at an especially high and generalized risk for developing adult psychopathology. McGue, M. and Iacono, W.G. The Association of Early Adolescent Problem Behavior with Adult Psychopathology. *American Journal of Psychiatry*, 162(6), pp. 1118-1124, 2005.

#### Child Psychopathology and Early Substance Use

This study examined the relationships between childhood externalizing and internalizing disorders and early substance use and abuse, in a large community-based sample of twins of both genders, at ages 11 and 14. The sample was composed of twins participating in the Minnesota Twin Family Study, an epidemiological sample of twins and their families' representative of the largely-Caucasian population of Minnesota. A total of 699 twin girls and 665 twin boys participated at both time-points. Twins participated in in-person, life-time diagnostic assessments of the following childhood DSM III-R externalizing and internalizing disorders at age 11: conduct disorder, oppositional defiant disorder, attention deficit hyperactivity disorder, major depressive disorder and in addition, for girls only, overanxious disorder and separation anxiety disorder. At ages 11 and 14, substance use and abuse were assessed. Consistent with the literature, externalizing disorders at age 11, particularly conduct and oppositional disorders, were related to substance use and abuse in both boys and girls, at ages 11 and 14. Among the internalizing disorders, only major depression among girls at age 11 showed a relationship to substance use and abuse at age 14. These findings can help refine populations that may benefit from interventions for early substance abuse. King, S.M., Iacono, W.G. and McGue, M. Childhood Externalizing and Internalizing Psychopathology in the Prediction of Early Substance Use. *Addiction*, 99, pp. 1548-1559, 2004.

#### Heritability of Cigarette Smoking and Family Dysfunction in Women

Previous studies using adoption samples have found that the impact of genetic risk factors on alcoholism in women have a stronger influence when there is a history of conflict in the family. The authors of this study investigated a similar impact on cigarette smoking in a population-based twin sample. A sample of 1676 female twins from a population-based registry provided data on maximum lifetime cigarette smoking and family dysfunction assessed as the mean report of up to four informants (twin, co-twin, mother, father). Using a variety of statistical approaches and models, the hypothesis was not confirmed; on the contrary, the heritability (proportion of variance due to genetic factors) of cigarette smoking was reduced at higher levels

of family dysfunction, and unique environmental factors became more significant. Further work, with different populations and substances, is needed; in the meantime, the authors caution against a broad assumption that adverse childhood environments always increase heritability. Kendler, K.S., Aggen, S.H., Prescott, C.A., Jacobson, K.C. and Neale, M.C. Level of Family Dysfunction and Genetic Influences on Smoking in Women. *Psychological Medicine*, 34, pp. 1263-1269, 2004.

#### Partitioning Common and Specific Influences on Drug Use and Abuse

Previous studies of the genetic epidemiology of drug abuse have generally modeled drug use and drug abuse and dependence separately. However, the authors of this paper note that drug use disorders are contingent on drug use (one cannot develop the disorder without first using the drug) and so they apply a model that can partition the genetic and environmental influences into those that are common to both stages and those that are stage-specific. Using the SCID, data on use and abuse/dependence of cannabis, cocaine, sedatives, stimulants and any illicit drug were obtained from 1191 male and 934 female Caucasian twin pairs in the Mid-Atlantic Twin Registry. Results provide evidence for both genetic, shared environmental and unique environmental influences that are common to illicit drug use and abuse/dependence, and factors that are specific to abuse/dependence. Similarities among different types of drugs and between both sexes were noted in the patterns of risk influences. Thus, it is likely that there are some genetic and environmental factors that influence both drug use and abuse/dependence regardless of the drugs used or gender of the user, and that there are other factors that operate specifically to predispose to abuse and dependence once use has onset. Agrawal, A., Neale, M.C., Jacobson, K.C., Prescott, C.A. and Kendler, K.S. Illicit Drug Use and Abuse/Dependence: Modeling of Two-Stage Variables Using the CCC Approach. *Addictive Behaviors*, 30(5), pp. 1043-1048, 2005.

#### Attitudes of Emergency Medical Service Providers Towards Naloxone Distribution Programs

Training and distributing naloxone to drug users is a promising method for reducing deaths associated with heroin overdose. Emergency Medical Service (EMS) providers have experience responding to overdose, administering naloxone, and performing clinical management of the patient. Little is known about the attitudes of EMS providers toward training drug users to use naloxone. An anonymous survey was conducted of 327 EMS providers to assess their attitudes toward a pilot naloxone program. Of 176 who completed the survey, the majority were male (79%) and Caucasian (75%). The average number of years working as an EMS provider was 7 (SD = 6). Overall attitudes toward training drug users to administer naloxone were negative, with 56% responding that this training would not be effective in reducing overdose deaths. Differences in attitudes did not vary by gender, level of training, or age. Providers with greater number of years working in EMS were more likely to view naloxone trainings as effective in reducing overdose death. Provider concerns included drug users' inability to properly administer the drug, program condoning and promoting drug use, and unsafe disposal of used needles. The study concludes that incorporating information about substance abuse and harm reduction approaches in continuing education classes may improve the attitudes of providers toward naloxone training programs. Tobin, K., Gaasch, W., Clarke, C., MacKenzie, E. and Latkin, C. Attitudes of Emergency Medical Service Providers towards Naloxone Distribution Programs. *J Urban Health*, 82(2), pp. 296-302, 2005.

#### The Effect of Serostatus on HIV Risk Behavior Change among Women Sex Workers in Miami, Florida

HIV prevention and risk reduction are especially salient and timely issues for women, particularly among those who are drug-involved or who exchange sex for drugs or money. Studies suggest that HIV-prevention measures can be effective with highly vulnerable women, and have the potential to produce significant reductions in risk behaviors among both HIV-negative and HIV-positive women. Within this context, this paper examines risk behaviors and HIV serostatus among 407 drug-involved women sex workers in Miami, Florida, and investigates the effects of participation in HIV testing, counseling, and a risk-reduction intervention on subsequent behavioral change among this population. Overall, at follow-up, the HIV-

positive women were 2.4 times more likely than the HIV-negative women to have entered residential treatment for drug abuse, 2.2 times more likely to have decreased the number of their sex partners, 1.9 times more likely to have decreased the frequency of unprotected sex, 1.9 times more likely to have reduced their levels of alcohol use, and 2.3 times more likely to have decreased their crack use. These data support the importance of HIV testing and risk-reduction programs for drug-involved women sex workers. Inciardi, J., Surratt, H., Kurtz, S. and Weaver, J. The Effect of Serostatus on HIV Risk Behavior Change among Women Sex Workers in Miami, Florida. *AIDS Care*, 17 (Supplement 1): S88-S101, June 2005.

### Predictors of High Rates of Suicidal Ideation among Drug Users

Several studies have attempted to understand the link among substance abuse, depression, and suicidal ideation (SI). Assessment of this link is important to develop specific interventions for persons in substance abuse treatment. This association was tested among 990 drug users in and out of treatment with significant criminal justice histories from two NIDA-sponsored studies. The Diagnostic Interview Schedule and Substance Abuse Module assessed DSM-III-R depression, number of depression criteria met, antisocial personality disorder (ASPD), and substance use disorders. Compared with men, women were twice as likely to report depression (24% vs. 12%), whereas men were nearly twice as likely to report ASPD (42% vs. 24%). High rates of SI were found, with women more likely than men to report thoughts of death (50% vs. 31%), wanting to die (39% vs. 21%), thoughts of committing suicide (47% vs. 33%), or attempting suicide (33% vs. 11%); 63% of women and 47% of men reported at least one of these suicidal thoughts or behaviors. Male and female ideators were more likely than nonideators to report depressed mood and to meet criteria for depression, ASPD, and alcohol use disorders. Male ideators were more likely than male nonideators to meet criteria for cocaine use disorders. Using logistic regression, SI among men was predicted by alcohol use disorder (OR - 1.60), ASPD (OR - 1.59), and number of depression criteria (OR - 9.38 for five criteria). Among women, SI was predicted by older age, marital status, alcohol use disorder (OR - 2.77), and number of depression criteria (OR - 9.12 for five criteria). These original findings point out the need to discuss suicidal thoughts among depressed drug users for early treatment and prevention. Cottler, L., Campbell, W., Krishna, V., Cunningham-Williams, R. and Abdallah, A. Predictors of High Rates of Suicidal Ideation among Drug Users. *J Nerv Ment Dis*, 193, pp. 431–437, 2005.

### Barriers to Health and Social Services for Street-Based Sex Workers

Homelessness, poverty, drug abuse and violent victimization faced by street-based women sex workers create needs for a variety of health and social services, yet simultaneously serve as barriers to accessing these very services. Researchers utilized interview (n = 586) and focus group (n = 25) data to examine the service needs and associated barriers to access among women sex workers in Miami, Florida. Women most often reported acute service needs for shelter, fresh water, transportation, crisis intervention, and drug detoxification, as well as long-term needs for mental and physical health care, drug treatment, and legal and employment services. Barriers included both structural (e.g., program target population, travel costs, office hours, and social stigma) and individual (e.g., drug use, mental stability, and fear) factors. Bridging these gaps is tremendously important from a public health perspective given the disease burden among this population. The findings support additional efforts to improve service staff training and outreach and to reduce marginalization and stigma in this population through peer education, empowerment, and accessing care and treatment. Kurtz, S., Surratt, H., Kiley, M. and Inciardi, J. Barriers to Health and Social Services for Street-Based Sex Workers. *J Health Care for the Poor and Underserved*, 16, pp. 345-361, 2005.

### The Social Structural Production of HIV Risk among IDUs

In this paper, researchers discuss the increasing appreciation for and need to understand how social and structural factors shape HIV risk. Drawing on a review of recently published literature, they describe the social structural production of HIV risk associated with injecting drug use. They use an inclusive definition of the HIV 'risk environment' as the space, whether social or physical, in which a variety of factors

exogenous to the individual interact to increase vulnerability to HIV. Factors identified as critical in the social structural production of HIV risk associated with drug injecting include cross-border trade and transport links; population movement and mixing; urban or neighborhood deprivation and disadvantage; specific injecting environments (including shooting galleries and prisons); the role of peer groups and social networks; the relevance of 'social capital' at the level of networks, communities and neighborhoods; the role of macro-social change and political or economic transition; political, social and economic inequities in relation to ethnicity, gender and sexuality; the role of social stigma and discrimination in reproducing inequity and vulnerability; the role of policies, laws and policing; and the role of complex emergencies such as armed conflict and natural disasters. The researchers argue that the HIV risk environment is a product of interplay in which social and structural factors intermingle but where political-economic factors may play a predominant role; moreover, 'structural HIV prevention' implies community actions and structural changes within a broad framework concerned to alleviate inequity in health, welfare and human rights. Rhodes, T., Singer, M., Bourgois, P., Friedman, S. and Strathdee, S. The Social Structural Production of HIV Risk among IDUs. *Social Science and Medicine*, 61, pp. 1026-1044, 2005.

#### Herpes Simplex Virus 2 and Syphilis among Young Drug Users in Baltimore, Maryland

To examine the sex specific seroprevalence and correlates of herpes simplex virus 2 (HSV-2) and syphilis among a cohort of young drug users, researchers recruited drug users aged 15–30 years old who used heroin, cocaine, or crack between October 1999 and August 2002. Baseline interviews gathered information on socio-demographics, drug use and sexual behaviors. Serum was tested at baseline for HSV-2 and syphilis seroreactivity. For each sexually transmitted infection (STI), infected and non-infected participants were stratified by sex and compared using  $\chi^2$ , Mann-Whitney tests, and logistic regression. The study found that, of the 543 participants recruited, 42.4% were female and 39.3% were African-American. The seroprevalence of STIs among females and males, respectively, were HSV-2: 58.7% and 22.0%; syphilis: 4.3% and 0.3%. In multivariate models, older age, African-American race, having over 30 lifetime sex partners, current HIV infection and previous incarceration were independently associated with HSV-2 infection among males. For females, older age, African-American race, sex trade, and daily heroin use were independently associated with HSV-2. For females, only a self reported previous syphilis diagnosis was associated with current syphilis seroreactivity in multivariate analyses. Examination of this cohort revealed a particularly high seroprevalence of HSV-2 and syphilis, especially among female drug users. Few infected participants had been previously diagnosed with these infections. Plitt, S., Sherman, S., Strathdee, S. and Taha, T. Herpes Simplex Virus 2 and Syphilis Among Young Drug Users in Baltimore, Maryland. *Sex Transm Inf.*, 81, pp. 248-253, 2005.

#### The Relationship between College Fraternity/Sorority Membership and Substance Use

Nationally representative probability samples of US high school seniors (modal age 18 years) were followed longitudinally across two follow-up waves during college (modal ages 19/20 and 21/22). The longitudinal sample consisted of 10 cohorts (senior years of 1988–97) made up of 5883 full-time undergraduate students, of whom 58% were women and 17% were active members of fraternities or sororities. Analysis of the longitudinal data revealed that active members of fraternities and sororities had higher levels of heavy episodic drinking, annual marijuana use and current cigarette smoking than non-members at all three waves. Although members of fraternities reported higher levels than non-members of annual illicit drug use other than marijuana, no such differences existed between sorority members and non-members. Heavy episodic drinking and annual marijuana use increased significantly with age among members of fraternities or sororities relative to non-members, but there were no such differential changes for current cigarette use or annual illicit drug use other than marijuana. These findings indicate that the higher rates of substance use among US college students who join fraternities and sororities predate their college attendance, and that membership in a fraternity or sorority is associated with considerably greater than average increases in heavy episodic drinking and annual marijuana use during college. These findings have important implications for prevention and intervention efforts aimed toward college students,

especially members of fraternities and sororities. McCabe, S.E., Schulenberg, J.E., Johnston, L.D., O'Malley, P.M., Backman, J.G. and Kloska, D.D. Selection and Socialization Effects of Fraternities and Sororities on US College Student Substance Use: A Multi-cohort National Longitudinal Study, *Addiction*, 100, pp. 512-524, 2005.

## **PREVENTION RESEARCH**

### Parents' Beliefs Synergistically Affect Children's Drinking

This research examined whether mother's and father's beliefs about their children's alcohol use had cumulative self-fulfilling effects on their children's future drinking behavior. Researchers analyzed longitudinal data from 115 seventh-grade children and their mothers and fathers. Questionnaire data were collected at two points in time 12 months apart. At the first time point, researchers measured parents' beliefs about their child's alcohol use, the child's alcohol use and intentions to use and other risk and protective factors for substance use. At the second time point, child's recent alcohol use was measured. Findings suggest that the inaccurate portion (e.g., overestimation or underestimation) of parent's beliefs about their children's behavior at time 1 uniquely accounted for variance in a model predicting alcohol use at time 2. Mothers' beliefs that overestimated children's alcohol use more strongly predicted time 2 alcohol use when father's beliefs also overestimated time 2 use, a process the authors call synergistic accumulation. However, synergistic accumulation did not occur when parents' beliefs underestimated children's alcohol use. Madon, S., Gyll, M., Spoth, R. and Willard, J. Self-Fulfilling Prophecies: The Synergistic Accumulative Effect of Parents' Beliefs on Children's Drinking Behavior. *Psychological Science*, 15(12), pp. 837-845, 2004.

### Higher Impulsivity Related to Fewer Negative Expectancies and More Marijuana Use

The current study evaluated a model of marijuana use by examining the relationship between a distal risk factor (impulsivity) and a proximal risk factor (marijuana use expectancies) and marijuana use. An impulsive personality style has been identified as both a risk factor and a predictor of substance use and abuse. Marijuana expectancies, or evaluations of marijuana's expected effects (positive, negative, or neutral) have emerged as a strong predictor of marijuana use. Estimated probabilities and subjective evaluations of personally expected marijuana effects, along with impulsivity and frequency of marijuana use, were assessed in a sample of 337 college undergraduates (248 females, 89 males, average age of 20.84 years). Tests of mediation indicated that negative expectancies were a significant mediator for both males and females. That is, participants who were higher on impulsivity had fewer negative expectancies and in turn used more marijuana. Vangsness, L., Bry, B.H. and LaBouvie, E.W. Impulsivity, Negative Expectancies, and Marijuana Use: A Test of the Acquired Preparedness Model. *Addictive Behaviors*, 30, pp. 1071-1076, 2005.

## **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

### Anxiety Disorders among Patients with Co-occurring Bipolar and Substance Use Disorders

Dr. Kolodziej and colleagues at Harvard and Boston University examined the prevalence and nature of anxiety disorder among treatment seeking patients diagnosed with current bipolar and substance use disorders, and investigated the association between anxiety disorders and substance use. Among 90 participants diagnosed with bipolar disorder I (n=75, 78%) or II (n=15, 22%), 43 (48%) had a lifetime anxiety disorder, with posttraumatic stress disorder (PTSD) occurring most frequently (n=21, 23%). They found that those with PTSD, but not with the other anxiety disorders assessed, began using drugs at an earlier age and had more lifetime substance use disorders, particularly cocaine and amphetamine use disorders, than those without PTSD. Most participants with PTSD were women, sexual abuse was the most frequently reported index trauma, and the mean age of the earliest index trauma occurred before the mean

age of initiation of drug use. These findings highlight the heterogeneity of dually diagnosed patients, and the importance of further investigating the ramifications of a trauma history among those who are diagnosed with bipolar and substance use disorders. Kolodziej, M.E., Griffin, M.L., Najavits, L.M., Otto, M.W., Greenfield, S.F. and Weiss, R.D. Anxiety Disorders among Patients with Co-Occurring Bipolar and Substance Use Disorders. *Drug and Alcohol Dependence*, 80, pp. 251-257, 2005.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

### Effect of Nicotine Replacement Therapy on Post-cessation Weight Gain and Nutrient Intake: A Randomized Controlled Trial of Postmenopausal Female Smokers

This study of 94 postmenopausal female smokers evaluated the effect of nicotine replacement therapy (NRT) and hormone therapy (HT) on change in weight, energy intake, and physical activity during 2 weeks of smoking abstinence. Women, stratified by current use of HT, were randomized to nicotine or placebo patch. After 2 weeks of abstinence, women on nicotine patch had significantly larger increases in total caloric and fat intake than women on placebo patch and a trend toward larger increases in carbohydrates (total and sweet). Conversely, the nicotine group had less weight gain, 0.47 kg, than the placebo group, 1.02 kg ( $F=10.31, p=0.002$ ). No effects were observed for hormone therapy. It appears that in short-term smoking abstinence, postmenopausal women on NRT gain less weight than do women on placebo, in spite of consuming more calories. This may be beneficial in the critical first 1-2 weeks of tobacco cessation, especially in light of postmenopausal weight gain. Allen, S.S., Hatsukami, D., Brintnell, D.M. and Bade, T. Effect of Nicotine Replacement Therapy on Post-cessation Weight Gain and Nutrient Intake: A Randomized Controlled Trial of Postmenopausal Female Smokers. *Addict. Behav.*, 30, pp. 1273-1280, 2005.

### Spontaneous Smoking Cessation during Pregnancy Among Ethnic Minority Women: A Preliminary Investigation

This study examined the postpartum relapse rates and characteristics of pregnant women who stopped smoking without professional intervention. Baseline characteristics of women who spontaneously quit were compared to women who continued to smoke. Women who spontaneously quit were also randomized to a psychotherapy relapse prevention treatment, or to usual care. The sample was ethnically diverse, containing 141 low-income women who were predominantly Hispanic, 23% ( $n=33$ ) of whom spontaneously quit smoking. The variables that significantly differentiated between "spontaneous quitters" and ongoing smokers were entered into a regression analysis, which revealed that higher self-confidence, smoking fewer cigarettes per day, and younger age accounted for 25% of the variance in spontaneous cessation. Adding the psychotherapy intervention conferred no additional protection against relapse in this subgroup of spontaneous quitters. The six-month abstinence rate of 36% is similar to that found in Caucasian and higher-income populations. These results extend research with pregnant smokers to a new population and may have implications for healthcare providers and policy makers. Morasco, B.J., Dornelas, E.A., Fischer, E.H., Oncken, C. and Lando, H.A. Spontaneous Smoking Cessation during Pregnancy among Ethnic Minority Women: A Preliminary Investigation. *Addict. Behav.*, 31, pp. 203-210.

## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE**

### Disorders of Glucose Metabolism among HIV-infected Women

Abnormal glucose metabolism in HIV-infected patients has largely been attributed to the use of protease inhibitors. However, most studies of glucose metabolism in HIV-infected patients have focused on men or have lacked appropriate control groups. Authors assessed the factors associated with previously diagnosed diabetes among 620 middle-aged women with or at risk for HIV infection. For a subset of 221 women without previously diagnosed diabetes, we performed an oral glucose tolerance test (OGTT) to measure



glucose and insulin levels, and we assessed factors associated with abnormal glucose tolerance, insulin resistance, and insulin secretion. Thirteen percent of the women in the present study had previously diagnosed diabetes. Among women without previously diagnosed diabetes who underwent an OGTT, 6% had previously undiagnosed diabetes, and 12% had impaired glucose tolerance (IGT). According to multivariate analysis, factors that were associated with previously diagnosed diabetes included current methadone treatment, body mass index of  $\geq 25$ , family history of diabetes, and physical inactivity. Factors that were independently associated with an abnormal result of an OGTT (i.e., a result consistent with IGT or diabetes) included age  $\geq 50$  years, family history of diabetes, physical inactivity, and a high number of pack-years of smoking. Factors independently associated with insulin resistance included waist circumference, Hispanic ethnicity, physical inactivity, and, among HIV-infected women, use of HAART that did not include protease inhibitors. Factors associated with lower levels of insulin secretion included current opiate use (i.e., methadone or heroin) and older age. The authors conclude that abnormal glucose metabolism is highly prevalent among middle-aged women with or at risk for HIV infection, particularly women who use opiates. Screening for diabetes in the HIV primary care setting should occur for women who have classic risk factors for diabetes, rather than solely for women who are taking PIs. Interventions that target modifiable risk factors, including obesity and physical inactivity, are also warranted. Howard, A.A., Floris-Moore, M., Arnsten, J.H., Santoro, N., Fleischer, N., Lo, Y. and Schoenbaum, E.E. Disorders of Glucose Metabolism Among HIV-infected Women. *Clin Infect Dis.*, 40(10), pp. 1492-1499, 2005.

#### Depressive Symptoms, Quality of Life, and Neuropsychological Performance in HIV/AIDS: The Impact of Gender and Injection Drug Use

Limited attention has been paid to the potential impact of gender and injection drug use (IDU) on mood, quality of life, and neuropsychological performance in human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). Several studies that describe the natural history of HIV/AIDS in terms of mental health and neuropsychological ability have focused solely on men or have excluded injection drug users. Women and injection drug users are two groups for whom the incidence of HIV infection is increasing. Additionally, the National Academy of Sciences recently recommended that studies concerned with health-related research include males and females, and that researchers analyze their data for gender differences. The goals of the current study were to investigate possible relationships between HIV and IDU status and depressive symptoms, quality of life, and neuropsychological performance in women and men matched for age, race, and education. Overall, women reported more depressive symptoms than men, and this gender difference was most evident in women who were both infected with HIV and who were also injection drug users. Women and HIV-infected individuals reported the poorest quality of life scores. Women outperformed men on a measure of verbal memory and HIV(-) participants outperformed HIV(+) participants on a measure of perceptual speed. Finally, gender and HIV status interacted such that uninfected women performed the best, and infected men performed the worst, on a test of verbal memory. A better understanding of how men and women with different drug use profiles respond to HIV/AIDS may substantially improve survival, as well as aspects of daily functioning, of affected individuals. Thus, further study and development of treatment protocols targeted at including women and IDU are needed. Wisniewski, A.B., Apel, S., Selnes, O.A., Nath, A., McArthur, J.C., Dobs, A.S. Depressive Symptoms, Quality of Life, and Neuropsychological Performance in HIV/AIDS: The Impact of Gender and Injection Drug Use. *J Neurovirol.*, 11(2), pp. 138-143, 2005.

#### Gender Effects Following Repeated Administration of Cocaine and Alcohol in Humans

Use of cocaine, alcohol, and the two drugs simultaneously is common and the risk of morbidity and mortality associated with these drugs is widely reported. This double-blind, placebo-controlled, randomized study examined gender differences in response to administration of these drugs alone and in combination. Current users of cocaine and alcohol ( $n = 17$ ) who met diagnostic criteria (DSM-IV) for cocaine dependence and alcohol abuse or dependence (not physiologically dependent on alcohol) and who were not seeking treatment for substance use disorders gave voluntary, written, informed consent to

participate in three drug administration sessions: 1) four doses of intranasal cocaine (1 mg/kg every 30 min) with oral alcohol (1 g/kg following the initial cocaine dose and a second drink at +60 min (120 mg/kg) calculated to maintain a plasma alcohol concentration of approximately 100 mg/dL; 2) four doses of cocaine and alcohol placebo; 3) cocaine placebo and alcohol. Pharmacokinetics were obtained by serial blood sampling, physiological measurements (heart rate and blood pressure) were obtained with automated equipment, and subjective effects were assessed using visual analog scales over 480 min. Responses to cocaine, alcohol, and cocaine-alcohol were equivalent by gender for most measurements. Women had higher heart rates following alcohol administration ( $p = .02$ ). Women consistently reported higher ratings for "Feel Good", a measure of overall mental/physical well-being, for all study conditions, reaching statistical significance for cocaine ( $p = .05$ ) and approaching significance for alcohol administration ( $p = .1$ ). Women showed equivalent responses to drug administration with the exception of perception of well-being, which was significantly increased for women. These findings may have implications for differential risk for acute and chronic toxicity in women. McCance-Katz, E.F., Hart, C.L., Boyarsky, B., Kosten, T. and Jatlow, P. Gender Effects Following Repeated Administration of Cocaine and Alcohol in Humans. *Subst Use Misuse*, 40(4), pp. 511-528, 2005.

## **SERVICES RESEARCH**

### Chemically Dependent Youth Benefit from Psychiatric Services

Many adolescents with alcohol and drug problems have mental health co-morbidities. The literature suggests that patients entering chemical dependency (CD) treatment with co-occurring problems have less successful outcomes, including treatment dropout and relapse. Researchers examine the impact of psychiatric services on treatment initiation, retention, and alcohol and drug abstinence outcomes for adolescents in CD treatment. Participants were 419 adolescents aged 12-18 years who were seeking treatment at four CD programs of a nonprofit, managed care, group model health system. A parent or guardian for each adolescent also participated. Participants were surveyed at intake and at 6 months and the researchers were exposed to clinical and administrative data pertaining to their diagnoses for CD and psychiatric utilization. Six-month response rates were 91% for adolescents and 93% for parents. Fifty-five percent of the patients with treatment intakes had at least one psychiatric diagnosis in addition to a substance use disorder. Compared with matched controls, patients with CD intakes had higher rates of depression, anxiety, eating disorders, attention deficit hyperactivity disorder, conduct disorder, and conduct disorder including oppositional defiant disorder. Thirty-one percent of the full sample had psychiatric visits in the 6 months after intake; among those with a psychiatric diagnosis, 54% had a psychiatric visit. Girls and those with higher Youth Self-Report internalizing scores were more likely to have a psychiatric visit (OR = 2.27,  $p < 0.001$  and OR = 1.05,  $p < 0.0001$ , respectively). Adolescents receiving psychiatric services were more likely to be abstinent from both alcohol and drugs than those not receiving these services (OR = 1.57, 95% CI = 0.98-2.5) and more likely to be alcohol abstinent (OR = 1.68, 95% CI = 1.00-2.85). Those adolescents at co-located clinics had higher odds of abstinence from both alcohol and drugs (OR = 1.57, 95% CI = 1.03-2.39) and drugs (OR = 1.84, 95% CI = 1.87-2.85) and of returning after intake to initiate CD treatment (OR = 2.28, 95% CI = 1.44-3.61,  $p < 0.001$ ) than others. The results demonstrate the need for psychiatric treatment of adolescents in CD treatment and highlight the importance of their receiving such services. Sterling, S. and Weisner, C. Chemical Dependency and Psychiatric Services for Adolescents in Private Managed Care: Implications for Outcomes. *Alcoholism: Clinical and Experimental Research*, 25(5), pp. 801-809, 2005.

### Juvenile Offenders at Increased Risk for HIV Infection

The purpose of this study was to examine the prevalence, multiple correlates, and gender differences in chlamydia and gonorrhea infections among adolescents incarcerated in a youth detention center in the southern region of the United States. STD screening was conducted on 1816 youth, ages 10-18, as they entered the facility. Rates of undiagnosed chlamydia were 24.7% for incarcerated girls and 8.1% for boys.

Gonorrhea was detected in 7.3% of the girls and 1.5% of the boys. Only youth 13 years or older were asked to complete a survey: 763 assented to participate, and 690 gave permission to link their STD test results to their survey responses. The majority of the juveniles who participated in the study were African American (89%) and male (67%). Predictors of STD positivity differed for boys and girls. Demographic characteristics (gender, race, and age) account for 52% of the total variance in STD infections; youths' behavior (alcohol use, sex under the influence of alcohol, history of STD and sexual risk reduction strategy) accounts for about one-third of the total variance, psychological (sexual abuse, alcohol and drug expectancies) and family variables (family structure/living arrangements, supervision and monitoring, parental involvement, family communication) account for 8.6% (boys) and 7.2% (girls) of the total variance. An approach that considers psychological and social influences on adolescent sexual behavior is useful for identifying potential risk and protective factors of adolescent STD/HIV risk that are amenable to intervention. Robertson, A.A., Baird-Thomas, C., St. Lawrence, J.S. and Pack, R. Predictors of Infection with Chlamydia or Gonorrhea in Incarcerated Adolescents. *Sexually Transmitted Diseases*, 32(2), pp. 115-122, 2005.

### Effectiveness of Highly Regarded Adolescent Substance Abuse Treatment Programs

This study conducted the first systematic evaluation of the quality of highly regarded adolescent substance abuse treatment programs in the United States. An advisory panel of 22 experts defined 9 key elements of effective treatment for adolescent substance abuse based on a review of the literature. In-depth telephone and written surveys were conducted with 144 highly regarded adolescent substance abuse treatment programs identified by panel members and by public and private agencies. There was a 100% response rate to the initial interviews, and a 65% response rate to the follow-up surveys. The open-ended survey responses were coded by defining 5 components deemed to be crucial in addressing each of the 9 key elements, and quality scores were calculated overall and for each of the 9 key elements. Out of a possible total score of 45, the mean score was 23.8 and the median was 23. Top-quartile programs were not more likely to be accredited. The majority of programs scored at least 4 of a possible 5 on only 1 of the 9 key elements (qualified staff). The elements with the poorest-quality performance were assessment and treatment matching, engaging and retaining teens in treatment, gender and cultural competence, and treatment outcomes. Most of the highly regarded programs surveyed are not adequately addressing the key elements of effective adolescent substance abuse treatment. Expanded use of standardized assessment instruments, improved ability to engage and retain youths, greater attention to gender and cultural competence, and greater investment in scientific evaluation of treatment outcomes are among the most critical needs. Expanding awareness of effective elements in treating adolescents will lead the way to program improvement. Brannigan, R., Schackman, B.R., Falco, M. and Millman, R.B. The Quality of Highly Regarded Adolescent Substance Abuse Treatment Programs: Results of an In-depth National Survey. *Archives of Pediatric Adolescence Medicine*, 158, pp. 904-909, 2004.

### Quality of Social Support Affects Employment Outcomes

This study examined social support and its association with employment, income, and drug use in a sample of 534 low-income women. Social support was operationalized as two distinct categories. Functional support was defined as the perceived quality of one's interactions with others, considered as either actual or perceived assistance from others. Structural support was defined as the number of individuals within a network as well as the social ties or links within the network. Such networks as social, employment, drug, and emergency are characterized by size and density. Over the two-year study period, significant increases attributable to the quality of these relationships were observed in hours-worked, income from work, income from other sources, and total income. There was also a significant decrease in welfare income. Results suggest that the perceived quality of support received is an important factor in achieving positive employment outcomes. Simply using a quantitative measure of social support was not sufficient in this analysis. For welfare populations a beneficial change in the quality of functional support could lead to

improvements in work hours. Brown, V.L. and Riley, M.A. Social Support, Drug Use, and Employment among Low-Income Women. *American Journal of Drug and Alcohol Abuse*, 31, pp. 203-223, 2005.

## **INTRAMURAL RESEARCH**

### **TREATMENT SECTION**

#### **CLINICAL PHARMACOLOGY AND THERAPEUTICS RESEARCH BRANCH**

##### Menstrual Cycle Length during Methadone Maintenance

While heroin's menstrual disruption has been demonstrated, there are few published data concerning methadone maintenance (MM) and menstrual function. This study was conducted to evaluate whether cycles were more regular during MM. Start/end dates of each menses were collected from 191 drug-using women from two clinical trials, lasting 25-29 weeks, while on 70-100 mg of methadone. Participants were classified as regular, irregular, transient amenorrhea, persistent amenorrhea, or cycle restarters. Repeated-measures regression modeling was used to determine correlates of cycle length, probability of long cycles (>40 days), and short cycles (<20 days). Bleeding episodes (days from "start" to "stop") were defined as one or more bleeding days, bound by at least two non-bleeding days. Correlates of cycle length, body mass index, drug use, methadone dose, and race were calculated. Women had a high prevalence of cycle length irregularity; 133 participants: regular 37 (27.8%); irregular 62 (46.7%); transient amenorrhea 7 (5.3%); persistent amenorrhea 11 (8.3%); cycle restarters 16 (12%). Each additional week on MM was associated with decreased risk of long (OR=0.96, p=0.001) and short (OR=0.92, p=0.001) cycles. Of 27 women with secondary amenorrhea pre-study, 16 (59%) restarted menses. Positivity for opioids or cocaine was not significantly associated with short or long cycles. Cycle length begins to normalize during MM. Menses resumption may occur. MM, despite interfering with menstrual function in an absolute sense, may interfere less than illicit heroin abuse. Schmittner, J., Schroeder, J.R., Epstein, D.H., and Preston, K.L. *Addiction*, 100(6), pp. 829-836, 2005.

### **CLINICAL PHARMACOLOGY SECTION**

#### **CLINICAL PHARMACOLOGY AND THERAPEUTICS RESEARCH BRANCH**

##### Calorie Restriction Increases Cigarette Use In Adult Smokers

Cigarette smokers weigh less than nonsmokers, and smokers often gain weight when they quit. This is a major barrier to smoking cessation, especially among women. However, strict dieting is not recommended during smoking cessation out of concern that it might promote relapse. One reason is that calorie restriction increases self-administration of drugs of abuse in animals. This relationship has never been experimentally demonstrated in humans. This study evaluated whether calorie restriction increases cigarette smoking in humans. Seventeen (9M, 8F) healthy, normal-weight smokers not attempting to quit were cycled in partially counterbalanced order, double-blind, through four diets: normal calorie (2000-2800 kcal/day), low calorie (700 kcal/day deficit), low carbohydrate (CHO)-normal calorie, and low CHO-low calorie, for six days per diet on an inpatient research ward. Smoking was assessed by cigarette counts, breath carbon monoxide (CO) levels, and cigarette craving. Compared with the normal calorie diet, while on the low calorie diet, subjects smoked 8% more cigarettes (p<0.02) and had 11% higher breath CO levels (p<0.01). The low CHO- normal calorie diet showed no significant effect on either variable, but there was a 15% increase in breath CO levels (p<0.05) on the low CHO-low calorie diet. There were no changes in self-reported cigarette craving or mood. Consistent with animal studies, moderate calorie restriction was associated with a small but statistically significant increase in cigarette smoking, with no independent effect of carbohydrate deprivation. These findings suggest that dieting may increase smoking behavior, and could impede smoking cessation attempts. Cheskin, L.J., Hess, J.M., Henningfield, J., and Gorelick, D.A. *Psychopharmacology* 179, pp. 430-436, 2005.

# DIRECTOR'S REPORT TO COUNCIL

February 2006

## BASIC NEUROSCIENCES RESEARCH

### Prenatal Cocaine Exposure and Brain Development

It has been demonstrated that exposure to cocaine increases cell death (i.e., apoptosis) in the fetal brain. To examine the molecular mechanisms of this effect, Dr. Michael Lidow and his group conducted studies in a mouse model of prenatal cocaine exposure. These studies demonstrate that maternal cocaine use is capable of interfering with a range of apoptosis-related genes in the cells of the fetal cerebral wall making these brain cells more sensitive to death-inducing signals. However, this increase in potential for apoptosis is likely to result in actual cell death only when and where the affected cells are subjected to a death-promoting local environment, with the distribution and harshness of such tissue environment depending not only on the cocaine exposure itself but also on fetal developmental stage, maternal health, nutritional status, etc. Consequently, the severity and scope of structural and functional impacts of the pro-apoptotic gene alterations in the offspring of cocaine-abusing mothers should be prone to significant variability due to idiosyncratic use of cocaine and a great diversity in the quality of prenatal care. Furthermore, apoptosis represents just one of several potentially negative influences of cocaine exposure on fetal corticogenesis, with proliferation, migration, and differentiation of cortical cells also being affected by this drug.

Novikova, S.I., He, F., Bai, J., Badan, I., Lidow, I.A. and Lidow, M.S. Cocaine-induced Changes in the Expression of Apoptosis-related Genes in the Fetal Mouse Cerebral Wall. *Neurotoxicology and Teratology*, 27, pp. 3-14, 2005.

### Melanocortin-1 Receptor Gene Variants Affect Pain and Mu-Opioid Analgesia in Mice and Humans

Melanocortin-1 receptor (MCR1) was recently found to mediate  $\kappa$ -opioid receptor analgesia, especially in female mice and human volunteers. This was an unexpected finding because MCR1 is thought to be primarily involved in skin/hair pigmentation and immunomodulation. Mogil and colleagues tested MCR1 mutant mice and humans of various hair color for sensitivity to pain and  $\mu$ -opioid analgesia. Mice were tested for their basal sensitivity on six different assays of acute and tonic nociception. Human volunteers were also tested for tolerance to acute pain. For both mice and humans, morphine and its derivative, morphine-6-glucuronide (M6G), were assessed for their effectiveness in reducing pain. In mice, mutants for MCR1 displayed reduced nociceptive responses to morphine and M6G and this effect was significant for both sexes. Studies in human volunteers with two or more variant alleles of the MCR1 gene in amino acids known to abolish MCR1 functionality, compared to volunteers with no or one variant, showed that baseline tolerance differed significantly between genotypes, with greater tolerance for pain in volunteers with the MCR1 variant. In addition, analgesic responses after M6G were greater in MCR1 variant subjects compared to controls. In contrast to the  $\kappa$ -opioid receptor analgesia, the effect on the  $\mu$ -opioid receptor is not sex-dependent. This study eloquently demonstrates the power of direct mouse to human translation in genetic studies. Mogil and colleagues show a significant link between MCR1 gene variants, pain tolerance, and potential efficacy of analgesics acting on the  $\mu$ -opioid receptor. Larger human studies are needed to validate these findings in this important area of pain research. [Mogil, J.S., Ritchie, J., Smith S.B., Strasburg, K., Kaplan, L., Wallace, M.R., Romberg, R.R., Bijl, H., Sarton, E.Y., Fillingim, R.B. and Dahan, A.](#) Melanocortin-1 Receptor Gene Variants Affect Pain and Mu-opioid Analgesia in Mice and Humans. *Journal of Medical Genetics*, 42, pp. 583-587, 2005.

## **BASIC BEHAVIORAL RESEARCH**

### Sex and Estrous Cycle Phase Influence Conditioned Cue-Induced Reinstatement of Cocaine-Seeking Behavior in Rats

Studies comparing cocaine self-administration in male and female rats have found that females exhibit greater sensitivity in a variety of outcomes; for example, they acquire self-administration more quickly, a greater percentage of females acquire self-administration, females exhibit greater disruption in the diurnal control over cocaine intake, and they exhibit greater motivation for cocaine. Additionally, females exhibit greater cocaine-primed reinstatement of cocaine-seeking behavior. Dr. Ron See and colleagues at the Medical University of South Carolina now report sex differences in reinstatement of cocaine seeking behavior using a conditioned-cue procedure. Separate groups of rats were trained to bar press for varying doses of i.v. cocaine (0.25, 0.4, 0.5, 0.6, and 1.0 mg/kg per infusion). Each infusion was paired with a compound conditioned stimulus (CS) consisting of a light and tone. Following the establishment of stable cocaine self-administration, cocaine responding was extinguished and during reinstatement, the ability of the CS alone (without cocaine) was assessed. During the extinction period, females exhibited more extinction responses (i.e., greater resistance to extinction) than males, perhaps reflecting greater cocaine motivation. During the reinstatement period in which bar-presses produced the CS, but not cocaine, both males and females in all the training dose groups exhibited increased bar-pressing relative to the extinction responding. At intermediate training doses (0.4, 0.5, 0.6 mg/kg) there were no sex differences in reinstatement. Females trained at the lowest dose (0.25 mg/kg) and the highest dose (1.0mg/kg), however, exhibited less bar pressing for the CS than did males. Analysis of reinstatement by females tested during the estrous phase (*versus* non-estrous) indicated that those trained on the 0.25 mg/kg dose did not show reinstatement, although estrous status did not affect reinstatement at the other training doses. In summary, sex differences in reinstatement occurred at the highest and lowest training dose wherein reinstatement was greater in males than females and at the lowest training dose reinstatement was not observed in estrous females. Given that prior research has shown greater cocaine-primed reinstatement in females than males, the authors suggest that there are sex differences in the variables that control reinstatement. Specifically, females may be more vulnerable to pharmacologically induced reinstatement, whereas males may be more vulnerable to conditioned cue-induced reinstatement. Further research on these sex differences, including hormonal control, and their implications for relapse in humans is warranted. Fuchs, R.A., Evans, A., Mehta, R.H., Case, J. M. and See, R.E. Influence of Sex and Estrous Cyclicity on Conditioned Cue-induced Reinstatement of Cocaine-seeking Behavior in Rats. *Psychopharmacology*, 179, pp. 662-672, 2005.

### Exogenous Progesterone Attenuates the Subjective Effects of Smoked Cocaine in Women, But Not In Men

Several preclinical studies have shown greater sensitivity to cocaine in females as compared to males. Further, many of these behavioral effects are modulated by the estrous cycle, and are eliminated by ovariectomy and subsequently restored by administration of estradiol, suggesting a role for estradiol in male-female differences in cocaine sensitivity. On the other hand, there is suggestive evidence from both preclinical and clinical studies that progesterone may also play a role in cocaine's subjective effects and may contribute to male-female differences in cocaine sensitivity. Drs. Suzette Evans and Richard Foltin of the New York State Psychiatric Institute and Columbia University pursued this possibility by comparing the subjective effects of exogenously administered progesterone in males and in females. In inpatient sessions, each female was studied in the mid-luteal phase (when both progesterone and estradiol were elevated), in the follicular phase (when progesterone was negligible and estradiol was elevated), and in a follicular phase in which progesterone was administered. A dose of 150 mg oral micronized progesterone was given so that the progesterone levels approximated those of the mid-luteal phase. Each male was studied under progesterone administration and under placebo. For each subject a full cocaine dose-response curve (0, 6, 12, and 25 mg cocaine) was obtained in each session. Replicating prior studies, cocaine's subjective effects were greater in the follicular phase than the luteal. Progesterone administration

during the follicular phase resulted in an attenuation of the positive subjective effects, but did not alter the subjective effects in males. Drs. Evans and Foltin are now conducting a study to determine whether the administration of progesterone will attenuate cocaine self-administration. Evans, S.M. and Foltin, R.W. Exogenous Progesterone Attenuates the Subjective Effects of Smoked Cocaine in Women, But Not in Men. *Neuropsychopharmacology*, 31(3), pp. 659-674, 2006.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Maternal Cocaine Use during Pregnancy and Physiological Regulation in 4- to 8-Week-Old Infants

In their report on associations between maternal cocaine use during pregnancy and physiological regulation in infants at 4 to 8 weeks of age, Drs. Schuetze and Eiden provided data for 141 mother-infant dyads (77 cocaine-exposed and 64 nonexposed) recruited at birth. Physiological measures of regulation included heart rate (HR) and respiratory sinus arrhythmia (RSA), assessed during a 15-minute period of sleep. Results indicated a dose-dependent relationship between prenatal exposure to cocaine and RSA. The analyses found no evidence that fetal growth or other prenatal exposure to substances mediated this association or that fetal growth or maternal age moderated this association. Analyses did indicate that birth weight (BW), but not birth length (BL), head circumference (HC) or other substance use mediated the association between prenatal exposure to cocaine and HR. In their conclusions, the researchers note that the findings highlight the importance of considering level of exposure when assessing infant outcomes. Schuetze, P. and Eiden, R.D. The Association between Maternal Cocaine Use during Pregnancy and Physiological Regulation in 4- to 8-Week-Old Infants: An Examination of Possible Mediators and Moderators. *Journal of Pediatric Psychology*, 31, pp. 15-26, 2006.

### Prenatal Drug Exposure and Mother-Infant Interaction

Based on data from the Maternal Lifestyle Study, a multi-site investigation of development following prenatal drug exposure, this report provides findings for mother-infant interactions observed at 4 months infant age. Specifically, the face-to-face still-face (FFSF) paradigm was used, a standardized procedure in which infants engage in face-to-face interaction with the caregiver, and also have to deal with a stressful interaction during which the caregiver becomes poker-faced as well as vocally and gesturally unresponsive. The sample involved 236 cocaine-exposed and 459 non-cocaine-exposed infants (49 were opiate-exposed and 646 non-opiate-exposed). No opiate exposure effects were observed. Mothers of cocaine-exposed infants showed more negative engagement than other mothers. The cocaine-exposed dyads also showed higher overall levels of mismatched engagement states than other dyads, including more maternal negative engagement when the infants were in states of neutral engagement. Infants exposed to heavier levels of cocaine showed more passive-withdrawn negative engagement and engaged in more negative affective matching with their mothers than other infants. The study authors conclude that although effect sizes were small, cocaine exposure, especially heavy cocaine exposure, was associated with subtly negative interchanges, which may have a cumulative impact on infants' later development and their relationships with their mothers. Tronick, E.Z., Messinger, D.S., Weinberg, M.K., et al. Cocaine Exposure is Associated with Subtle Compromises of Infants' and Mothers' Social-Emotional Behavior and Dyadic Features of Their Interaction in the Face-to-Face Still-Face Paradigm. *Developmental Psychology*, 41, pp. 711-722, 2005.

### Prenatal Cocaine/Polydrug Use and Maternal-Infant Feeding Interactions during the First Year of Life

In research conducted at Case Western Reserve University, relationships between prenatal cocaine use and quality of maternal-infant interactions were examined. The Nursing Child Assessment Feeding Scale (NCAFS) was used with a sample of 341 mothers (155 with prenatal cocaine use and 186 without prenatal cocaine use) and their infants at 6.5 and 12 months infant age. Analyses included a number of sociodemographic and maternal covariates, including postnatal substance use. Women who used cocaine

during pregnancy were found to be less sensitive to infant cues at 6.5 and 12 months than were non-cocaine-using women. At 6.5 months, heavier prenatal cocaine use was related to less maternal responsiveness to infants. In infants, prenatal cocaine exposure was related to poorer clarity of cues. The investigators found no significant cocaine effects on maternal social-emotional growth fostering, cognitive growth fostering, or infant responsiveness to mother. The study authors note implications of the findings for clinicians and intervention programs. Minnes, S., Singer, L.T., Arendt, R. and Satayathum, S. Effects of Prenatal Cocaine/Polydrug Use on Maternal-Infant Feeding Interactions during the First Year of Life. *Developmental and Behavioral Pediatrics*, 26, pp. 194-200, 2005.

#### Cocaine Use during Pregnancy and Preschool Development at 3 Years of Age

In this University of Florida longitudinal cohort study, 154 pregnant cocaine users were recruited and were matched on race, parity, socioeconomic status, and perinatal risk with 154 noncocaine users. The study protocol involves examining development of the children at multiple ages. This report presents findings for the children at 3 years of age based on two measures, the Bayley Scales of Infant Development, and the Vineland Adaptive Behavior Scales (the latter involving caregiver report). A preschool development variable was created, using the Bayley Mental and Psychomotor Development Indices, and the Communication and Motor Skills subscales of the Vineland. Based on structural equation modeling analyses, the researchers concluded that environmental factors accounted for most of the variance in the preschool development variable, and that prenatal cocaine exposure exerted an indirect effect on preschool development through its effect on birth head circumference. Behnke, M., Eyler, F.D., Warner, T.D., et al. Outcome from a Prospective, Longitudinal Study of Prenatal Cocaine Use: Preschool Development at 3 Years of Age. *Journal of Pediatric Psychology*, 31, pp. 41-49, 2006.

#### Aggression at Age 5 Years Relative to Prenatal Cocaine Exposure, Gender, and Environmental Risk

In a project conducted by researchers from Robert Wood Johnson Medical School, childhood aggression at age 5 years was examined using a multiple risk model that included prenatal cocaine exposure, environmental risk, and gender as predictors. Aggression was assessed in 206 children using multiple methods, including teacher report, parent report, child's response to hypothetical provocations, and child's observed behavior. Also examined was a composite score that reflected high aggression across contexts. Multiple aspects of the environment were assessed and quantified using a cumulative environmental risk score. Analyses indicated that a significant amount of variance in each of the aggression measures and the composite was explained by the predictors. The factors that were independently related differed depending on the outcome. Prenatal cocaine exposure, gender, and environmental risk were all related to the composite aggression score. The investigators concluded that prenatal cocaine exposure, being male, and living in a high-risk environment were all predictive of aggressive behavior at 5 years. They also suggested that it is this group of exposed boys at high environmental risk that is most likely to show continued aggression over time. Bendersky, M., Bennett, D. and Lewis, M. Aggression at Age 5 as a Function of Prenatal Exposure to Cocaine, Gender, and Environmental Risk. *Journal of Pediatric Psychology*, 31, pp. 71-84, 2006.

#### Prenatal Cocaine Exposure and Language Functioning at 6 and 9.5 Years: Moderating Effects of Child Age, Birthweight, and Gender

In this report from an ongoing longitudinal cohort study of development following prenatal drug exposure, results are presented for language functioning at 6 and 9.5 years relative to prenatal cocaine exposure (PCE) and other individual and environmental variables. Analyses involved data for 160 low-income, urban children who completed a standardized language assessment. Based on multivariate longitudinal analyses using generalized estimating equations (GEE), the authors concluded that age, birthweight, and gender moderated the relation between PCE and school-aged children's language. For example, children with PCE had lower receptive language than unexposed children at 6 but not at 9.5 years, lower expressive language if they had lower birthweight, and lower expressive and total language if they were female. Other



risk (e.g., violence exposure) and protective factors (e.g., preschool experience) were related to language outcomes regardless of PCE status. Beeghly, M., Martin, B., Rose-Jacobs, R., et al. Prenatal Cocaine Exposure and Children's Language Functioning at 6 and 9.5 Years: Moderating Effects of Child Age, Birthweight, and Gender. *Journal of Pediatric Psychology*, 31, 98-115, 2006.

### fMRI Reveals Alterations in Spatial Working Memory Networks Across Adolescence

Dr. Susan Tapert and her colleagues at the University of California – San Diego have used functional neuroimaging to characterize the development of spatial working memory in adolescents. Their findings show that the frontal and parietal networks that are involved in working memory change over the course of adolescence, with activation of the left prefrontal and bilateral inferior posterior parietal regions increasing with age and activation of bilateral superior parietal cortex decreasing. Their data also demonstrate gender differences, with males showing greater activation of the anterior cingulate cortex and frontopolar cortex than females. Over the age range tested, there were no differences in performance on the working memory task, suggesting that the alterations in activation patterns with age represent the evolution of the strategies used in the task. Schweinsburg, A.D., Nagel, B.J. and Tapert, S.F. *J. Int. Neuropsych. Soc.* 11, pp. 631-644, 2005.

## **CLINICAL NEUROSCIENCE RESEARCH**

### Frontal Glucose Hypometabolism in Abstinent Methamphetamine Users

Renshaw and colleagues at McLean Hospital and in Korea examined changes in relative regional cerebral glucose metabolism (rCMRglc) and potential gender differences in abstinent methamphetamine (METH) users. Relative rCMRglc was measured by 18F-fluorodeoxyglucose PET. Frontal executive functions, as assessed by Wisconsin card sorting test (WCST), were compared between 35 abstinent METH users and 21 healthy comparison subjects. In addition, male and female METH users and their gender-matched comparison subjects were compared to investigate potential gender differences. METH users had lower rCMRglc levels in the right superior frontal white matter and more perseveration and nonperseveration errors in the WCST, relative to healthy comparison subjects. Relative rCMRglc in the frontal white matter correlated with number of errors in the WCST in METH users. In the subanalysis for gender differences, lower rCMRglc in the frontal white matter and more errors in the WCST were found only in male METH users, not in female METH users, relative to their gender-matched comparison subjects. The current findings suggest that METH use causes persistent hypometabolism in the frontal white matter and impairment in frontal executive function. These findings also suggest that the neurotoxic effect of METH on frontal lobes of the brain might be more prominent in men than in women. Kim, S.J., Lyoo, I.K., Hwang, J., Young, H.S., Lee, H.L., Lee, D.S., Jeong, D. and Renshaw P. *Neuropsychopharmacology*, 30, pp. 1383–1391, 2005.

### Increased White Matter Hyperintensities in Male Methamphetamine Abusers

Renshaw and colleagues at McLean Hospital and in Korea used structural MRI to compare the prevalence, severity, and location of white matter signal hyperintensities (WMH) in methamphetamine (METH) abusers. Thirty-three METH abusers and 32 age- and gender-matched healthy comparison subjects were studied. Axial T-2 weighted images and fluid attenuated inversion recovery axial images were obtained using a 3.0 T MR scanner. The severity of WMH was assessed separately for deep and periventricular WMH. Ordinal logistic regression models were used to assess the odds ratio for WMH. The METH abusers had greater severity of WMH than the healthy comparison subjects (odds ratio: 7.06, 8.46, and 4.56 for all, deep, and periventricular WMH, respectively). Severity of deep WMH correlated with total cumulative dose of METH. Male METH abusers had greater severity of WMH than female METH abusers. Although male METH abusers had greater severity of WMH than male comparison subjects, there was no significant difference in WMH severity between female METH abusers and female comparison subjects.

The current study reports increased WMH in METH abusers, which may be related to METH-induced cerebral perfusion deficits. In addition, female METH abusers had less severe WMH than male METH abusers, possibly due to estrogen's protective effect against ischemic or neurotoxic effects of METH. Bae, C.S, Lyoo, I.K., Sung, Y.H., Yoo, J., Yoon, C.S.J., Kimd, D-J., Hwang, D.W., Kime, S.J. and Renshaw, P. *Drug and Alcohol Dependence*, 81, pp. 83-88, 2006.

## **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

### Differentiating Risk Factors for Drug Use and Drug Abuse/Dependence

This study asked whether there are risk factors that associate specifically with illicit drug use or illicit drug abuse/dependence, and whether the magnitude of the association is the same for use and abuse/dependence, across different categories of drugs. Data from 1943 female adult twins in a population-based Virginia sample were used to assess the association of 26 putative risk factors with use and abuse/dependence of six illicit psychoactive drugs. These factors, which include socio-demographic variables, religiosity, personality measures, childhood factors, and psychiatric diagnoses, were each examined in relation to drug use, abuse/dependence, or both. Several findings are notable: First, factors associate in similar patterns with different drug categories; second, there is a stronger association of significant socio-demographic factors with drug use, while the psychiatric diagnoses are more strongly associated with progression to abuse/dependence. Third, childhood sexual abuse was associated with drug use and with progression to abuse/dependence. This suggests complex, interacting pathways that determine drug habits in individuals. These results are hypothesis generating. Future studies of causal relationships may draw from the outcomes presented in these analyses. Agrawal, A., Gardner, C., Prescott, C. and Kendler, K. *The Differential Impact of Risk Factors on Illicit Drug Involvement in Females. Soc Psychiatry Psychiatr Epidemiol*, 40(6), pp. 454-466, 2005.

### Risk of Becoming Cocaine Dependent 24 Months after First Use

This study explores estimates for the risk of becoming cocaine dependent within 24 months after first use of the drug, and study subgroup variation in this risk. The study estimates are based on the National Household Survey on Drug Abuse conducted during 2000-2001, with a representative sample of US residents aged 12 years and older (n=114 241). A total of 1081 respondents were found to have used cocaine for the first time within 24 months prior to assessment. Between 5 and 6% of these recent-onset users had become cocaine dependent since onset of use. Less [corrected] risk of recent cocaine dependence soon after onset of cocaine use was found for female subjects, young adults aged 21-25 years, and non-Hispanic Black/African-Americans. Use of crack-cocaine and taking cocaine by injection were associated with having become cocaine dependent soon after onset of use. These epidemiologic findings help to quantify the continuing public health burden associated with new onsets of cocaine use in the 21st century. O'Brien, M., and Anthony, J. *Risk of Becoming Cocaine Dependent: Epidemiological Estimates for the United States, 2000-2001. Neuropsychopharmacology*, 30(5), pp. 1006-1018, 2005.

### Receptive Syringe Sharing among IDUs during ESAP

Effective January 1, 2001, New York State enacted the Expanded Syringe Access Demonstration Program (ESAP), which allows syringes to be sold in pharmacies without a prescription or dispensed through doctors, hospitals, and clinics to persons 18 years of age or older and permits the possession of those syringes for the purposes of injecting drugs. In this study, researchers assessed changes in receptive syringe sharing since the inception of the ESAP. Sociodemographic characteristics and syringe use data regarding the last injection episode were combined from 3 projects (n = 1181) recruiting injection drug users in ongoing studies in Harlem and the Bronx in New York City from January 2001 through June 2003. These data were analyzed as serial cross sections by calendar quarter. Findings showed that receptive sharing decreased significantly over time, from 13.4% in the first quarter to 3.6% in the last quarter.

Obtaining the last injection syringe from an ESAP source (mostly pharmacies) increased significantly over time, from 7.5% in the first quarter to 25.0% in the last quarter. In multiple logistic regression analysis, variables that were significantly associated with less receptive sharing were syringe exchange and ESAP syringe source as well as time since ESAP inception. Female gender and white race/ethnicity were significantly associated with greater receptive sharing. These data show that the increase in the use of pharmacies and other ESAP syringe sources in this sample has been accompanied by a decline in receptive sharing. Pouget, E., Deren, S., Fuller, C., Blaney, S., McMahon, J., Kang, S., Tortu, S., Andia, J., Des Jarlais, D. and Vlahov, D. Receptive Syringe Sharing Among Injection Drug Users in Harlem and the Bronx during the New York State Expanded Syringe Access Demonstration Program. *J Acquir Immune Defic Syndr*, 39(4), pp. 471-477, 2005.

### Influences of Early Attachment, Depression, Illicit Drug Use, and Perceived Support on Drug-dependent Mothers' Parenting

In this study, the authors used an attachment framework to examine how drug-dependent mothers' early bonding experience, depression, illicit drug use, and perceived support work together to influence the family environment. The authors hypothesized that (a) depression and drug use function as proxies for a stronger risk factor, the perceived absence of support available in everyday life, and (b) associations between mothers' early bonding experience and family environment are mediated by perceptions of support and nurture available in everyday life. The authors used a "building block" analytic approach and data collected from 125 mothers enrolled in methadone maintenance to test hypotheses. They expected that associations between mothers' early bonding experience and their perceptions of relationships with their children would be mediated by their perceptions of support and nurture available in their everyday life. Each of these hypotheses was supported for the first outcome, mothers' perceptions of family adaptability. Few psychosocial factors were associated with the second outcome, mothers' perceptions of family cohesion, and a majority of mothers (87.2%) in the sample reported no cohesion in their relationships with their children. Although preliminary, the findings suggest that perceptions of relationships in everyday life play a critical role in the etiology of drug-dependent mothers' parenting. Suchman, N., McMahon, T., Slade, A. and Luthar, S. How Early Bonding, Depression, Illicit Drug Use, and Perceived Support Work Together to Influence Drug-Dependent Mothers' Care Giving. *Am J Orthopsychiatry*, 75(3), pp. 431-445, 2005.

## **PREVENTION RESEARCH**

### Assertiveness and Alcohol Use in Rural Adolescents

There is evidence of higher prevalence rates for alcohol use among rural adolescents relative to urban adolescents. Strategies aimed at preventing adolescent alcohol use typically include the development of social skills to resist peer pressure; among the social skills frequently targeted is assertiveness. Self-report data were collected from a sample of rural adolescents (N=470) participating in a longitudinal preventive intervention study. Five hypothesized dimensions of assertiveness were validated with confirmatory factor analysis: specific substance refusal, individual rights, transaction, justice and social approach. Using gender as a between-subject factor, plus time and assertiveness as within-subject factors to predict an alcohol use composite index, repeated measures analysis revealed a number of significant findings. Several assertiveness dimensions were found to have significant effects on the alcohol use index (specific substance refusal, individual rights, and justices associate lower alcohol involvement; social assertiveness was associated with higher involvement). Moreover, there were significant two and three way interaction effects with time and gender. Goldberg-Lillehoj, C.J., Spoth, R. and Trudeau, L. Assertiveness among Young Rural Adolescents: Relationship to Alcohol Abuse. *J. Child and Adol Sub Abuse*, 14(3), pp. 39-67, 2005.

## Rural Youth Attitudes towards Substance Use and Violence

To determine the effectiveness of multi-component prevention campaigns (media and other community wide interventions) the authors conducted 15 focus groups with 169 male and female 6th-, 7th-, and 8th-graders. Participants were recruited from small to mid-size communities across the US. The focus groups examined youth attitudes towards their own use and their peers' use of alcohol, tobacco, drugs, and violence. Several key findings emerged that may be utilized in future multi-component campaigns. First, youth value spending unstructured time with their friends. In terms of tobacco use, both boys and girls are worried about getting caught by their parents; but girls are more concerned about the physical effects of smoking in terms of their attractiveness to members of the opposite sex. In terms of alcohol use, girls were concerned about the dangers of drinking and driving (especially girls in 8th grade) and the pressure to have sex if a date is inebriated. Hispanic youth were more concerned about being a good role model for younger siblings than Caucasian youth. In terms of violence, girls were more likely to spread rumors while boys were more likely to engage in verbal and or physical violence. Finally, both boys and girls preferred prevention and intervention campaigns that were based on real situations and experiences, reflected their culture, were positive, and stress the capabilities of an individual to take action. Kelly, K.J., Comelle, M.G. and Edwards, R.W. Attitudes of Rural Middle-School Youth toward Alcohol, Tobacco, Drugs, and Violence. *The Rural Educator*, 25(3), pp. 19-24, 2004.

## Which Comes First in Adolescence - Sex and Drugs or Depression

The notion that adolescents self-medicate for depression with substance use and sexual behaviors is widespread, but the temporal ordering of depression and these risk behaviors is not clear. This study tests whether gender-specific patterns of substance use and sexual behavior precede and predict depression or vice versa. Data from the National Longitudinal Study of Adolescent Health were weighted to produce population estimates. The sample includes 13,491 youth, grades 7 to 11, interviewed in 1995 and again one year later. Multivariate logistic regression analyses, conducted in 2004, tested temporal ordering, controlling for covariates. The main outcome measures were depression, as measured by a modified Center for Epidemiological Studies-Depression Scale (CES-D), and three behavior patterns: (1) abstaining from sexual intercourse and drug use, (2) experimental behavior patterns, and (3) high-risk behavior patterns. Results showed that overall, sex and drug behaviors predicted an increased likelihood of depression, but depression did not predict sex and drug behaviors. Among girls, both experimental and high-risk behavior patterns predicted depression. Among boys, only high-risk behavior patterns increased the odds of later depression. Depression did not predict behavior in boys, or experimental behavior in girls; but it decreased the odds of high-risk behavior among abstaining girls (RRR=0.14) and increased the odds of high-risk behavior (RRR=2.68) among girls already experimenting with substance use. Engaging in sex and drug behaviors placed adolescents, especially girls, at risk for future depression. Mechanisms of these relationships are yet to be determined. Hallfors, D.D., Waller, M.W., Bauer, D. and Ford, C.A. Which Comes First in Adolescence - Sex and Drugs or Depression? *Am J Prev Med*, 29(3), pp. 163-170, 2005.

## Consistent Predictors of Substance Use in Emerging Adulthood are Male Gender and Previous Use

This 5-year longitudinal study followed a group of 848 adolescents attending an alternative high school in the emerging adulthood years and measured their adult role taking and substance use. Psychological factors at baseline, and adult role taking at the follow-up were examined as correlates of substance use during emerging adulthood. At this stage of life 74% of subjects were employed, 30% were married or engaged, and 53% had at least one child. One third of subjects were daily cigarette smokers, and 24% had used marijuana in the past 30 days. Forty-seven percent had experienced negative consequences of alcohol or drug use in the last year. The most consistent positive predictors of substance use in emerging adulthood were male gender and previous drug use. Addiction concern was a consistent negative predictor. After controlling for baseline psychosocial variables, attending school and being married at the five-year follow-up were negative correlates of both personal consequences and problems related to alcohol or drug use.

Pentz, M.A., Mares, D., Schinke, S. and Rohrbach, L.A. Tobacco, Alcohol, and Other Drug Use among High-risk Young People: A Five-year Longitudinal Study from Adolescence to Emerging Adulthood. *Journal of Drug Issues*, 35(2), pp. 333-356, 2005.

#### Coping Strategies and Mental Health Services

This study examined the relationship among trauma, coping, depression, and mental health service seeking in a probability sample of sheltered homeless and low-income housed women. Results highlight the diversity of trauma. In a longitudinal analysis, women who lived in shelters or experienced major violence had a twofold increase in their risk of depression over the 6-month follow-up. In a cross-sectional analysis, childhood sexual abuse, living in a shelter, physical violence, childhood physical abuse, and death or injury of a friend or relative predicted avoidant coping and symptoms of depression. Active coping and depression predicted mental health service seeking among traumatized women. Modifying coping strategies may ameliorate some of the negative impact of trauma and potentially enhance mental health service use among at-risk women. Rayburn, N.R., Wenzel, S.L., Elliott, M.N., Hambarsoomians, K., Marshall, G.N. and Tucker, J.S. Trauma, Depression, Coping, and Mental Health Service Seeking Among Impoverished Women. *J Consult Clin Psychol*, 73(4), pp. 667-677, 2005.

#### American Indian Girls Exceed American Indian Boys, White Girls and White Boys in Cigarette, Marijuana, Alcohol and Inhalant Use

This article documents the prevalence of self-reported substance use among White and American Indian adolescents enrolled in 7th grade in 1997 in a Northern Plains state. Data were collected by self-administered questionnaire preceding adolescents' participation in a randomized field trial of Project Alert (a 7th and 8th grade prevention curriculum). Rates of lifetime and past-month use of cigarettes and marijuana were higher among American Indians than among Whites of the same gender. American Indian girls exceeded American Indian boys as well as White girls and White boys on lifetime and past-month use of cigarettes, marijuana, alcohol and inhalants; differences in cigarette and inhalant use reached statistical significance. These findings add to the sparse literature on substance use among adolescents as young as 12 through 13 years old and underscore the importance of examining gender-specific substance use patterns early in adolescence. Spear, S., Longshore, D. and McCaffrey, D. Prevalence of Substance Use among White and American Indian Young Adolescents in a Northern Plains State. *Journal of Psychoactive Drugs*, 37(1), pp. 1-16, 2005.

### **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

#### Gamblers with Antisocial Personality Disorder (ASPD) Exhibit More Drug Problems

Nancy Petry and colleagues at University of Connecticut School of Medicine examined problems of 237 compulsive gamblers entering a treatment program and found that approximately 16.5% of participants met diagnostic criteria for ASPD. Male gender, history of illicit substance use, Addiction Severity Index Medical composite score, and the number of criteria for compulsive gambling diagnosis all were positive predictors of Antisocial Personality Disorder. These individuals were more likely to have had a history of substance abuse treatment and to have used a wider variety of substances at higher lifetime rates. The results add to the body of literature supporting a subtype of gambler characterized by high levels of other risk taking and illegal behavior such as substance abuse. Pietrzak R.H. and Petry N.M. Antisocial Personality Disorder is Associated with Increased Severity of Gambling, Medical, Drug and Psychiatric Problems among Treatment-seeking Pathological Gamblers. *Addiction*, 100, pp. 1183-1193, 2005.

### Computer-based Brief Motivational Intervention for Perinatal Drug Use in Primary Care

Computer based brief motivational interventions may be able to reach a high proportion of at risk- individuals and thus have potential for significant population impact. Dr. Ondersma and colleagues at Wayne State University conducted a series of studies to determine the feasibility of delivering a computer-based brief motivational intervention, the Motivation Enhancement System (MES) for perinatal drug use. Overall, the women rated the MES as highly acceptable and easy to use and reported significant increases in state motivation at post-intervention and at one month follow up. These preliminary results suggest the feasibility of this approach. Ondersma, S.J., Chase, S.K., Svikis, D.S. and Schuster, C.R. Computer-based Brief Motivational Intervention for Perinatal Drug Use. *Journal of Substance Abuse Treatment*, 28, pp. 305-312, 2005.

### Anxiety Disorders among Patients with Co-occurring Bipolar and Substance Use Disorders

Dr. Kolodziej and colleagues at Harvard and Boston University examined the prevalence and nature of anxiety disorder among treatment seeking patients diagnosed with current bipolar and substance use disorders, and investigated the association between anxiety disorders and substance use. Among 90 participants diagnosed with bipolar disorder I (n=75, 78%) or II (n=15, 22%), 43 (48%) had a lifetime anxiety disorder, with posttraumatic stress disorder (PTSD) occurring most frequently (n=21, 23%). They found that those with PTSD, but not with the other anxiety disorders assessed, began using drugs at an earlier age and had more lifetime substance use disorders, particularly cocaine and amphetamine use disorders, than those without PTSD. Most participants with PTSD were women, sexual abuse was the most frequently reported index trauma, and the mean age of the earliest index trauma occurred before the mean age of initiation of drug use. These findings highlight the heterogeneity of dually diagnosed patients, and the importance of further investigating the ramifications of a trauma history among those who are diagnosed with bipolar and substance use disorders. Kolodziej, M.E., Griffin, M.L., Najavits, L.M., Otto, M.W., Greenfield, S.F. and Weiss, R.D. Anxiety Disorders among Patients with Co-occurring Bipolar and Substance Use Disorders. *Drug and Alcohol Dependence*, 80(2), pp. 251-257, 2005.

### Gender Differences among HIV-Positive Methadone Maintenance Patients Enrolled in a Medication Adherence Trial

Dr. Haug and colleagues at UCSF examined gender differences among HIV + methadone maintained patients on antiretroviral medications. Participants were enrolled in a larger clinical trial, which included a 4 week observation period using electronic monitors to track medication adherence. Contrary to previous literature, no significant differences were detected between men (n=42) and women (n=36) on medication adherence or depression. Both groups showed poor adherence during baseline (M=56% of doses taken on time), high overall prevalence of depression (47%) and illicit cocaine use (47%). Women reported significantly more medication side effects (M=21.4 vs.14.9), higher severity of ASI psychiatric problems (M=0.50 vs. 0.40), and lower SF-36 health related quality of life in physical (M=42.1 vs. 63.3) and emotional functioning (M=26.9 vs. 58.9) than men. Women tested positive for opioids at higher rates than men (53% vs. 29%, respectively), whereas men were more likely to be positive for benzodiazepines than women (26% vs. 6%, respectively). The findings suggest that gender differences between male and female methadone maintenance patients have relevance to treatment providers. Comprehensive assessment, specialized medical care and mental health services may be necessary in the treatment of HIV positive female drug abusers. Haug, N.A., Sorensen, J.L., Lollo, N.D., Gruber, C.A., Delucchi, K.L. and Hall, S.M. Gender Differences among HIV-positive Methadone Maintenance Patients Enrolled in a Medication Adherence Trial. *AIDS Care*, 17(8), pp. 1022-1029, 2005.

## RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE

### Buprenorphine versus Methadone in the Treatment of Pregnant Opioid-dependent Patients: Effects on the Neonatal Abstinence Syndrome

Buprenorphine may be shown to be an alternate medication to methadone in pregnant women. The purpose of this study was to compare the neonatal abstinence syndrome (NAS) in neonates of methadone and buprenorphine maintained pregnant opioid-dependent women and provide preliminary safety and efficacy data for a larger multi-center trial. In this randomized, double-blind, double-dummy, flexible dosing, parallel-group controlled trial, treatment involved daily administration of either sublingual buprenorphine or oral methadone using flexible dosing of 4-24 mg or 20-100 mg, respectively. Primary outcome measures were number of neonates treated for NAS; amount of opioid agonist medication used to treat NAS; length of neonatal hospitalization; and peak NAS score. Two of 10 buprenorphine-exposed and 5 of 11 methadone-exposed neonates were treated for NAS. Total amount of opioid-agonist medication administered to treat NAS in methadone-exposed neonates was three times greater than for buprenorphine-exposed neonates. Length of hospitalization was shorter for buprenorphine-exposed than for methadone-exposed neonates. Peak NAS total scores did not significantly differ between groups. Results suggest that buprenorphine is not inferior to methadone on outcome measures assessing NAS and maternal and neonatal safety when administered starting in the second trimester of pregnancy. Jones, H.E., Johnson, R.E., Jasinski, D.R., O'Grady, K.E., Chisholm, C.A., Choo, R.E., Crocetti, M., Dudas, R., Harrow, C., Huestis, M.A., Jansson, L.M., Lantz, M., Lester, B.M. and Milio, L. Buprenorphine Versus Methadone in the Treatment of Pregnant Opioid-dependent Patients: Effects on the Neonatal Abstinence Syndrome. *Drug Alcohol Depend.* 79(1), pp. 1-10, 2005.

### Males and Females Differ in Response to Opioid Agonist Medications

Few clinical trials include sex as a factor. This analysis explored within-sex differences in response to opioid agonist medications. Males and females randomly assigned to buprenorphine, LAAM, or methadone were compared on opioid use and retention in treatment. Females receiving buprenorphine had less objective drug use than females receiving methadone, while males receiving LAAM had less objective drug use than males receiving buprenorphine. Retention in treatment was longer for both sexes receiving methadone versus LAAM. Within-subject change results indicate that all three medications benefit both sexes. Clinical trials should be designed to examine the impact of sex on outcomes. Jones, H.E., Fitzgerald, H. and Johnson, R.E. Males and Females Differ in Response to Opioid Agonist Medications. *Am. J. Addict.* 14(3) pp. 223-233, 2005.

### Gender Effects Following Repeated Administration of Cocaine and Alcohol in Humans

Use of cocaine, alcohol, and the two drugs simultaneously is common and the risk of morbidity and mortality associated with these drugs is widely reported. This group carried out a double-blind, placebo-controlled, randomized study examining gender differences in response to administration of these drugs alone and in combination. Current users of cocaine and alcohol (n = 17) who met diagnostic criteria (DSM-IV) for cocaine dependence and alcohol abuse or dependence (not physiologically dependent on alcohol) and who were not seeking treatment for substance use disorders gave voluntary, written, informed consent to participate in three drug administration sessions: 1) four doses of intranasal cocaine (1 mg/kg every 30 min) with oral alcohol (1 g/kg following the initial cocaine dose and a second drink at +60 min (120 mg/kg) calculated to maintain a plasma alcohol concentration of approximately 100 mg/dL; 2) four doses of cocaine and alcohol placebo; 3) cocaine placebo and alcohol. Pharmacokinetics were obtained by serial blood sampling, physiological measurements (heart rate and blood pressure) were obtained with automated equipment, and subjective effects were assessed using visual analog scales over 480 min. The results showed that responses to cocaine, alcohol, and cocaine-alcohol were equivalent by gender for most

measurements. Women had higher heart rates following alcohol administration ( $p = .02$ ). Women consistently reported higher ratings for “Feel Good”, a measure of overall mental/physical well-being, for all study conditions, reaching statistical significance for cocaine ( $p = .05$ ) and approaching significance for alcohol administration ( $p = .1$ ). Women showed equivalent responses to drug administration with the exception of perception of well-being, which was significantly increased for women. These findings may have implications for differential risk for acute and chronic toxicity in women. McCance-Katz, E.F., Hart, C.L., Boyarsky, B., Kosten, T. and Jatlow, P. Gender Effects Following Repeated Administration of Cocaine and Alcohol in Humans. *Subst. Use Misuse* 40(4), pp. 511-528, 2005.

#### What Came First, Major Depression or Substance Use Disorder? Clinical Characteristics and Substance Use Comparing Teens in a Treatment Cohort

This study utilized data on a treatment cohort from a randomized clinical trial that recruited adolescents with co-occurring major depression and substance use disorder ( $N=126$ ). The purpose of this study was to compare adolescents for whom the onset of depression was first versus those for whom the onset of substance use disorder was first or in the same year as depression. Intake clinical evaluations were abstracted to yield common stressors that included childhood abuse, early loss or death, exposure to violence, and attachment problems. Tobacco, alcohol, and cannabis initiation and dependence were compared for the depression first and substance use disorder first groups, and within those groups by gender. Among the substances studied, only cannabis dependence was significantly more prevalent among those with depression first. Comparisons suggest some differences in the developmental path toward comorbid depression and substance use disorders, but remarkable similarity in measures of dependence and severity. Although small samples limited statistical significance, observed differences suggest possible avenues for prevention or intervention. Libby, A M., Orton, H.D., Stover, S.K. and Riggs, P.D. What Came First, Major Depression or Substance Use Disorder? Clinical Characteristics and Substance Use Comparing Teens in a Treatment Cohort. *Addict Behav.*, 30, pp. 1649-1662, 2005.

### **SERVICES RESEARCH**

#### Hospital and Outpatient Health Services Utilization among HIV-Infected Adults In Care: 2000-2002

Rapid changes in HIV epidemiology and antiretroviral therapy may have resulted in recent changes in patterns of healthcare utilization. The objective of this study was to examine sociodemographic and clinical correlates of inpatient and outpatient HIV-related health service utilization in a multi-state sample of patients with HIV. Demographic, clinical, and resource utilization data were collected from medical records for 2000, 2001, and 2002. The study was conducted at 11 U.S. HIV primary and specialty care sites in different geographic regions. Chosen for inclusion, for each year, were HIV-positive patients with at least one CD4 count and any use of inpatient, outpatient, or emergency room services. Sample sizes were 13,392 in 2000, 15,211 in 2001, and 14,403 in 2002. Main outcome measures were the number of hospital admissions, total days in the hospital, and the number of outpatient clinic/office visits per year. Inpatient and outpatient costs were estimated by applying unit costs to numbers of inpatient days and outpatient visits. Findings show that mean numbers of admissions per person per year decreased from 2000 (0.40) to 2002 (0.35), but this difference was not significant in multivariate analyses. Hospitalization rates were significantly higher among patients with greater immunosuppression, women, blacks, patients who acquired HIV through drug use, those 50 years of age and over, and those with Medicaid or Medicare. The mean annual outpatient visits decreased significantly between 2000 and 2002, from 6.06 to 5.66 visits per person per year. Whites, Hispanics, those 30 years of age and over, those on highly active antiretroviral therapy (HAART), and those with Medicaid or Medicare had significantly higher outpatient utilization. Inpatient costs per patient per month (PPPM) were estimated to be 514 dollars in 2000, 472 dollars in 2001, and 424 dollars in 2002; outpatient costs PPPM were estimated at 108 dollars in 2000, 100 dollars in 2001, and 101 dollars in 2002. In conclusion, changes in utilization over this 3-year period, although statistically significant in some cases, were not substantial. Hospitalization rates remain relatively high among



minority or disadvantaged groups, suggesting persistent disparities in care. Combined inpatient and outpatient costs for patients on HAART were not significantly lower than for patients not on HAART. Fleishman, J., Gebo, K., Reilly, E., Conviser, R., Christopher Mathews, W., Todd Korthuis, P., Hellinger, J., Rutstein, R., Keiser, P., Rubin, H. and Moore, R. Hospital and Outpatient Health Services Utilization among HIV-Infected Adults in Care 2000-2002. *Med Care*, 43(9), pp. 40-52, 2005.

#### HIV Intervention for Indigent Substance Abusing Women in the USVI

As the HIV/AIDS epidemic continues to expand and penetrate new communities around the globe, risk reduction intervention initiatives must continue to evolve and adapt to new challenges and populations. This is especially true in the Caribbean Basin, where the feminization of the HIV epidemic is tied to a cultural milieu characterized by pervasive gender inequality. HIV intervention programs in the Caribbean must treat women's risks as a function of the social context, standards, and meanings of sexual behaviors and practices in the local community. As such, this article describes an initiative to develop an HIV prevention-intervention protocol for the cultural context of substance abusing women in the US Virgin Islands. Through street-based survey research combined with focus groups and in-depth interviews with such "cultural insiders" as members of the substance-abusing target population, members of the local public health and social services system, and community leaders, a culturally sensitive HIV/AIDS protocol was developed which addresses the supports and barriers to risk reduction faced by substance abusing women in the Virgin Islands. Surratt, H.L. and Inciardi, J. A. Developing an HIV Intervention for Indigent Women Substance Abusers in the United States Virgin Islands. *J Urban Health*, 82(3-4), pp. iv74-iv83, 2005.

#### The Intersection of Violence with Culture and HIV Risk among Sex Workers

The Republic of South Africa has become an epicentre of heterosexual HIV transmission among Black women, and the interface between violence against women, substance abuse, and HIV risk is becoming evident. This article describes the characteristics of Black South African women who engage in sex work in Pretoria and examines their intersecting experiences of high-risk sexual behaviour, substance abuse, and victimization. Ninety-three women were recruited into the study. Field staff collected biological measures of drug use and administered a structured, self-report interview. Findings indicate that young South African women who engage in sex work and use drugs rely on this activity as their main source of income and are supporting other family members. The majority of sample women reported experiencing some victimization at the hand of men, either clients or boyfriends, with many reporting childhood abuse histories; young women also report great fear of future victimization. Findings also suggest that as a result of their decreased likelihood of using protection, women who reported any sexual or physical victimization are at increased risk for HIV and other STIs. Results support the critical need for targeted, comprehensive interventions that address substance abuse, sexual risk, and violence as interrelated phenomena.

Wechsberg, W.M., Luseno, W.M. and Lam, W.K. Violence against Substance-Abusing South African Sex Workers: Intersection with Culture and HIV Risk. *AIDS Care*, 17, Supplement 1, pp. s55-s64, 2005.

#### Women in Outpatient Treatment for Methamphetamine Improved Family Relationships and Their Medical Condition Relative to Men

This prospective longitudinal study examined treatment outcomes among 1,073 methamphetamine-abusing patients (567 women, 506 men) from 32 community-based outpatient and residential programs in 13 California counties. Data were collected at intake and at 3 months and 9 months after admission. With one exception, improvements from baseline to follow-up were observed in all areas measured by the Addiction Severity Index for both women and men in either modality. Compared to men, women demonstrated greater improvement in family relationships and medical problems, and similar improvement in all other areas, despite the fact that more women were unemployed, had childcare responsibilities, were living with someone who also used alcohol or drugs, had been physically or sexually abused, and reported more psychiatric symptoms. Implications for service improvement are discussed. Hser, Y., Evans, E. and

Huang, Y. Treatment Outcomes among Women and Men Methamphetamine Abusers in California. *J Subst Abuse Treat*, 28(1), pp. 775-785, 2005.

#### Patterns of Diagnoses In Hospital Admissions In A Multi-State Cohort of HIV-Positive Adults In 2001

Admissions for AIDS-related illnesses decreased soon after the introduction of highly active antiretroviral therapy (HAART), but it is unclear if the trends have continued in the current HAART era. The investigators examined the diagnoses for hospitalizations of patients with HIV in 2001. Demographic and healthcare data were collected for 8,376 patients from 6 U.S. HIV care sites. Diagnoses were categorized into 18 disease groups and Poisson regression was used to analyze the number of admissions for each of the 4 most common groups. Investigators also compared patients with admissions for AIDS-defining illnesses (ADI) with patients admitted for other diagnoses. Findings revealed that twenty-one percent of patients had at least 1 hospitalization. Among patients hospitalized at least once, 28% were hospitalized for an ADI. Comparing diagnosis categories, the most common hospitalizations were AIDS-defining illnesses (21.6%), gastrointestinal (GI) diseases (9.5%), mental illnesses (9.0%), and circulatory diseases (7.4%). In multivariate analysis, women had higher hospitalization rates than men for ADI (incidence rate ratio [IRR], 1.50; 95% confidence interval [CI], 1.25-1.79) and GI diseases (IRR, 1.52; 95% CI, 1.15-2.00). Compared with whites, blacks had higher admission rates for mental illnesses (IRR, 1.70; 95% CI, 1.22-2.36), but not for ADI. As expected, CD4 count and viral load were associated with ADI admission rates; CD4 counts were also related to hospitalizations for GI and circulatory conditions. Thus, five years after the introduction of HAART, AIDS-defining illnesses continue to have the highest hospitalization rate among the diagnosis categories examined. This result emphasizes the importance of vaccination for pneumonia and influenza, as well as prophylaxis for *Pneumocystis jiroveci* pneumonia. The relatively large number of mental illness admissions highlights the need for co-management of psychiatric disease, substance abuse, and HIV. Overall, the majority of patients were hospitalized for reasons other than ADI, illustrating the importance of managing comorbid conditions in this population. Data from this cohort of patients with HIV may help guide the allocation of healthcare resources by enhancing our understanding of factors associated with variation in inpatient utilization rates. An understanding of healthcare utilization patterns is important for optimization of care and resource allocation. Betz, M., Gebo, K., Barber, E., Sklar, P., Fleishman, J., Reilly, E. and Christopher Mathews, W. Patterns of Diagnoses in Hospital Admissions in a Multistate Cohort of HIV-Positive Adults in 2001. *Med Care*, 43(9), pp. 3-14, 2005.

#### High Rates of Primary Mycobacterium Avium Complex and Pneumocystis Jiroveci Prophylaxis In The U.S.

National data from the mid-1990s demonstrated that many eligible patients with HIV infection do not receive prophylaxis for opportunistic infections (OIs) and that racial and gender disparities existed in OI prophylaxis receipt. The investigative team examined whether demographic disparities in the use of OI prophylaxis persisted in 2001 and whether outpatient care was associated with OI prophylaxis utilization. Demographic, clinical, and pharmacy utilization data were collected from 10 U.S. HIV primary care sites in the HIV Research Network (HIVRN). This study consisted of adult patients ( $\geq 18$  years old) in longitudinal HIV primary care. Indications for *Pneumocystis jiroveci* pneumonia (PCP) or *Mycobacterium avium* complex (MAC) prophylaxis were 2 or more CD4 counts less than 200 or 50 cells/mm<sup>3</sup> during calendar year (CY) 2001, respectively. Using multivariate logistic regression, they examined demographic and clinical characteristics associated with receipt of PCP or MAC prophylaxis and the association of outpatient utilization with appropriate OI prophylaxis. As for findings, among eligible patients, 88.1% received PCP prophylaxis and 87.6% received MAC prophylaxis. Approximately 80% had 4 or more outpatient visits during CY 2001. Adjusting for care site, male gender (odds ratio [OR], 1.47), Medicare coverage (OR, 1.60), and having 4 or more outpatient visits in a year (OR, 2.34) were significantly associated with increased likelihood of PCP prophylaxis. Adjusting for care site, having 4 or more outpatient visits in a year (OR, 1.85) was associated with increased likelihood of receipt of MAC prophylaxis. There were no demographic or insurance characteristics associated with receipt of MAC

prophylaxis. In conclusion, the overall prevalence of OI prophylaxis has increased since the mid-1990s, and previous racial and HIV risk factor disparities in receipt of OI prophylaxis were found to have waned. Integration into the healthcare system is considered an important correlate to receiving OI prophylaxis. Gebo, K., Fleishman, J., Reilly, E., Moore, R. and Moore, R. High Rates of Primary Mycobacterium Avium Complex and Pneumocystis Jiroveci Prophylaxis in the United States. *Med Care*, 43(9), pp. 23-30, 2005.

## **INTERNATIONAL RESEARCH**

### Interactive Skills of Infants With Their High-Risk Mothers

Savonlahti, E., Pajulo, M., Ahlqvist, S., Helenius, H., Korvenranta, H., Tamminen, T. and Piha J. *Nord J Psychiatry*, 59(2), pp. 139-147, 2005. (INVEST Fellow: Marjaterstu Pajulo, Finland, 2003-2004). In this pilot study, the interactive skills of infants with their high-risk, substance-dependent mothers were explored in residential treatment from pregnancy until the infant was 6 months of age. Fourteen mother-infant pairs were videotaped in feeding and free play situations at 6 months after birth. A comparison, low-risk group consisted of 12 ordinary Finnish mother-infant pairs with minimal clinical risks. The findings show significantly higher levels of dyadic interactive deficiencies among the high-risk mother-infant pairs compared to the low-risk pairs, displayed especially in the feeding situation as lack of mutuality and flat, empty, constricted affective tone of interaction. Also, more interactive deficiencies were found among the high-risk infants compared to the low-risk infants, but the differences were not significant. In this study, this finding might reflect the reduced amount of somatic complications and the benefits of treatment, the impacts of which were not explored. The differences between the high- and low-risk infants were displayed as more withdrawal, depressed mood and avoiding behavior and as less alertness and attentional abilities, robustness and focus on parent's emotional state among the high-risk group.

# DIRECTOR'S REPORT TO COUNCIL

May 2006

## **BASIC NEUROSCIENCE RESEARCH**

### Pregnancy & Cigarette Smoking

Children of women who smoked during pregnancy are at increased risk of dependence when smoking is initiated during adolescence. Studies conducted in experimental animals demonstrate that gestational nicotine exposure attenuated dopamine release induced by nicotine delivered during adolescence. In a recent study, NIDA supported researchers report that exposing pregnant rats to nicotine for a period equivalent to the three trimesters of human brain development period reduced nicotine cholinergic receptor (nAChR) expression in dopaminergic regions during adolescence. This reduction reflects lower nAChR subunits transcript levels and fewer neurons in the VTA, as well as other undefined mechanisms. These data indicate that gestational nicotine exposure affected the developmental regulation of nAChR expression and these effects can endure at least into adolescence. These findings are important from a public health perspective because the down-regulation of nAChR expression during brain development may result in heightened vulnerability to dependence on cigarette smoking that affects adolescent offspring of women who smoked tobacco during pregnancy. Chen, H., Parker, S.L., Matta, S.G., and Sharp, B.M. Gestational Nicotine Exposure Reduces Nicotinic Cholinergic Receptor (nAChR) Expression in Dopaminergic Brain Regions of Adolescent Rats. *European Journal of Neuroscience*, 22, pp. 380-388, 2005.

### Estradiol Selectively Reduces the Stimulated Release of GABA in Rat Striatum

NIDA-supported research has shown that females (rats and humans) appear to be more sensitive to the effects of psychostimulants than males. Research conducted in Dr. Jill Becker's laboratory suggests that the naturally occurring higher concentrations of estrogen in females relative to males may be related to this observation. Becker and her colleagues ovariectomized female rats, replaced the estradiol in some of them, and monitored the efflux of GABA, taurine, and glutamate in the striatum after local application of 75 mM  $K^+$ . They found that GABA and taurine were both enhanced in the striatum after the  $K^+$  challenge, but that the increase in GABA was much less in rats that also were given estradiol; glutamate did not change after challenge in either group. As GABA is the predominant inhibitory transmitter in the brain, this finding may be important for our understanding of how estradiol can alter neurotransmission and how that may be related to the differential effects of stimulants on males and females. Hu, M., Watson, C.J., Kennedy, R.T. and Becker, J.B. Estradiol Attenuates the  $K^+$ -induced Increase in Extracellular GABA in Rat Striatum. *Synapse*, 59, pp. 122-124, 2006.

### Estrogen Neuroprotection from HIV Protein-Induced Oxidative Stress

Estrogen replacement therapy in older women is associated with improvement of symptoms of dementia and Parkinson's Disease, so it is believed that estradiol may have neuroprotective qualities in some circumstances. Although the mechanisms of such neuroprotection are unknown, it is possible that estradiol acts as a free-radical scavenger to reduce oxidative stress. Some HIV infected patients experience similar neurological problems, likely involving glutamate and/or oxidative stress-mediated neurotoxicity that may be caused in part by extracellular HIV proteins gp120 and Tat. This study used human neuronal cells grown in culture to test whether estrogen could reverse damage by tat and gp120, as well as the free-radical generator SIN-1. Both tat and gp120, alone and combined, increased oxidative stress as measured by a fluorescent indicator. This increase was greatly diminished in the presence of estradiol but not progesterone or estradiol plus a selective antagonist. When exposed to tat or gp120, synaptosomes made from rat striatal tissue showed reduced dopamine uptake, and this effect was blocked by preincubation with

estradiol. Reduced dopamine transporter activity in the striatum is a component of HIV-associated neuropathology; so together these findings suggest that estradiol may be a useful strategy for neuroprotection in the context of HIV-associated neurological disease. Wallace, D.R., Dodson, S., Nath, A. and Booze, R.M. Estrogen Attenuates gp120- and Tat(1-72)-Induced Oxidative Stress and Prevents Loss of Dopamine Transporter Function. *Synapse*, 59, pp. 51-60, 2006.

## **BASIC BEHAVIORAL RESEARCH**

### An Animal Model of Disruption of Maternal Behavior and Intergenerational Effects of Cocaine Treatment

Pregnant women who use cocaine are more likely to abuse or neglect their children and to exhibit deficits in bonding and interacting with their infants. In addition, numerous studies have shown an intergenerational transfer of childhood maltreatment: daughters with a history of abuse or neglect are more likely to exhibit these same behaviors in rearing their own offspring. Dr. Josephine Johns and her colleagues have developed a rat model to investigate the causal factors involved in disruption of maternal behavior and intergenerational transfer. During gestation, they treated rat dams with cocaine, or with saline, or merely handled them as a control condition. Then, after the litters were culled to form comparable sized groups, the dams reared either their natural or cross-fostered litters such that some pups that were not themselves exposed to cocaine were reared by cocaine exposed dams and vice versa. Measures of maternal behavior were then collected on postpartum days 1, 5, 10, and 15. Subsequently, first generation daughters from these various litters were bred with no cocaine exposure, and their maternal behavior towards their natural litters was also studied. The authors found: 1) Dams treated with cocaine, regardless of whether they reared exposed or unexposed pups, showed disruption of the onset of maternal behavior, with a diminishing effect over the postpartum period; 2) Pups prenatally exposed to cocaine were treated differently by all dams, regardless of their own treatment condition. Overall, the dams had a tendency to spend less time caring for these pups, consistent with other animal studies suggesting that drug-exposed rat pups have attributes that may make them vulnerable to neglect; 3) Intergenerational deficits in maternal behavior were apparent in the first generation daughters. This effect largely resulted from prenatal exposure to cocaine, but it was also influenced by the treatment of the dams that had reared them. Johns, J.M., Elliott, D.L., Hofler, V.E., Joyner, P.W., McMurray, M.S., Jarrett, T.M., Haslup, A.M., Middleton, C.L., Elliott, J.C. and Walker, C.H. Cocaine Treatment and Prenatal Environment Interact to Disrupt Intergenerational Maternal Behavior in Rats. *Behavioral Neuroscience*, 119, pp. 1605-1618, 2005.

### Psychological Processes Underlying Risky Decisions

Poor self-control or disinhibition is a characteristic feature of young adults with drug addiction. NIDA researcher Julie Stout and her colleagues recently applied mathematical decision models with a simulated gambling task (SGT) to investigate the processes underlying decision making in 66 drug abusers and 58 control participants. The mathematical model enabled these investigators to separately examine the effects of wins and losses on the SGT. The investigators also assessed impulsivity, social deviance and harm avoidance. The results of the study showed that drug abusers differed from controls in SGT performance and in the processes underlying performance. The results showed also that individual differences, such as personality and drug abuse characteristics, are related to SGT performance. For the men, for example, drug group participants performed more poorly than did controls. Moreover, male drug abusers were more influenced by rewards than by punishments, consistent with other studies that have found drug abusers are hypersensitive to rewards and relatively insensitive to future consequences. In contrast to the findings from men, the performance of women was not straightforward. Control women performed at chance level, which is unusual for a control group on this task. By contrast, performance of the drug-abusing women fell below that of control men, but was slightly better than that of the drug-abusing men. Overall the findings suggest a difference between men and women in their approach to the SGT. Thus, generalizations from studies that have focused on male participants may not be germane to understanding cognitive aspects of drug abuse in women. Finally, individual differences in the decision processes used in performing the SGT

task are related not only to drug abuse but also to personality factors. Stout, J.C., Rock, S.L., Campbell, M.C., Busemeyer, J.R. and Finn, P.R. Psychological Processes Underlying Risky Decisions in Drug Abusers. *Psychology of Addictive Behaviors*, 19, pp. 148-157, 2005.

#### Potentiation of Cocaine-Primed Reinstatement of Drug Seeking in Female Rats During Estrus

Researchers at the Medical University of South Carolina previously reported that cue-induced reinstatement of cocaine-seeking was greater in male than in female rats at the highest (1.0 mg/kg) and lowest training dose (0.25 mg/kg), but did not differ at the intermediate training doses (0.4, 0.5, 0.6 mg/kg). At the lowest training dose, females in estrus failed to exhibit reinstatement. (Fuchs, R.A., Evans, A., Mehta, R.H., Case, J. M., and See, R.E. Influence of Sex and Estrous Cyclicity on Conditioned Cue-induced Reinstatement of Cocaine-seeking Behavior in Rats. *Psychopharmacology*, 179, pp.662-672, 2005.) In a follow up study, the researchers sought to determine whether sex and estrous cycle phase play a role in cocaine-primed reinstatement. Following the acquisition of cocaine self-administration (0.5 mg/kg per infusion) and subsequent extinction, reinstatement was assessed with a priming infusion of i.p. cocaine (0, 5.0 or 10.0 mg/kg) in males and in females tested in either the diestrus, proestrus, or estrus phase. Both males and females exhibited a dose-related increase in reinstatement. The effects, however, were opposite those previously observed under conditioned cue-reinstatement. At the 10.0 mg/kg priming dose, females in estrus were more susceptible to reinstatement than both males and non-estrus females (that did not differ). These sex differences in cocaine-induced versus conditioned cue-induced reinstatement could have implications for sex differences in relapse in humans, suggesting perhaps that the factors leading to relapse may differ in males and females. The neuroendocrine basis for the sex differences observed in the present study is unknown, although prior work has shown that dopamine transmission in the prefrontal cortex is associated with cocaine-primed reinstatement, whereas dopamine transmission in the basolateral amygdala is associated with conditioned cue-reinstatement. Further investigation into sex differences and hormonal factors involved in these brain regions and the relationship to reinstatement is warranted. Kippen, T.E., Fuchs, R.A., Mehta, R.H., Case, J.M., Parker, M.P., Bimonte-Nelson, H.A. and See, R.E. Potentiation of Cocaine-primed Reinstatement of Drug Seeking in Female Rats during Estrus. *Psychopharmacology*, 182, pp. 245-252, 2005.

#### Exogenous Estrogen Enhances Reinstatement of Cocaine-Seeking Behavior in Ovariectomized Female Rats

In recent studies from the Medical University of South Carolina, reinstatement of cocaine-seeking behavior was found to be affected by phase of the estrous cycle. In a separate investigation by researchers at the University of Minnesota, the role of estrogen as a modulator of reinstatement of cocaine-seeking behavior has been explicitly examined by comparing reinstatement in ovariectomized female rats administered estrogen replacement (OVX+EST), OVX females administered vehicle (OVX+VEH), and sham-operated females administered vehicle (SH+VEH). In the first of two experiments, in the OVX+EST females EST was administered long-term, during training of self-administration, maintenance, extinction and reinstatement. Results indicated that cocaine-primed reinstatement of responding was greater in the OVX+EST and the SH+VEH females than in the OVX+VEH females, indicating that estrogen mediates cocaine-primed reinstatement of responding. In order to distinguish between estrogen's effects on motivation versus learning, in the second experiment, EST was administered short-term, over 3 days prior to and during the reinstatement phase in OVX+EST. As in the first experiments, greater reinstatement occurred in the OVX+EST females compared to OVX+VEH controls. Comparison of OVX+EST rats in the two experiments (i.e., those receiving long versus short-term EST), however, revealed no differences in reinstatement, suggesting to the authors that estrogen's enhancing effects on reinstatement reflects a direct effect of estrogen's enhancement of motivation for cocaine as opposed to an effect of estrogen on associative learning. Larson, E.B., Roth, M.E., Anker, J.J. and Carroll, M.E. Effect of Short- vs. Long-term Estrogen on Reinstatement of Cocaine-seeking Behavior in Female Rats. *Pharmacology, Biochemistry and Behavior*, 82, pp. 98-108, 2005.

### Nicotine Reward More Influenced by Dose Instructions in Female than Male Smokers

Studies on smoking behavior have shown that females are more sensitive to the non-pharmacological cues associated with nicotine and less sensitive to nicotine dose compared to males. These findings suggest that different interventions may be effective in smoking cessation strategies for men and women. Ken Perkins and his colleagues investigated the effects of accurate or inaccurate instructions about nicotine content on smoking reward. The investigators report that accurate instructions increased smoking reward more in women than in men. In a follow-up study, these investigators enrolled 60 subjects who smoked more than 10 cigarettes per day for at least one year to assess the influence of dose instruction *versus* no instruction on male and female smokers. Subjects were abstinent overnight and were randomly assigned to one of four conditions on the study day. Subjects smoked either a normal cigarette with 0.6mg nicotine (nic) or a denicotinized brand with <0.05 mg. Half of each group was given instructions and half were not. After two puffs, they completed the Rose Sensory Questionnaire to assess smoking reward, and the Diener and Emmons Mood Scale. Craving was also measured and smoking behavior was quantified by number of puffs and latency to first puff during a 30-min ad lib smoking period. Data analysis revealed the following: For women, nic increased reward only in the *presence* of dose instructions, whereas for men, nic increased reward only in the *absence* of dose instructions. Nic increased positive affect overall. Craving decreased from baseline to post-puffs, but this decrease was greater for men than for women. Also, for men but not women, nic decreased craving in the presence, but not the absence, of instructions (opposite from the observation for smoking reward). In the 30-min ad lib smoking period, nic decreased the latency to the first puff for women, only in the presence of dose instruction; this effect was not seen in men. These observations add to a rapidly accumulating body of evidence that women's smoking behavior is guided by a different set of influences from those that are important for men. Perkins, K.A., Doyle, T., Ciccocioppo, M. Conklin, C., Sayette, M. and Caggiula, A. Sex Differences in the Influence of Nicotine Dose Instructions on the Reinforcing and Self-reported Rewarding Effects of Smoking. *Psychopharmacology*, 184, pp. 600-607, 2006.

### Sibutramine Decreases the Appetitive and Consummatory Aspects of Feeding in Baboons

This study examined how sibutramine (0.06–4.0 mg/kg, i.m.), a clinically effective weight-loss medication that increases extracellular serotonin and norepinephrine levels, affected the appetitive and consummatory aspects of feeding of nonhuman primates (baboons) with task-dependent 24-hour access to food. Sibutramine effects were compared to those of dexfenfluramine (2.0–6.0 mg/kg, p.o.), which primarily increases extracellular serotonin levels. The baboons had to complete a two-response sequence to obtain food: responding on one lever during a 30-min appetitive phase was required before animals could start a consumption phase, where responding on a second lever led to food delivery. Responding during the appetitive phase resulted in presentations of food-related light stimuli only. Both males and females ate significantly less when treated with dexfenfluramine, but not sibutramine. Animals also ate fewer meals when treated with dexfenfluramine, but not with sibutramine. Although sibutramine had no effect on number of light presentations and did not alter performance during the appetitive phase, it did reduce consummatory behavior. Sibutramine increased the latency to the first meal of the session in females, but not males. By contrast, dexfenfluramine increased the latency to the first meal of the session, and decreased both appetitive and consummatory behavior in males and females. The presence of sibutramine's gender-specific effects suggests that sex may play a role in determining its effects on feeding behavior. The behavioral mechanism by which sibutramine decreases food intake appears distinct from anorectic drugs such as dexfenfluramine. That is, sibutramine has its anorectic effect by reducing consummatory behavior (eating), whereas dexfenfluramine reduces both consummatory and appetitive behavior (food seeking). Applied to drug abuse, this behavioral paradigm might be useful for understanding appetitive drug seeking and consummatory drug taking. Foltin, R.W. Effects of Sibutramine on the Appetitive and Consummatory Aspects of Feeding in Non-human Primates. *Physiology and Behavior*, 87, pp. 280-286, 2006.

## Differential Responsivity to Non-Drug Reinforcers Predicts Vulnerability for Relapse in Female Rats

Previous studies have demonstrated that rats that freely explore novel environments, rats that have high activity levels, rats that are impulsive and rats that have a preference for highly palatable tastes readily acquire drug self-administration. Recently, Marilyn Carroll and colleagues examined the maintenance of i.v. cocaine intake and subsequent drug-primed relapse after an extended period of abstinence. In this study, female rats were allowed six hours per day access to running wheels for 21 days and then divided into groups that had high wheel running rates (H) or low rates (L) on the basis of a median split (mean revolutions/day). Patterns of wheel running over the 21 days increased in animals that were subsequently assigned to an H group, while steady rates were observed in the L group. Also, the investigators found that H rats took significantly more cocaine (0.4 mg/kg/infusion) over 14 days on a fixed ratio reinforcement schedule, than their low wheel running counterparts. Following self-administration tests, rats were withdrawn from cocaine by replacing saline in the infusion cannulae for 22 days. In response to a priming dose of cocaine on Day 23, both groups showed drug seeking by increasing their responses on the lever previously associated with drug, but the H group had a 7-fold increase over their prior response rates during extinction, as compared to a 3-fold increase by L animals. These differences cannot be accounted for by responses during extinction because both groups showed similar response rates during this phase. These findings support previous observations suggesting that inherent differences in an individual's behavior for non-drug reinforcers predict the propensity to engage in drug taking and drug seeking. Still to be determined is whether the increased vulnerability seen in maintenance and reinstatement reflects inherent differences in the sensitivity of motivational systems or more rapid neuroadaptations to cocaine exposure. However, as non-drug rewards and drugs of abuse activate similar neurobiological substrates, and H animals showed an escalating pattern of running wheel behavior, these animals may experience deprivation of hedonic effects produced by running. The authors suggest that they may show higher rates of drug intake and relapse in order to compensate for this loss. Larson, E.B. and Carroll, M.E. Wheel Running as a Predictor of Cocaine Self-administration and Reinstatement in Female Rats. *Pharmacology Biochemistry and Behavior*, 82, pp. 590-600, 2005.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Methamphetamine and Other Substance Use during Pregnancy: Preliminary Estimates from the Infant Development, Environment, and Lifestyle (IDEAL) Study

Methamphetamine use is a continuing problem in several regions of the United States yet few studies have focused on prenatal methamphetamine exposure. Dr. Barry Lester and his colleagues are conducting a study to estimate the prevalence and correlates of alcohol, tobacco, and other substance use-including methamphetamine-during pregnancy in four areas of the country (Los Angeles, CA; De Moines, IA; Tulsa, OK; and Honolulu, HI). The sample consists of the first 1632 eligible mothers who consented to participate in a large-scale multi-site study focused on prenatal methamphetamine exposure. This unselected screening sample includes both users and nonusers of alcohol, tobacco, methamphetamine, and other drugs. Substance use was determined by maternal self-report and/or GC/MS confirmation of a positive meconium screen. Overall, 5.2% of women used methamphetamine at some point during their pregnancy. One quarter of the sample smoked tobacco, 22.8% drank alcohol, 6.0% used marijuana, and 1.3% used barbiturates prenatally. Less than 1% of the sample used heroin, benzodiazepenes, and hallucinogens. Multivariate modeling results showed that tobacco smokers and illicit drug users were more likely to be single and less educated, have attended less than 11 prenatal visits, and utilize public financial assistance. IDEAL is the first large-scale investigation to report the prevalence of methamphetamine use during pregnancy in areas of the United States where methamphetamine is a notable concern. Given that this research extends and confirms previous findings showing that high-risk groups of pregnant women can be identified on the basis of basic demographic characteristics, targeted interventions are greatly needed to reduce serious adverse outcomes associated with prenatal alcohol and tobacco use. Arria, A.M., Derauf, C., Lagasse, L.L., Grant, P., Shah, R., Smith, L., Haning, W., Huestis, M., Strauss, A., Grotta, S. D., Liu, J.



and Lester, B. Methamphetamine and Other Substance Use during Pregnancy: Preliminary Estimates from the Infant Development, Environment, and Lifestyle (IDEAL) Study. *Maternal Child Health Journal*, pp. 10, pp. 293-302, 2006.

### Cocaine Exposure during Pregnancy and Neonatal Outcomes

Data in this report are for newborns in the Maternal Lifestyle Study, a multi-site longitudinal investigation of health and development following prenatal drug exposure. Associations between cocaine exposure in utero and newborn conditions were examined. One of the strengths of this study is its large sample size; these analyses were carried out for 717 cocaine-exposed infants and 7442 infants not exposed to cocaine. Cocaine-exposed infants were about 1.2 weeks younger, weighed 536 grams less, measured 2.6 cm shorter, and had head circumference 1.5 cm smaller than nonexposed infants. Results did not confirm previous reports in the literature of abnormal anatomic outcomes. Central and autonomic nervous system symptoms were more frequent in the exposed group (i.e., jittery/tremors, high-pitched cry, excessive suck, hyperalertness, and autonomic instability); they were usually transient. No differences were detected in organ systems by ultrasound examination. Exposed infants had more infections, including hepatitis, syphilis, and HIV. Exposed infants were also less often breastfed, had more child protective services referrals, and were more often not living with their biological mother. Bauer, C.R., Langer, J.C., Shankaran, S., et al. Acute Neonatal Effects of Cocaine Exposure during Pregnancy. *Archives of Pediatrics and Adolescent Medicine*, 159, pp. 824-834, 2005.

### Anthropometric and Dymorphologic Assessments in 6-Year-Old Children Prenatally-Exposed to Cocaine

Anthropometric and dymorphologic assessments were carried out for 154 6-year-old children prenatally-exposed to cocaine (PCE) and 131 high-risk controls of similar race and social class. Dose-response relationships were observed for adjusted mean height z scores and for weight-for-height z scores, with higher cocaine exposure associated with lower height and lower weight for height. Severity of marijuana use also predicted lower height for age but greater weight for height. Higher average alcohol exposure throughout pregnancy and 3rd trimester predicted lower head circumference and weight z scores, respectively. After controlling for covariates, higher average prenatal cigarette exposure predicted higher incidence of cranial facial abnormalities. First trimester alcohol exposure predicted greater rates of ear abnormalities and third trimester marijuana exposure predicted greater rates of chest and head shape abnormalities. There was not an increased rate of minor anomalies among the PCE cohort, nor was a consistent phenotype identified, leading the authors to conclude that prenatal cocaine exposure is negatively related to specific growth outcomes, including standardized height and weight-for-height, but is not associated with a systematic pattern of structural abnormalities. The dymorphologic examination utilized a standardized checklist of presence or absence of 271 common dymorphic characteristics. The authors discuss limitations of the study in detail, such as implications for generalizability as a result of exclusion of children with birth defects (including suspected or diagnosed fetal alcohol syndrome) prior to recruitment. Minnes, S., Robin, N.H., Alt, A.A., et al. Dymorphic and Anthropometric Outcomes in 6-Year-Old Prenatally Cocaine-Exposed Children. *Neurotoxicology and Teratology*, 28, pp. 28-38, 2006.

### Prenatal Exposure to Substances of Abuse in Children Residing in Russian Orphanages

Over 600,000 children reside in institutional care in Russia, most of them in baby homes and orphanages. The actual prevalence of fetal alcohol spectrum disorders (FASD) and exposure to drugs of abuse among these children is unknown. In this study, a team of researchers from Boston and the Murmansk Region of Russia, led by Dr. Laurie Miller from Tufts-New England Medical Center conducted a systematic survey of phenotypic features associated with prenatal alcohol exposure among institutionalized Russian children and related these findings to their growth, development, medical, and social histories. Phenotypic screening was conducted for all 234 children residing in three baby homes in the Murmansk region of Russia (mean age 21+12.6 months). These baby homes care not only for orphaned children but also abandoned and relinquished children and children whose parents' rights were terminated. Phenotypic expression scores were devised based on facial dysmorphology and other readily observable physical findings. Growth measurements from birth, time of placement in the baby home, and at present were analyzed. In addition, the charts of 64% of the children were randomly selected for retrospective review. Information collected included maternal, medical, developmental, and social histories. Thirteen percent of children had facial phenotype scores highly compatible with prenatal alcohol exposure and 45% had intermediate facial phenotype scores. These scores correlated with maternal gravidity and age. At least 40% of mothers in whom history was available ingested alcohol during pregnancy; some also used illicit drugs and tobacco. Z scores for growth measurements corresponded to phenotypic score, as did the degree of developmental delay. Children with no or mild delay had significantly lower phenotypic scores than those with moderate or severe delay ( $p = 0.04$ ); more than 70% of children with high phenotypic scores were moderately or severely delayed. More than half of residents of the baby homes in Murmansk, Russia, have intermediate (45%) or high (13%) phenotypic expression scores suggesting prenatal exposure to alcohol. Despite good physical care, stable daily routine, availability of well-trained specialists, and access to medical care, these vulnerable children show significant growth and developmental delays compared with their institutionalized peers. Miller, L.C., Chan, W., Litvinova, A., Rubin, A., Comfort, K., Tirella, L., Cermak, S., Morse, B., Kovalev, I., and Boston-Murmansk Orphanage Research Team. Fetal Alcohol Spectrum Disorders in Children Residing in Russian Orphanages: A Phenotypic Survey. *Alcohol: Clinical and Experimental Research*, 30 (3), pp. 531-538, 2006.

### Caregiver Substance Abuse Associated with Violence Exposure among Young Urban Children

Dr. Delaney-Black and her colleagues at Wayne State University examined the relative importance of caregiver substance abuse as a correlate of child-reported exposure to violence in this study of 407 female African-American primary caregivers and their children 6 to 7 years of age. The association between child report of violence and exposure to substance abuse by others (both within and outside the home) was considered after controlling for variance accounted for by child characteristics, caregiver characteristics, home environment, and neighborhood environment (including neighborhood crime). Caregiver alcohol abuse, children's witnessing of drug use in the home, and children's witnessing of drug deals all explained significant additional variance in violence exposure. These findings suggest that for early elementary-age children, meaningful prevention of violence exposure may be possible via addressing their exposure to substance abuse in their home and community. Ondersma, S.J., Delaney-Black, V., Covington, C.Y., Nordstrom, B. and Sokol, R.J. The Association between Caregiver Substance Abuse and Self-Reported Violence Exposure among Young Urban Children. *Journal of Traumatic Stress*, 19 (1), pp. 107-118, 2006.

### Maternal Acceptance Moderates Relationship between Community Violence Exposure and Child Functioning

Children in the United States are exposed to considerable community violence that has been linked to child functioning, however, not all those exposed experience negative outcomes. Dr. Delaney-Black and her colleagues examined the potential buffering or moderating role of maternal acceptance in the relationship between child-reported community violence exposure (reports of witnessing and being a victim of

community violence) and internalizing and externalizing problems. In a sample of 268 urban African American first graders community violence exposure was significantly related to symptoms of post-traumatic stress, but did not correlate with either internalizing or externalizing problems for all children, after control for demographics, maternal mental health, and general life stress. However, children's perceptions of maternal acceptance moderated the relationship between violence exposure and internalizing and externalizing problems that included being withdrawn, anxious-depressed, and demonstrating delinquent behavior. Children with the lowest levels of self-reported maternal acceptance were most impacted by community violence. In this sample of urban first graders, low levels of maternal acceptance placed children at greater risk for adverse outcomes associated with community violence exposure compared to moderate and high levels of maternal acceptance. Bailey, B.N., Hannigan, J.H., Delaney-Black, V., Covington, C.Y., Covington, C.Y. and Sokol, R.J. The Role of Maternal Acceptance in the Relation between Community Violence Exposure and Child Functioning. *Journal of Abnormal Child Psychology*, 34, pp. 57-70, 2006.

#### Maternal Behavior among Drug Using Mothers

In this report, Dr. Rina Eiden and her colleagues examined the association between maternal cocaine use and maternal behavior in an infant feeding context. The investigators also tested a conceptual model predicting maternal insensitivity during mother-infant interactions. The analyses involved 130 mother-infant dyads (68 cocaine-exposed and 62 noncocaine-exposed) recruited after birth and assessed at 4–8 weeks of infant age. Results indicated that when the effects of prenatal cocaine use were examined in the context of polydrug use, maternal psychopathology, maternal childhood history, and infant birth weight, only postnatal cocaine use and maternal depression/anxiety were unique predictors of maternal insensitivity during the mother-infant interactions. Eiden, R.D., Stevens, A., Schuetze, P. and Dombkowski, L.E. A Conceptual Model for Maternal Behavior among Polydrug Cocaine-Using Mothers: The Role of Postnatal Cocaine Use and Maternal Depression. *Psychology of Addictive Behaviors*, 20, pp. 1-10, 2006.

#### Gender Differences in the Prediction of Condom Use among Incarcerated Juvenile Offenders

Dr. Angela Robertson and her colleagues at Mississippi State University examined the predictive value of the Information-Motivation-Behavioral Skills (IMB) model of HIV prevention for sexually active juvenile offenders at risk for substance abuse and explored gender differences in IMB model constructs for condom-protected vaginal intercourse. Self-report measures of HIV/AIDS knowledge, pro-condom peer influence, risk perception, condom attitudes, condom use self-efficacy, frequency of vaginal intercourse, and frequency of condom-protected vaginal intercourse were collected from predominantly African-American detainees 13-18 years of age. Analysis consisted of structural equation models for the combined sample (N = 523) and for separate gender groups (328 males and 195 females). In the combined model, condom use was significantly predicted by male gender, peer influence, positive condom attitudes, and condom self-efficacy. In separate gender analyses, condom use among adolescent males was predicted by peer influence (modestly) and by positive condom attitudes, whereas condom use among females was predicted by peer influence, self-efficacy, and condom attitudes. Compared with males, females reported significantly greater knowledge, less peer influence, higher perceived risk for infection, more positive condom attitudes, and more self-efficacy, but they reported less condom use. The authors conclude that females may find it difficult to use condoms consistently despite their awareness of their efficacy. Power imbalances or other dynamics operating in their relationships with males need further exploration. Gender differences in the relationship between condom self-efficacy and condom use were masked in the analysis of the total sample, indicating the value of testing theories of HIV prevention separately by gender. Robertson, A.A., Stein, J.A., and Baird-Thomas, C. Gender Differences in the Prediction of Condom Use among Incarcerated Juvenile Offenders: Testing the Information-Motivation-Behavior Skills (IMB) Model. *Journal of Adolescent Health*, 38 (1), pp. 18-25, 2006.

## **CLINICAL NEUROSCIENCE RESEARCH**

### Ambiguity in Groups of Emotional Faces Recruits Ventromedial Prefrontal Cortex

Paulus and colleagues at the University of California, San Diego, used fMRI in a social neuroscience study of affective appraisal of the mood of a group of people. Affective neuroimaging research often uses individual faces as stimuli when exploring the neural circuitry involved in social appraisal, but single face paradigms may not generalize to settings where multiple faces are simultaneously processed. In this study groups of multiple matrices of affective faces were briefly presented during fMRI scans. Subjects were asked to decide whether there were more angry or happy faces (emotional decision) or whether there were more male or female faces (gender decision). In each condition, the array contained either an equal (ambiguous trials) or an unequal (unambiguous trials) distribution of one affect or gender. Ambiguous trials relative to unambiguous trials activated regions implicated in conflict monitoring and cognitive control, including the dorsal anterior cingulate cortex (ACC), dorsolateral PFC, and posterior parietal cortex. The ventromedial PFC (including the ventral ACC) was activated specifically by ambiguous affective decisions compared with ambiguous gender decisions. This supports the dissociation of the ACC into dorsal cognitive and ventral affective divisions, and suggests that the ventromedial PFC may play a critical role in appraising affective tone in a complex display of multiple human faces. This study forms the foundation for investigating whether drug abusers show impairment in brain systems involved in affective appraisal of groups. Since many treatment approaches involve group therapy, such a dysfunction could have substantial implications for treatment development. Simmons, A., Stein, M.B., Matthews, S.C., Feinstein, J.S. and Paulus, M.P. Affective Ambiguity for a Group Recruits Ventromedial Prefrontal Cortex. *Neuroimage*, 29(2), pp. 655-661, 2006.

### Increased White Matter Hyperintensities in Male Methamphetamine Abusers

Renshaw and colleagues at McLean Hospital used structural MRI to assess the prevalence, severity, and location of white matter signal hyperintensities (WMH) in methamphetamine (MA) abusers. Axial T-2 weighted images and fluid attenuated inversion recovery axial images were obtained using a 3T MR scanner from 33 MA abusers and 32 age- and gender-matched healthy comparison subjects. The severity of WMH was assessed separately for deep and periventricular WMH. Ordinal logistic regression models were used to assess the odds ratio for WMH. MA abusers had greater severity of WMH than the healthy comparison subjects (odds ratio: 7.06, 8.46, and 4.56 for all, deep, and periventricular WMH, respectively). Severity of deep WMH correlated with total cumulative dose of MA ( $p = 0.027$ ). These differences were mainly due to increased WMH in male MA abusers. There was greater severity of WMH in male than female MA abusers (odds ratio = 10.00). Male MA abusers had greater severity of WMH than male comparison subjects (odds ratio = 18.86), but there was no significant difference in WMH severity between female MA abusers and female comparison subjects. Increased WMH in MA abusers may be related to MA-induced cerebral perfusion deficits. The lower severity of WMH in female MA abusers may be due to estrogen's protective effect against ischemic or neurotoxic effects of MA. Bae, S.C., Lyoo, I.K., Sung, Y.H., Yoo, J., Chung, A., Yoon, S.J., Kim, D.J., Hwang, J., Kim, S.J. and Renshaw, P.F. Increased White Matter Hyperintensities in Male Methamphetamine Abusers. *Drug and Alcohol Dependence*, 81(1), pp. 83-88, 2006.

### Sex, Stress, and Fear: Gender and Individual Differences in Conditioned Learning

LaBar and colleagues at Duke University investigated the relationship among sex, stress hormones, and fear conditioning in humans in order to elucidate factors that contribute to individual variation in emotional learning. Forty-five healthy adults (22 females) underwent differential delay conditioning, using fear-relevant conditioned stimuli and a shock unconditioned stimulus. Salivary cortisol samples were taken at baseline and after acquisition training and a 24-h-delayed retention test. Acquisition of conditioning significantly correlated with postacquisition cortisol levels in males, but not in females. This sex-specific

relationship was found despite similar overall levels of conditioning, unconditioned responding, and cortisol. There was no effect of postacquisition cortisol on consolidation of fear learning in either sex. These findings have implications for the understanding of individual differences in fear acquisition and risk factors for stress-elicited relapse in substance abusers. Zorawski, M., Cook, C.A., Kuhn, C.M. and LaBar, K.S. Sex, Stress, and Fear: Individual Differences in Conditioned Learning. *Cognitive Affective & Behavioral Neuroscience*, 5(2), pp. 191-201, 2005.

#### Gender and Functional Asymmetry of Ventromedial Prefrontal Cortex

Bechara and colleagues at the University of Iowa investigated whether gender plays a role in the development of defects in social conduct, emotional functioning and decision-making, following unilateral VMPC damage. A previous lesion study found that the more right-sided sector of the ventromedial prefrontal cortices (VMPCs) was critical for social/emotional functioning and decision-making than the left side. However, all but one of the subjects in that study were men, and the one woman did not fit the pattern very well. The study sample consisted of same-sex pairs of men or women patients who had comparable unilateral VMPC damage in either the left or right hemisphere. Two male pairs and one female pair were formed, and authors included two additional women with unilateral right VMPC damage (8 patients in all). The domains of measurement covered social conduct, emotional processing and personality, and decision-making. A systematic effect of gender was found on the pattern of left-right asymmetry in VMPC. Men had severe function defects following unilateral right VMPC damage, but not following left-sided damage. In contrast, functional defects were only found in women with unilateral left VMPC damage, whereas with right-sided damage the defects were mild or absent. The findings suggest that asymmetric, gender-related differences exist in the neurobiology of left and right VMPC sectors and as a result men and women may use different strategies to solve similar problems that parallel differences in information processing between hemispheres. Such differences could reflect. Tranel, D., Damasio, H., Denburg, N.L. and Bechara, A. Does Gender Play a Role in Functional Asymmetry of Ventromedial Prefrontal Cortex? *Brain*, 128(12), pp. 2872-2881, 2005.

#### COMT SNPs and Haplotypes Differentially Associated with European and African American, Male and Female Smokers

Li and colleagues studied 5 SNPs and associated haplotypes in over 600 nuclear families. Results showed the Val/Met polymorphism (rs4680) was associated with three different (but related) measures of smoking. Haplotype analysis revealed one SNP trio was a protective factor for European Americans; another three-SNP haplotype was protective for African Americans while a third was high-risk. However, further analysis showed the protective factors were only for the African American females and the European American males. Both SNPs and haplotypes had different frequencies in the two ethnic groups. These data suggest that COMT variants are related to nicotine dependence but that the effects are both sex and ethnic specific. Other studies have shown the val/met polymorphism to be related to low extraversion and high neuroticism usually in females. Beuten, J., Payne, T.J., Ma, J.Z. and Li, M.D. Significant Association of Catechol-O-Methyltransferase (COMT) Haplotypes with Nicotine Dependence in Male and Female Smokers of Two Ethnic Populations *Neuropsychopharmacology*, 31, pp. 675-684, 2006.

#### Sex Differences in Smoking Initiation and Consumption and in Linkage Analysis

Madden and her colleagues queried their sample of Australian twins with regard to smoking onset and continuation as a "smoker" in both males and females. Results demonstrated the presence of sex differences in the magnitude of genetic and genetic and environmental influences. Heritability was higher for men; shared environment was important only for women in a group where self-described non-smokers were excluded. For smoking initiation, the strongest linkage peak was at 20p13; for cigarette consumption where non-smokers were included, the highest peak was at 11q23 with secondary peaks at 4q35 and 6p34. The peaks were similar but not the same when non-smokers were excluded. Also males tended to have the

stronger peaks. These results support some recent studies and add to the growing list of possible susceptibility genes for smoking. Morley, K.I., Medland, S.E., Ferreira, M.A., Lynsky, M.T., Montgomery, G.W., Heath, A.C., Madden, P.A. and Martin, N.G. A Possible Smoking Susceptibility Locus on Chromosome 11p12: Evidence from Sex-Limitation Linkage Analyses in a Sample of Australian Twin Families. *Behavior Genetics*, 36(1), pp. 87-99.

#### Low Socialization Is Correlated with Increased Activity in the Medial Prefrontal Cortex in Cocaine-Dependent Women

Rajita Sinha, T. R. Kosten and C.S. Li assessed antisocial personality using the California Psychological Inventory socialization scale and compared it to brain activation during a script-guided induction of stress. Three (right inferior frontal cortex, right anterior cingulate and medial prefrontal cortex (MDFC)) of eight brain regions which showed greater activation during stress imagery than at baseline and which were within the corticolimbic circuitry were correlated with the socialization score separately for males and females. The scores were all correlated but only the MPFC in females was (negatively) significant. A low socialization score means a lower arousal to stress and has been previously related to physiological measurements such as skin conductance and heart rate. In other words, females seemed to be underaroused during stress imagery (a suggestion of antisocial pathology) which is shown to be related to increased brain activity in the MDFC. Li, C.S., Kosten, T.R. and Sinha, R. Antisocial Personality and Stress-Induced Brain Activation in Cocaine-Dependent Patients. *Neuroreport*, 17(3), pp. 243-247, 2006.

#### The Alpha-4 Subunit of the Nicotinic Acetylcholine Receptor Is Ethnically-Specific and Gender-Specific Associated with Nicotine Dependence

M.D. Li and associates assessed over 2,000 European or African American subjects from over 600 families. Two (different) single nucleotide polymorphisms are associated with measures of smoking in each of the two ethnic origin groups. After correction, one SNP and a haplotype remained significant in African American females. There were no associations with the beta-2 subunit of the receptor. These data suggest that there is involvement of the alpha 4 subunit of the nicotinic acetylcholine receptor in nicotine addiction. Li, M.D., Beuten, J., Ma, J.Z., Payne, T.J., Lou, X.Y., Garcia, V., Duenes, A.S., Crews, K.M. and Elston, R.C. Ethnic- and Gender-Specific Association of the Nicotinic Acetylcholine Receptor Alpha4 Subunit Gene (CHRNA4) with Nicotine Dependence. *Human Molecular Genetics*, 14(9), pp. 1211-1219, 2005.

## **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

#### Cigarette Smoking in Two American Indian Reservation Populations

This study describes the prevalence and correlates of cigarette smoking in two American Indian reservation populations using multinomial logistic regression on data from a population-based, cross-sectional study of Southwest and Northern Plains American Indians aged 15-54. 19% of Southwest men, 10% of Southwest women, 49% of Northern Plains men and 51% of Northern Plains women were current smokers. Male gender and younger age were associated with higher odds of smoking in the Southwest tribe, whereas current or former marriage and less time spent on a reservation were associated with higher odds of smoking in the Northern Plains population. Alcohol consumption was strongly associated with higher odds of smoking in both groups. Nez Henderson, P., Jacobsen, C., Beals, J. and the AI-SUPERPPF Team. Correlates of Cigarette Smoking Among Selected Southwest and Northern Plains Tribal Groups: The AI-SUPERPPF Study. *Am J Public Health*, 95, pp. 867-872, May 2005.

#### Exposure to Trauma among Two American Indian Tribes

This study examined the prevalence of trauma in 2 large American Indian communities in an attempt to describe demographic correlates and to compare findings with a representative sample of the US

population. The researchers determined differences in exposure to each of 16 types of trauma among 3084 tribal members aged 15 to 57 years through structured interviews. The researchers compared prevalence rates of trauma, by gender, across the 2 tribes and with a sample of the US general population. The researchers used logistic regression analyses to examine the relationships of demographic correlates to trauma exposure. Lifetime exposure rates to at least 1 trauma (62.4%-67.2% among male participants, 66.2%-69.8% among female participants) fell at the upper limits of the range reported by other researchers. Unlike the US general population, female and male American Indians exhibited equivalent levels of overall trauma exposure. Members of both tribes more often witnessed traumatic events, experienced traumas to loved ones, and were victims of physical attacks than their counterparts in the overall US population. Many American Indians live in adverse environments that place them at high risk for exposure to trauma and harmful health sequelae. Manson, S., Beals, J., Klein, S., Croy, C., and Croy, C. Social Epidemiology of Trauma among 2 American Indian Reservation Populations. *Am J Public Health*, 95(5), pp. 851-859, 2005.

### Psychosocial Adjustment among Drug Using Suburban Adolescents

Despite ongoing concern about substance use during adolescence, very little is known about alcohol and drug use among teens living in affluent social settings. In this longitudinal study, cluster analysis was used to characterize patterns of substance use and change in other dimensions of psychosocial adjustment within a cohort of 292 high school students (54% girls) living in an affluent, suburban community. When compared with a cluster of students reporting minimal use, clusters reporting escalating, declining, and persistently high use consistently demonstrated relatively poorer psychosocial adjustment. Moreover, other dimensions of psychosocial adjustment remained relatively stable despite changes in substance use, and there were relations involving substance use and other aspects of psychosocial adjustment that may be specific to this social setting. McMahan, T. and Luthar, S. Patterns and Correlates of Substance Use among Affluent, Suburban High School Students. *J Clin Child Adolesc Psychol*, 35(1), pp. 72-89, 2006.

### Late Onset Antisocial Behavior and Risk for SUD

This study compared late onset antisocial behavior with the more commonly recognized two courses, persisting (beginning by early adolescence and continuing through late adolescence) and desisting (stopping by mid-adolescence) antisocial behavior, in terms of risk for later substance dependence and background risk factors (gender, IQ, socioeconomic status, parental antisocial behavior, and parental divorce). A population-based sample of 500 twins from the Minnesota Twin Family Study, evaluated at ages 17 and 20, was used. The results indicated that youths with late onsets were similar to those with persisting antisocial behavior and that both groups were at higher risk of later nicotine, alcohol, and cannabis dependence than controls; both also had similarly high levels of background risk factors. The late-onset group included a significant overrepresentation of females, whereas the persisting and desisting groups included more males. The authors conclude that late-onset antisocial behavior has many of the same negative correlates of persisting antisocial behavior but includes significantly more females. Clinical implications include the need to recognize this pathway, particularly for vulnerable young women, even though they do not meet criteria for the diagnosis of antisocial personality disorder, for both etiologic studies and preventive interventions. Marmorstein, N. and Iacono, W. Longitudinal Follow-Up of Adolescents with Late-Onset Antisocial Behavior: A Pathological Yet Overlooked Group. *J Am Acad Child Adolesc Psychiatry*, 44(12), pp. 1284-1291, 2005.

### Social Competence among Children of Alcoholics

In the current study, the authors tested the hypothesis that children of alcoholic parents (COAs) show deficits in social competence that begin in early childhood and escalate through middle adolescence. A community sample of families with high levels of alcohol use disorder and control families was used (n=110 COAs and 263 controls). Teachers, parents, and children reported on the social competence of

COAs and matched controls assessed from ages 6 to 15. Hierarchical linear growth models revealed different patterns of change in social competence across development as a function of the reporter of various indicators of competence. Moreover, female COAs showed deficits in social competence in early childhood that receded in adolescence and that varied across subtypes of parent alcoholism. Implications of these findings for understanding the development of social competence in children, and at-risk children in particular, are discussed. Hussong, A., Zucker, R., Wong, M., Fitzgerald, H., and Puttler, L. Social Competence in Children of Alcoholic Parents over Time. *Dev Psychol*, 41(5), pp. 747-759, 2005.

### Behavior Problems among Maltreated Children

Maltreated children are at increased risk for behavior problems. This study examines a model in which shame mediates the potential relation between maltreatment and anger, and anger mediates the potential relation between shame and behavior problems. Participants were 177 children (ages 3 to 7 years) and their mothers, 90 of whom had histories of perpetrating neglect and/or physical abuse. Physical abuse, but not neglect, was related to increased shame during an evaluative task; shame was related to increased anger; and anger to teacher ratings of total behavior problems and externalizing problems. Age moderated the relation between physical abuse and adjustment, as abuse was related to more total problems only among the younger children. Anger was a significant mediator of shame and both behavior problems and externalizing problems. Shame, anger, age, and type of maltreatment appear to be important factors in explaining variance in behavioral adjustment following a history of maltreatment. Bennett, D., Sullivan, M., and Lewis, M. Young Children's Adjustment as a Function of Maltreatment, Shame, and Anger. *Child Maltreat*, 10(4), pp. 311-323, 2005.

### Predictors of Early Initiation of Vaginal and Oral Sex among Urban Young Adults in Baltimore, Maryland

Over the past three decades, most research on adolescent sexual behavior has focused on vaginal intercourse and related behaviors, including contraception and unintended pregnancy. In this study, researchers describe the prevalence and correlates of vaginal, oral, and anal sex in an epidemiologically defined population in Baltimore, Maryland. Young adults (ages 18-24), who had been enrolled in a behavioral intervention trial during elementary school, were interviewed by telephone between 1998 and 2002 to assess their sexual behavior. Of 1679 respondents interviewed, 70.8% were Black and 55% were women. Overall, 93% of the young adults reported vaginal intercourse, 78% reported receiving oral sex, 57% reported performing oral sex, and 10% reported receptive anal intercourse. Among men, 27% reported insertive anal intercourse. Blacks initiated vaginal intercourse at an earlier age than Whites; White women performed oral sex earlier than Black women. Significant interactions were observed between age of first vaginal partner and both gender and race/ethnicity. Blacks with older partners initiated sex at an earlier age than both Blacks with a partner the same age or younger and Whites. A relationship between older female sex partners and earlier vaginal sex initiation among men was observed. These findings indicate that older sex partners play an important role in sexual initiation among young adults. In light of the rates of oral and anal sex, sexual education and intervention programs should address the risk for unintended consequences of these behaviors. Ompad, D., Strathdee, S., Celentano, D. and Latkin, C. Predictors of Early Initiation of Vaginal and Oral Sex among Urban Young Adults in Baltimore, Maryland. *Arch Sex Behav*, 35(1), pp. 53-65, 2006.

### The Impact of Emotional Distress on HIV Risk Reduction among Women

This study evaluated whether 333 seronegative African American female drug users (aged 18-59 years) participating in an HIV intervention and with higher levels of emotional distress, specifically symptoms of depression and anxiety, reduced HIV risk behaviors to a lesser extent than those with lower levels of emotional distress. Participants were recruited between June 1998 and January 2001 from inner-city Atlanta (Georgia, U.S.) neighborhoods and were randomly assigned to one of two enhanced gender-specific and culturally specific HIV intervention conditions or to the NIDA standard condition.



Participants were interviewed at baseline, post-intervention and at 6-month follow-up with a structured questionnaire including information on sociodemographics, sexual and drug-using behavior, and psychosocial characteristics. Despite a significant decline in symptoms of emotional distress during the study period, the women in this sample reported high levels of depressive and anxiety symptoms at baseline and 6-month follow-up. Higher levels of emotional distress were positively associated with post-intervention sexual and drug-taking risk. Women in both enhanced intervention conditions reduced their sexual and drug-taking risks more than women in the standard intervention. Those in the motivation intervention arm experienced a greater reduction in depressive symptoms, accompanied by a greater reduction in sexual risk behavior. Findings suggest the need for effective interventions and mental health resources among subgroups of high-risk women who may be most resistant to behavioral change. Sterk, C., Theall, K. and Elifson, K. The Impact of Emotional Distress on HIV Risk Reduction Among Women. *Subst Use Misuse*, 41(2), pp. 157-173, 2006.

#### Drug Treatment Disparities among Hispanic Drug-Using Women in Puerto Rico and New York City

This paper reports findings on 334 out-of-treatment drug users in Puerto Rico and 617 in New York City, at the 6-month follow-up interview of a longitudinal survey. Main outcomes were health care and drug treatment utilization since baseline, assessed by asking participants if they had received physical or mental health services (including HIV medications), and if they had been in methadone maintenance, inpatient or outpatient drug treatment, or drug treatment while incarcerated. Chi-square tests were used to evaluate associations between gender and other correlates. Logistic regression was used to calculate the contribution of each variable in predicting use of drug treatment. The analysis suggests that women in both sites were likely to suffer from disparities in health care and drug treatment utilization when compared with men, although women in New York utilized more drug treatment resources and were more embedded in the immediate family than their female peers in Puerto Rico. Further research to specify the impact of contextual factors at the organizational and community levels, among members of the same ethnic group residing in different sites, may prove valuable in identifying the health needs and factors that impede or facilitate drug-using women in obtaining the most appropriate treatment. Findings from these studies can help in developing appropriate public health policy and science-based drug treatment programs to eliminate such disparities as those identified in this study. Robles, R., Matos, T., Deren, S., Colón, H., Sahai, H., Marrero, C., Reyes, J., Andía, J., and Shepard, E. Drug Treatment Disparities among Hispanic Drug-Using Women in Puerto Rico and New York City. *Health Policy*, 75(2), pp. 159-169, 2006.

#### Physical Victimization Related to Alcohol and Cigarette Use

This study examined associations between two forms of peer victimization, physical and relational, and externalizing behaviors including drug use, aggression, and delinquent behaviors among a sample of 276 predominantly African American eighth graders attending middle school in an urban public school system. Regression analyses indicated that physical victimization was significantly related to cigarette and alcohol use but not to advanced alcohol and marijuana use; relational victimization contributed uniquely to all categories of drug use after controlling for physical victimization. Physical victimization was also significantly related to physical and relational aggression and delinquent behaviors, and relational victimization made a unique contribution in the concurrent prediction of these behaviors. Physical victimization was more strongly related to both categories of alcohol use, aggression, and to delinquent behaviors among boys than among girls. In contrast, relational victimization was more strongly related to physical aggression and marijuana use among girls than among boys, but more strongly related to relational aggression among boys than among girls. These findings provide information about the generalizability of prior research and have important implications for intervention efforts. This research was supported by Cooperative Agreement U81/CCU309966 from the Centers for Disease Control and Prevention (CDC). Sullivan, T., Farrell, A., and Kliewer, W. Peer Victimization in Early Adolescence: Association between Physical and Relational Victimization and Drug Use, Aggression, and Delinquent Behaviors among Urban Middle School Students. *Dev. Psychopathol.*, 18(1), pp. 119-137, 2006.

### Psychiatric and Drug Use Disorders in Children of Antisocial Parents

The authors examined the prevalence of common externalizing and internalizing disorders in the pre-adolescent and late adolescent offspring of antisocial parents. Lifetime diagnoses for a sample of 11-year-old twins (958 males, 1042 females) and a sample of 17-year-old twins (1332 males, 1434 females) from the Minnesota Twin Family Study, as well as their parents, were obtained through in-person interviews. Odds ratios were calculated for the effect of the parent's diagnosis on the child's diagnosis, controlling for the effect of the co-parent's diagnosis. For the 11 year olds, antisocial behavior in either parent was associated with increased odds of a variety of externalizing disorders. For the 17 year olds, parental antisociality was associated with increased risk for a range of externalizing and internalizing disorders, including paternal antisociality with abuse and dependence on nicotine, alcohol, and drugs. This study extends the previous literature by using a population-based sample and looking at gender of both parents and offspring, finding that each parent has an effect net any effects of the co-parent. Herndon, R., and Iacono, W. Psychiatric Disorder in the Children of Antisocial Parents. *Psychol Med*, 35(12), pp. 1815-1824, 2005.

### HIV, HBV, and HCV Infections among Drug-Involved, Inner-City, Street Sex Workers in Miami, Florida

This study describes the rates of HIV, HBV, and HCV seropositivity among drug-involved, female street sex workers in low-income, inner-city sections of Miami, Florida; further, their sociodemographic characteristics, drug use, and sexual risk behaviors were assessed; and predictors of infection were reported. A sample of 586 sex workers was recruited through targeted sampling methods, interviewed, and counseled and tested for the presence of antibody to HIV, HBV, and HCV. Respondents' median age was 38 years, median time in sex work was 14 years, all were heavily involved in the use of alcohol and drugs, and 42% were homeless. More than half (51.0%) had engaged in unprotected vaginal sex in the past month. Prevalences were HIV, 22.4%; HBV, 53.4%; HCV, 29.7%. A multidimensional public health program must address not only issues related to unsafe sex, but also the problems of drug abuse, homelessness, and other lifestyle factors that contribute to risk behaviors. Inciardi, J., Surratt, H.L., and Kurtz, S.P. HIV, HBV, and HCV Infections among Drug-Involved, Inner-City, Street Sex Workers in Miami, Florida. *AIDS Behav*, 10(2), pp. 139-147, 2006.

### Sex, Touch, and HIV Risk among Ecstasy Users

This study examined HIV risk among heavy and non-heavy ecstasy users, focusing specifically on touch and sexual behavior as part of the ecstasy experience. Structured interviews were conducted with 268 young adult (age 18-25) ecstasy users in Atlanta, Georgia. Heavy ecstasy users were more likely to have been tested for HIV than non-heavy users (79 vs. 68%). However, they also were more likely to perceive no chance of contracting HIV (36 vs. 26%). Touch, both sensual and sexual, was a significant part of the ecstasy experience. In addition, ecstasy use seemed to increase the sexual desire, however, not the ability to achieve an orgasm. Heavy users reported more sexual risk-taking than their non-heavy using counterparts. Results suggest that the setting of ecstasy use also may influence involvement in risk behaviors. Future longitudinal studies are needed on the relationship between ecstasy use, touch, sexual arousal and ability, and risk behavior. Theall, K.P., Elifson, K.W. and Sterk, C.E. Sex, Touch, and HIV Risk among Ecstasy Users. *AIDS Behav*, 10(2), pp. 169-178, 2006.

### Needle-Sharing among Young IV Drug Users and Their Social Network Members: The Influence of the Injection Partner's Characteristics on HIV Risk Behavior

Injection drug use is a risk factor for HIV among adolescents and young adults, yet the interpersonal dynamics of needle-sharing among young injectors remain poorly understood. Research has focused on identifying the characteristics of injecting drug users (IDUs) that increase their risk of needle-sharing. Most studies have not taken into consideration IDUs' decisions to share needles with certain partners but

not with other partners. This study examined partner characteristics associated with needle-sharing among 96 male and 77 female young adult IDUs who had shared needles previously. Men were most likely to share needles with partners who gave them emotional support, partners who they injected or who injected them, and partners with whom they had had sex. Women were most likely to share needles with partners who they injected or who injected them, partners with whom they had discussed HIV risk, and partners with whom they had had sex. Results indicate that needle-sharing occurs within the context of mutual injection rituals and close emotional and sexual relationships. These findings point to the need for targeted interventions to help young IDUs avoid needle-sharing with intimate partners. Unger, J.B., Kipke, M.D., De Rosa, C.J., Hyde, J., Ritt-Olson, A., and Montgomery, S. Needle-Sharing Among Young IV Drug Users and Their Social Network Members: The Influence of the Injection Partner's Characteristics on HIV Risk Behavior. *Addict Behav*, 31(9), pp. 1607-1618, 2006.

### Alcohol and Other Drug Use in the US and Australia

Although youth drug and alcohol harm minimization policies in Australia are often contrasted with the abstinence and zero tolerance policies adopted in the United States, there has been little research directly comparing youth substance use behaviour in the two countries. Three state representative samples in Victoria, Australia (n = 7898) and in the US states of Oregon (n = 15,224) and Maine (n = 16,245) completed a common cross-sectional student survey. Rates of alcohol use (lifetime alcohol use, recent use in the past 30 days), alcohol use exceeding recommended consumption limits (binge drinking: five or more drinks in a session), other licit drug use (tobacco use), and norm-violating substance use (substance use at school, use in the past 30 days of marijuana or other illicit drug use) were compared for males and females at ages 12-17. Rates were lower (odds ratios 0.5-0.8) for youth in Maine and Oregon compared to Victoria for lifetime and recent alcohol use, binge drinking and daily cigarette smoking. However, rates of recent marijuana use and recent use of other illicit drugs were higher in Maine and Oregon, as were reports of being drunk or high at school. In contradiction of harm minimization objectives, Victoria, relative to the US states of Oregon and Maine, demonstrated higher rates of alcohol use exceeding recommended consumption limits and daily tobacco use. However, findings suggested that aspects of norm-violating substance use (substance use at school, marijuana use and other illicit drug use) were higher in the US states compared to Victoria. Toumbourou, J., Beyers, J., Catalano, R., Hawkins, J., Arthur, M., Evans-Whipp, T., Bond, L., and Patton, G. Youth Alcohol and Other Drug Use in the United States and Australia: A Cross-National Comparison of Three State-Wide Samples. *Drug Alcohol Rev*, 24(6), pp. 515-523, 2005.

### For Females, Marriage at Any Age is Protective from Alcohol Use

Previous research shows that marriage leads to reductions in alcohol use, especially for women. Because marriage prior to age 20 (early marriage) is a marker for deviance, the protective effects of marriage may not extend to those who marry in adolescence. This study compared the effects of marriage in adolescence versus young adulthood on alcohol consumption, negative alcohol-related consequences and heavy episodic drinking at age 29. They analyzed data from 1,138 women in a longitudinal cohort followed from ages 18 to 29. The original sample was recruited from 30 California and Oregon middle schools and first surveyed at age 13. Women who had not married, had married early or had married between ages 20 and 29 did not differ on alcohol use at age 18. Women who married as young adults were less likely than singles to engage in any alcohol use, heavy episodic drinking or experience negative consequences and reported less alcohol use at age 29. Women who married in adolescence reported fewer negative consequences at age 29 than did singles and (if they had not divorced) were less likely to engage in heavy episodic drinking or experience any negative consequences, reported fewer consequences and consumed less alcohol. The protective effects of marriage in young adulthood were observed whether or not women divorced. Parenthood and college attendance before age 23 did not explain the marriage effect. Results support role theory, which posits that individuals who marry are socialized into conventional adult roles that discourage deviant behavior. Bogart, L., Collins, R., Ellickson, P., Martino, S., and Klein, D. Effects

of Early and Later Marriage on Women's Alcohol Use in Young Adulthood: A Prospective Analysis. *J Stud Alcohol*, 66(6), pp. 729-737, 2005.

### Personality Traits and Externalizing Disorders in Adolescence

The authors examined personality profiles among children who differed in their co-morbidity of externalizing disorders: attention-deficit/hyperactivity disorder (ADHD) and conduct disorder (CD). 11- and 17-year-old male and female twins from a community sample of 2876 twin pairs in the Minnesota Twin Family Study were categorized as ADHD only, CD only, co-morbid CD-ADHD, and controls (no ADHD or CD) based on threshold and subthreshold CD and ADHD diagnoses assessed with structured interviews. Multivariate analyses were used to identify patterns of personality that differentiate these four diagnostic groups. The authors found that the co-morbid group had a pattern of personality marked by higher Negative Emotionality and lower Constraint than the other diagnostic groups. This pattern was evidenced across gender and age cohort. They concluded that an extreme personality profile may represent a liability toward the occurrence of ADHD and CD with more extreme profiles contributing to the occurrence of both disorders among boys and girls. The significance of this study lies in prediction and understanding of risk based on childhood psychiatric diagnosis and personality traits, given the findings from other groups that co morbid ADHD and CD represent a particularly strong risk group for substance use disorders. Significance is further strengthened by the use of a large, population-based sample and the extension of findings across ages and gender. Cukrowicz, K., Taylor, J., Schatschneider, C., and Iacono, W. Personality Differences in Children and Adolescents with Attention-Deficit/Hyperactivity Disorder, Conduct Disorder, and Controls. *J Child Psychol Psychiatry*, 47(2), pp. 151-159, 2006.

### Measuring Violence Risk and Outcomes among Mexican American Adolescent Females

Central to the development of culturally competent violence prevention programs for Hispanic youth is the development of psychometrically sound violence risk and outcome measures for this population. A study was conducted to determine the psychometric properties of two commonly used violence measures, in this case for Mexican American adolescent females. The Conflict Tactics Scales (CTS2) and the Past Feelings and Acts of Violence Scale (PFAV) were analyzed to examine their interitem reliability, criterion validity, and discriminant validity. A sample of 150 low-risk and 150 high-risk adolescent females was studied. Discriminant validity was indicated by the perpetrator negotiation scale and by the victim psychological aggression and sexual coercion scales of the CTS2 and the PFAV. Analysis indicates that the CTS2 scales and the PFAV demonstrate adequate reliability, whereas strong criterion validity was evidenced by eight of the CTS2 scales and the PFAV. Cervantes, R., Duenas, N., Valdez, A., and Kaplan, C. Measuring Violence Risk and Outcomes among Mexican American Adolescent Females. *J. Interpers. Violence*, 21(1), pp. 24-41, 2006.

### Assessing Parenting Behaviors among Mothers with a History of Maltreatment

Parenting assessments (the Parent-Child Conflict Tactics Scale, CTSPC; and a mother-child observation) were examined for their ability to identify mothers with a history of physically abusing or neglecting their child. Participants were mothers of 139 children (age 3 to 6 years; 58 with a history of maltreatment). Mothers with a history of maltreatment reported higher scores on the Neglect, Nonviolent Discipline, and Psychological Aggression subscales of the CTSPC. These group differences, however, were limited to mothers who acknowledged a history of maltreatment, as mothers who concealed their maltreatment history rated themselves similar to controls. Observation of parental behaviors during a brief, non-stressful task did not discriminate mothers who maltreated from mothers who did not maltreat. The findings suggest that parental report using the CTSPC may be useful in assessing parenting behaviors among mothers with a history of maltreatment, although socially desirable responding is a significant problem. Bennett, D., Sullivan, M., and Lewis, M. Relations of Parental Report and Observation of Parenting to Maltreatment History. *Child Maltreat*, 11(1), pp. 63-75, 2006.

## **PREVENTION RESEARCH**

### Definition and Outcome of the ATHENA Program to Prevent Disordered Eating and Body-Shaping Drug Use in Female Athletes

This study examined the outcomes of the Athlete Targeting Healthy Exercise and Nutrition Alternatives (ATHENA) intervention in female high school athletes. The ATHENA program is based on the Athletes Training and Learning to Avoid Steroids (ATLAS) curriculum, a sport team-centered drug-use prevention program for male high school athletes, which has been shown to reduce alcohol and illicit drug use. Just as anabolic steroid use is associated with male athletes, female sport participants may be at a greater risk for disordered eating and body-shaping drug use. Extending sport team-centered programs to young women athletes required defining and ranking factors related to developing those harmful behaviors. Survey results from a cross-sectional cohort of female middle and high school student athletes were used to identify and prioritize potential curriculum components, including mood and self-esteem, norms of behavior, perceptions of healthy body weight, effects of media depictions of women, and societal pressures to be thin. The derived sport team-centered program was prospectively assessed among a second group of female student athletes from 18 high schools, randomized to receive the intervention or the usual care control condition. The ATHENA intervention is a scripted, coach-facilitated, peer-led 8-session program, which was incorporated into a team's usual training activities. The ATHENA program significantly altered the targeted risk factors and reduced ongoing and new use of diet pills and body-shaping substances (amphetamines, anabolic steroids, and sport supplements). These findings illustrate the utility of a structured process to define curriculum content, and the program's positive results also confirm the sport team's potential as a vehicle to effectively deter health-harming behaviors. Elliot, D., Moe, E., Goldberg, L., Defrancesco, C., Durham, M., and Hix-Small, H. Definition and Outcome of a Curriculum to Prevent Disordered Eating and Body-Shaping Drug Use. *J Sch Health*, 76(2), pp. 67-73, 2006.

### Intervention Outcomes for Girls Referred From Juvenile Justice: Effects on Delinquency

An increasing number of girls are entering the juvenile justice system. However, intervention programs for delinquent girls have not been examined empirically. The authors examined the 12-month outcomes of a randomized intervention trial for girls with chronic delinquency (N = 81). Girls were randomly assigned into an experimental condition (Multidimensional Treatment Foster Care; MTFC) or a control condition (group care; GC). Analysis of covariance indicated that MTFC youth had a significantly greater reduction in the number of days spent in locked settings and in caregiver-reported delinquency and had 42% fewer criminal referrals than GC youth (a trend) at the 12-month follow-up. Implications for reducing girls' chronic delinquency are discussed. Leve, L., Chamberlain, P., and Reid, J. Intervention Outcomes for Girls Referred From Juvenile Justice: Effects on Delinquency. *J Consult Clin Psychol*, 73(6), pp. 1181-1185, 2005.

### Ethnic and Gender-specific Substance Use Patterns in Adolescence

This article documents the prevalence of self-reported substance use among White and American Indian adolescents enrolled in seventh grade (ages 12 through 13) in 1997 in a Northern Plains state. Data were collected by self-administered questionnaire preceding adolescents' participation in a randomized field trial of Project Alert, a seventh and eighth grade substance use prevention curriculum. Rates of lifetime and past-month use of cigarettes and marijuana were higher among American Indians than among Whites of the same gender. American Indian girls exceeded American Indian boys as well as White girls and White boys on lifetime and past-month use of cigarettes and marijuana as well as alcohol and inhalants; differences on cigarette and inhalant use reached statistical significance. These findings add to the sparse literature on substance use among adolescents as young as 12 through 13 years old and underscore the importance of examining gender-specific substance use patterns early in adolescence. Spear, S., Longshore, D.,

McCaffrey, D., and Ellickson, P. Prevalence of Substance Use among White and American Indian Young Adolescents in a Northern Plains State. *J Psychoactive Drugs*, 37(1), pp. 1-6, 2005.

### Externalizing Behavior & Gender Predict Drug Initiation Trajectories

The purpose of the current study was to investigate the influence of externalizing behaviors on substance initiation trajectories among rural adolescents over a 42-month period. Data were obtained from 198 rural adolescents who were participating in a longitudinal study. At the baseline assessment, subjects were on average 12.3 years old. Controlling for gender, higher baseline levels of externalizing were associated with a greater number of substances initiated over time. The initiation trajectory was curvilinear. Girls, compared with boys, reported a lower number of substances initiated at baseline, a greater linear growth trajectory, and a deceleration of growth over time. Lillehoj, C., Trudeau, L., Spoth, R., and Madon, S. Externalizing Behaviors as Predictors of Substance Initiation Trajectories among Rural Adolescents. *J Adolesc Health*, 37(6), pp. 493-501, 2005.

### Female Caregivers' Experiences with Intimate Partner Violence Are Related to Child Functioning

This study examined the relationship between women's experiences with intimate partner violence and their reports of child behavior problems. Data were from the National Survey of Child and Adolescent Well-Being, a national probability study of children who were the subjects of child abuse and neglect investigations. The sample consisted of 2020 female caregivers of children between the ages of 4 and 14 years who were interviewed about demographic characteristics, child behavior problems, female caregiver mental health, parenting behaviors, experiences with intimate partner violence, and community characteristics. Information on child abuse and neglect was obtained in interviews with child protective services workers. Multiple-regression analyses were used to investigate the association between caregiver victimization and child behavior problems while controlling for the effects of child, family, and environmental characteristics. The potential moderating effects of caregiver depression and parenting practices on the relation between intimate partner violence and child behavior problems were examined also. Severe intimate partner violence was associated with both externalizing and internalizing behavior problems when other risk factors were controlled. Use of corporal punishment and psychological aggression were significant moderators, but maternal depression did not moderate the relation between intimate partner violence and behavior problems. This study adds to the evidence that maternal caregivers' experiences with intimate partner violence are related to child functioning. The findings suggest that systematic efforts are needed to ensure that mental health needs are identified and addressed appropriately in children exposed to this violence. Hazen, A., Connelly, C., Kelleher, K., Barth, R., and Landsverk, J. Female Caregivers' Experiences With Intimate Partner Violence and Behavior Problems in Children Investigated as Victims of Maltreatment. *Pediatrics*, 117(1), pp. 99-109, 2006.

### Measuring Adolescents' Smoking Expectancies

Outcome expectancies have been related to smoking behavior among adults, but less attention has been given to expectancies about smoking among adolescents at differing levels of smoking experience. The present study reports the psychometric properties and predictive validity of a brief expectancy scale across two samples of adolescents. Sample 1 (N = 349) consisted of high school students (54% female) who were regular smokers enrolled in a cessation program. Sample 2 (N = 273) consisted of 8th- and 10th-grade early experimenters (54% female) involved in a natural history study of smoking trajectories. In both samples, a principal component analysis of a 13-item expectancy scale yielded four factors (taste, weight control, boredom relief, and negative affect management), each with high internal consistency (coefficient alphas >.77) and accounting for 73% and 80% of the total variance for each sample, respectively. Expectancies were significantly higher among current smokers than among early initiators. In Sample 1, boredom relief and weight management expectancies predicted smoking status 6 months later. In Sample 2, students whose smoking increased over 18 months had higher overall expectancies at baseline compared

with those who tried smoking and did not escalate. These findings support the predictive validity of expectancies in predicting escalation and cessation. Wahl, S., Turner, L., Mermelstein, R., and Flay, B. Adolescents' Smoking Expectancies: Psychometric Properties and Prediction of Behavior Change. *Nicotine Tob Res*, 7(4), pp. 613-623, 2005.

#### Psychometric Examination of English and Spanish Versions of Scales

The psychometric properties of the Revised Conflict Tactics Scales (CTS2) are examined for English-speaking (n = 211) and Spanish-speaking (n = 194) Latino women. Internal consistency of total scale scores is satisfactory (Cronbach's alpha of .70 to .84). However, subscale alphas range from .46 to .80. Confirmatory factor analysis supported five factors of negotiation, minor and severe psychological aggression, and minor and severe physical assault. In unconstrained two-group models, loadings are of similar magnitude across language of administration, with the exception of the Physical Assault scales. Unconstrained and constrained model comparisons show scale structure varied by language group for physical assault. Although results of this study show some comparability for English-speaking and Spanish-speaking Latinas, simply combining results across language groups may obscure important differences in rates of endorsement and patterns of responses reflecting cultural, educational, and economic differences. Connelly, C., Newton, R., and Aarons, G. A Psychometric Examination of English and Spanish Versions of the Revised Conflict Tactics Scales. *J Interpers Violence*, 20(12), pp. 1560-1579, 2005.

#### Measurement Properties of the Communities That Care Youth Survey Across Demographic Groups

Prevention science has produced information about risk and protective factors that predict adolescent use and related problem behaviors. This paper investigates the Communities That Care Youth survey that measures multiple risk and protective factors. Using a sample of 172,628 students who participated in surveys administered in seven states in 1998, analyses were conducted to test the factor structure of these risk and protective factors and to test the equivalence of the factor models across five racial/ethnic groups (African Americans, Asians or Pacific Islanders, Caucasians, Hispanic Americans, and Native Americans), four grade levels (6th, 8th, 10th and 12th), and both gender groups. Results support the construct validity of the survey's risk and protective factor scales and indicate that the measures are equally reliable across males and females and five racial/ethnic groups. Implications of these findings for science-based prevention planning are discussed. Glaser, R.R., Van Horn, M.L., Arthur, M.W., Hawkins, J.D., and Catalano, R.F. Measurement Properties of the Communities That Care Youth Survey Across Demographic Groups. *J Quantitative Crim*, 21(1), pp. 73-101, 2005.

### **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

#### Cardiovascular Risk Behavior among Sedentary Female Smokers and Smoking Cessation Outcomes

Researchers from the Harvard School of Dental Medicine conducted this study to determine if female sedentary smokers with additional cardiovascular disease (CVD) health risk behaviors, like diet and alcohol use, predict abstinence from tobacco use. This study was part of a randomized controlled trial testing the effectiveness of exercise and nicotine gum in smoking cessation. Included in the analysis were 148 participants. This study suggested that high alcohol consumption alone and accumulation of two added risk behaviors predicted poorer smoking cessation outcome in a quit attempt. Dietary behavior alone was not related to cessation outcome. However, the high-fat diet interacted with depression, suggesting that depressed women engaging in high-fat diet are significantly more likely to relapse in their quit attempt compared to other subgroups. The authors conclude that non-moderate alcohol use alone and accumulation of multiple CVD risk behaviors seem to be associated with lower success in smoking cessation. Korhonen,

T., Kinnunen, T., Quiles, Z., Leeman, R.F., Terwal, D.M. and Garvey, A.J. Tobacco Induced Diseases, 3, pp. 7-26, 2005.

### Comprehensive Treatment Including Provision of Housing Reduced Drug Use for Homeless, Dually-Diagnosed Cocaine Abusers

Drs. Jesse Milby and Joseph Schumacher and colleagues at the University of Alabama delivered a cognitive behaviorally-based day treatment and work therapy platform to 196 homeless cocaine abusers, along with one of 3 randomly-assigned housing conditions: 1) provision of housing contingent upon abstinence from drugs; 2) provision of housing without an abstinence contingency; and 3) no provision of housing. Treatment occurred in phases, beginning with a skills-based day treatment and free housing for those receiving housing (months 1 - 2), followed by work therapy, group treatment, and low-cost rent for those receiving housing (months 3 - 6), and finally less intensive support group meetings (months 7 - 12). Participants who were provided housing had significantly better abstinence rates and retention rates than did those who were not provided housing, and there were few significant differences in outcomes between the two housing groups. However, among participants who were engaged into the day-treatment phase, those with abstinent-contingent housing had better abstinence than the other groups. Also, all housing recipients were successful in earning and paying rent during the work therapy phase of treatment. Sex/gender did not appear to moderate the relationships between interventions and outcomes. This study contributes to a line of related research highlight the value of housing in recovery, and suggests several methods for successfully integrating provisions of housing and work skills into substance abuse treatment. Milby, J.B., Schumacher, J.E., Wallace, D., Freedman, M.J. and Vuchinich, R.E. To House or Not to House: The Effects of Providing Housing to Homeless Substance Abusers in Treatment. American Journal of Public Health, 95, pp. 1259-1265, 2005.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

### Gender Effects Following Repeated Administration of Cocaine and Alcohol in Humans

Use of cocaine, alcohol, and the two drugs simultaneously is common and the risk of morbidity and mortality associated with these drugs is widely reported. This double-blind, placebo-controlled, randomized study examined gender differences in response to administration of these drugs alone and in combination. Current users of cocaine and alcohol (n = 17) who met diagnostic criteria (DSM-IV) for cocaine dependence and alcohol abuse or dependence (not physiologically dependent on alcohol) and who were not seeking treatment for substance use disorders gave voluntary, written, informed consent to participate in three drug administration sessions: 1) four doses of intranasal cocaine (1 mg/kg every 30 min) with oral alcohol (1 g/kg following the initial cocaine dose and a second drink at +60 min (120 mg/kg) calculated to maintain a plasma alcohol concentration of approximately 100 mg/dL; 2) four doses of cocaine and alcohol placebo; 3) cocaine placebo and alcohol. Pharmacokinetics were obtained by serial blood sampling, physiological measurements (heart rate and blood pressure) were obtained with automated equipment, and subjective effects were assessed using visual analog scales over 480 min. Responses to cocaine, alcohol, and cocaine-alcohol were equivalent by gender for most measurements. Women had higher heart rates following alcohol administration (p = .02). Women consistently reported higher ratings for "Feel Good" a measure of overall mental/physical well-being, for all study conditions, reaching statistical significance for cocaine (p = .05) and approaching significance for alcohol administration (p = .1). Women showed equivalent responses to drug administration with the exception of perception of well-being, which was significantly increased for women. These findings may have implications for differential risk for acute and chronic toxicity in women. McCance-Katz, E.F., Hart, C.L., Boyarsky, B., Kosten, T. and Jatlow, P. Gender effects following repeated administration of cocaine and alcohol in humans. Subst Use Misuse, 40(4), pp. 511-528, 2005.



### Early Impact of Methadone Induction for Heroin Dependence: Differential Effects of Two Dose Sequences in a Randomized Controlled Study

The pharmacodynamic and pharmacokinetic effects of 2 methadone (METH) induction dose sequences were evaluated in this 15-day outpatient experimental protocol. Heroin-dependent, non-treatment-seeking volunteers were randomly assigned (stratified for gender, race, and route of heroin use) to 2 groups. In 1 sequence, METH doses ascended (28, 56, then 84 mg/day; stepwise, n = 18), whereas in the other sequence doses escalated, then tapered (28-84 mg on Days 1-6 to 56 mg/day; rapid, n = 16). A contingency-management intervention was common to both groups. Drug use and heroin craving and opioid withdrawal symptoms decreased, whereas agonist symptoms and positive mood increased overall across days for both groups. Plasma concentrations and the acute reinforcing effects of METH paralleled each dose sequence. Stepwise relative to rapid METH induction significantly decreased heroin craving and opioid withdrawal symptoms and increased agonist symptoms and positive mood but did not significantly improve drug use or retention. Although these specific dosing procedures would not necessarily be used in clinical settings, they provide a procedural template that might be applied safely and effectively with a broader range of treatment-seeking individuals. Greenwald, M.K. Early Impact of Methadone Induction for Heroin Dependence: Differential Effects of Two Dose Sequences in a Randomized Controlled Study. *Exp. Clin. Psychopharmacol.*, 14, pp. 52-67, 2006.

### Effects of Topiramate in Combination with Intravenous Nicotine in Overnight Abstinent Smokers

Topiramate, an anticonvulsant medication, may be effective as a treatment for alcohol and cocaine addiction. While a recent clinical study has demonstrated the potential utility of topiramate for smoking cessation in alcohol-dependent smokers, the effects of topiramate on tobacco addiction have not been systematically examined in humans. The purpose of this study is to determine topiramate's effects on acute physiological and subjective responses to intravenous (IV) nicotine in overnight abstinent smokers. Seven male and five female smokers participated in a double-blind, placebo-controlled, crossover study, which consisted of one adaptation and three experimental sessions. Before each session, participants were treated orally with either a single 25 or 50 mg topiramate dose or with placebo. Starting 2 h following the medication treatment, participants received an IV saline injection, followed by 0.5 and 1.0 mg/70 kg IV nicotine. Topiramate treatment at 50 mg, compared to 25 mg or placebo, attenuated heart rate increases induced by nicotine. Topiramate, compared to placebo, enhanced the ratings of subjective effects from nicotine including "drug strength," "good effects," "head rush," and "drug liking." Topiramate treatment did not affect performance on the Stroop test. These results suggest that topiramate may enhance the subjective effects of nicotine and attenuate the heart rate response to nicotine. While the exact mechanisms are unclear, enhancement of the dopaminergic system and attenuation of the noradrenergic system may mediate topiramate's effects on the subjective and cardiovascular responses to nicotine, respectively. The utility of topiramate for smoking cessation needs to be examined further in controlled clinical trials. Sofuoglu, M., Poling, J., Mouratidis, M. and Kosten, T. Effects of Topiramate in Combination with Intravenous Nicotine in Overnight Abstinent Smokers. *Psychopharmacology (Berl)*, 184, pp. 645-651, 2006.

## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE AND INFECTIONS**

### **DRUGS OF ABUSE AND THE ENDOCRINE SYSTEM**

#### Cortisol Levels and Depression in Men and Women Using Heroin and Cocaine

Abnormalities in the hypothalamic-pituitary-adrenal (HPA) axis are well documented in men using illicit drugs and/or infected with HIV; however, less is known about HPA function, or the health consequence of HPA dysfunction, in their female counterparts. People with depression exhibit hypercortisolemia, and depression is common in people with HIV or substance use problems. The current study investigated cortisol secretion in 209 demographically matched men and women, stratified by their HIV and drug use status. Self-reported depressive symptoms were evaluated using a standardized, validated questionnaire (CES-D). Women reported more depressive symptoms than men ( $p=.01$ ). Male and female drug users exhibited higher cortisol concentrations ( $p=.03$ ), and were more likely to report depressive symptoms ( $p=.04$ ), than non-users. Depression was related to elevated cortisol concentrations for the study population ( $p=.03$ ), and women with elevated cortisol concentrations were significantly more depressed than all other participants ( $p=.05$ ). While it is unknown whether high cortisol concentrations precede depressive symptoms or vice versa, these data indicate that higher cortisol concentrations are associated with depressive symptoms in heroin and cocaine users, and that this association is more pronounced in women than men. HIV status did not act in an additive or synergistic way with drug use for either cortisol or CES-D measures in the current study. Unique therapies to treat the endocrine and mental health consequences of illicit drug use in men and women deserve consideration as depressive symptoms, and high cortisol concentrations associated with depressive symptoms, differ by gender. Wisniewski, A.B., Brown, T.T., John, M., Cofranceso, J. Jr., Golub, E.T., Ricketts, E.P., Wand, G. and Dobs, A.S. Cortisol Levels and Depression in Men and Women Using Heroin and Cocaine *Psychoneuroendocrinology*, 31(2), pp. 250-255, 2006.

### **DRUG-DRUG INTERACTIONS**

#### Effect of Buprenorphine and Antiretroviral Agents on the QT Interval in Opioid-Dependent Patients

Cardiac arrhythmias have been linked to treatment with methadone and levacetylmethadol. HIV-positive patients often have conditions that place them at risk for QT interval prolongation including HIV-associated dilated cardiomyopathy, coronary artery disease as a consequence of highly active antiretroviral (ARV) therapy-associated metabolic syndrome, and uncorrected electrolyte abnormalities. As of February 14, 2006, no cases of adverse events related to QT interval prolongation have been reported in patients receiving buprenorphine, an opioid partial agonist and the newest drug approved for the treatment of opioid dependence. The objective of this study was to evaluate the effects of buprenorphine/naloxone alone and in combination with 1 of 5 ARV agents (efavirenz, nelfinavir, delavirdine, ritonavir, lopinavir/ritonavir) on the QT interval. This study was prospective, open-label, and within-subject in design, with subjects serving as their own controls. In 50 HIV-negative, opioid-dependent subjects, electrocardiogram recordings were obtained at baseline, after receiving buprenorphine/naloxone for 2 weeks, and then following buprenorphine/naloxone plus ARV administration for 5-15 days at steady-state. QTc interval measurements were compared using mixed-model, repeated-measures ANOVA. Recent cocaine use and gender were considered covariates. Buprenorphine/naloxone alone and often in the presence of evidence for recent use of cocaine did not significantly alter the QT interval ( $p = 0.612$ ). Buprenorphine/naloxone in combination with ARVs caused a statistically, but not clinically, significant increase ( $p = 0.005$ ) in the QT interval. Subjects receiving buprenorphine/naloxone in combination with either delavirdine or ritonavir had the greatest increase in QTc intervals. Prolonged QT intervals were not observed in opioid-dependent subjects receiving buprenorphine/naloxone alone. QT interval increases were observed with buprenorphine/naloxone in combination with either delavirdine or ritonavir, which inhibit CYP3A4.

Baker, J.R., Best, A.M., Pade, P.A. and McCance-Katz, E.F. Effect of Buprenorphine and Antiretroviral Agents on the QT Interval in Opioid-Dependent Patients. *Ann Pharmacother.* 40(3), pp. 392-396, 2006.

#### Medical Illness and Comorbidities in Drug Users: Implications for Addiction Pharmacotherapy Treatment

Providing effective medical care to those with substance use disorders can be a challenge to clinicians. In this article, the authors briefly summarize issues that occur frequently in the medical treatment of substance users. The focus of this article is twofold. The first is to briefly summarize common co-occurring medical illnesses in those manifesting substance use disorders with an emphasis on issues related to providing effective treatment for these diseases in this population. Using specific examples of frequently occurring comorbid medical illness in substance users, including infectious diseases (hepatitis C and HIV disease), sexually transmitted diseases, and pregnancy as examples, the complexities of medical care for this population is demonstrated. Second, this article addresses some of the difficulties encountered in pharmacotherapy aimed specifically at treatment of substance use disorders. For example, difficulties in managing concomitant opiate therapy in those requiring medications for medical illness that may have strong and adverse interactions with opiates are addressed. Adverse events reported for some substance use disorder pharmacotherapies are also highlighted. The authors conclude with a brief review of models of care that have been effective in addressing the needs of this challenging population that can provide additional means for enhancing the clinical care of substance users. Draper, J.C. and McCance-Katz, E.F. Medical Illness and Comorbidities in Drug Users: Implications for Addiction Pharmacotherapy Treatment. *Subst Use Misuse.* 40(13), pp. 1899-1921, 2005.

### **SERVICES RESEARCH**

#### Pathways in the Relapse, Treatment, Recovery Cycle

For many individuals, substance use leads to a chronic cycle of relapse, treatment reentry, and recovery, often lasting for decades. This study replicates earlier work, documents the transition patterns within the cycle during a 3-year period, and identifies variables that predict these transitions. Data are from 1,326 adults recruited from sequential admissions to 12 substance abuse treatment facilities in Chicago, IL, between 1996 and 1998. Participants were predominantly female (60%) and African American (88%) adults. Participants were interviewed at intake, and at 6, 24, and 36 months post-intake. Follow-up rates ranged from 94% to 98% per wave. At each observation, participants' current status in the cycle was classified as (1) in the community using, (2) incarcerated, (3) in treatment, or (4) in the community not using. The transitional probabilities and correlates of pathways between these states were estimated. Over 83% of the participants transitioned from one point in the cycle to another during the 3 years (including 36% two times, 14% three times). For the people in the community, about half remained in the same status (either using or abstinent) and just under half transitioned to incarceration or treatment. The majority of people whose beginning status was incarceration or in-treatment also transitioned to *in the community* by the end of the observation period. While there was some overlap, predictors typically varied by pathway and direction (e.g., using to not using vs. not using to using). These results help demonstrate the need to adopt a chronic vs. acute care model for substance use. While exploratory and observational, several of the predictors are time-dependent and identify promising targets for interventions designed to shorten the cycle and increase the long-term effectiveness of treatment. Scott, C., Foss, M. and Dennis, M. Pathways in the Relapse--Treatment--Recovery Cycle Over 3 Years. *J Subst Abuse Treat*, 28(Suppl 1), pp. S63-S72, 2005.

#### HIV Intervention for Indigent Women Substance Abusers in the US Virgin Islands

As the HIV/AIDS epidemic continues to expand and penetrate new communities around the globe, risk reduction intervention initiatives must continue to evolve and adapt to new challenges and populations. This is especially true in the Caribbean Basin, where the feminization of the HIV epidemic is tied to a cultural milieu characterized by pervasive gender inequality. HIV intervention programs in the Caribbean

must treat women's risks as a function of the social context, standards, and meanings of sexual behaviors and practices in the local community. As such, this article describes an initiative to develop an HIV prevention-intervention protocol for the cultural context of substance abusing women in the US Virgin Islands. Through street-based survey research combined with focus groups and in-depth interviews with such "cultural insiders" as members of the substance-abusing target population, members of the local public health and social services system, and community leaders, a culturally sensitive HIV/AIDS protocol was developed which addresses the supports and barriers to risk reduction faced by substance abusing women in the Virgin Islands. The intervention, which is delivered in three sessions, was pilot tested with 20 active or former substance abusing women. Results from the pilot test revealed that the women were engaged and found the material relevant to their lifestyles and concerns. Surratt, H., and Inciardi, J. Developing an HIV Intervention for Indigent Women Substance Abusers in the United States Virgin Islands. *J Urban Health*, 82(3-4), pp. iv74-iv83, 2005.

#### Substance Use, Sexual Risk, and Violence: HIV Prevention Intervention with Sex Workers in Pretoria

This paper describes an HIV prevention intervention designed in the US that was adapted and implemented in South Africa. Using an experimental design, 93 women who reported recent substance use and sex trading were randomly assigned to a modified Standard HIV intervention or to a Woman-Focused HIV prevention intervention. Eighty women completed the one-month follow-up interview. Participants reported high rates of sexual risk and violence at baseline. At follow-up, findings showed decreases in the proportion of women reporting unprotected sex and the daily use of alcohol and cocaine. Daily alcohol and cocaine use decreased more for women receiving the Woman-Focused intervention. Although violence continued to be a problem, at follow-up Woman-Focused participants reported being victimized less often than women receiving the Standard intervention. This study demonstrates the feasibility of implementing cross-cultural behavioral HIV prevention interventions, and supports the need for future studies of women's contextual issues and the effectiveness of targeted interventions. Wechsberg, W.M., Luseno, W.K., Lam, W.K., Parry, C.D. and Morojele, N.K. Substance Use, Sexual Risk, and Violence: HIV Prevention Intervention with Sex Workers in Pretoria. *AIDS & Behavior*, pp. 1-5, 2006.

#### Sexual Risk Behavior and Substance Use among a Sample of Asian Pacific Islander Transgendered Women

This study examined the prevalence and correlates of HIV-related sexual risk and substance use behaviors among Asian Pacific Islander (API) male-to-female (MTF) transgendered individuals, referred to here as API transgendered women. As part of a larger study on HIV risk among transgendered women of color (Nemoto, Operario, Keatley, Han, & Soma, 2004), a sample of 110 API transgendered women in San Francisco completed individual interviews, of which 13% reported being HIV-positive. In the past 30 days, one fifth of the sample engaged in unprotected receptive anal intercourse (URAI) with any male partner, nearly one half had sex while under the influence of substances, and over half used illicit drugs. In multivariate models, URAI was associated with commercial sex work (odds ratio [OR] = 4.23, 95% confidence interval [CI] = 1.10, 16.25) and previous attempted suicide (OR = 5.83, 95% CI = 1.02, 33.44). Sex under the influence of substances was associated with commercial sex work (OR = 3.35, 95% CI = 1.11, 10.13) and having a college degree (OR = 5.32, 95% CI = 1.34, 21.18). Illicit drug use was associated with commercial sex work (OR = 7.15, 95% = 2.26, 22.63). Findings suggest that API MTF transgendered are on the front line of HIV risk for the API community, and provide insight into factors within this group that might contribute to unsafe sex and substance use. Operario, D., and Nemoto, T. Sexual Risk Behavior and Substance Use among a Sample of Asian Pacific Islander Transgendered Women. *AIDS Educ Prev*, 17(5), pp. 430-443, 2005.

### Addiction Treatment Utilization among Homeless and Housed

Research on addiction treatment utilization in indigent samples mainly has been retrospective, without the measures of three factors: addictive consequences, social network influences, and motivation. In this prospective study, the researchers focus upon these three factors as they are associated with utilization of addiction treatment and mutual help groups among substance-dependent persons with high rates of homelessness. Patients detoxified from alcohol or drugs at baseline were followed for 2 years in a randomized clinical trial of linkage to primary care (n = 274). Outcomes included utilization of Inpatient/Residential, Outpatient, Any Treatment, and Mutual Help Groups. Predictor variables in longitudinal regression analyses came from the literature and clinical experience, organized according to theoretical categories of Need, and non-Need (e.g., Predisposing and Enabling). Many subjects used Inpatient/Residential (72%), Outpatient (62%), Any Treatment (88%) or Mutual Help Groups (93%) at least once. In multivariable analyses, addictive consequences (odds ratio [OR] 1.38, 95% confidence interval [CI] 1.12-1.71), motivation (OR 1.32, 95% CI 1.09-1.60), and female gender (OR 1.80, 95% CI 1.13-2.86) were associated with most treatment types. Homelessness was associated with Residential/Inpatient (for Chronically Homeless vs. Housed, OR 1.75, 95% CI 1.04-2.94). Living with one's children (OR 0.51, 95% CI 0.31-0.84) and substance-abusing social environment (OR 0.65, 95% CI 0.43-0.98) were negatively associated with Any Treatment. Addictive consequences, social network variables, and motivation were associated with treatment utilization in this sample. Non-need factors, including living with one's children and gender, also were found to be significant influences on treatment utilization. Kertesz, S., Larson, M., Cheng, D., Tucker, J., Winter, M., Mullins, A., Saitz, R., and Samet, J. Need and Non-Need Factors Associated with Addiction Treatment Utilization in a Cohort of Homeless and Housed Urban Poor. *Med Care*, 44(3), pp. 225-233, 2006.

### Gender Differences in the Prediction of Condom Use among Incarcerated Juveniles

This research study applied the Information-Motivation-Behavioral skills (IMB) model in predicting condom-protected vaginal intercourse among incarcerated youth. The IMB model is a three-factor conceptualization of HIV preventive behavior. According to the IMB Model, there are three fundamental determinants of AIDS risk reduction including: information on HIV/AIDS transmission and information on specific prevention methods, motivation to act on the knowledge and change risky behavior, and behavioral skills in performing the specific prevention acts. Self-report measures of AIDS knowledge, pro-condom peer influence, risk perception, condom attitudes, condom use self-efficacy, frequency of vaginal intercourse, and frequency of condom-protected vaginal intercourse were collected from predominately African-American adolescent juvenile detainees (N=523). Study results found that for males and females combined condom use was significantly predicted by being male, peer influence, positive condom attitudes, and condom self-efficacy. In separate gender analyses, condom use among adolescent males was predicted by peer influence and positive condom attitudes, whereas condom use among females was predicted by peer influence, self-efficacy, and influence, higher perceived risk for infection, more positive condom attitudes, and more self-efficacy, but females also reported less condom use. The investigators conclude that girls may find it more difficult to consistently use condoms despite awareness of their efficacy. Power imbalances or other dynamics operating in their relationships with boys need further exploration. Robertson, A.A., Stein, J.A., and Baird-Thomas, C. Gender Differences in the Prediction of Condom Use among Incarcerated Juvenile Offenders: Testing the Information-Motivation-Behaviors Skills (IMB) Model. *Journal of Adolescent Health*, 38, pp. 18-25, 2006.

# DIRECTOR'S REPORT TO COUNCIL

September 2006

## **BASIC NEUROSCIENCE RESEARCH**

### Uterine Anandamide Levels and Pregnancy

Anandamide, an endogenous cannabinoid, plays an important role in implantation of the fertilized ovum. Uterine implantation requires a reciprocal interaction between a blastocyst and a receptive uterus. NIDA supported research in mice has illuminated anandamide's role in mediating this interaction. During early pregnancy, anandamide is at lower levels in both the receptive uterus and at the implantation site. However, the mechanism by which differential uterine anandamide gradients are established is not clearly understood. NIDA researchers Dr. Dey and his associates have recently demonstrated that uterine anandamide levels are primarily regulated by *Nape-Pld*, the gene encoding *N*-acylphosphatidylethanolamine-hydrolyzing phospholipase D (NAPE-PLD) that generates anandamide. This suggests that aberrant uterine NAPE-PLD activity may cause implantation failure or defective implantation. These findings may be relevant to human abuse of cannabinoids, since elevated anandamide is associated with spontaneous pregnancy failure. Guo, Y., Wang, H., Okamoto, Y., Ueda, N., Kingsley, P.J., Marnett, L.J., Schmid, H.H.O., Das, S.K., and Dey S.K., *N*-Acylphosphatidylethanolamine-hydrolyzing Phospholipase D Is an Important Determinant of Uterine Anandamide Levels during Implantation. *Journal of Biological Chemistry*, 280, pp. 23429-23432, 2005.

## **BASIC BEHAVIORAL RESEARCH**

### Rats Given Prolonged Access to Nicotine Display Age, But Not Gender, Differences

In a recent study by NIDA grantee Dr. B. M. Sharp, adolescent rats were housed in operant chambers allowing 23 hr access to self-administered nicotine via lever-pressing on one of two available levers (one active, one inactive). During acquisition of self-administration behavior, males displayed greater variation in responding on the active lever, but there were no significant gender differences in acquisition. Thus, both genders rapidly learned to self-administer nicotine and there were no gender differences in sensitivity to dose. However, adult female rats acquired nicotine self-administration at a slower rate than adolescent females and the adult females self-administered significantly less drug than their adolescent counterparts. (Adult male rats were not tested in this phase of the study). The procedure used by Dr. Sharp and his colleagues differs from those previously employed to establish nicotine self-administration in that animals were not food restricted (which may affect growth, especially in animals that are continuing to develop). This experimental paradigm more closely mimics the conditions under which humans self-administer nicotine. Additionally, since the "adolescent" phase of development is short in rats, this model allows for rapid acquisition of the self-administration behavior for study. Chen, H., Matta, S.G. and Sharp, B.M. Acquisition of Nicotine Self-Administration in Adolescent Rats Given Prolonged Access to the Drug. *Neuropsychopharmacology*, 32(3), 700-709, 2007.

### Sex Difference in Visual Cue Enhancement of Nicotine Reinforcement

Human laboratory studies have shown that sensitivity to nicotine is lower in females than in males but that sensitivity to nonpharmacological stimuli associated with cigarette use is higher in females than in males. The importance of stimuli associated with nicotine to the reinforcing effects of nicotine has been established by researchers at the University of Pittsburg. That research was conducted previously in male rats and the researchers have now extended this work to female rats and have observed sex differences in

this effect. Following acquisition of i.v. self-administration of either 0.03, 0.06, or 0.15 mg/kg nicotine and stable responding, nicotine deliveries were subsequently paired with a visual cue. In the absence of the visual cue, nicotine alone functioned as a reinforcer in both males and females at the .06 and 0.15 mg/kg doses, but not the 0.03 mg/kg dose. Addition of the visual cue produced a robust enhancement of nicotine reinforcement (response rate, infusions earned, and nicotine intake) in both males and females at the lower doses, and this enhancement at the 0.06 mg/kg dose was greater in females than males. The authors suggest possible explanations for this greater enhancement in females, including a greater synergistic interaction between nicotine and the visual cue and sex differences in limbic responses to nicotine and nicotine cues. This sex difference in visual cue enhancement of nicotine reinforcement could have implications for the use of pharmacologic versus non-pharmacologic strategies for nicotine cessation in males versus females. Chaudhri, N., Cagguila, A.R., Donny, E.C., Booth, S., Gharib, M.A., Craven, L.A., Shannon, S.A., Alan, F.S., and Perkins, K.A. Sex Differences in the Contribution of Nicotine and Nonpharmacological Stimuli to Nicotine Self-Administration in Rats. *Psychopharmacology*, 180, pp. 258-266, 2005.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Prenatal Smoking and Disruptive Behavior in Early Development

An association between prenatal smoking and disruptive behaviors in children has been documented in the research literature, but little is known about the possible emergence of these behaviors in early development. Dr. Lauren Wakschlag and colleagues investigated very early precursors to disruptive behavior problems, examining behaviors of prenatally-exposed children and non-exposed children at 12, 18, and 24 months of age. Maternal reports were recorded at 12, 18, and 24 months, and behavioral observations were carried out at 24 months. Analyses took into account multiple covariates (e.g., other substances used during pregnancy, parenting practices, and cumulative family risk, which included demographic, psychiatric, and psychosocial factors). The investigators report that exposed toddlers exhibited higher levels of behavior problems from 12 to 24 months, and that virtually all of the toddlers with clinically significant problems at age 2 years had been exposed. They also report that exposure was associated with social, rather than emotional aspects of early problem behaviors. Those exposed were more likely to exhibit stubbornly defiant and aggressive behavior, and lower social engagement. The two groups did not differ on difficulty regulating negative emotion. While pointing out that the data do not prove a causal relationship, the researchers do note that the findings allow generating ideas concerning which areas of the brain may be affected by exposure, and highlight a potential window of opportunity for early interventions aimed at altering disruptive behavior pathways before they become serious clinical patterns. Wakschlag, L.S., Leventhal, B.L., Pine, D.S., Pickett, K.E., and Carter, A.S. Elucidating Early Mechanisms of Developmental Psychopathology: The Case of Prenatal Smoking and Disruptive Behavior. *Child Development*, 77, pp. 893-906, 2006.

### Postnatal Cocaine Use and Parental Behavior during Mother-Infant Interactions

Within a broader conceptual model for maternal behavior among polydrug cocaine-using mothers, this study investigated the relationship between maternal cocaine use (prenatal and postnatal) and maternal behavior during mother-infant interactions. Specifically, behaviors were observed in a feeding context between 4 and 8 weeks of infant age. The categories of maternal behaviors analyzed were maternal insensitivity (e.g., position without support, misses infant cues) and maternal warmth (e.g., talks to infant, pleasure toward infant). The conceptual model used by Dr. Eiden and her colleagues included prenatal and postnatal polydrug use, maternal psychopathology, maternal childhood history, and infant birth weight. There were no group differences in maternal warmth or between maternal psychological functioning and maternal warmth. Results of conceptual model testing indicated that only postnatal cocaine use was a significant and unique predictor of maternal insensitivity during feeding. Maternal depression/anxiety was marginally associated with maternal insensitivity. The investigators point out that the results add to a

growing body of evidence that indicates the importance of examining postnatal caregiving as a predictor of child outcome among children exposed to substances in the prenatal period. Eiden, R.D., Stevens, A., Schuetze, P., and Dombkowski, L.E. A Conceptual Model for Maternal Behavior Among Polydrug Cocaine-Using Mothers: The Role of Postnatal Cocaine Use and Maternal Depression. *Psychology of Addictive Behaviors*, 20, pp. 1-10, 2006.

#### Prediction of Parenting Stress and Perception of Infant Temperament

This investigation was conducted from the perspective that prenatal cocaine exposure is a marker of developmental risk, and the risk may involve a range of social, environmental, and biological factors. The researchers note that two factors likely to mark heightened risk are the degree to which mothers perceive their parental role as highly stressful and the degree to which they perceive their infant as temperamentally difficult. Therefore, the goal of this study was to understand processes that may heighten or attenuate levels of parenting stress and perceptions of infant temperament for infants prenatally-exposed to cocaine. Neonatal behavior, infant temperament, parenting stress, and maternal psychopathology were assessed in a large sample of mother-infant dyads (394 prenatally-exposed infants and 590 comparison infants). The sample was drawn from the multi-site longitudinal Maternal Lifestyle Study, and infants were selected for inclusion if they were in the care of their biological mother. Neonatal behavior was observed at 1 month corrected age, and other assessments were carried out at 4 months corrected age. Results indicated that neonatal behavioral characteristics and certain maternal psychological characteristics interacted to predict maternal ratings of infant temperament, and maternal self-reports of parenting stress. Results were not related to drug exposure history. The researchers conclude that for mothers of at risk infants, with or without prenatal cocaine exposure, psychological distress affects the degree to which infant behavioral characteristics are experienced as stressful or difficult. The researchers also discuss implications of the findings for interventions. Sheinkopf, S.J., Lester, B.M., LaGasse, L.L., et al. Interactions between Maternal Characteristics and Neonatal Behavior in the Prediction of Parenting Stress and Perception of Infant Temperament. *Journal of Pediatric Psychology*, 31, pp. 27-40, 2006.

#### Predicting Caregiver-Reported Behavior Problems in Cocaine-Exposed Children

The purpose of this study was to investigate predictors of caregiver-reported behavior problems in a sample of 3-year-old children. The children were either in a group exposed to cocaine prenatally, or in a comparison group. Two measures of behavior problems were used: the Conners' Parent Report Scale, and the Eyberg Child Behavior Inventory. The Conners' Scale has scales assessing conduct problems and impulsive/hyperactive behaviors. The Eyberg Inventory was designed to assess disruptive behaviors, especially those associated with oppositional-defiant and conduct disorders. Concurrent maternal/caregiver depression as measured by the Center for Epidemiologic Studies-Depression (CES-D) Scale was the only significant predictor of reported child behavior problems in a model that included prenatal drug exposure, child sex, and the quality of the child's environment. Comparisons involving maternal and non-maternal caregivers relative to depression scores and child behavior ratings are also provided in the report. The researchers discuss implications of the findings for clinical care and for future research on behavioral functioning of prenatally exposed children. Warner, T.D., Behnke, M., Hou, W., et al. Predicting Caregiver-Reported Behavior Problems in Cocaine-Exposed Children at 3 Years. *Journal of Developmental and Behavioral Pediatrics*, 27, pp. 83-92, 2006.

#### Behavioral Reactivity and Regulation in Preschoolers Prenatally-Exposed to Cocaine

Based on concerns in the literature that prenatal exposure to cocaine may increase risk for problems related to reactivity and regulation in infancy and childhood, this study examined whether cocaine-exposed children show such difficulties during the preschool period, a time of increased social and cognitive demands, and a time of rapid changes in reactivity and regulation. The procedure involved observing reactivity and regulation during a frustrating problem-solving task at 4.5 years of age. Frustration reactivity



was measured by latency to show frustration and number of disruptive behaviors. Regulation was measured by latency to approach and attempt the problem-solving task and by the number of problem-solving behaviors. Results indicated that cocaine-exposed children took longer to engage in the problem-solving task, and that cocaine-exposed boys showed the most difficulties. The cocaine-exposed boys expressed frustration more rapidly and had a larger number of disruptive behaviors compared to non-exposed children and cocaine-exposed girls. The researchers make note that the effect sizes were relatively small, and feel that the results indicate both resilience and vulnerabilities. They also comment on implications for intervention and prevention. Dennis, T., Bendersky, M., Ramsay, D., and Lewis, M. Reactivity and Regulation in Children Prenatally Exposed to Cocaine. *Developmental Psychology*, 42, pp. 688-697, 2006.

### Neuroimaging and Prenatal Drug Exposure

This article is a summary report of a symposium that brought together researchers who are investigating effects of prenatal substance abuse in humans and primates, and who are utilizing neuroimaging techniques in their studies. The purpose of the symposium was to assess strengths and weaknesses of the neuroimaging and data processing techniques, and to discuss strategies that may facilitate collection of imaging data in exposed and comparison children. Various imaging techniques were discussed, i.e., magnetic resonance imaging (MRI), positron emission tomography (PET), diffusion tensor imaging (DTI), magnetic resonance spectroscopy (MRS), and molecular imaging. Papers were presented by five groups, and are provided in this article. While the findings in this report are very preliminary, they emphasize the potential that neuroimaging methodologies have for understanding how drug exposure may affect brain development. Dow-Edwards, D.L., Benveniste, H., Behnke, M., et al. Neuroimaging of Prenatal Drug Exposure. *Neurotoxicology and Teratology*, 28, pp. 386-402, 2006.

### Depression, Sensation Seeking, and Maternal Smoking as Predictors of Adolescent Cigarette Smoking

This study examined maternal and adolescent depression, maternal and teen sensation seeking, and maternal smoking, and their associations with adolescent smoking. Data were collected from a sample of 47 male and 66 female adolescents (ages 11-18 years) and their mothers from three different health clinics. The findings indicate that maternal sensation seeking was linked indirectly with adolescent smoking through teen sensation seeking, both of which were significantly associated with teen smoking (beta = 0.29,  $p < 0.001$  and beta = 0.32,  $p < 0.001$ , respectively). Teen depression was associated positively with teen smoking (beta = 0.24,  $p < 0.01$ ) when controlling for sensation seeking behaviors. Maternal smoking was also directly linked to adolescent smoking (beta = 0.20,  $p < 0.05$ ). These findings underscore a potentially important role of sensation seeking in the origins of adolescent smoking, and clarify pathways of influence with regard to maternal attitudes and behaviors in subsequent teenage nicotine use. Van de Venne, J., Bradford, K., Martin, C., Cox, M., and Omar, H.A. Depression, Sensation Seeking, and Maternal Smoking as Predictors of Adolescent Cigarette Smoking. *Scientific World Journal*, 6, pp. 643-652, 2006.

## **CLINICAL NEUROSCIENCE RESEARCH**

### Affect Modulates Appetite-Related Brain Activity To Images Of Food

Deborah Yugelen-Todd and colleagues used fMRI to determine whether affect ratings predicted regional brain responses to high and low-calorie foods in healthy individuals. Thirteen normal-weight adult women viewed photographs of high and low-calorie foods during BOLD functional magnetic resonance imaging (fMRI). Positive and negative affect had different effects on several important appetite-related regions depending on the calorie content of the food images. When viewing high-calorie foods, positive affect was associated with increased activity in satiety-related regions of the lateral orbitofrontal cortex, but when viewing low calorie foods, positive affect was associated with increased activity in hunger-related regions including the medial orbitofrontal and insular cortex. The opposite pattern of activity was observed for

negative affect. These findings describe the neurobiologic substrates involved in the commonly reported increase in cravings for calorie-dense foods during heightened negative emotions. Killgore, W.D.S., and Yurgelun-Todd, D.A. Affect Modulates Appetite-related Brain Activity to Images of Food. *International Journal of Eating Disorders*, 39, pp. 357-363, 2006.

#### Gender Differences among Recreational Gamblers: Association with the Frequency of Alcohol Use

Marc Potenza and colleagues at Yale School of Medicine investigated the interactive effects of alcohol use and gender on health and gambling attitudes and behaviors in recreational gamblers. The Gambling Impact and Behavior Study surveyed by telephone 2,417 adults targeted to be representative of the U.S. adult population. Male and female recreational gamblers (n = 1,471) were stratified by frequency of alcohol use on measures of health and gambling. Significant Gender x Alcohol Use group interactions were observed such that moderate-to-high frequency alcohol consumption correlated with heavier gambling in men than in women, whereas such an association did not exist among abstinent or low frequency drinkers. There were few gender differences in the correlations between alcohol consumption and health. Future research should consider gender-related influences when examining alcohol use and gambling behaviors. Desai, R.A., Maciejewski, P.K., Pantalon, M.V., and Potenza, M.N. Gender Differences among Recreational Gamblers: Association with the Frequency of Alcohol Use. *Psychology of Addictive Behaviors*, 20, pp. 145-153, 2006.

#### Cognitive Deficits Were Found In Non-Clinically-Referred College Women Who Were Sexually Abused Prior To Age 18

Clinically-reported sexual abuse is associated with several disorders appearing in adulthood including drug abuse. Teicher and colleagues at Mclean Hospital assessed cognitive effects in community-based subjects recruited by advertisement and assessed college women who endorsed at least three episodes of “forced contact sexual abuse” and were physically healthy on a number of cognitive tests. Some of the subjects had either current or past diagnoses of Major Depressive Disorder, Post-Traumatic Stress Disorder, or General Anxiety Disorder. Results showed that there were a constellation of deficits in some but not all tests. In particular, the abused group had a diminished capacity on a test requiring response inhibition, performed less well on the Math SAT tests (in spite of normal level verbal scores), and demonstrated memory deficits as a function of abuse duration. Navalta, C.P., Polcari, A., Webster, D.M., Boghossian, A., and Teicher, M.H. Effects of Childhood Sexual Abuse on Neuropsychological and Cognitive Function in College Women. *Journal of Neuropsychiatry and Clinical Neuroscience*, 18(1), pp. 45-53, 2006.

#### Genes Contributed to the Covariance between Conduct Disorder and Dependence Vulnerability

Stallings and Hewitt in Crowley’s group at Boulder’s Institute for Behavioral Genetics examined the genetic, shared and non-shared environmental factors contributing to both conduct disorders and dependence vulnerability or to dependence vulnerability alone. The subjects were nearly 900 twin pairs encompassing all five groups—monozygotic males and females, dizygotic males and female, and dizygotic male/female pairs. Symptoms of both disorders were significantly heritable and all three factors contributed to the co-variation: genes contributed 35% of the phenotypic covariance, shared environment contributed 46%, and non-shared environment contributed the remaining 19%. Finally, it was noted that the etiology of the comorbidity was similar in males and females. Button, T.M.M., Hewitt, J.K., Rhee, S.H., Young, S.E., Corley, R.P., Stallings, M.C. Examination of the Causes of Covariation between Conduct Disorder symptoms and Vulnerability to Drug Dependence. *Twin Research and Human Genetics*, 9(1), pp. 38-45, 2006.

## **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

### Is Prenatal Smoking Associated with a Developmental Pattern of Conduct Problems in Young Boys?

Prenatal smoking is robustly associated with increased risk of conduct problems in offspring. This study used a developmental framework to examine the association of exposure with (1) oppositional defiant disorder and attention-deficit/hyperactivity disorder in young boys and (2) the pattern of delinquent behavior at adolescence. Using diagnostic measures and repeated measures of delinquency, the researchers compare exposed and non-exposed boys from the youngest cohort of the Pittsburgh Youth Study (N = 448). Exposed boys were significantly more likely to (1) develop oppositional defiant disorder and comorbid oppositional defiant disorder-attention-deficit/hyperactivity disorder but not attention-deficit/hyperactivity disorder alone and (2) to have an earlier onset of significant delinquent behavior. The early emergence and developmental coherence of exposure-related conduct problems is striking and is consistent with a behavioral teratological model. Phenotypically, exposure-related conduct problems appear to be characterized by socially resistant and impulsively aggressive behavior. Whether prenatal smoking plays an etiological role in or is a risk marker for the development of conduct problems, exposed offspring are at increased risk of an early-starter pathway to conduct problems. Wakschlag, L., Pickett, K., Kasza, K., and Loeber, R. Is Prenatal Smoking Associated with a Developmental Pattern of Conduct Problems in Young Boys? *J Am Acad Child Adolesc Psychiatry*, 45(4), pp. 461-470, 2006.

### The Growth in Marijuana Use among American Youths during the 1990s and the Extent of Blunt Smoking

Marijuana use among American youths and young adults increased substantially during the 1990s. This paper reviews that trend using data collected 1979-2003 by the National Survey on Drug Use and Health (NSDUH). The data suggest that the increase in marijuana use started first among persons age 12-20. Among 18-20 year-olds, the increase started earlier among whites and blacks than Hispanics, among males before females, and surprisingly in areas that are not part of an MSA as opposed to those with a population in excess of a million. Much of the increase in marijuana use could have been attributable to the growing popularity of blunts. Starting in 2000, the NSDUH explicitly asked youth's age 12-17 (but not older respondents) about smoking blunts. Of the 9% of youths who reported past-30-day use of marijuana 2000-03, more than half reported smoking blunts. On the other hand, the data also indicate that blunts have not fully supplanted other ways that youths consume marijuana. Blunts were more common among youths that were black, older, male, and from metropolitan areas. Many blunt smokers reported they had not used marijuana, which suggests that they did not define smoking blunts as marijuana use. Even fewer reported that they had used cigars, suggesting they did not define smoking blunts as cigar use. Golub, A., Johnson, B., and Dunlap, E. The Growth in Marijuana Use among American Youths during the 1990s and the Extent of Blunt Smoking. *J Ethn Subst Abuse*, 4(3-4), pp. 1-21, 2005.

### Childhood and Adolescent Antecedents of Drug and Alcohol Problems A Longitudinal Study

Despite the serious health and economic consequences of drug and alcohol abuse and dependence, few studies have prospectively examined the etiology of this problem in non-clinical populations. This longitudinal study examines childhood and adolescent antecedents of drug and alcohol problems in adulthood among an African American cohort (n=1242; 51% female) from Woodlawn, a neighborhood in Chicago. The participants were followed from age 6 to 32 years, and data were collected in first grade, adolescence, and adulthood. Structural equation modeling showed that, for both males and females, educational attainment was directly associated with a reduced risk for substance use problems. For males, first grade shyness was directly associated with a reduced risk of substance use problems, and adolescent substance use was directly associated with an increased risk. First grade aggression, low family socioeconomic status (SES), and low school bonds were indirectly associated with substance use problems for both males and females. For males, first grade underachievement had an indirect effect, and, for females, first grade shyness and strong parental supervision had indirect effects. This study is among the

first to identify life course trajectories to substance use problems among an African American, community-based population. These results help to identify the targets and timing of interventions that may help to reduce the risk of drug and alcohol problems in adulthood. Fothergill, K., and Ensminger, M. Childhood and Adolescent Antecedents of Drug and Alcohol Problems: A Longitudinal Study. *Drug Alcohol Depend*, 82(1), pp. 61-76, 2006.

#### Estimates of IDU at the National and Local Level in Developing and Transitional Countries, and Gender and Age Distribution

This study sought to update available national and sub national estimates of IDUs in developing/transitional countries, and provide indicative estimates of gender and age distribution. Literature reviews were conducted of both "grey" and published literature, including updates from previously reported estimates, on estimates of IDU population and data sources giving age and gender breakdowns. The scope area was developing/transitional countries and the reference period was 1998-2005. Estimates of IDU numbers were available in 105 countries and 243 sub national areas. The largest IDU populations were reported from Brazil, China, India, and Russia. Sub national areas with the largest IDU populations (35,000-79,000) were: Warsaw (Poland); Barnadul, Irkutsk, Nizhny-Novgorod, Penza, Voronez, St. Petersburg, and Volgograd (Russia); New Delhi and Mumbai (India); Jakarta (Indonesia), and Bangkok (Thailand). By region, Eastern Europe and Central Asia have the largest IDU prevalence, followed by Asia and Pacific. In the Middle East and Africa the median value equals 0.2% and in Latin America and the Caribbean, 0.12%. Greater dispersion of national IDU prevalence's was observed in Eastern Europe and Central Asia, and Asia and Pacific. Sub national areas with the highest IDU prevalence among adults (8-14.9%) were Shymkent (Kazakhstan), Balti (Moldova), Astrakhan, Barnadul, Irkutsk, Khabarovsk, Kaliningrad, Naberezhnyje Chelny, Penza, Togliatti, Volgograd, Voronez, and Yaroslavl (Russia), Dushanbe (Tajikistan), Ashgabad (Turkmenistan), Ivano-Frankivsk and Pavlograd (Ukraine) and Imphal, Manipur (India). Data on the IDU age/gender distributions are scarce or unavailable for many countries. The proportion of IDU men was 70%-90% in Eastern Europe and Central Asia, and there was a marked absence of data on women outside this region. In conclusion, data on IDU prevalence available to national and international policymakers are of an unknown and probably yet to be tested quality. This study provides baseline figures, but steps need to be taken to improve the reporting and assessment of these critical data. Aceijas, C., Friedman, S., Cooper, H., Wiessing, L., Stimson, G., and Hickman, M. Estimates of Injecting Drug Users at the National and Local Level in Developing and Transitional Countries, and Gender and Age Distribution. *Sex Transm Infect*, 82(3), pp. 10-17, 2006.

#### Impact of Marriage on HIV Risk Behaviors

Studies among normative samples generally demonstrate a positive impact of marriage on health behaviors and other related attitudes. This study used a multilevel latent variable approach to examine the impact of marriage on HIV/AIDS risk behaviors and attitudes among impoverished, highly stressed, homeless couples, many with severe substance abuse problems. A multilevel analysis of 368 high-risk sexually intimate married and unmarried heterosexual couples assessed individual and couple-level effects on social support, substance use problems, HIV/AIDS knowledge, perceived HIV/AIDS risk, needle sharing, condom use, multiple sex partners, and HIV/AIDS testing. More variance was explained in the protective and risk variables by couple-level latent variable predictors than by individual latent variable predictors, although some gender effects were found (e.g., more alcohol problems among men). The couple-level variable of marriage predicted lower perceived risk, less deviant social support, and fewer sex partners but predicted more needle sharing. Stein, Nyamathi, Ullman, and Bentler. Impact of Marriage on HIV/AIDS Risk Behaviors among Impoverished, At-Risk Couples: A Multilevel Latent Variable Approach. *AIDS Behav*, 11(1), pp. 87-98, 2007.

### Estimated Numbers of Men and Women Infected with HIV/AIDS in Tijuana, Mexico

Tijuana, Mexico, just south of San Diego, California, is located by the busiest land border crossing in the world. Although UNAIDS considers Mexico to be a country of "low prevalence, high risk," recent surveillance data among sentinel populations in Tijuana suggests HIV prevalence is increasing. The aim of this study was to estimate the number of men and women aged 15 to 49 years infected with HIV in Tijuana. Gender and age-specific estimates of the Tijuana population were obtained from the 2000 Mexican census. Population and HIV prevalence estimates for at-risk groups were obtained from published reports, community based studies, and data from the Centro Nacional para la Prevención y Control del VIH/SIDA (CENSIDA). Age-specific fertility rates for Mexico were used to derive the number of low and high-risk pregnant women. Numbers of HIV-positive men and women were estimated for each at-risk group and then aggregated. A high growth scenario based on current HIV prevalence and a conservative, low growth estimate was determined. A total of 686,600 men and women in Tijuana were aged 15 to 49 years at the time of the 2000 census. Considering both scenarios, the number of infected persons ranged from 1,803 to 5,472 (HIV prevalence: 0.26 to 0.80%). The majority of these persons were men (>70%). The largest number of infected persons were MSM (N = 1,146 to 3,300) and IDUs (N = 147 to 650). Data from this study suggest that up to one in every 125 persons aged 15-49 years in Tijuana is HIV-infected. Interventions to reduce ongoing spread of HIV are urgently needed. Brouwer, K., Strathdee, S., Magis-Rodríguez, C., Bravo-García, E., Gayet, C., Patterson, T., Bertozzi, S., and Hogg, R. Estimated Numbers of Men and Women Infected with HIV/AIDS in Tijuana, Mexico. *J Urban Health*, 83(2), pp. 299-307, 2006.

### Psychiatric Disorders and Their Correlates among Young Adult MDMA Users in Ohio

This study describes the lifetime prevalence, correlates, and age of onset of selected psychiatric disorders among a community sample of MDMA users (n = 402), aged 18 to 30, in Ohio. Participants responded to interviewer-administered questionnaires, including sections of the computerized Diagnostic Interview Schedule for DSM-IV. Fifty-five percent of the sample had at least one lifetime disorder, with major depression (35.3%) and antisocial personality disorder (ASPD) (25.4%) the most common. Proportionately more women were diagnosed with depression, generalized anxiety disorder, and posttraumatic stress disorder (PTSD), while proportionately more men were diagnosed with ASPD. Proportionately more non-White participants had attention deficit/hyperactivity disorder (AD/HD). Higher levels of education were associated with proportionately less PTSD, ASPD, and AD/HD. Higher frequencies of MDMA use were associated with proportionately more ASPD and AD/HD. Comparing the age of first MDMA use with the age of onset for selected psychiatric disorders revealed that for most participants' disorders preceded use. Multivariate analysis revealed participants with more than a high school education were less likely to have experienced a lifetime disorder, while those who had used MDMA more than 50 times were more likely. Variations in the prevalence of psychiatric disorders have practical implications for drug abuse prevention and treatment programs. Falck, R., Carlson, R., Wang, J., and Siegal, H. Psychiatric Disorders and Their Correlates among Young Adult MDMA Users in Ohio. *J Psychoactive Drugs*, 38(1), pp. 19-29, 2006.

### Correlates of Rural Methamphetamine and Cocaine Users: Results from a Multi-state Community Study

Use and production of methamphetamine (MA) has dramatically increased in the United States, especially in rural areas, with concomitant burdens on the treatment and criminal justice systems. However, cocaine is also widely used in many rural areas. The purpose of this article is to contrast MA and cocaine users in three geographically distinct rural areas of the US. Participants were recent not-in-treatment adult cocaine and MA users living in rural Ohio, Arkansas, and Kentucky, who were recruited by a referral recruitment method for sampling hidden community populations. Participants were interviewed for demographics, drug and alcohol use, criminal justice involvement, and psychological distress (Brief Symptom Inventory). The sample of 706 comprised 29% nonwhite and 38% female participants; the average age was 32.6 years; 58% had a high school education or higher, and 32% were employed. In the past 6 months, they had used

either MA only (13%), cocaine only (52%), or both (35%). MA users were seldom (8.2%) nonwhite, but type of stimulant use did not vary by gender. Combined MA/cocaine users reported significantly greater use of alcohol and other drugs, including marijuana and non-prescribed opiates and tranquilizers, and reported significantly higher psychological distress. MA users (with or without cocaine use) had greater odds of recent criminal justice involvement compared with cocaine-only users. There is a clear need for accessible substance-use treatment and prevention services in rural areas of the United States, including services that can address MA, cocaine, poly-drug use, and mental health needs. There is a particular need of these services for poly-drug users. Booth, B., Leukefeld, C., Falck, R., Wang, J., and Carlson, R. Correlates of Rural Methamphetamine and Cocaine users: Results from a Multi-state Community Study. *J Stud Alcohol*, 67(4), pp. 493-501, 2006.

#### Sexual Risk Behaviors among Adolescent Mothers in an HIV Prevention Program

The purpose of this study was to determine the following: (1) whether adolescent mothers in a human immunodeficiency virus (HIV) prevention program had significantly greater perceived self-efficacy and perceived behavioral control to use condoms, and more favorable outcome expectancies and subjective norms regarding condom use than those in a health education control group, 3 months after intervention; and (2) the impact of the 3-month post-intervention theoretical variables on intentions to use condoms at 3 months and sexual risk behaviors at 6 months. Structural equation modeling with latent variables was used to assess the influence of theoretical variables and treatment condition using data from 496 participants (78% Latinas, 18% African-Americans) who completed questionnaires at baseline and at 3- and 6-month follow-up evaluations. Substantial improvements were shown by both groups, with a slight advantage for the HIV prevention group, on all theoretical variables between pretest and the follow-up evaluations. In the predictive model, the intervention group reported significantly fewer sex partners. By using intentions to use condoms as a mediator, greater self-efficacy, hedonistic beliefs, positive subjective norms, and less unprotected sex predicted intentions to use condoms, which, in turn, predicted less unprotected sex. Lower subjective norms modestly predicted multiple partners. Significant indirect paths mediated through intentions to use condoms were observed. These data support a relationship among several constructs from social cognitive theory and the theory of reasoned action, and subsequent sexual risk behaviors. HIV-prevention programs for adolescent mothers should be designed to include these theoretical constructs and to address contextual factors influencing their lives. Koniak-Griffin, D., and Stein, J. Predictors of Sexual Risk Behaviors among Adolescent Mothers in a Human Immunodeficiency Virus Prevention Program. *J Adolesc Health*, 38(3), pp. 297-311, 2006.

#### The Role of Coping and Problem Drinking in Men's Abuse of Female Partners

This article examines the relationship of coping and problem drinking to men's abusive behavior towards female partners. While previous research has demonstrated a consistent association between problem drinking and male abuse of intimate partners, virtually no studies have assessed the role of coping in relation to men's violence. An ethnically diverse sample of 147 men in a court-mandated program for domestic violence offenders completed questionnaires at the first session. Path modeling was conducted to test the extent to which coping and problem drinking predicted both physical and psychological abuse. In addition, the relationships of problem drinking and physical abuse to injury of the men's female partners were examined. Results indicated that both the use of avoidance and problem-solving coping to deal with relationship problems were related indirectly to abusive behavior through problem drinking. Greater use of avoidance coping strategies was more likely among problem drinkers. By contrast, men who used higher levels of problem-solving coping were less likely to be problem drinkers. Avoidance, but not problem-solving coping also was directly and positively related to physical and psychological abuse. Men identified as problem drinkers were more likely to use both physical and psychological abuse. Finally, greater use of physical violence was strongly related to higher levels of injury among female partners, and served to mediate the relationship between problem drinking and injury. Snow, D., Sullivan, T., Swan, S., Tate, D.,

and Klein, I. The Role of Coping and Problem Drinking in Men's Abuse of Female Partners: Test of a Path Model. *Violence Vict*, 21(3), pp. 267-285, 2006.

#### Partner Concurrency among Drug Users with Large Numbers of Partners

The objective of this study was to measure the nature of concurrent sex partnering in two samples of drug users having large numbers of sex partners, and in which some or all participants were trading sex-for-money. The two samples included drug-using male sex workers (MSW) and male and female crack cocaine smokers (CS) having vaginal sex. Three measures were used to reflect the quality of concurrent partnering: the proportion of the samples having concurrent partners; the proportions of the samples having intimate, casual, and sex-for-money of partners; and overlap in concurrent partners. Proportions of each sample having concurrent partners were essentially the same. However, the kinds of concurrent partners and overlap in concurrent partners were significantly different. Concurrent partners in the MSW sample were mostly sex-for-money or sex-for-drugs partners. Most concurrent partners in the CS sample were intimate or casual sex partners. Overlap in concurrent partners was also significantly different. The measure of overlap for the CS sample was three times higher than that of the MSW sample. These data suggest that concurrent sex partnering in the two samples, beyond the proportion having concurrent partners, was different. The patterns of concurrent sex partners in each sample may reflect different reasons for engaging in concurrent partnering, and may be reflected in different overlap scores between the two samples. Efforts should be made in future studies to better capture the complexities of concurrent partnering and to examine the implications of these for disease spread and control. Williams, M., Ross, M., Atkinson, J., Bowen, A., Klovdahl, A., and Timpson, S. An Investigation of Concurrent Sex Partnering in Two Samples of Drug Users Having Large Numbers of Sex Partners. *Int J STD AIDS*, 17(5), pp. 309-314, 2006.

#### Drug Use, Drug Severity, and Help-seeking Behaviors of Lesbian and Bisexual Women

Illicit substance use and abuse may be an important contributor to behavioral health problems of lesbian and bisexual women. This paper describes the nature and extent of self-reported illicit and licit drug use, associated severity, and substance use-related help-seeking behaviors in an urban/metropolitan community sample of sexual minority women in California. Self-administered questionnaire data from 2011 lesbian and bisexual women recruited through multiple strategies were used. Multiple logistic regression was employed to describe patterns of reported drug use and to compare lifetime severity of drug use with demographic characteristics, recent drug use, indicators of current social and emotional problems, and help-seeking behaviors. Drug use, especially marijuana (33% used in the past year), was fairly common. Overall, 16.2% of the women in the study reported lifetime drug use that was associated with self-reported severity of substance use, and another 10.8% indicated moderate-risk use. Extent of lifetime drug use was positively correlated with self-reported recent drug use as well as current life problems. Of the respondents who evidenced more problematic drug use, 41.5% indicated that they had received professional help for a substance use problem, and 16.3% wanted but had not received such help. The women in this study reported elevated rates of illicit drug use that were frequently associated with impairment and specific life problems. A significant proportion wanted and had not received professional treatment for their drug use problems, suggesting an important need to examine pathways by which lesbians and bisexual women can obtain referrals and treatment for substance use problems. Corliss, H., Grella, C., Mays, V., and Cochran, S. Drug Use, Drug Severity, and Help-Seeking Behaviors of Lesbian and Bisexual Women. *J Womens Health (Larchmt)*, 15(5), pp. 556-568, 2006.

#### Prevalence and Correlates of Current Depressive Symptomatology among a Community Sample of MDMA Users in Ohio

Research suggests that MDMA can cause serotonin depletion as well as serotonergic neurodegradation that may result in depression among users of the drug. Several small-scale studies have used various editions of

the Beck Depression Inventory (BDI) to quantify depressive symptomatology among MDMA users. This study represents the largest application of the BDI to date to explore symptoms of current depression among a community sample of young adult MDMA users (n = 402). Internal consistency testing of the BDI-II with this sample revealed Cronbach's alpha = .92. Results show a mean BDI-II score of 9.8, suggesting low levels of depressive symptomatology among study participants. Two-thirds of the sample had scores that placed them in the non-depressed/minimal depression category, while 4.7% had scores indicative of severe depression. Logistic regression analysis revealed that men were significantly less likely than women and people who used opioids were significantly more likely than non-users to have higher levels of depressive symptomatology. Higher lifetime occasions of MDMA use were marginally related to symptoms of serious depression. Falck, R., Wang, J., Carlson, R., and Siegal, H. Prevalence and Correlates of Current Depressive Symptomatology among a Community Sample of MDMA Users in Ohio. *Addict Behav*, 31(1), pp. 90-101, 2006.

#### Factors Associated with Buying and Selling Syringes among IDUs in a Setting of one of North America's Largest Syringe Exchange Programs

Researchers performed analyses of syringe buying and syringe selling among Vancouver injection drug users, recruited from May 1996 and followed up between November 2002 and August 2003, in the context of one of North America's largest syringe exchange programs (SEPs). An interviewer-administered questionnaire, approximately 45 minutes in duration, was used to collect information regarding risk factors for HIV infection and sources of sterile syringes. Seventy participants (15%) reported syringe selling and 122 (26%) reported syringe buying. Syringe sellers were more likely to be female, reside in unstable housing, need help injecting, and have visited the SEP at least once weekly. Syringe buyers were more likely to need help injecting, have difficulty finding new syringes, have binged on drugs, and have visited the SEP at least once weekly. Syringe buying most frequently occurred when the SEP was closed. Kuyper, L., Kerr, T., Li, K., Hogg, R., Tyndall, M., Montaner, J., and Wood, E. Factors Associated with Buying and Selling Syringes among Injection Drug Users in a Setting of one of North America's Largest Syringe Exchange Programs. *Subst Use Misuse*, 41(6-7), pp. 883-899, 2006.

#### Factors Associated With Non-IDUs Having IDU Sex Partners

This study examined factors associated with non-injectors having 1 or more IDUs as sex partners. Data were collected as part of the Self-Help in Eliminating Life Threatening Diseases study, a network-oriented experimental HIV prevention intervention. All eligible participants were administered a detailed face-to-face interview on their socio-demographic background, patterns of drug use, HIV prevention and risk behaviors, and social networks. The sample for these analyses consisted of 863 non-injectors, 97 of whom had 1 or more injection drug-using sex partners. The study found that the factors associated with an increased odds of having 1 or more IDU sex partners were long-term unemployment, increasing proportion of women in network (among male non-injectors), increasing number of recent sex partners (among former injectors), increasing number of injecting non-sex partners in the network, and increasing network size above 15. These findings indicate that there are specific network characteristics associated with non-injectors having injecting sex partners. Howard, D., and Latkin, C. A Bridge Over Troubled Waters: Factors Associated With Non-Injection Drug Users Having Injection Drug-using Sex Partners. *J Acquir Immune Defic Syndr*, 42(3), pp. 325-330, 2006.

#### Substance Use among Adolescent Children with Drug Abusing Fathers

This longitudinal study examined paternal, perceived maternal, and youth risk factors at Time 1 (T1) (e.g., substance use, violent victimization, parental rules) as predictors of the stage of substance use in the adolescent child at Time 2 (T2). Participants (N = 296) consisted of drug-abusing fathers and one of their adolescent children, aged 12 to 20 years. Fathers and youths were each administered structured interviews separately and in private. Adolescents were re-interviewed approximately one year later. Pearson



correlation analyses showed that the paternal, perceived maternal, and youth risk factors were significantly related to adolescent stage of substance use at T2. With an increase in risk factors, there was an increase in T2 stage of substance use in the child. Findings imply that father-oriented treatment programs should focus on how paternal behaviors, such as illegal drug use, inadequate parenting skills, and a poor father-child relationship contribute to youth problem behaviors, including alcohol, tobacco, and illicit drug use. Castro, F., Brook, J., Brook, D., and Rubenstone, E. Paternal, Perceived Maternal, and Youth Risk Factors as Predictors of Youth Stage of Substance Use A Longitudinal Study. *J Addict Dis*, 25(2), pp. 65-75, 2006.

#### Parent Drug Use and Personality Attributes: Child Rearing in African-American and Puerto Rican Young Adults

This study assessed the effect of the interrelationship of mothers' and fathers' tobacco and marijuana use with their personality attributes on some of their child rearing behaviors. A longitudinal design was used to analyze the data of 258 males and females who were seen four times over a 13-year period from early adolescence through young adult parenthood. Thirty-one percent of the multiple regression analyses revealed significant interactions between the effect of tobacco or marijuana use and a personality attribute on child rearing. The majority of these significant interactions suggested that protective personality characteristics were offset by substance use risks resulting in less adequate child rearing. If these results are substantiated in an experimental intervention, it suggests that having resilient personality attributes does not protect against the negative effects of tobacco or marijuana use on child rearing. Brook, Balka, Fei, and Whiteman. The Effects of Parental Tobacco and Marijuana Use and Personality Attributes on Child Rearing in African-American and Puerto Rican Young Adults. *J Child Fam Stud*, 15(2), pp. 153-164, 2006.

#### Contextual Determinants of Condom Use Among Female Sex Exchangers in East Harlem, NYC: An Event Analysis

Recent studies have identified a variety of contexts involving HIV risk behaviors among women who exchange sex for money or drugs. Event analysis was used to identify the individual, relationship, and contextual factors that contribute to these high-risk sex exchange practices. Analyses were conducted on data obtained from 155 drug-using women who reported details of their most recent sex exchange event with male clients. The majority of sex exchange encounters (78%) involved consistent condom use. In multivariable analysis, protective behavior was associated primarily with situational and relationship variables, such as exchange location, substance use, sexual practices, and respondent/client discussion and control. To inform HIV prevention programs targeted to women sex exchangers, research should focus on the contextual determinants of risk, especially with regard to condom-use negotiation and factors involving substance use that adversely affect women's ability to manage protective behavior in the context of sex exchange. McMahon, Tortu, Pouget, Hamid, and Neaigus. Contextual Determinants of Condom Use among Female Sex Exchangers in East Harlem, NYC: An Event Analysis. *AIDS Behav*, 10(6), pp. 731-741, 2006.

#### Borderline Personality and Substance Use in Women

The association between borderline personality disorder (BPD) and substance use disorder (SUD) was examined in a predominantly psychiatric (77.6%) sample of 232 women. BPD proved to be a significant predictor of a lifetime diagnosis of SUD across four different categories: any SUD (including alcohol); alcohol use; drug use; and heroin, cocaine, or poly-substance use. BPD continued to be a predictor of SUD even when the effects of other cluster B and all cluster C PDs were controlled statistically. Antisocial personality disorder generally yielded larger odds ratios than BPD and emerged as a partial mediator of the relation between BPD and SUD. Histrionic PD was the only other PD that showed meaningful relations with SUD. Feske, U., Tarter, R., Kirisci, L., and Pilkonis, P. Borderline Personality and Substance Use in Women. *Am J Addict*, 15(2), pp. 131-137, 2006.

### Prenatal Cocaine Exposure not linked to Child Behavior Problems at Age 7

This study examined the relationship between prenatal cocaine exposure and parent-reported child behavior problems at age 7 years. Data were from 407 African-American children (210 cocaine-exposed, 197 non-cocaine-exposed) enrolled prospectively at birth in a longitudinal study on the neurodevelopmental consequences of in utero exposure to cocaine. Prenatal cocaine exposure was assessed at delivery through maternal self-report and bioassays (maternal and infant urine and infant meconium). The Achenbach Child Behavior Checklist (CBCL), a parent report measure of childhood externalizing and internalizing behavior problems, was completed by the child's current primary caregiver during an assessment visit scheduled when the child was seven years old. Structural equation and GLM/GEE models disclosed no association linking prenatal cocaine exposure status or level of cocaine exposure to child behavior (CBCL Externalizing and Internalizing scores or the eight CBCL subscale scores). This evidence, based on standardized ratings by the current primary caregiver, fails to support hypothesized cocaine-associated behavioral problems in school-aged children with in utero cocaine exposure. A next step in this line of research is to secure standardized ratings from other informants (e.g., teachers, youth self-report). Accornero, V., Anthony, J., Morrow, C., Xue, L., and Bandstra, E. Prenatal Cocaine Exposure: An Examination of Childhood Externalizing and Internalizing Behavior Problems at Age 7 Years. *Epidemiol Psychiatr Soc*, 15(1), pp. 20-29, 2006.

### Psychiatric Disorders among Parents/Caretakers of American Indian Early Adolescents in the Midwest

This study reports prevalence and comorbidity of five DSM-III-R diagnoses (alcohol abuse, alcohol dependence, drug abuse, major depressive episode, and generalized anxiety disorder) among American Indian and Canadian First Nations parents/caretakers of children aged 10-12 years from the Northern Midwest United States and Canada. Lifetime prevalence rates were compared to adults in the National Comorbidity Survey (NCS) and Southwest and Northern Plains cultures from the AI-SUPERPFP study. Native interviewers used computer-assisted personal interviews to administer the University of Michigan Composite International Diagnostic Interview (UM-CIDI) to 861 tribally enrolled parents and caretakers (625 females; 236 males) of 741 tribally enrolled children aged 10-12 years. Fathers/male caretakers ranged in age from 21 years to 68 years with an average age of 41 years; mothers/female caretakers ranged in age from 17 years to 77 years with an average of 39 years. About three-fourths (74.6%) of the adults met lifetime criteria for one of the five disorders; approximately one-third (31.6%) met lifetime criteria for two or more of the five disorders. Prevalence of the substance use disorders was higher than those in the general population (NCS); prevalence of internalizing disorders (major depressive disorder and generalized anxiety disorder) was very similar to those in the general population. Prevalence rates for alcohol abuse among the Northern Midwest adults were higher than those reported for Southwest and Northern Plains Tribes, but rates of alcohol dependency were very similar across cultures. The higher prevalence rates for some mental disorders found for the Northern Midwest are discussed in terms of potential method variance. The Northern Midwest results reflect unique patterns of psychiatric disorders in the ubiquity of substance abuse disorders and the co-occurrence of substance abuse disorders with internalizing disorders. Reducing lifetime occurrences of substance abuse disorders would have an enormous positive impact on the mental health of this population. Whitbeck, Hoyt, Johnson, and Chen. Mental Disorders among Parents/caretakers of American Indian Early Adolescents in the Northern Midwest. *Soc Psychiatry Psychiatr Epidemiol*, 41(8), 2006.

### Drug Use Related to Suicide Ideation in Midwestern American Indian Youth

This study examined correlates of suicidal ideation among 212 American Indian youth who lived on or near three reservations in the upper Midwestern United States. The youths were, on average, 12 years old, and 9.5% reported current thoughts about killing themselves. Females were over 2 times more likely than males to think about suicide. Multivariate logistic regression results indicated that gender, enculturation, negative life events, perceived discrimination, self-esteem, and drug use were related to the likelihood of

thinking about suicide. Drug use was the strongest correlate of suicidal ideation, and both enculturation and perceived discrimination emerged as important culturally specific variables. It was suggested that suicide prevention programs should draw on the strengths of American Indian culture. Yoder, K., Whitbeck, L., Hoyt, D., and LaFromboise, T. Suicidal Ideation among American Indian Youths. *Arch Suicide Res*, 10(2), pp. 177-190, 2006.

## **PREVENTION RESEARCH**

### Results of Two Methods of Delivery of Life Skills Training

The study reported here assessed two methods of delivery of a prevention program called Life Skills Training (LST), implemented in nine rural disadvantaged school districts. This study tested the effectiveness of both standard LST curriculum, which is usually taught by one or two teachers in classes dedicated to substance abuse prevention), and the infused LST (I-LST) condition, which integrates LST and alcohol, tobacco and other drug information into the existing grade-level subject curricula, taught by the regular teachers for these subject areas. The results indicate that neither standard LST nor an infused LST delivery methods were effective for the entire sample, although some encouraging results were found for the females in the study. This study, conducted by researchers independent of the original LST program, is useful for school decision makers in determining what programs are most effective with which groups. It included all students with parental permission, controlling for prior use levels, unlike some previous LST studies. The results of the program, as implemented by regular classroom teachers, reflect many issues relevant to recruitment, training, implementation, adaptation, and institutionalization of prevention programming. Vicary, J., Smith, E., Swisher, J., Hopkins, A., Elek, E., Bechtel, L., and Henry, K. Results of a 3-year Study of Two Methods of Delivery of Life Skills Training. *Health Educ Behav*, 33(3), pp. 325-339, 2006.

### Prenatal Care Providers' Role in Reducing Risk for Smoking, Alcohol Use, Illicit Drug Use and Domestic Violence during Pregnancy

This qualitative study explored prenatal care providers' methods for identifying and counseling pregnant women to reduce or stop 4 high risk behaviors: smoking, alcohol use, illicit drug use, and the risk of domestic violence. Six focus groups were conducted (five with OB/Gyn physicians, one with nurse practitioners and certified nurse midwives), with 49 care providers, using open-ended questions that assessed: providers' specific issues or interests in preventing the risk behaviors; providers' reactions and opinions to ACOG recommendations for handling the risk behaviors and whether providers feel they can have a positive impact on the risk behaviors; providers' challenges with assessing and counseling patients; providers' opinions about whether pregnancy is an opportune time to effect behavior change; whether providers should counsel patients about risk behaviors; best ways for providers to ask about the risky behaviors; and specific strategies providers have found effective for the risky behaviors. Three major themes emerged: (1) specific risk-prevention tactics or strategies exist that are useful during pregnancy; (2) some providers address patients' isolation or depression; and (3) providers can adopt a policy of "just chipping away" at risks. Specific tactics included normalizing risk prevention, using specific assessment techniques and counseling strategies, employing a patient-centered style of smoking reduction, and involving the family. Providers generally agreed that addressing behavioral risks in pregnant patients is challenging, and that patient-centered techniques and awareness of patients' social contexts help patients disclose and discuss risks. Herzig, K., Danley, D., Jackson, R., Petersen, R., Chamberlain, L., and Gerbert, B. Seizing the 9-month Moment: Addressing Behavioral Risks in Prenatal Patients. *Patient Educ Couns*, 61(2), pp. 228-235, 2006.

### HIV Risk is Common among Older (Age 49-60) Substance Users, Particularly Men

Gender differences and other factors associated with current heroin and cocaine use were assessed among middle-aged drug users in New York City. Baseline data were merged from 2 studies of men and women with or at risk for HIV infection, and those age 49-60 years who had ever used heroin or cocaine were selected for analysis. HIV-antibody status, drug-use history, and psychosocial and sociodemographic data were examined. Logistic regression models were used to assess factors independently associated with current heroin and cocaine use. Of 627 persons who ever had used heroin and/or cocaine, 250 (39.9%) reported using these drugs within 6 months of the study interview. Men were more likely to be using drugs currently, compared with women (42.3% vs. 28.2%;  $p = .007$ ). In multivariate analysis, men, unemployed persons, and HIV-seronegative persons were more likely to be using heroin or cocaine at the time of the interview. In addition, current marijuana users, persons drinking alcohol on a daily basis, and persons who had been homeless in the 6 months before the interview were also more likely to be using these drugs. It appears that a relatively high proportion of middle-aged substance users with or at risk for HIV infection, especially men, may continue to use illicit drugs into the sixth decade of life. Special attention needs to be given to aging and gender issues in framing HIV-prevention and drug-treatment programs. Hartel, D.M., Schoenbaum, E.E., Lo, Y., and Klein, R.S. Gender Differences in Illicit Substance Use among Middle-Aged Drug Users with or at Risk for HIV Infection. *Clin Infect Dis*, 43(4), pp. 525-531, 2006.

### In India Sixth Graders Use More Tobacco Than Eighth Graders

The epidemic of tobacco use is shifting from developed to developing countries, including India, where increased use is expected to result in a large disease burden in the future. Changes in prevalence of tobacco use in adolescents are important to monitor, since increased use by young people might be a precursor to increased rates in the population. A survey of 11,642 students in the sixth and eighth grades in 32 schools in Delhi and Chennai, India about their tobacco use and psychosocial factors related to onset of tobacco use was conducted. Schools were representative of the range of types of school in these cities. Students who were in government schools, male, older, and in sixth grade were more likely to use tobacco than students who were in private schools, female, younger, and in eighth grade. Students in sixth grade were, overall, two to four times more likely to use tobacco than those in eighth grade. 24.8% (1529 of 6165) of sixth-grade students and 9.3% (509 of 5477) of eighth-grade students had ever used tobacco; 6.7% (413 of 6165) and 2.9% (159 of 5477), respectively, were current users. Psychosocial risk factors were greater in sixth-grade than in eighth-grade students. The increase in tobacco use by age within each grade was larger in sixth grade than in eighth grade in government schools, with older sixth-grade students at especially high risk. The finding that sixth-grade students use significantly more tobacco than eighth-grade students is unusual, and might indicate a new wave of increased tobacco use in urban India that warrants confirmation and early intervention. Reddy, K., Perry, C., Stigler, M., and Arora, M. Differences in Tobacco use Among Young People in Urban India by Sex, Socioeconomic Status, Age, and School Grade: Assessment of Baseline Survey Data. *Lancet*, 367(9510), pp. 589-594, 2006.

### Direct and Mediated Effects of Aggressive Marital Conflict on Child Aggressive-Disruptive Behavior

Direct associations between aggressive marital conflict and child aggressive-disruptive behavior at home and school were explored in this cross-sectional study of 360 kindergarten children. In addition, mediated pathways linking aggressive marital conflict to maternal harsh punishment to child aggressive-disruptive behavior were examined. Moderation analyses explored how the overall frequency of marital disagreement might buffer or exacerbate the impact of aggressive marital conflict on maternal harsh punishment and child aggressive-disruptive behavior. Participants were a sub-sample of the normative and high risk groups in the Fast Track Project, and were included in this analysis if the biological mother of the study child was married and living with a spouse, and if the mother completed the measure of aggressive marital conflict during the child's kindergarten year. The Hierarchical regressions revealed direct pathways linking aggressive marital conflict to child aggressive-disruptive behavior at home and school, and maternal harsh

punishment partially mediated the pathway linking aggressive marital conflict to child aggressive-disruptive behavior at home. Further analyses revealed that rates of marital disagreement moderated the association between aggressive marital conflict and child aggressive-disruptive behavior at home, with an attenuated association at high rates of marital disagreement as compared with low rates of marital disagreement. These preliminary findings suggest that marital conflict may be another important target for the prevention of child conduct problems and related high-risk trajectories. Erath, S., Bierman, K., and Bierman, K.C. Aggressive Marital Conflict, Maternal Harsh Punishment, and Child Aggressive-disruptive Behavior: Evidence for Direct and Mediated Relations. *J Fam Psychol*, 20(2), pp. 217-226, 2006.

### Influences of Social Norms on Early Adolescent Substance Use

Social norms play an important role in adolescent substance use. Norm focus theory (Cialdini et al., 1990) distinguishes three types of norms: injunctive, descriptive, and personal. This study examines the relative influence of these three norms, as well as the moderating effects of gender and ethnicity, on the concurrent substance use of 2,245 Mexican or Mexican-American students, 676 other Latino students, 756 non-Hispanic White students, and 353 African-American students. Personal norms appear to be the strongest significant predictor of substance use. Descriptive, parental injunctive, and friend injunctive norms also demonstrate significant, though weaker influences. Controlling for intentions reduces the predictive ability of each type of norm, especially personal norms. Gender moderates the relationship between norms and substance use with the relationships generally stronger for males. Personal norms act as stronger predictors of some types of substance use for Mexican/Mexican Americans. Elek, E., Miller-Day, M., and Hecht, M.L. Influences of Personal, Injunctive, and Descriptive Norms on Early Adolescent Substance Use. *Journal of Drug Issues*, 36(1), pp. 147-171, 2006.

### Victimization and Health among Indigent Young Women in the Transition to Adulthood: A Portrait of Need

To understand victimization by physical and sexual violence and its association with physical and behavioral health in a probability sample of sheltered homeless and low-income-housed young women in the transition to adulthood (ages 18 through 25). Participants were 224 women ages 18 through 25 who were selected by means of a stratified random sample from 51 temporary shelter facilities (N = 94) and 66 Section 8 private project-based Housing and Urban Development (HUD)-subsidized apartment buildings (N = 130) in Los Angeles County, California. Women completed structured interviews. Forty-one percent of the sample had been physically or sexually victimized as children and 51% had been victimized since turning 18. Young women who experienced victimization were significantly ( $p < .05$ ) more likely than non-victimized women to have a sexually-transmitted disease (STD) other than HIV/AIDS or Hepatitis B or C, vaginal discharge or bleeding and pelvic pain in the past 6 months, and past-12 month screening diagnoses of drug abuse/dependence and depression. Victimized women were also significantly more likely to use alcohol to intoxication and drugs, including crack and amphetamines, during the past 6 months, and to have experienced psychological distress and poor self-esteem. This study highlights striking rates of victimization and its association with physical and behavioral health problems among indigent young women during the period of emerging adulthood. This portrait of need communicates an urgency to develop multifaceted programs for such women to help them successfully navigate the transition to adulthood and realize their full potential as adults. Wenzel, S., Hambarsoomian, K., D'Amico, E., Ellison, M., and Tucker, J. Victimization and Health among Indigent Young Women in the Transition to Adulthood: A Portrait of Need. *J Adolesc Health*, 38(5), pp. 536-543, 2006.

### HIV Infection is a Significant Risk Factor for Human Papillomavirus (HPV) Among Drug Using Women

A total of 230 female former and current drug users in New York City were prospectively studied at 6 month intervals. Each assessment included interviews, HIV testing, and cervicovaginal lavage sampling for human papillomavirus (HPV). Incidence rates of and factors associated with HPV infections of all

types and high-risk types were analyzed. Baseline median age was 40 years (range 24-65); 62% of women were Hispanic, 20% black, and 16% white; 54 (24%) were HIV seropositive; 172 (75%) were without detectable HPV; 58 (25%) had only low-risk or untypeable HPV. The incidence rate for any HPV 9.5/100 person-years type and for high-risk types was 4.8/100 person-years. HIV-seropositive women had a significantly increased hazard rate for any HPV (HRadj: 3.4; 95% CI: 1.4 to 8.0) and for high-risk HPV (HRadj 3.0; 95% CI: 1.4 to 6.6), adjusted for race, sexual behaviors, condom use, and history of other sexually transmitted infections. HIV infection was independently associated with a substantial and significantly increased risk for any and for high-risk genital HPV infection and was the most important risk factor found. Dev, D., Lo, Y., Ho, G.Y., Burk, R.D., and Klein, R.S. Incidence of and Risk Factors for Genital Human Papillomavirus Infection in Women Drug Users. *J Acquir Immune Defic Syndr*, 41(4), pp. 527-529, 2006.

## **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

### Characterizing Nicotine Withdrawal in Pregnant Cigarette Smokers

The aim of this study was to characterize nicotine withdrawal and craving in pregnant cigarette smokers. These data were collected as part of prospective clinical trials assessing the efficacy of voucher-based incentives to promote abstinence from cigarette smoking during pregnancy and postpartum. Results from 27 abstainers and 21 smokers during the first 5 days of a cessation attempt were examined. Abstinent pregnant smokers reported more impatience, anger and difficulty concentrating than did smokers. The results also suggest that pregnant smokers generally may have elevated baseline levels of withdrawal, which need to be considered in the design and analysis of future studies. Heil, S.H., Higgins, S.T., Mongeon, J.A., Badger, G.J., and Bernstein, I.M. Characterizing Nicotine Withdrawal in Pregnant Cigarette Smokers. *Experimental and Clinical Psychopharmacology*, 14, pp. 165-170, 2006.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

### Cognitive Deficits Predict Low Treatment Retention in Cocaine Dependent Patients

Impaired cognition predicted treatment dropout from cognitive behavioral therapy (CBT) in a small sample of cocaine dependent patients. To further address the role of impaired cognition in retention and treatment outcome of cocaine-dependent patients in CBT, the P.I. expanded a previous investigation to a larger sample, added depressed cocaine patients, and added an additional cognitive assessment. Fifty-six cocaine dependent patients receiving CBT in outpatient clinical trials were assessed for cognitive performance at treatment entry with the computerized MicroCog (MC) and the Wisconsin Card Sort Test (WCST). Treatment completion was defined as 12 or more weeks. Treatment dropouts had significantly lower MC scores (poorer cognitive functioning) than completers on attention, memory, spatial ability, speed, accuracy, global functioning, and cognitive proficiency, with effect sizes in the moderate to large range. These findings were not affected by depression, demographics (age, gender, race, sex, marital status) or drug use (years of cocaine use or average weekly cocaine expenditure in the prior 30 days). In contrast, patients' performance on the WCST was in the average or near-average range, and WCST scores did not differentiate between completers and dropouts. Consistent with previous research, results suggest that mild cognitive impairments (< or =1 S.D. below the mean) negatively affect retention in outpatient CBT treatment for cocaine dependence. Future studies should examine whether there are specific effects of different executive functioning abilities on treatment outcome. Modified behavioral and pharmacologic interventions should be considered to target mild cognitive impairments to improve substance treatment outcome. Aharonovich, E., Hasin, D. S., Brooks, A. C., Liu, X., Bisaga, A., & Nunes, E. V. Cognitive Deficits Predict Low Treatment Retention in Cocaine Dependent Patients. *Drug Alcohol Depend.*, 81, pp. 313-322, 2006.

### Preliminary Observations of Paranoia in a Human Laboratory Study of Cocaine

Cocaine-induced paranoia (CIP) has recently shown a relationship to genetic factors that may moderate disulfiram treatment response in cocaine-dependent individuals. However, little research has examined CIP under controlled laboratory conditions. This study examined subjective and physiological responses to a 0.4 mg/kg dose of smoked cocaine in a human laboratory setting with 23 male and 21 female cocaine users. Twenty-nine of 44 participants (67%) reported feeling Paranoid/Suspicious in response to cocaine. Those who reported feeling Paranoid/Suspicious were more likely to be older and male. Further studies are warranted to investigate the mechanisms of gender influence on CIP, and CIP in pharmacotherapy development for cocaine-dependent individuals. Mooney, M., Sofuoglu, M., Dudish-Poulsen, S., and Hatsukami, D.K. Preliminary Observations of Paranoia in a Human Laboratory Study of Cocaine. *Addict. Behav.*, 31, pp. 1245-1251, 2006.

## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE AND INFECTIONS**

### Comorbid Medical and Psychiatric Conditions and Substance Abuse in HCV Infected Persons on Dialysis

The burden of comorbidity in the Hepatitis C virus (HCV) infected persons on dialysis is unknown. Authors identified all HCV infected and uninfected subjects in the United States Renal Data System in the years 1997-1998 using ICD-9 codes. Controls were matched on the date of first dialysis. ICD-9 codes and claims data was used to identify medical and psychiatric comorbidities. Authors identified 5,737 HCV infected persons and 11,228 HCV uninfected subjects. HCV infected subjects were younger, more likely to be black race and male and more likely to have the following comorbidities: hypertension; hepatitis B; cirrhosis; wasting; anemia; human immunodeficiency virus (HIV) infection; major depression; mild depression; bipolar disorder; schizophrenia; post-traumatic stress disorder; drug use; alcohol use; smoking and less likely to have the following comorbidities: coronary artery disease; stroke; peripheral vascular disease; diabetes; cancer; erythropoietin use. After adjusting for age, gender and race, HCV infected subjects were more likely to have hypertension, hepatitis B, cirrhosis, wasting, anemia and HIV infection and less likely to have coronary artery disease and stroke. Authors concluded that HCV infected persons on dialysis are more likely to have psychiatric comorbidities and substance abuse, as well as certain medical comorbidities. These factors should be considered when developing future intervention strategies. Butt, A.A., Evans, R., Skanderson, M., and Shakil, A.O. Comorbid Medical and Psychiatric Conditions and Substance Abuse in HCV Infected Persons on Dialysis. *J Hepatol.*, 44(5), pp. 864-868, 2006.

### (C2) Saliva, Breast Milk, and Mucosal Fluids in HIV Transmission

The oral environment has received various amounts of attention in association with HIV infection and pathogenesis. Since HIV infection occurs through mucosal tissue, oral factors-including tissue, fluids, and compartments-are of interest in furthering our understanding of the diagnosis, infectivity, transmission, and pathogenesis of disease. This report reviews: (1) HIV testing and diagnoses with oral fluids; (2) post-natal acquisition of HIV in association with breast-feeding from HIV-positive mothers; and (3) oral sex and HIV transmission. In the first, authors examine how oral fluids are used to detect HIV infection and review current consensus on the role of salivary molecules as markers for immunosuppression. Second, lactation-associated HIV acquisition is reviewed, with special consideration of emerging issues associated with the impact of anti-retroviral therapies. Last, authors consider current data on the risk of HIV infection in association with oral sex. Investigation of these diverse topics has a common goal: understanding how HIV presents in the oral environment, with an aim to rapid and accessible HIV diagnosis, and improved prevention and treatment of infection. Page-Shafer, K., Sweet, S., Kassaye, S., and Ssali, C. (C2) Saliva, Breast Milk, and Mucosal Fluids in HIV Transmission. *Adv Dent Res.*, 19, pp. 152-157, 2006.

### Cardiovascular Function in Multi-Ethnic Study of Atherosclerosis: Normal Values by Age, Sex, and Ethnicity

MRI provides accurate and high-resolution measurements of cardiac anatomy and function. The purpose of this study was to describe the imaging protocol and normal values of left ventricular (LV) function and mass in the Multi-Ethnic Study of Atherosclerosis (MESA). Eight hundred participants (400 men, 400 women) in four age strata (45-54, 55-64, 65-74, 75-84 years) were chosen at random. Participants with the following known cardiovascular risk factors were excluded: current smoker, systolic blood pressure > 140 mm Hg, diastolic blood pressure > 90 mm Hg, fasting glucose > 110 mg/dL, total cholesterol > 240 mg/dL, and high-density lipoprotein (HDL) cholesterol < 40 mg/dL. Cardiac MR images were analyzed using MASS software (version 4.2). Mean values, SDs, and correlation coefficients in relationship to patient age were calculated. There were significant differences in LV volumes and mass between men and women. LV volumes were inversely associated with age ( $p < 0.05$ ) for both sexes except for the LV end-systolic volume index. For men, LV mass was inversely associated with age (slope =  $-0.72$  g/year,  $p = 0.0021$ ), but LV mass index was not associated with age (slope =  $-0.179$  g/m<sup>2</sup>/year,  $p = 0.075$ ). For women, LV mass (slope =  $-0.15$  g/year,  $p = 0.30$ ) and LV mass index (slope =  $0.0044$  g/m<sup>2</sup>/year,  $p = 0.95$ ) were not associated with age. LV mass was the largest in the African-American group (men,  $181.6 \pm 35.8$  [SD] g; women,  $128.8 \pm 28.1$  g) and was smallest in the Asian-American group (men,  $129.1 \pm 20.0$  g; women,  $89.4 \pm 13.3$  g). The normal LV differs in volume and mass between sexes and among certain ethnic groups. When indexed by body surface area, LV mass was independent of age for both sexes. Studies that assess cardiovascular risk factors in relationship to cardiac function and structure need to account for these normal variations in the population. Natori, S., Lai, S., Finn, J.P., Gomes, A.S., Hundley, W.G., Jerosch-Herold, M., Pearson, G., Sinha, S., Arai, A., Lima, J.A., and Bluemke, D.A. Cardiovascular Function in Multi-Ethnic Study of Atherosclerosis: Normal Values by Age, Sex, and Ethnicity. *AJR Am J Roentgenol*, 186(6 Suppl 2):S357-365, 2006.

### Caffeine Metabolites in Umbilical Cord Blood, Cytochrome P-450 1A2 Activity, and Intrauterine Growth Restriction

Studies investigating antenatal caffeine consumption and reproductive outcomes show conflicting results, and most studies have used maternal self-reported caffeine consumption to estimate fetal exposure. This study ( $n=1,606$ ) was specifically designed to test the association of caffeine and its primary metabolites in umbilical cord blood with intrauterine growth restriction (IUGR). Pregnant women were recruited from 56 obstetric practices and 15 clinics affiliated with six hospitals in Connecticut and Massachusetts between September 1996 and January 2000. In an adjusted model including caffeine only, levels in all quartiles were associated with reduced risk of IUGR. In adjusted analyses including paraxanthine and caffeine, serum paraxanthine levels in the highest quartile were associated with increased risk of IUGR (adjusted odds ratio=3.29, 95% confidence interval: 1.17, 9.22); caffeine remained protective. These conflicting findings suggest that cytochrome P-450 1A2 (CYP1A2) metabolic activity may be associated with IUGR, so the ratio of paraxanthine to caffeine was then modeled. The likelihood of IUGR increased 21% for every one standard deviation change in the ratio (adjusted odds ratio=1.21, 95% confidence interval: 1.07, 1.37), suggesting that CYP1A2 activity, and not the absolute levels of paraxanthine, influences fetal growth. No associations were observed between caffeine or any metabolites and preterm delivery. Grosso, L.M., Triche, E.W., Belanger, K., Benowitz, N.L., Holford, T.R., and Bracken, M.B. Caffeine Metabolites in Umbilical Cord Blood, Cytochrome P-450 1A2 Activity, and Intrauterine Growth Restriction. *Am J Epidemiol.*, 163(11), pp. 1035-1041, 2006.

### Caffeine Metabolism, Genetics, and Perinatal Outcomes: A Review of Exposure Assessment Considerations During Pregnancy

The purpose of this study was to review the methodologic issues complicating caffeine exposure assessment during pregnancy; to discuss maternal and fetal caffeine metabolism, including genetic



polymorphisms affecting caffeine metabolism; and to discuss the endogenous and exogenous risk factors known to influence caffeine metabolism. Methods consisted of a review of the relevant literature. Results indicated that there is wide inter-individual variation in caffeine metabolism, primarily due to variations in CYP1A2 enzyme activity. Some variability in CYP1A2 activity is due to genetic polymorphisms in the CYP1A2 gene that can cause increased or decreased inducibility of the enzyme. Considerable evidence exists that maternal caffeine metabolism is influenced by a variety of endogenous and exogenous factors and studying the genetic polymorphisms may improve understanding of the potential effects of caffeine and its metabolites on perinatal outcomes. There is substantial evidence that measurement of maternal, fetal, and neonatal caffeine metabolites may allow for a more precise measure of fetal caffeine exposure. Authors conclude that research on the genetic polymorphisms affecting caffeine metabolism may further explain the potential effects of caffeine and its metabolites on perinatal outcomes. Grosso, L.M. and Bracken, M.B. Caffeine Metabolism, Genetics, and Perinatal Outcomes: A Review of Exposure Assessment Considerations during Pregnancy. *Ann Epidemiol.*, 15(6), pp. 460-466, 2005.

## **SERVICES RESEARCH**

### Survival Benefits of AIDS Treatment

As widespread adoption of potent combination antiretroviral therapy (ART) reaches its tenth year, the objective of this study was to quantify the cumulative survival benefits of acquired immunodeficiency syndrome (AIDS) care in the United States. Eras were defined that corresponded to advances in standards of human immunodeficiency virus (HIV) disease care, including opportunistic infection prophylaxis, treatment with ART, and the prevention of mother-to-child transmission (pMTCT) of HIV. Per-person survival benefits for each era were determined using a mathematical simulation model. Published estimates provided the number of adult patients with new diagnoses of AIDS who were receiving care in the United States from 1989 to 2003. Compared with survival associated with untreated HIV disease, per-person survival increased 0.26 years with *Pneumocystis jirovecii* pneumonia prophylaxis alone. Four eras of increasingly effective ART in addition to prophylaxis resulted in per-person survival increases of 7.81, 11.05, 11.57, and 13.33 years, compared with the absence of treatment. Treatment for patients with AIDS in care in the United States since 1989 yielded a total survival benefit of 2.8 million years. pMTCT averted nearly 2900 infant infections, equivalent to 137,000 additional years of survival benefit. In conclusion, at least 3.0 million years of life have been saved in the United States as a direct result of care of patients with AIDS, highlighting the significant advances made in HIV disease treatment. Walensky, R., Paltiel, A., Losina, E., Mercincavage, L., Schackman, B., Sax, P., Weinstein, M., and Freedberg, K. The Survival Benefits of AIDS Treatment in the United States. *J Infect Dis*, 194(1), pp. 11-19, 2006.

### Prevalence of DSM/ICD-Defined Nicotine Dependence

In this study techniques of systematic review were used to estimate for adults (1) the lifetime and current prevalence of DSM/ICD-defined nicotine dependence and (2) the prevalence of individual DSM/ICD dependence criteria. Systematic computer searches and other methods located eleven population-based surveys of adults ( $\geq 18$  year olds) and two of young adults (18-30 year olds). In the USA and Germany, about 25% of adults had been dependent on nicotine in their lifetime, including 15% who were currently dependent. Similar or higher rates were seen in Asian men but  $<5\%$  of Asian women had been dependent. About a third of ever-smokers and half of current smokers either had been or were currently dependent on nicotine and this did not consistently differ by age, country or sex. Impaired control over tobacco use was the most commonly endorsed criteria and giving up activities to use and spending lots of time with nicotine were the least commonly endorsed. This study is consistent with others that show that nicotine dependence is one of the most common mental disorders; however, about half of current smokers do not meet DSM/ICD dependence criterion, perhaps because they have not tried to stop, nicotine is more legal than other drugs of dependence, and nicotine causes fewer behavioral disturbances than other drugs of abuse. However none of these possible explanations have been empirically tested as yet. Hughes, J.R., Helzer,

J.E., and Lindberg, S.A. Prevalence of DSM/ICD-defined Nicotine Dependence. *Drug Alcohol Depend*, 85(2), pp. 91-102, 2006.

#### Utilization of Medicaid Substance Abuse Services among Adolescents

This study examined race and gender disparities in utilization of substance abuse treatment among adolescents enrolled in Medicaid in Tennessee. By using Medicaid enrollment, encounter, and claims data, utilization of substance abuse services for the population of adolescents enrolled in TennCare was examined in two ways. The first utilization measure considered annual utilization rates and probability of use of substance abuse services for the statewide population of enrolled adolescents (approximately 170,000 per year). The second examined the age at which the first substance abuse service was received for the 8,473 youths who had that service paid for by TennCare during state fiscal years 1997 to 2001. Proportionally, among adolescents, more whites than blacks and more males than females used substance abuse services. The disparities were greater than differences in prevalence rates explain. Black females had the greatest disparity in service utilization. Whites and females received their first substance abuse service at a younger age than blacks or males in this Medicaid population. However, the age difference may not be clinically significant. The low utilization rates, in general, and the disparities in service use by race and gender raise questions about the identification of substance use problems at both provider and system levels. Heflinger, C., Chatman, J., and Saunders, R. Racial and Gender Differences in Utilization of Medicaid Substance Abuse Services among Adolescents. *Psychiatr Serv*, 57(4), pp. 504-511, 2006.

#### Gender Differences in the Prediction of Condom Use among Incarcerated Juvenile Offenders

This study seeks to predict condom-protected vaginal intercourse among incarcerated youth using the Information-Motivation-Behavioral skills (IMB) model as the theoretical framework. The IMB model is a three-factor conceptualization of HIV preventive behavior including information on HIV/AIDS transmission and prevention methods, motivation to act on the knowledge and change risky behavior, and behavioral skills in performing the specific prevention act. Data was collected from youth held in a detention center located in a Southern city. Adolescents 13 years of age or older and recently incarcerated (within 3 days of booking) were eligible for the study. The study sample included 523 adolescents (328 male and 195 female). Participants were predominately African-American (90%), with an average age of 15, and average level of highest education was 9th grade. Survey data was collected for a self-report measure of AIDS knowledge, pre-condom peer influence, risk perception, condom attitudes, condom use self-efficacy, frequency of vaginal intercourse, and frequency of condom-protected vaginal intercourse. Results revealed that being male, peer influence, positive condom attitudes, and condom self-efficacy significantly predicted condom use. Separate gender analyses revealed that condom use among males was predicted by peer influence and positive condom attitudes, whereas condom use among females was predicted by peer influence, self-efficacy, and condom attitudes. Compared with males, females reported significantly greater knowledge, less peer influence, higher perceived risk for infection, more positive condom attitudes, and more self-efficacy. Despite these findings, females reported less condom use than males. The authors conclude that females find it difficult to use condoms consistently despite their awareness. They suggest that power imbalances and other dynamics operating within relationships between boys and girls need to be explored further in developing effective HIV prevention interventions. Robertson, A.A., Stein, J.A., and Baird-Thomas, C. Gender Differences in the Reduction of Condom Use among Incarcerated Juvenile Offenders: Testing the Information-motivation-behavior Skills (IMB) Model. *J Adolesc Health*, 38(2006), pp. 18-25, 2006.

### Pregnant Women Treated in Women-only Versus Mixed-gender Programs Receive More Services

This study compared characteristics of pregnant women treated in women-only (WO) and mixed-gender (MG) substance abuse treatment programs and compared services provided by these two types of programs. Participants were 407 pregnant women who were admitted to 7 WO programs and 29 MG programs in 13 counties across California during 2000–2002. Pregnant women treated in WO programs demonstrated greater severity in drug use, legal problems, and psychiatric problems than those treated in the MG programs. They were also less likely to be employed and more likely to be homeless. Women-only programs were more likely to offer childcare, children's psychological services, and HIV testing. The greater problem severity of pregnant women treated in WO programs suggests that these specialized services are filling an important gap in addiction services, although further expansion is warranted in psychiatric, legal, and employment services. Hser, Y., and Niv, N. Pregnant Women in Women-Only and Mixed-Gender Substance Abuse Treatment Programs: A Comparison of Client Characteristics and Program Services. *J Behav Health Serv Res*, 33(4), pp. 431-442, 2006.

### Exposure to Transphobia and HIV Risk Behavior Among Transgendered Women

This study examined the relationship between exposure to transphobia -societal discrimination and stigma of individuals who do not conform to traditional notions of gender--and risk for engaging in unprotected receptive anal intercourse (URAI) among 327 transgendered women of color. Overall, 24% of participants had engaged in URAI at least once in the past 30 days. Individuals who self-identified as pre-operative transsexual/transgendered women were significantly more likely than self-identified females to have engaged in URAI. Although exposure to transphobia was not independently related to URAI, an interaction between age and experiencing discrimination was observed. Among transgendered women 18-25 years old, those reporting higher levels of exposure to transphobia had a 3.2 times higher risk for engaging in URAI compared to those reporting lower levels. Findings from this study corroborate the importance of exposure to transphobia on HIV risk, particularly among transgendered young adults. Sugano, E., Nemoto, T., and Operario, D. The Impact of Exposure to Transphobia on HIV Risk Behavior in a Sample of Transgendered Women of Color in San Francisco. *AIDS Behav*, 10(2), pp. 217-225, 2006.

## **INTERNATIONAL RESEARCH**

Alumni of the NIDA International Program research training and exchange programs authored or coauthored the following articles indexed by PubMed:

### Prevalence and Correlates of Drug Use Disorders in Mexico

The objective of this study was to describe the prevalence of drug use disorders, the correlates of drug use, and the utilization of specialized treatment services for drug users among the Mexican urban population 18-65 years old. The data were collected in 2001 and 2002 in the Mexican National Comorbidity Survey. The sample design was stratified probabilistically for six geographical areas of the country in a multistage process for census count areas, city blocks, groups of households, and individuals. The data were weighted, taking into account the probability of selection and the response rate. The information was collected using a computerized version of the World Mental Health Survey edition of the Composite International Diagnostic Interview. The weighted response rate for individuals was 76.6%. Overall, 2.3% of the population reported any illicit use of drugs in the preceding 12 months; marijuana and cocaine were the substances most often used. Low levels of education were significantly associated with use, abuse, and dependence. Use of any drug was significantly more common among those who were in the youngest age group (18-29 years), were male, or were living in the Northwest region of the country. Overall, 1.4% had a lifetime history of drug abuse or dependence, with this being much more common for men (2.9%) than for women (0.2%). The 12-month prevalence of drug abuse or dependence was 0.4% overall (0.9% for men, and 0.0% for women). The rate of treatment during the preceding 12 months for those with the 12-month

criteria for abuse or dependence was 17.1%; 14.8% were seen in specialized treatment centers; 2.8% reported having attended self-help groups. A noticeable number of Mexicans have a drug use disorder, but demand for treatment is limited, in part due to stigma. These results indicate that there is an urgent need to organize the specialized services for persons with a substance abuse disorder according to the prevalence of dependence on different substances and the variation in prevalence in the different regions of the country. Medina-Mora, M.E., Borges, G., Fleiz, C., Benjet, C., Rojas, E., Zambrano, J., Villatoro, J., and Aguilar-Gaxiola, S. *Rev Panam Salud Publica*. 19(4), pp. 265-276, April 2006. INVEST Fellow: Guilherme Borges, Mexico, 1997-1998.

#### Leber's Hereditary Optic Neuroretinopathy (LHON) Associated with Mitochondrial DNA Point Mutation G11778A in Two Croatian Families

Leber's hereditary optic neuroretinopathy (LHON) is manifested as a bilateral acute or subacute loss of central vision due to optic atrophy. It is linked to point mutations of mitochondrial DNA, which is inherited maternally. The most common mitochondrial DNA point mutations associated with LHON are G3460A, G11778A and T14484C. These mutations are linked with the defects of subunits of the complex I (NADH-dehydrogenase-ubiquinone reductase) in mitochondria. The G11778A mitochondrial DNA point mutation is manifested by a severe visual impairment. In this paper two Croatian families with the LHON G11778A mutation are presented. Three LHON patients from two families were younger males who had the visual acuity of 0.1 or below, the ophthalmoscopy revealed telangiectatic microangiopathy and papilloedema, while Goldmann kinetic perimetry showed a central scotoma. The mothers and female relatives were LHON mutants without symptoms, whereas their sons suffered from a severe visual impairment. Molecular diagnosis helps to explain the cause of LHON disease. Martin-Kleiner, I., Gabrilovac, J., Bradvica, M., Vidovic, T., Cerovski, B., Fumic, K., and Boranic, M. *Coll Antropol*. 30(1), pp. 171-174, March 2006. INVEST Fellow: Irena Martin-Kleiner, Croatia, 1995-1996.

#### **FORMER HUBERT H. HUMPHREY DRUG ABUSE RESEARCH FELLOWS**

##### Assessing Prescribing and Patient Care Indicators for Children Under Five Years Old With Malaria and Other Disease Conditions in Public Primary Health Care Facilities

A prospective descriptive observational study using WHO indicator forms and questionnaire was carried out in Kibaha district public primary health care facilities. Authors assessed knowledge about drugs in mothers/guardians of sick children under age five years immediately after consulting clinicians and after receiving drugs from the dispenser. The questionnaires had closed- and open-ended questions. Interviews were administered by trained nurses and the authors. The prescribing, dispensing practices, including drug labeling and instructions given to mothers/guardians on how to use drugs at home, in these health facilities which are under the Essential Drugs Program (EDP), was assessed. A total of 652 prescriptions from mothers/ guardians with sick children under age five years were observed, recorded and analyzed. Prescribing indicators were used as stipulated by the WHO/DAP/93.1 how to investigate drug use in health facilities. The diagnosis for malaria cases made by the clinicians on average per facility were as follows: malaria alone 25, diarrhea alone 3, pneumonia alone 3, malaria and diarrhea 4 cases, malaria and pneumonia 2 cases and malaria and other conditions 14 cases. The average number of drugs per prescription in these facilities was 2.3 and the percentage generic prescribing was 87.0, antibiotics 30.5, and injections 26.2, with 93.5 % of all prescribed drugs being within the Essential Drugs List (EDL). The overall average dispensing time was 1.4 minutes per patient, of the drugs prescribed, 54.7 % were dispensed, whereas 21.4 % of drugs dispensed to mothers/guardians were adequately labeled, and 37.2 % of mothers knew how to administer drugs correctly to their sick children after receiving the drugs from the dispenser. These results suggest the need for educational intervention for prescribers (health care providers) on rational prescribing of drugs, such as antimalarials, antibiotics, injections, proper dispensing, and adequate labeling drugs in packets, while the dispensing time for drugs was too short. It is necessary to correct these malpractices of irrational prescribing and dispensing drugs for treatment of malaria and other

childhood illnesses in public primary health care facilities (PHC). Furthermore, inadequate physical examination and short consultation time needs to be improved. There is a need to advise the Ministry of Health to develop health education programs on a regular basis for all health care providers in the country and mothers/guardians of children in general public/rural communities on how to use/administer antimalarials and other drugs at home. All these can be achieved through well planned health education training programs. Nsimba, S.E. Southeast Asian J Trop Med Public Health. 37(1):206-214, January 2006. HHH Fellow: Stephen Nsimba, Tanzania, 2005-2006.

#### Poor Educational Attainment and Sexually Transmitted Infections Associated with Positive HIV Serostatus among Female In-Patient Substance Abusers in Trinidad and Tobago

Female crack cocaine users are at high risk for HIV infection. Data from 121 female substance abusers admitted to an all-female rehabilitation center in Trinidad and Tobago between 1996 and 2002 were reviewed retrospectively to determine human immunodeficiency virus (HIV) seroprevalence and associated risk factors. HIV seroprevalence was 19.8%, which is six times higher than in the general population. The univariate analysis identified the following factors associated with HIV infection: poor educational attainment, history of a sexually transmitted infection (STI), and use of crack cocaine. In the multivariate analysis, only poor educational attainment and history of an STI were independently associated with HIV seroprevalence. Female substance abusers, especially female crack cocaine users, are at high risk of acquiring and transmitting the HIV virus. To reduce risk of HIV infection, rehabilitation programs should address risky sexual behaviors and screen for STIs, and they also should improve educational attainment, develop skills, and provide vocational training. Reid, S.D. Drug Alcohol Depend. 82 Suppl 1, pp. S81-84, April 2006. HHH Fellow: Sandra Reid, Trinidad and Tobago, 1992-1993.

### **INTRAMURAL RESEARCH**

#### **TREATMENT SECTION, CLINICAL PHARMACOLOGY AND THERAPEUTICS RESEARCH BRANCH**

##### Adverse Events among Patients in a Behavioral Treatment Trial for Heroin and Cocaine Dependence: Effects of Age, Race, and Gender

Safety monitoring is a critical element of clinical trials evaluating treatment for substance dependence, but is complicated by participants' high levels of medical and psychiatric comorbidity. This paper describes AEs reported in a large (N = 286), 29-week outpatient study of behavioral interventions for heroin and cocaine dependence in methadone-maintained outpatients. A total of 884 AEs were reported (3.1 per patient, 0.12 per patient-week), the most common being infections (26.8%), gastrointestinal (20.5%), musculoskeletal (12.3%), and general (10%) disorders. Serious AEs were uncommon (1.6% of total). Female participants reported significantly higher rates of AEs (incidence density ratio, IDR = 1.38,  $p < 0.0001$ ); lower rates of AEs were reported by African Americans (IDR = 0.73,  $p < 0.0001$ ) and participants over age 40 reported lower rates of AEs (IDR = 0.84,  $p = 0.0095$ ). AE incidence was not associated with the study intervention or with psychiatric comorbidity. Further work is needed to adapt AE coding systems for behavioral trials for substance dependence; the standard Medical Dictionary for Regulatory Activities, International Federation of Pharmaceutical Manufacturers Associations (MedDRA) coding system used in this report did not contain a separate category for one of the most common types of AE, dental problems. Nonetheless, the data reported here should help provide a context in which investigators and IRBs can interpret the patterns of AEs they encounter. Schroeder, J.R., Schmittner, J.P., Epstein, D.H., and Preston, K.L. Drug and Alcohol Dependence, 80, pp. 45-51, 2005.

### Menstrual Cycle Length during Methadone Maintenance

While the menstrual disruption of heroin has been demonstrated, there are few published data concerning methadone maintenance and menstrual function. This study was conducted to evaluate whether cycle length was more regular during methadone maintenance. A total of 191 heroin and cocaine-using women who were maintained on methadone therapy (70-100 mg/day) in two clinical trials, lasting 25-29 weeks. Start/end dates of each menses were collected weekly. Menstrual patterns were classified as regular, irregular, transient amenorrhea, persistent amenorrhea or cycle restart. Repeated-measures regression modeling determined correlates of cycle length and predictors of long cycles (> 40 days) and short cycles (< 20 days). Bleeding episodes were defined as 1 or more bleeding days, bound by at least 2 non-bleeding days. Correlates/predictors examined were body mass index, drug use, methadone dose and race. In the 133 women for whom menstrual patterns could be determined, cycle-length irregularity was common: irregular, 62 (46.7%); regular, 37 (27.8%); cycle restart, 16 (12%); persistent amenorrhea, 11 (8.3%); transient amenorrhea, seven (5.3%). Each additional week on methadone maintenance was associated with decreased risk of long (OR = 0.96,  $P < 0.01$ ) and short (OR = 0.92,  $P < 0.01$ ) cycles. Of 27 women with secondary amenorrhea pre-study, 16 (59%) restarted menses. Positivity for opioids or cocaine was not significantly associated with short or long cycles. Cycle length begins to normalize during methadone maintenance. Menses resumption may occur. Methadone maintenance, despite interfering with menstrual function in an absolute sense, may interfere less than illicit heroin abuse. Schmittner, J., Schroeder, J.R., Epstein, D.H., and Preston, K.L. *Addiction*, 100, pp. 829-836, 2005.

# DIRECTOR'S REPORT TO COUNCIL

February 2007

## **BASIC NEUROSCIENCE RESEARCH**

### Paternal Cocaine Exposure & Its Consequences

In a recent study, NIDA supported researchers, Dr. Michael Lidow and his associates report that paternal cocaine abuse may have a significant negative impact on offspring development and that such paternal impact could be brought about by long-term cocaine exposure of males prior to coitus. This study conducted using a novel drug inhalation model revealed that male mice were capable of learning self-administration of cocaine via inhalation route as well as achieving and maintaining blood levels of this drug during daily inhalation sessions comparable to that reported for females. Authors also noted a reduction in biparietal head diameter in newborn pups sired by cocaine-inhaling males suggesting a decreased cerebral volume. Most importantly, they observed a greater negative impact in female offspring compared to males with respect to working memory and light stimulus duration. This study also showed that chronic cocaine exposure in male mice did not result in substantial breakage of spermatozoal DNA, but significantly altered expression of DNA methyltransferase 1 and 3a in the germ cell-rich seminiferous tubules of the testis. Since these enzymes are essential for generating and maintaining parental gene imprinting in germ cells, the authors' observations point to an intriguing possibility that cocaine may cause paternally induced neuroteratological effects by interfering with gene-imprinting patterns in male gametes. He, F., Lidow, I.A., and Lidow, M.S. Consequences of Paternal Cocaine Exposure in Mice, *Neurotoxicology and Teratology*, 28, pp. 198-209, 2006.

## **BASIC BEHAVIORAL RESEARCH**

### Gestational Nicotine Exposure Changes Basal Neuronal Activity in Areas Associated with Motivated Behavior

Dr. Frances Leslie and colleagues investigated whether nicotine, infused into a pregnant dam during gestation, would affect the neuronal response to acute nicotine during adolescence. One of three challenge doses of nicotine, or saline, was administered during postnatal days 38-40 (i.e., adolescence in the rat), and c-fos mRNA was used as a measure of neuronal activity. Gestational exposure to nicotine did not alter response to acute nicotine challenge during adolescence. The highest dose of acute nicotine challenge, however, did result in a significant increase in c-fos mRNA in the nucleus accumbens, the superior colliculus and the dorsolateral geniculate nucleus. Stress-sensitive areas of the lateral bed nucleus of the stria terminalis and the paraventricular nucleus also showed increased neuronal activity in response to acute nicotine. Two brain areas showed significant increases in c-fos mRNA as a result of gestational treatment, independently of nicotine challenge during adolescence: the infralimbic cortex and the nucleus accumbens core. These regions are important mediators of executive function and inhibitory control. These data suggest that gestational nicotine exposure results in long-term changes in neuronal activity, that it does not interact with acute adolescent exposure, but that the neuronal activity of adolescent rats can be significantly altered by a single, acute dose of nicotine. Park, M.K., Loughlin, S.E. and Leslie, F.M. Gestational Nicotine-Induced Changes in Adolescent Neuronal Activity. *Brain Research*, 1094, pp. 119-126, 2006.

### Salvinorin-A, a $\kappa$ -Opioid Hallucinogen, Produces Time- and Dose-Dependent Neuroendo-crine Effects

Salvinorin A is a potent kappa-opioid agonist *in vitro* and salvinorin A-containing products have been emerging as drugs of abuse for their hallucinogenic effects. NIDA researcher Dr. Eduardo Butelman recently tested the drug for kappa effects *in vivo* using serum prolactin levels as biomarkers of efficacy, and also cloned the Macaca mulatto (*M. mulatto*) OPRK1 gene, which codes for the kappa opioid receptor. He treated *M. mulattos* with salvinorin A, U69,593 (a kappa-agonist) or vehicle, followed by blood sampling at 5-120 minutes post-injection. Both kappa agonists produced robust, dose-and time-dependent increases in prolactin levels in males. U69,593 produced a longer-lasting effect; however the maximum effect and potency were the same as produced by salvinorin A. In females in the follicular phase, salvinorin A produced robust prolactin release. This was longer lasting, and had a faster onset than in males. In antagonist challenge studies the opioid antagonist nalmefene and/or the serotonin antagonist ketanserin was administered prior to a dose of salvinorin A. In both males and females, antagonist pretreatment with nalmefene produced robust antagonism of salvinorin A-stimulated prolactin release at the high, but not low, dose. Ketanserin produced no antagonism and did not affect prolactin levels, indicating that serotonin receptors were not involved. In these studies, salvinorin A was shown to be a potent kappa agonist, and was effective in both males and females. Butelman, E.R., Mandau, M., Priszano, T.E., Yufarov, V. and Kreek, M.J. Effects of Salvinorin A, a  $\kappa$ -Opioid Hallucinogen, on a Neuroendocrine Biomarker Assay in Non-human Primates with High  $\kappa$ -Receptor Homology to Humans. *Journal of Pharmacology and Experimental Therapeutics*, 320(1), pp. 300-306, 2006.

### Sex Differences in Decision Making on the Iowa Gambling Task

On the Iowa Gambling Task subjects choose cards from four decks that provide monetary gains or monetary losses. Selections from two of the decks result in an overall net gain, but choices from the other two produce an overall net loss. Optimal performance requires the subject to identify and select from a low pay/low loss deck, and men typically select significantly more cards from these advantageous decks whereas women consistently choose more cards from disadvantageous decks with high penalties. Successful performance depends on integrity of the prefrontal cortex (PFC) and measurement of PFC activation during the task reveals that men activate bilateral areas of the dorsolateral PFC, right lateral orbital PFC, and right parietal lobe. By contrast, women activate a smaller region of the left medial orbital PFC. Recently, Dr. William Overman conducted a study to determine if a task known to activate dorsolateral PFC areas might improve IGT performance in women. One task that activates this region is deliberation of moral personal dilemmas. In the present study, 200 participants were divided into three groups and asked to contemplate a scenario every 10 trials – either a moral personal dilemma, a moral impersonal dilemma, or a nonmoral dilemma. Results show that sex differences on the Iowa Gambling Task were eliminated in groups contemplating PM whereas men in the other two conditions selected a significantly greater proportion of cards from advantageous decks than did the women. Finally, in order to test whether improvement might be due to generalized emotional arousal, another 229 students were tested after moral personal dilemma deliberation on a Wisconsin Card Sort Task that relies upon dorsolateral and dorsomedial PFC substrates. Wisconsin Card Sort Task scores were unaffected by moral personal dilemma deliberation suggesting that improvement by females on the Iowa Gambling Task is due to a shift in activation of PFC regions and enhanced cognitive control over an emotional response to rewards in the disadvantageous decks. Overman, W., Graham, L., Redmond, A. Eubank, R., Boettcher, L., Samplawski, O. and Walsh, K. Contemplation of Moral Dilemmas Eliminates Sex Differences on the Iowa Gambling Task. *Behavioral Neuroscience*, 120, pp. 817-825, 2006.

### Conditioned Psychostimulant Effects Are Moderated by Age and Sex

Individual differences in locomotor response to novelty predict the behavioral activating effects and self-administration of psychomotor stimulants. Rats that are more reactive in a novel environment (high responders, HR) show greater drug-induced stimulation and more readily acquire self-administration of



amphetamine, cocaine, and nicotine, than their low-responding (LR) counterparts. Dr. Michael Bardo and colleagues recently completed a study to determine if individual differences in novelty response predict: 1) Locomotor sensitization to the psychostimulant, methylphenidate or 2) methylphenidate-conditioned locomotion in the drug-paired environment. Moreover, they sought to determine if novelty response would predict behavioral change differentially for male versus female rats and for adolescent (25 days old) versus adult (60 days old). A median split between HR and LR rats was based on locomotor counts and time spent in a novel compartment. Rats were then treated with saline, 3.0 or 10.0 mg/kg methylphenidate, for 10 days. After 14 days of withdrawal animals were assessed for conditioned locomotor activity with saline and for sensitization with a single 10.0mg/kg methylphenidate injection in the test cage. The investigators found: 1) Adolescent rats selected novelty in a free choice situation significantly more than adults; however, choice did not predict methylphenidate sensitization or conditioning; 2) HR showed greater methylphenidate behavioral activation and adult females had greater dose-dependent activity than adult males; 3) Adolescent Rats developed sensitization at 3.0 mg/kg METH, whereas adults only sensitized to 10 mg/kg; 4) Only HR adult females had increased sensitization to 5) All animals showed a methylphenidate conditioned to the test environment except the adult males; 6) HR rats showed a greater methylphenidate conditioned locomotor activity but a HR>LR difference was only significant for adolescent males and adult females; 7) Only HR adult females showed greater sensitization on the methylphenidate challenge. These findings suggest that: 1) Gender differences in sensitization emerge during development; 2) Adolescent rats in general are more sensitive to psychomotor stimulant sensitization; 3) Initial response to novelty predicts methylphenidate -induced conditioned locomotion to the test chamber and sensitized behavioral response to methylphenidate; and 4) This individual difference is moderated by both age and gender. Wooters, T.E., Dwoskin, L.P. and Bardo, M.T. Age and Sex Differences in the Locomotor Effect of Repeated Methylphenidate in Rats Classified as High or Low Novelty Responders. *Psychopharmacology*, 188, pp. 18-27, 2006.

#### Menstrual Cycle Phase Effects on Nicotine Withdrawal and Cigarette Craving: A Review

Research over the past several years has uncovered numerous male-female differences in cigarette smoking. In studies of quitting, for example, women are less successful than men, and there is clinical and laboratory evidence that nicotine versus non-nicotine factors play a differential role in smoking for men versus women. The menstrual cycle has been shown to be a factor in smoking for women with several studies finding more smoking in the luteal phase (post-ovulation/premenstrual) of the cycle than in the follicular phase (menses/pre-ovulation). Researchers at the Medical University of South Carolina conducted a literature review to examine whether this higher level of smoking in the luteal phase reflects greater nicotine withdrawal and craving. Using MEDLINE and PsychInfo databases, a total of 13 studies were identified, of which 3 examined the naturalistic time course of withdrawal and craving under *ad libitum* smoking, 6 examined these measures under laboratory conditions of abstinence, and 4 conducted comparisons of the two conditions. The review yielded mixed results although there was evidence for greater withdrawal and craving in the luteal phase. The authors conclude that “the most striking implication from this review is the need for further research,” noting that inconsistencies in outcomes among studies could be due to heterogeneity of methods including differences in statistical power to detect cycle effects, inconsistency in identification and corroboration of menstrual cycle phase, definition of cycle phase (two phases versus four-phases), and inclusion versus exclusion of women with a history of premenstrual dysphoric disorder. The authors recommend that future research in this area uses hormonal verification of menstrual phase status and follows a four-phase conceptualization: early follicular, late follicular, early luteal, and late luteal. This area of research has important clinical implications for choice of quit date for nicotine cessation and thus warrants future study. Carpenter, M.J., Upadhyaya, H.P., LaRowe, S.D., Saladin, M.E., and Brady, K.T. Menstrual Cycle Phase Effects on Nicotine Withdrawal and Cigarette Craving. A Review. *Nicotine & Tobacco Research*, 8, pp. 627-638, 2006.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Effects of Prenatal Methamphetamine Exposure, Polydrug Exposure, and Poverty on Intrauterine Growth

Methamphetamine use among pregnant women is an increasing problem in the United States. Effects of methamphetamine use during pregnancy on fetal growth have not been reported in large, prospective studies. Dr. Barry Lester and his colleagues at four clinical centers in California, Oklahoma, Hawaii and Iowa examined the neonatal growth effects of prenatal methamphetamine exposure. Of 13,808 subjects screened, 1,618 were eligible and consented, among which 84 were methamphetamine exposed, and 1,534 were unexposed. Both groups included prenatal alcohol, tobacco, or marijuana use, but excluded use of opiates, LSD, PCP or cocaine only. The methamphetamine exposed group was 3.5 times more likely to be small for gestational age than the unexposed group. Mothers who used tobacco during pregnancy were nearly two times more likely to have small-for-gestational-age infants. In addition, less maternal weight gain during pregnancy was more likely to result in a small-for-gestational-age infant. Birth weight in the methamphetamine exposed group was lower than the unexposed group. These findings suggest that prenatal methamphetamine use is associated with fetal growth restriction after adjusting for covariates. Continued follow-up will determine if these infants are at increased risk for growth and/or neurodevelopmental deficits in the future. Smith, L.M., LaGasse, L.L., Derauf, C., Grant, P., Shah, R., Arria, A., Huestis, M., Haning, W., Strauss, A., Della Grotta, S., Liu, J., and Lester, B.M. The Infant Development, Environment, and Lifestyle Study: Effects of Prenatal Methamphetamine Exposure, Polydrug Exposure, and Poverty on Interuterine Growth, *Pediatrics*, 118(3), pp. 1149-1156, 2006.

### Neuroimaging of Frontal White Matter and Executive Functioning in Cocaine-Exposed Children

Researchers at the University of Florida have reported on the use of Diffusion Tensor Imaging (DTI) to assess frontal white matter development in prenatally cocaine-exposed and non-exposed children, and also have reported on associations between frontal white matter development and executive functioning in these children. DTI uses magnetic resonance imaging (MRI) to investigate white matter microstructure by measuring the movement, or diffusion, of water molecules in tissues. Using different DTI quantification indices, researchers study maturation of white matter tracts. Executive functioning is a concept that describes a diverse set of skills involved in goal-directed behavior such as problem solving, and includes skills such as attention control, inhibition abilities, and management of cognitive, emotional, and behavioral functions. Executive functioning was assessed using two frequently used instruments (the Stroop color and word test and the Trail Making Test). The sample for these analyses (tested and scanned in the age range 9.6 to 12.2 years) was drawn from an ongoing longitudinal study of development following prenatal cocaine exposure, and involved 28 cocaine-exposed children and 25 non-exposed children with similar sociodemographic characteristics. The investigators conclude that prenatal cocaine exposure, alone and in combination with exposure to other drugs, is associated with slightly poorer executive functioning and with subtle microstructural characteristics that may suggest less mature development of frontal white matter pathways. They also state that the relative contribution of postnatal environmental factors (e.g., caregiving environment) on brain development and behavioral functioning in polydrug-exposed children awaits further research. Warner, T.D., Behnke, M., Eyler, F.D., et al. Diffusion Tensor Imaging of Frontal White Matter and Executive Functioning in Cocaine-Exposed Children. *Pediatrics*, 118, pp. 2014-2024, 2006.

### Discrete Opioid Gene Expression Impairment in the Human Fetal Brain Associated with Maternal Marijuana Use

The most commonly used illicit drug by pregnant women is marijuana. In light of the strong interactions between the cannabinoid and Opioid systems, Dr. Yasmin Hurd and her colleagues investigated the effects of in utero marijuana exposure on expression levels of Opioid-related genes in the human fetal forebrain. The Opioid peptide precursors (preprodynorphin and preproenkephalin (PENK)) and receptor (mu, kappa and delta) mRNA expression were assessed in distinct brain regions in 42 midgestation fetuses from saline-

induced voluntary abortions and the effects of prenatal cannabis exposure was analyzed while controlling for confounding variables such as maternal alcohol and cigarette use, fetal age, sex, growth measure and post-mortem interval. Prenatal cannabis exposure was found to be significantly correlated with increased mu receptor expression in the amygdala, reduced kappa receptor mRNA in mediodorsal thalamic nucleus and reduced preproenkephalin expression in the caudal putamen. Prenatal alcohol exposure was found to primarily influence kappa receptor mRNA, with reduced levels in the amygdala, claustrum, putamen and insula cortex. No significant effect of prenatal nicotine exposure was seen in the analyses performed. These results indicate that maternal cannabis and alcohol exposure during pregnancy differentially affect opioid-related genes in distinct brain circuits; alterations that may have long-term effects on cognitive and emotional behaviors. Wang, X., Dow-Edwards, D., Anderson, V., Minkoff, H., and Hurd, Y.L. Discrete Opioid Gene Expression Impairment in the Human Fetal Brain Associated with Maternal Marijuana Use. *Pharmacogenomics Journal*, 6(4), pp. 255-264, 2006.

### Prenatal Cocaine Exposure and Risk for Developing Learning Disabilities

Dr. Emmalee Bandstra and her colleagues at the University of Miami examined prenatal cocaine exposure and risk for developing a learning disability (LD) or impaired intellectual functioning by age seven in a sample of 409 children (212 cocaine-exposed, 197 non-cocaine-exposed) born full term and enrolled prospectively at birth. LDs were categorized based on ability-achievement discrepancy scores. The cocaine-exposed children had 2.8 times greater risk of developing a LD by age seven than non-cocaine-exposed children. No differences were found in the estimate of relative risk for impaired intellectual functioning (IQ below 70) between children with and without prenatal cocaine exposure. Results remained stable with adjustment for multiple child and caregiver covariates including but not limited to maternal education, caregiver substance use, the home environment, and attendance in Head Start/prekindergarten suggesting that children with prenatal cocaine exposure are at increased risk for developing a learning disability by age seven when compared to their non-cocaine-exposed peers. Morrow, C.E., Culbertson, J.L., Accornero, V.H., Xue, L., Anthony, J.C., and Bandstra, E.S. Learning Disabilities and Intellectual Functioning in School-Aged Children with Prenatal Cocaine Exposure. *Developmental Neuropsychology*, 30(3), pp. 905-931, 2006.

### Prenatal Smoking Exposure and Developmental Patterns of Conduct Problems in Boys

There are reports in the research literature of associations between prenatal smoking exposure and increased risk of conduct problems among offspring. This report examines associations of prenatal smoking exposure with oppositional defiant disorder (ODD) and attention-deficit/hyperactivity disorder (ADHD) in young boys (during first grade), and with developmental patterns of delinquent behavior during adolescence. Researchers from the University of Illinois at Chicago and from the University of Pittsburgh examined data from the Pittsburgh Youth Study, a prospective, population-based study of conduct problems in boys. In the analyses for this report, prenatal smoking exposure was examined relative to the presence of ODD and ADHD, singly and as comorbid conditions at age 7 years. Also investigated was the association of prenatal exposure with the timing of onset of both mild and more serious conduct problems, using in-depth measures of delinquency administered prospectively from early school age through age 19 years. Multiple potentially confounding factors were controlled in multivariate analyses. The investigators report that exposed boys were more likely to show evidence of ODD and comorbid ODD-ADHD, but not ADHD alone. They also report that exposed boys were more likely to have an earlier onset of significant delinquent behavior. The authors note that whether prenatal smoking plays an etiological role in, or is a marker for risk of antisocial behavior, it is clear that the offspring of prenatal smokers as a group are at increased risk for an early-starter pathway to antisocial behavior that is evident as early as first grade. Wakschlag, L.S., Pickett, K.E., Kasza, K.E., and Loeber, R. Is Prenatal Smoking Associated with a Developmental Pattern of Conduct Problems in Young Boys? *Journal of the American Academy of Child and Adolescent Psychiatry*, 45, pp. 461-467, 2006.

### Prenatal Cannabis Exposure Increases Heroin Seeking with Allostatic Changes in Limbic Enkephalin Systems in Adulthood

Very little is known about the long-term consequences of prenatal cannabis exposure on behavior and neural systems. Dr. Yasmin Hurd and her colleagues used an animal model to study the effects of prenatal exposure to  $\Delta^9$ -tetrahydrocannabinol (THC) on heroin self-administration behavior and opioid neural systems in adult male rats (postnatal day 62) that were exposed to THC from gestational day five to postnatal day two. They found that THC-exposed rats exhibited shorter latency to pressing a lever for heroin, responded more for low heroin doses, and had more readily sought heroin when stressed and during drug extinction. Neurobiologically, they found that THC exposure reduced preproenkephalin (PENK) mRNA expression in the nucleus accumbens during early development, but this was elevated in adulthood. PENK mRNA was also increased in the central and medial amygdala in adult THC-exposed animals. Finally, THC animals had reduced heroin-induced locomotor activity and nucleus accumbens  $\mu$  opioid receptor coupling. This study demonstrates that the effects of prenatal THC exposure endure into adulthood and that these effects are evident on heroin-seeking behavior and in changes in mesocorticolimbic PENK systems relevant to drug motivation/reward and stress responses. Spano, M.S., Ellgren, M., Wang, X., and Hurd, Y.L. Prenatal Cannabis Exposure Increases Heroin Seeking with Allostatic Changes in Limbic Enkephalin Systems in Adulthood. *Biological Psychiatry*, July 27, 2006.

### Intrauterine Growth Restriction and Prenatal Substance Exposure in Term Infants and Risk for Hypertension at Age Six

Researchers from the Maternal Lifestyle Study, a prospective longitudinal multi-site study of prenatal cocaine and opiate exposure, investigated the association between intrauterine growth restriction (IUGR) status at birth among full-term infants, exposure to substance use during pregnancy, and risk of hypertension at six years of age. Of the 1,388 infants (600 cocaine exposed, 781 non-exposed, and seven indeterminate, matched by gestational age, race, and sex), enrolled in this study, 950 children (415 exposed, 535 non-exposed) completed the age six assessment, 891 had blood pressure data and of these, 516 were born at full term. One hundred and forty-four (28%) of the 516 children had a diagnosis of IUGR at birth. At six years of age, 93 (19%) of 516 children had hypertension, defined as either systolic or diastolic blood pressure higher than the 95th percentile for sex, age, and height. Of 144 children with IUGR, 35 (24%) had hypertension as compared with 58 (16%) of 372 children without IUGR. The study did not find any association with cocaine, opiate, marijuana, tobacco, or alcohol use during pregnancy and hypertension at 6 years of age. Twenty percent of cocaine-exposed children had hypertension as compared with 16% of nonexposed children. Intrauterine growth restriction status at birth was significantly associated with hypertension adjusting for site; maternal race, education, and tobacco, marijuana, alcohol, and cocaine use during pregnancy; and child's current body mass index. In term infants, IUGR is linked to risk of hypertension in early childhood, which may be a marker for adult cardiovascular disease. Shankaran, S., Das, A., Bauer, C.R., Bada, H., Lester, B., Wright, L., Higgins, R., and Poole, K. Fetal Origin of Childhood Disease: Intrauterine Growth Restriction in Term Infants and Risk for Hypertension at Age Six. *Archives of Pediatrics and Adolescent Medicine*, 160(9), pp. 977-981, 2006.

### Perinatal HIV Infection, In Utero Substance Exposure and Cognitive Development in Young Children

Researchers from the Women and Infants transmission study examined the effect of HIV in combination with other health and social factors including in utero exposure to drugs on the development of cognitive abilities of children perinatally exposed to HIV and substances of abuse. Serial cognitive assessments were performed for 117 children who were infected vertically and 422 children (50% African American, 32% Hispanic, and 12% Caucasian) who were exposed to but not infected with HIV. Forty-one percent of the children were exposed to cocaine, heroin, or methadone in utero as measured by self-report and/or urine screen and 63% were exposed to alcohol, tobacco, or marijuana as measured by self-report. Repeated-measures analyses were used to evaluate the neurocognitive development of these children between the

ages of three and seven years. Children with HIV/no Class C conditions were more likely to experience exposure to hard drugs during pregnancy than were children without HIV. (Class C refers to the CDC categorization of clinical conditions or symptoms of HIV infection considered severe including recurrent serious bacterial infections and encephalopathy). Children with HIV infection and class C status scored significantly lower in all domains of cognitive development, across all time points, than did those who were HIV infected without an AIDS-defining illness and those who were HIV exposed but not infected adjusting for presence of hard and soft substance exposure and other maternal factors during pregnancy and delivery, social demographic variables, test administration variables, and maternal and child disease stages. There were no significant differences between the two latter groups in General Cognitive Index or specific domain scores. Rates of change in cognitive development were parallel among all three groups over a period of four years. Factors that were associated consistently and significantly with lower mean scores were HIV status, number of times an examination had been completed previously, primary language, maternal education, and gender. No factors were related to rate of change of any mean domain score. An early AIDS-defining illness increased the risk of chronic static encephalopathy during the preschool and early school age years. Children with HIV infection but no class C event performed as well as non-infected children in measures of general cognitive ability. No significantly different profiles of strengths and weaknesses for verbal, perceptual-performance, quantitative, or memory functioning were observed among children with or without HIV infection. The authors recommend that future research include various environmental stressors in these children's lives including current parental drug use. Smith, R., Malee, K., Leighty, R., Brouwers, P., Mellins, C., Hittelman, J., Chase, C., Blasini, I., and the Women and Infants Transmission Study Group. Effects of Perinatal HIV Infection and Associated Risk Factors on Cognitive Development among Young Children. *Pediatrics*, 117(3), pp. 851-862, 2006.

#### Prenatal Exposure to Cocaine and Childhood Exposure to Violence: Association with Friends' and Own Substance Use

Children exposed to substances of abuse in utero may also be at risk for environmental stressors during childhood that can influence their neurodevelopmental trajectories and risk for substance use. This study examined the association between exposure to violence during childhood and own and friends' substance use in a sample of children from a prospective longitudinal study of in-utero cocaine exposure (IUCE). One hundred and four children were assessed at age 8.5, 9.5, and 11 years with the Violence Exposure Scale for Children-Revised (VEX-R) and the Substance Exposure Assessment, a child-report measure of their own and their friends' ATOD use. The sample consisted of 90% African-American/ Caribbean children (mean age 8.5 years, SD 3 years), 53% males, and 49% with IUCE. Twenty-eight percent of the sample reported own use of any ATOD by age 11. The percentage of children who reported having substance-using friends was 12% at 8.5 years, 25% by 9.5 years, and 45% by 11 years. In multivariate survival analyses controlling for caregiver type, in-utero cocaine exposure category (heavy, light, and none), and child gender, children in the upper quartile of violence exposure at age 8.5 years were at significantly greater risk of having reported friends' use of ATOD by age 11 compared to those in the first through third quartiles. Quartiles of the violence exposure score, however, were not significantly associated with children's acknowledgment of their own use. Findings suggest an association between exposure to violence in childhood and report of peer ATOD use at school age. Campaigns to prevent ATOD use should address the impact of childhood exposure to violence. Joseph, N.P., Augstyn, M., Cabral, H., and Frank, D.A. Preadolescents' Report of Exposure to Violence: Association with Friends' and Own Substance Use. *Journal of Adolescent Health*, 38(6), pp. 669-674, 2006.

#### Maternal Cocaine Use and Caregiving Status: Group Differences in Caregiver and Infant Risk Variables

This study examined differences between cocaine and non-cocaine-using mothers, and between parental and non-parental caregivers of cocaine-exposed infants on caregiver childhood trauma, psychiatric symptoms, demographic, and perinatal risks. Participants included 115 cocaine and 105 non-cocaine mother-infant dyads recruited at delivery. Approximately 19% of cocaine mothers lost custody of their

infants by one month of infant age compared to 0.02% of non-cocaine mothers. Mothers who used cocaine during pregnancy had higher demographic and obstetric risks and their infants had higher perinatal risks. Birth mothers who retained custody of their infants had higher demographic risks and perinatal risks, higher childhood trauma, and higher psychiatric symptoms compared to birth mothers who did not use cocaine and non-parental caregivers of cocaine-exposed infants. Results highlight the importance of addressing childhood trauma issues and current psychiatric symptoms in substance abuse treatment with women who engaged in substance use during pregnancy. Eiden, R.D., Foote, A., and Schuetze, P. Maternal Cocaine Use and Caregiving Status: Group Differences in Caregiver and Infant Risk Variables. *Addictive Behaviors*, 32(3), pp. 465-476, 2007.

#### Gender, Substance Exposure, Lymphocyte Populations, Plasma HIV RNA Levels, and Disease Progression in a Cohort of HIV Exposed Children

Researchers from the Women and Infants Transmission study analyzed blood samples from antiretroviral therapy-treated, HIV-infected children (n = 158) and HIV-uninfected children (n = 1801) to examine gender and substance exposure differences in lymphocyte subsets and plasma RNA levels. In terms of immunologic parameters, for anti-retroviral therapy (ART) treated, HIV-infected children, maternal hard drug use during pregnancy showed a trend toward children having lower CD4+ cell counts (p= .06). Children whose mothers did not use hard drugs during pregnancy also had, on average, greater CD16+ CD56+ natural killer cell counts. In contrast, children exposed to hard drugs during pregnancy but not HIV infected had a higher CD4+ percentage. In terms of virologic parameters and mortality rates, ART-treated, HIV-infected children whose mothers used hard drugs during pregnancy had a higher mean log RNA level. Maternal alcohol use during pregnancy had no effect on CD4+ cell counts or percentages, however, ART-treated, HIV-infected children whose mothers did not use alcohol during pregnancy had on average higher absolute CD19+ cell counts and higher mean log RNA level. ART-treated, HIV-infected female children had lower plasma RNA levels than did their male counterparts, but lymphocyte differences were not noted. Despite their higher plasma RNA level, a greater proportion of male children survived through 8 years of age. There were no gender differences with respect to the age of diagnosis of HIV, time to antiretroviral therapy after diagnosis of HIV, or type of antiretroviral therapy. Lymphocyte differences were noted for uninfected children. Plasma RNA levels differed among antiretroviral therapy-treated, HIV-infected children according to gender, in a manner similar to that noted in previous pediatric and adult studies. Lymphocyte subsets varied according to gender in a cohort of HIV-exposed but uninfected children. Most importantly, overall mortality rates for this cohort differed according to gender. Foca, M., Moye, J., Chu, C., Matthews, Y., Rich, K., Handelsman, E., Luzuriaga, K., Paul, M., Diaz, C., and the Women and Infants Transmission Study. Gender Differences in Lymphocyte Populations, Plasma HIV RNA Levels, and Disease Progression in a Cohort of Children Born to Women Infected with HIV. *Pediatrics*, 118(1) pp. 146-155, 2006.

#### A Framework to Monitor Environment-induced Major Genes for Developmental Trajectories: Implications for a Prenatal Cocaine Exposure Study

Whether there are specific genes involved in response to different environmental agents and how such genes regulate developmental trajectories during lifetime are of fundamental importance in health, clinical and pharmaceutical research. Drs. Fonda Eyler, Marylou Behnke and colleagues at the University of Florida developed a novel statistical model for monitoring environment-induced genes of major effects on longitudinal outcomes of a trait. This model is derived within the maximum likelihood framework, incorporated by mathematical aspects of growth and developmental processes. A typical structural model is implemented to approximate time-dependent covariance matrices for the longitudinal trait. This model allows for a number of biologically meaningful hypothesis tests regarding the effects of major genes on overall growth trajectories or particular stages of development. It can be used to test whether and how major genetic effects are expressed differently under altered environmental agents. In a well-designed case-control study, the model has been employed to detect cocaine-dependent genes that affect growth

trajectories for head circumference during childhood. The detected gene triggers significant effects on growth curves in both cocaine-exposed (case) and unexposed groups (control), but with different extents. Significant genotype-environment interactions due to this so-called environment-sensitive gene are promising for further studies toward its genomic mapping using polymorphic molecular markers. Hou, W., Garvan, C.W., Littell, R.C., Behnke, M., Eyler, F.D., and Wu, R. A Framework to Monitor Environment-Induced Major Genes for Developmental Trajectories: Implication for a Prenatal Cocaine Exposure Study. *Statistics in Medicine*, 25, pp. 4020-4035, 2006.

#### Prevalence of Primary HIV-1 Drug Resistance among Recently Infected Adolescents

Dr. Craig Wilson and his colleagues in the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) examined the prevalence of primary human immunodeficiency type 1 (HIV-1) drug resistance among recently infected youth in the United States. Previous studies on HIV drug resistance have been conducted primarily with adult, male, Caucasian samples. Fifty-five HIV+ youth were recruited from 15 clinical sites across the U.S. and Puerto Rico. Participants included male (65%) and female (35%), African American (47%), Hispanic (24%), Caucasian (22%) youth with an average age of 19.3 years (SD 1.9 yrs). Risk factors for HIV acquisition reported among the youth included having sex under the influence of drugs or alcohol (36% male, 21% female) and exchanging sex for money or drugs (14% male and 5% female). Major mutations conferring HIV drug resistance were present in 10 participants (18%). Eight (15%) had nonnucleoside reverse-transcriptase inhibitor (NNRTI) mutations, with the majority (6) having the K103N mutation; 2 (4%) had nucleoside reverse-transcriptase inhibitor (NRTI) mutations; and 2 (4%) had protease inhibitor (PI) mutations. Phenotypic drug resistance was present in 12 (22%) subjects: 10 (18%) for NNRTIs, 2 (4%) for NRTIs, and 3 (5.5%) for PIs. There was a high prevalence of primary HIV-1 drug resistance, particularly to NNRTIs, in this group of recently infected youth. Vivani, R.M., Peralta, L., Aldrovandi, G., Kapogiannis, B.G., Mitchell, R., Spector, S.A. Wilson, C.M. and the Adolescent Medicine Trials Network for HIV/AIDS Interventions. Prevalence of Primary HIV-1 Drug Resistance among Recently Infected Adolescents: A Multicenter Adolescent Medicine Trials Network for HIV/AIDS Interventions Study. *Journal of Infectious Diseases*, 194(11), pp. 1505-1509, 2006.

### **CLINICAL NEUROSCIENCE RESEARCH**

#### Sex Differences in Amphetamine-Induced Displacement of [F-18] Fallypride in Striatal and Extrastriatal Regions: A PET Study

Dr. David Zald and colleagues at Vanderbilt University used PET to examine gender differences in d-amphetamine-induced dopamine release striatal and extrastriatal brain regions. Dopamine release was indexed by displacements of [F-18]. In addition, these displacements were correlated with cognition and sensation seeking. Method: Six women and seven men underwent positron emission tomography (PET) with [F-18] fallypride before and after an oral dose of d-amphetamine. Percent displacements were calculated using regions of interest and parametric images of dopamine 2 (D-2) receptor binding potential. The results demonstrated that female subjects had greater dopamine release than the male subjects in the right globus pallidus and right inferior frontal gyrus. Gender differences were observed in correlations of changes in cognition and sensation seeking with regional dopamine release. The finding that women exhibit greater dopamine release in response to amphetamine as well as gender differences in the relationship between regional dopamine release and sensation seeking and cognition may underlie gender differences in vulnerability for the abuse of psychostimulants. Schmidt, D., Baldwin, R., and Kessler, R. *American Journal of Psychiatry*, 163(9), pp. 1639-1641, 2006.

#### Sex Differences in Orbitofrontal Cortex (OFC) As Assessed by SPECT in Cocaine Dependent Subjects

Dr. Brian Adinoff and associates studied regional cerebral blood (rCBF) flow in treatment-seeking cocaine abusers after at least 11 days abstinence. This study reported relative rCBF between patients and healthy

controls following saline infusion. The key finding was a decreased rCBF in the right and left lateral OFC in males but not female cocaine-dependent subjects in contrast with a decreased rCBF in the medial OFC in the female but not males. Additionally, it was found that increases in rCBF were found in diffuse regions in males with no significant increases in females. In other words, cerebral blood flow was disturbed to a greater extent in males and in different areas than in females. Post-hoc inferences based on other reported findings suggested sex differences in responsiveness or brain function during decision-making tasks or, possibly, assessment or suppression of reward saliency. In any case, it is concluded that these findings amplify the relevance of sex-specific differences in drug effects to the orbitofrontal cortex and the implications for clinical course and treatment. Adinoff, B., Williams, M.J., Best, S.E., Harris, T.S., Chandler, P., Devous, M.D. *Gender Med*, 3(3), pp. 206-222, 2006.

#### Individual Differences in the Functional Neuroanatomy of Inhibitory Control

Dr. Hugh Garavan of Trinity University performed combined the data of five event-related fMRI studies of response inhibition. Functional differences were observed between the sexes with greater activity in females in many of these cortical regions. Despite the relatively narrow age range (18-46), cortical activity, on the whole, tended to increase with age, echoing a pattern of functional recruitment often observed in the elderly. More absentminded subjects showed greater activity in fronto-parietal areas, while speed of Go trial responses produced a varied pattern of activation differences in more posterior and subcortical areas. Although response inhibition produces robust activation in a discrete network of brain regions, these results reveal that individual differences impact on the relative contribution made by the nodes of this network. These results provide a framework to interpret changes in brain activity during inhibitory control in substance abusers. Garavan, H., Hester, R., Murphy, K., Fassbender, C., and Kelly, C. *Brain Research*, 1105, pp. 130-142, 2006.

### **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

#### Modeling Initiation and Progression of Substance Use and Abuse

The authors note that twin data can provide valuable insight into the relationship between the stages of phenomena such as substance abuse, but existing models for the relationship between initiation and progression have been difficult to extend because they are usually expressed in terms of explicit integrals. In this paper, the problem is overcome by regarding the analysis of twin data on initiation and progression as a special case of missing data, in which individuals who do not initiate are regarded as having missing data on progression measures. Using the general framework for the analysis of ordinal data with missing values available in Mx makes extensions that include other variables much easier. The effects of continuous covariates such as age on initiation and progression becomes simple. Also facilitated are the examination of initiation and progression in two or more substances, and transition models with two or more steps. This paper describes and then applies these methods to twin data from 1942 adult female twins in the Virginia Twin Registry; models studied the effects of cohort on liability to cannabis use and abuse, bivariate analysis of tobacco use and dependence and cannabis use and abuse, and the relationships between initiation of smoking, regular smoking and nicotine dependence. In addition to the methodologic advances, this article offers substantive findings including a strong relationship between initiation of cannabis and smoking, and a stronger relationship between smoking initiation and regular smoking than either with nicotine dependence. These new methods hold much promise for making use of existing data and advancing our understanding of drug use progression and phenotypes. Neale, M., Harvey, E., Maes, H., Sullivan, P., and Kendler, K. *Extensions to the Modeling of Initiation and Progression: Applications To Substance Use and Abuse*. *Behav Genet*, 36(4), pp. 507-524, 2006.



### Childhood Trauma among Incarcerated Women in Substance Abuse Treatment

Authors sought to describe the prevalence of childhood traumatic events among incarcerated women in substance abuse treatment and to assess the relation between cumulative childhood traumatic events and adult physical and mental health problems. The study was modeled after the Adverse Childhood Events study's findings. In-depth baseline interview data for 500 women participating in the Female Offender Treatment and Employment Program evaluation were analyzed. Hypotheses were supported, and regression results showed that the impact of childhood traumatic events on health outcomes is strong and cumulative (greater exposure to childhood traumatic events increased the likelihood of 12 of 18 health-related outcomes, ranging from a 15% increase in the odds of reporting fair/poor health to a 40% increase in the odds of mental health treatment in adulthood). These findings suggest a need for early prevention and intervention, and appropriate trauma treatment, within correctional treatment settings. Messina, N., and Grella, C. Childhood Trauma and Women's Health Outcomes in a California Prison Population. *Am J Public Health*, 96(10), pp. 1842-1848, 2006.

### DAST Drug Abuse Screening of College Students

The present study assesses the prevalence of items from a modified version of the Drug Abuse Screening Test, Short Form (DAST-10) for substances other than alcohol among undergraduate students. More than 4,500 undergraduate students at a large Midwestern research university completed a web-based survey in 2005. Nearly 1 in every 10 undergraduate students experienced three or more DAST-10 items in the past 12 months. Although the prevalence of illicit drug use did not differ by gender, undergraduate men were significantly more likely than women to report DAST-10 items. Less than 6% of individuals who reported three or more drug DAST-10 items had ever used treatment services for substance use. As a brief screening instrument, the DAST-10 offers promise for detecting possible drug abuse among college students. Based on the prevalence of drug use, colleges and universities are encouraged to provide screening opportunities to identify and to provide services for students at high risk for drug abuse. McCabe, S., Boyd, C., Cranford, J., Morales, M., and Slayden, J. A Modified Version of the Drug Abuse Screening Test among Undergraduate Students. *J Subst Abuse Treat*, 31(3), pp. 297-303, 2006.

### Substance Abusing Mothers and Disruptions in Child Custody

Using an attachment framework, authors examined (1) whether substance-abusing mothers' perceptions of how they were parented were related to the severity of their substance abuse and psychological maladjustment and (2) whether these two factors mediated the association between mothers' perceptions of how they were parented and their children's placement out of home. There were 108 mothers of 248 children who completed interviews upon admission to a methadone maintenance program for women. A multilevel modeling approach was used to model effects of the hierarchically organized data (e.g., children nested within families). Findings are consistent with an attachment perspective on parenting suggesting that the internal psychological processes of a parent play a critical role in the continuity of parenting. When multiple risk domains associated with children's out-of-home placement were examined together within the same statistical model, maternal substance abuse severity and psychological maladjustment were the strongest predictors of children's out of home placement. Furthermore, mothers who perceived their own mothers as uncaring and intrusive were more likely to have lost custody of a minor child. There was also evidence that this effect was partially mediated by maternal substance abuse severity and psychological maladjustment. Suchman, N., McMahon, T., Zhang, H., Mayes, L., and Luthar, S. Substance-Abusing Mothers and Disruptions in Child Custody: An Attachment Perspective. *J Subst Abuse Treat*, 30(3), pp. 197-204, 2006.

### Parent-Child Attachment, Parenting, Family Ecology and Persistent Conduct Problems

A small proportion of children exhibit extreme and persistent conduct problems through childhood. The present study employed the multiple-domain model of Greenberg and colleagues as the framework for person-oriented analyses examining whether parent-child attachment combines with parenting, family ecology, and child characteristics in particular configurations of risk that are linked to this problematic developmental pathway. Using prospective data from a community sample of adolescent mothers and their children (n=255), latent variable growth mixture modeling identified a normative trajectory with declining problem behaviors during the preschool period. Consistent with research on early-starter pathways, a distinct group of children featured a higher intercept and a positive slope, indicating an escalation in disruptive behaviors. Attachment security played a role in defining specific risk profiles associated with the probability of exhibiting this problem trajectory. Given particular patterns of risk exposure, secure attachment served a protective function. Avoidant, but not disorganized, attachment was associated with significantly higher likelihood of the disruptive problem trajectory. The results also indicated the general accumulation of risk was detrimental, but the particular configuration of risk made a difference. Overall, the findings suggest that early attachment operates in conjunction with personal and contextual risk to distinguish the development of later problem behaviors. Keller, T., Spieker, S., and Gilchrist, L. Patterns of Risk and Trajectories of Preschool Problem Behaviors: A Person-oriented Analysis of Attachment in Context. *Dev. Psychopathol.*, 17(2), pp. 349-384, 2005.

### Early Risk Factors Predict Success in Transition to Adulthood among Adolescent Mothers

This prospective longitudinal study is based on a diverse sample of adolescent mothers in the Northwest. Data have been collected from pregnancy through adulthood. Five risk factors were used (individually and in a cumulative risk index) to predict young mothers' life course pathways from age 17 through 23 years. A multinomial logistic regression indicated that, relative to the normative group, the problem-prone group had significantly greater odds of having a history of school problems, delinquency, and hard substance use. The psychologically vulnerable group had significantly greater odds of mental health problems, hard substance use, and marginally more delinquency. Importantly, the cumulative risk index (the sum of the five risk factors) predicted the patterns of transition into adulthood and demonstrated significant sensitivity and specificity in distinguishing those in the normative pathway from those in either the problem-prone or psychologically vulnerable pathway. Results suggest that specific risk factors assessed at pregnancy can differentiate among adolescent mothers who experience varying levels of success in their transition into early adulthood. The cumulative risk index demonstrates applied utility as a risk assessment tool capable of distinguishing among life-course pathways. Oxford, M., Gilchrist, L., Gillmore, M., and Lohr, M. Predicting Variation in the Life Course of Adolescent Mothers as they Enter Adulthood. *J Adolesc Health*, 39(1), pp. 20-26, 2006.

### Heritability of DSM-IV Nicotine Withdrawal

The authors determined the heritability of the eight symptoms of DSM-IV symptoms of nicotine withdrawal in adult twins in the Australian Twin Registry. They examined both the genetic influences on nicotine withdrawal as well as the genetic factors specific to nicotine withdrawal, after controlling for factors responsible for risk of progression beyond experimentation with cigarettes and for quantity smoked (average number of cigarettes per day at peak lifetime use). Epidemiologic and genetic analyses were conducted using telephone diagnostic interview data from young adult Australian twins reporting any cigarette use (3026 women, 2553 men; mean age 30 years). Genetic analysis of the eight symptoms of DSM-IV nicotine withdrawal suggests heritability is intermediate for most symptoms (26-43%), and similar in men and women. The exceptions were depressed mood upon withdrawal, which had stronger additive genetic influences in men (53%) compared to women (29%), and decreased heart rate, which had low heritability (9%). Although prevalence rates were substantially lower for DSM-IV nicotine withdrawal syndrome (15.9%), which requires impairment, than for the DSM-IV nicotine dependence withdrawal

criterion (43.6%), heritability was similar for both measures: as high as 47%. Genetic modeling of smoking more than 1 or 2 cigarettes lifetime ( "progression " ), quantity smoked and nicotine withdrawal found significant genetic overlap across all three components of nicotine use/dependence (genetic correlations = 0.53-0.76). Controlling for factors associated with risk of cigarette smoking beyond experimentation and quantity smoked, evidence for genetic influences specific to nicotine withdrawal (up to 23% of total variance) remained. Their results suggest that at least some individuals become "hooked " or progress in the smoking habit, in part, because of a vulnerability to nicotine withdrawal. Pergadia, M., Heath, A., Martin, N., and Madden, P. Genetic Analyses of DSM-IV Nicotine Withdrawal in Adult Twins. *Psychol Med*, 36(7), pp. 963-972, 2006.

#### Examination of Transitions from Initiation through Dependence in Adolescent Substance Involvement

The present study examined Lengths of Times for important transitions in substance involvement from Initiation to Regular use (LOTIR), first Problem from drug use (LOTIP), and first experience of Dependence (LOTID) for alcohol, tobacco, cannabis, cocaine, and opiates. Data were from a longitudinal study of 590 children (22.2% female) at different levels of risk for substance use disorders based on their fathers' substance use-related diagnoses. Participants' substance involvement was assessed at four ages: 10-12, and follow-ups at two, five, and eight years later. Results suggested that faster transitions were more due to drug-related constructs (including possible social milieus of different drug classes and interactions between drug class and neurophysiology) than intrapersonal constructs. The shortest transition times (and greatest addictive liabilities) were for opiates followed respectively by cocaine, cannabis, tobacco, and alcohol. Females had shorter transition times, though gender differences were small. Some evidence was found for a familial influence on transition times above what was accounted for by differences between substances. Ridenour, T., Lanza, S., Donny, E., and Clark, D. Different Lengths of Times for Progressions in Adolescent Substance Involvement. *Addict Behav*, 31(6), pp. 962-983, 2006.

#### HTLV-2 Infection in Injection Drug Users in King County, Washington

Human T-cell lymphotropic virus type 2 (HTLV-2) is endemic in injection drug users (IDU), and Native American populations in the Americas. Transmission is associated with high-risk injection and sexual practices. A cohort of 2561 IDU in King County, Washington completed 2 study visits over 1 year. HTLV-2 infection was detected in 190 (7.4%) of 2,561 IDU, and 13 (7.8 cases per 1000 person-years) incident infections occurred during the study. Prevalent infection was associated with female gender, non-white race, longer duration as IDU, having a tattoo, combined injection of heroin and cocaine, and with serologic evidence of hepatitis B and C infection. Seroconversion was more common in women, and was associated with African American race, heterosexual identity and longer duration as IDU. Increased risk of HTLV-2 infection was associated with non-white race, and injection drug of choice, suggesting injection networks may play an important role in transmission of HTLV-2. The high correlation of HTLV-2 infection with HCV infection suggests the major route of transmission in IDU is via injection practices. This study points to the need for studies on the clinical manifestations of HTLV-2 infection, as well as the clinical and virological manifestations of HTLV-2/HCV coinfection. Zunt, J., Tapia, K., Thiede, H., Lee, R., and Hagan, H. HTLV-2 Infection in Injection Drug Users in King County, Washington. *Scand J Infect Dis*, 38(8), pp. 654-663, 2006.

#### Gender Differences in Sexual Behaviors, Sexual Partnerships, and HIV among Drug Users in New York City

Researchers sought to compare sexual behaviors/partnerships and sexual risk correlates associated with HIV by gender among sexually active, street-recruited drug users in New York City. The study sample included 818 men and women (average age 28 vs 30 years,  $p < .01$ ). Men were more likely to be Latino (63% vs 41%,  $p < .01$ ), recently homeless (61% vs 50%,  $p < .01$ ) or previously incarcerated (90% vs 79%,  $p < .01$ ) compared to women. More men than women reported being an IDU (29% vs 20%,  $p < .01$ ). Among

non-IDUs, men were less likely to report crack use, more likely to report marijuana use, and use of hallucinogens. Men reported higher risk sexual behaviors, yet fewer high-risk sexual partners than women. After adjustment, HIV seropositive men were more likely than seronegatives to be older, MSM, use condoms, and have an HIV-infected partner. HIV seropositive women were more likely to be older, have an HIV-infected partner, and not use non-injected heroin. IDU was not associated with HIV. These findings highlight the need to determine how gender-specific sexual behaviors/partnerships among drug users affect HIV acquisition. Absalon, J., Fuller, C.M., Ompad, D.C., Blaney, S., Koblin, B., Galea, S., and Vlahov, D. Gender Differences in Sexual Behaviors, Sexual Partnerships, and HIV among Drug Users in New York City. *AIDS Behav*, 10(6), pp. 707-715, 2006.

### Neglect and Later Externalizing Problems in Children of Adolescent Mothers

The present study examines the role of neglect potential in adolescent mother-child dyads, both in terms of antecedents and its consequences for children's development. Participants were 100 adolescent mother-child dyads who were part of a larger, longitudinal study. Data were collected from the third trimester of pregnancy until the children's 10th year. Histories of maternal neglect and the quality of mother-child interactions during early childhood were found to predict neglect potential during middle childhood. Mothers with high neglect potential had children who exhibited more externalizing problems and fewer adaptive behaviors, with neglect potential mediating the effects of both early abuse potential and the quality of parenting on children's later externalizing behaviors. Results suggest that neglect potential may be a mechanism through which early potential for child abuse and insensitive maternal interactions affect later externalizing problems in children of adolescent mothers. Lounds, J., Borkowski, J., and Whitman, T. The Potential for Child Neglect: The Case of Adolescent Mothers and their Children. *Child Maltreat*, 11(3), pp. 281-294, 2006.

## **PREVENTION RESEARCH**

### Recommendations for the Prevention of HIV Transmission in Hispanic Adolescents

This article reviews the state of the science in HIV prevention for Hispanic adolescents. Literature is reviewed in three broad areas: (1) the prevalence rates of drug and alcohol misuse, sexual practices, and HIV infection; (2) risk and protective factors for drug and alcohol misuse and unprotected sex (in general and specifically for Hispanics); and (3) the state of HIV prevention intervention development and evaluation targeting Hispanic youth. Little basic and intervention research has been conducted on HIV prevention in Hispanic adolescents, with even less attention given to Hispanic young men who have sex with men (YMSM). There are a number of areas in which further knowledge development and scientific advancement are needed. The seven areas identified in this review were (a) the need for analyses of nationwide epidemiological data examining risk and protective factors for substance use and unsafe sexual behavior for heterosexual and homosexual youth; (b) explaining variations in drug/alcohol use, unsafe sexual behavior, and HIV infection among Hispanic subgroups; (c) need for adaptive preventive interventions for Hispanic subgroups with varying risk and protection profiles; (d) incorporation of ethnic, cultural, and sexual identity into prevention programs for Hispanic adolescents; (e) examination of the role of gender in preventive interventions for Hispanic adolescents; (f) research on the effects of psychiatric comorbidity on drug/alcohol use and unsafe sex and on the efficacy of prevention programs; and (g) increased focus on intravenous drug use as a mode of HIV infection among Hispanics, particularly Puerto Ricans. Research addressing these research needs has the potential to facilitate progress toward achieving the two primary objectives of Healthy People 2010—improving the quality of life for all Americans and reducing health disparities between and among segments of the U.S. population. Prado, G., Schwartz, S.J., Pattatucci-Aragón, A., Clatts, M., Pantin, H., Fernández, M., Lopez, B., Briones, E., Amarof, H., and Szapocznik, J. The Prevention of HIV Transmission in Hispanic Adolescents. *Drug Alcohol Depend*, 84S pp. S43-S53, 2006.

### Predictors of HIV-Related Stigma among Young People Living with HIV

Enacted and perceived HIV stigma was examined among 147 substance-using young people living with HIV (YPLH) in Los Angeles, San Francisco, and New York City. Almost all YPLH (89%) reported perceived stigma, 31% reported enacted experiences in the past 3 months; and 64% reported experiences during their lifetime. The HIV stigma questions were characterized by factors of avoidance, social rejection, abuse, and shame. In multivariate models, enacted stigma was associated with gay or bisexual identity, symptomatic HIV or AIDS, and bartering sex. Perceived stigma was associated with female gender, symptomatic HIV or AIDS, bartering sex, lower injection drug use, and fewer friends and family knowing serostatus. Gay or bisexual YPLH who were also HIV symptomatic or AIDS diagnosed experienced more HIV stigma than their heterosexual peers. Swendeman, D., Rotheram-Borus, M., Comulada, S., Weiss, R., and Ramos, M. Predictors of HIV-Related Stigma Among Young People Living with HIV. *Health Psychol*, 25(4), pp. 501-509, 2006.

### Gender Differences in Associations between Depressive Symptoms and Patterns of Substance Use and Risky Sexual Behavior Among a Nationally Representative Sample of U.S. Adolescents

This study uses a cluster analysis of adolescents, based on their substance use and sexual risk behaviors, to 1) examine associations between risk behavior patterns and depressive symptoms, stratified by gender, and 2) examine gender differences in risk for depression. Data are from a nationally representative survey of over 20,000 U.S. adolescents. Logistic regression was used to examine the associations between 16 risk behavior patterns and current depressive symptoms by gender. Compared to abstention, involvement in common adolescent risk behaviors (drinking, smoking, and sexual intercourse) was associated with increased odds of depressive symptoms in both sexes. However, sex differences in depressive symptoms vary by risk behavior pattern. There were no differences in odds for depressive symptoms between abstaining male and female adolescents (OR = 1.07, 95% CI 0.70-1.62). There were also few sex differences in odds of depressive symptoms within the highest-risk behavior profiles. Among adolescents showing light and moderate risk behavior patterns, females experienced significantly more depressive symptoms than males. It was concluded that adolescents who engage in risk behaviors are at increased risk for depressive symptoms. Girls engaging in low and moderate substance use and sexual activity experience more depressive symptoms than boys with similar behavior. Screening for depression is indicated for female adolescents engaging in even experimental risk behaviors. Waller, M., Hallfors, D., Halpern, C., Iritani, B., Ford, C., and Guo, G. Gender Differences in Associations between Depressive Symptoms and Patterns of Substance use and Risky Sexual Behavior Among A Nationally Representative Sample of U.S. Adolescents. *Arch Womens Ment Health*, 9(3), pp. 139-150, 2006.

### Genetic Contribution to Suicidal Behaviors and Associated Risk Factors among Adolescents in the U.S.

This paper examines genetic contribution to suicidal behaviors and other risk factors associated with suicidal behavior among adolescents in the U.S. Using adolescent twin data in the National Longitudinal Study of Adolescent Health (N=1448), authors compared concordance in suicidal ideation and attempt among monozygotic (MZ) and dizygotic (DZ) twins. Heritability of risk factors for suicidal behaviors also was examined using Pearson correlation and mixed-model analyses. A trend of higher concordance in suicidal ideation and attempt was found among MZ than DZ twins but the difference was not statistically significant by the stringent test of bootstrapping analysis. Evidence of heritability was found for several suicide risk factors. The percentage of variance explained by heritability was larger among female twins for depression, aggression, and quantity of cigarettes smoked in comparison to heritability estimates for male twins. However, estimated heritability was larger among male than female twins for alcohol use and binge drinking. Heritability influence was negligible among both sexes for other drug use. Risk factors for suicidal behaviors among adolescents may be heritable. Gender differences found in the heritability of some suicide risk factors suggest these genetic contributions are gender specific. Future research

examining potential interactions between expression of genetic influence and particular environmental contexts may enhance prevention and intervention efforts. Cho, H., Guo, G., Iritani, B.J., and Hallfors, D.D. Genetic Contribution to Suicidal Behaviors and Associated Risk Factors Among Adolescents in the U.S. *Prev Sci*, 7(3), pp. 303-311, 2006.

#### In School Alcohol and Marijuana Use among High School Students

The problem of adolescent substance use has been examined extensively. Beyond simple prevalence estimates, however, little research has been conducted on substance use in the school context. The present investigation was an in-depth study of students' attitudes and behaviors regarding alcohol and marijuana use during the school day. Based on a representative sample of 1123 high school students, 48% male, in grades 9-12 in western New York state, this study assessed the frequency of alcohol and marijuana use at school among demographic subgroups, the accessibility of drugs in school, and students' perceived consequences of being caught using drugs in school. Twelve percent of the sample reported using alcohol during school hours in the past 6 months while 16% reported using marijuana at school. Among students who used alcohol outside of school, 18% also used alcohol at school. For marijuana users, 47% used marijuana at school. There was evidence of some demographic differences in school drug use. Specifically, male and Hispanic students had slightly higher levels of drug use at school compared to female and white students, respectively, and in school drug use was more prevalent among older students. In terms of accessibility, students reported that alcohol and marijuana were easily obtained and used on school grounds. Many students (40%) were not aware of the specific actions taken in their schools to punish drug use. The need for additional research on school-related drug use is emphasized. Finn, K. V. Patterns of Alcohol and Marijuana Use at School. *Journal of Research on Adolescence*, 16(1), pp. 69-77, 2006.

#### Time Varying Family and Peer Influences on Adolescent Daily Mood

The time-varying influences of peer and family support on adolescent daily mood were explored among 268 youth transitioning from middle school to high school (8th to 9th grade) as compared to 240 youth transitioning from 10th to 11th grade. The participants were part of a larger study examining the natural history of smoking. Real-time ecological momentary assessments measures of daily positive and negative affect were collected via palmtop computers at baseline, 6 months, and 12 months. Participants rated 12 mood adjectives in response to 5 to 7 random prompts per day for 7 consecutive days. Perceived peer and family support were assessed via self-report. Mixed-effects regression analyses revealed significant grade by time by peer support interactions for positive and negative mood, with the younger cohort showing greater increases in the relation between peer support and affect over time than the older cohort. Family support did not interact with cohort or time. The authors summarize that peer influences may increase as adolescents develop, thus developmental influences should be included in examinations of dynamic relations between peers and adolescent mood. Also, these results may help elucidate transitions that may be optimal times for preventive interventions targeting emotional well-being of adolescents, specifically transition to high school. This transition point also coincides with a growth in mood disorders in adolescents, in particular girls. Girls were found to exhibit higher levels of negative moods at lower levels of peer support, relative to boys. The authors call for future research that captures the bidirectional nature of support--mood relations across adolescence. Weinstein, S., Mermelstein, R., Hedeker, D., Hankin, B., and Flay, B. The Time-varying Influences of Peer and Family Support on Adolescent Daily Positive and Negative Affect. *J Clin Child Adolesc Psychol*, 35(3), pp. 420-430, 2006.

#### Trajectories of Depression in Male and Female Children of Depressed Mothers

This study reports on relationships among gender, maternal depressed mood, and children's trajectories of depressive phenomena across middle childhood and early adolescence. It tested the hypothesis that, compared to boys, girls become increasingly vulnerable to maternal depression as they enter adolescence.

The study sample consisted of 834 families from 10 Pacific Northwest schools that participated in the Raising Healthy Children project, a longitudinal study of the etiology of problem behaviors and test of a multicomponent, multiyear intervention targeting risk and protective factors within key child socializing domains of family, school, peer, group, and individual. Maternal depressed mood and children's depressive phenomena were assessed annually during an 8-year period that spanned Grade 3 through Grade 10 for the children. Mean scores for girls' depressive phenomena increased relative to those for boys as children matured. Maternal depressed mood was significantly and positively associated with children's level of depressive phenomena. An interaction effect of gender and maternal depressed mood on acceleration in children's depressive phenomena indicated that girls' trajectories of depressive phenomena were sustained in the presence of maternal depression while those of boys declined in the presence of maternal depression. Implications for the prevention and treatment of adolescent depression are discussed. Cortes, R.C., Fleming, C.B., Catalano, R.F., and Brown, E.C. Gender Differences in the Association between Maternal Depressed Mood and Child Depressive Phenomena from Grade 3 through Grade 10. *J Youth Adolescence*, 35, pp. 815-826, 2006.

## **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

### Smoking Status in the Initial Weeks of Quitting as a Predictor of Smoking-Cessation Outcomes in Pregnant Women

In the general population of smokers, seminal findings of Kenford et al. (1994) suggest a robust relationship between early smoking during a quit attempt and later smoking. The findings indicate that any smoking during the initial 2 weeks of a quit attempt predicts poor longer-term outcomes. However, it is not known whether this same predictor rule applies under conditions where patients are quitting related to a medical condition for which smoking is contraindicated, like pregnancy. Investigators at the University of Vermont conducted this study to examine the association between smoking status during the initial 2 weeks of attempting to quit and smoking status at an end-of-pregnancy assessment among women enrolled in smoking cessation studies. Data were obtained from 129 women participating in clinical trials on smoking-cessation examining the efficacy of voucher-based incentives delivered contingent on biochemically-verified abstinence or a control conditions wherein incentives were given independent of smoking status. Smoking status was assessed in weeks 1 and 2 of the cessation effort and again at an end-of-pregnancy. The findings show that women who smoked in the first 2 weeks of quitting had a greater than 80% chance of being classified as smokers at an end-of-pregnancy assessment and that relationship held across the two treatment conditions. These findings indicate that the predictor rule for the general population of smokers applies to pregnant women who are smokers. Thus, it is recommended that clinicians monitor smoking status during the initial weeks of a quit attempt and provide a change in treatment when smoking is detected. Higgins, S.T., Heil, S.H., Dumeer, A.M., Thomas, C.S., Solomon, L.J., and Bernstein, I.M. *Drug and Alcohol Dependence*, 85, pp. 138-141, 2006.

### Weight Concerns Affect Motivation to Remain Abstinent From Smoking Postpartum

This study assessed motivation for postpartum abstinence among pregnant women who had quit smoking and examined the relationship of weight concerns and mood to abstinence motivation. Participants (N=119) completed assessments of smoking, weight concerns, depressive symptoms, and perceived stress. Sixty-five percent were highly motivated to remain abstinent postpartum. Women who were and were not motivated were similar in age, race, and nicotine dependence. Motivated women reported more stress, greater self-efficacy for weight management, less hunger and less smoking for weight control than less motivated women. After controlling for intention to breast-feed, nicotine dependence, years of smoking, partner smoking, and race, self-efficacy for weight control was related to motivation to maintain postpartum abstinence. This study suggests that weight concerns are linked with motivation for postpartum smoking abstinence, and interventions designed to prevent postpartum smoking may need to target eating,

weight and shape concerns. Levine, M.D., Marcus, M.D., Kalarchian, M.A., Weissfeld, L., and Qin, L. *Annals of Behavioral Medicine*, 32, pp. 147-153, 2006.

### Relationship of DSM-IV-Based Depressive Disorders to Smoking Cessation and Smoking Reduction in Pregnant Smokers

Investigators at the University of Texas M.D. Anderson Cancer Center in Houston conducted this study to examine psychiatric disorders as predictors of smoking outcomes among pregnant smokers. Eighty-one pregnant women participating in a low-intensity smoking cessation trial were investigated. Thirty-two percent of the sample met criteria for current dysthymia, major depressive disorder in partial remission, or minor depression. The findings showed that no significant reduction in smoking among women with or without current depressive disorders was shown. Unexpectedly, compared to women without depressive disorders, women with dysthymia significantly increased the mean number of cigarettes smoked (from 8 to 23 cigarettes per day during the 2 to 30 days post-targeted quit date period) and were smoking significantly more at 30 days. A main effect approaching significance suggested that women with current depressive disorders were less likely to be abstinent than women without current depressive disorders. The current results add to previous findings indicating a correlation between depressive symptoms and continued smoking in pregnant women. These findings indicate that additional research is needed in evaluating the impact of depression on smoking outcomes in pregnant women and that investigation of mood-focused smoking cessation interventions may be warranted. Blalock, J.A., Robinson, J.D., Wetter, D.W., and Cinciripini, P.M. *The American Journal on Addictions*, 15, pp. 268-277, 2006.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

### Opioid Antagonism of Cannabinoid Effects: Differences between Marijuana Smokers and Nonmarijuana Smokers

In non-human animals, opioid antagonists block the reinforcing and discriminative-stimulus effects of Delta(9)-tetrahydrocannabinol (THC), while in human marijuana smokers, naltrexone (50 mg) enhances the reinforcing and subjective effects of THC. The objective of this study was to test a lower, more opioid-selective dose of naltrexone (12 mg) in combination with THC. The influence of marijuana-use history and sex was also investigated. Naltrexone (0, 12 mg) was administered 30 min before oral THC (0-40 mg) or methadone (0-10 mg) capsules, and subjective effects, task performance, pupillary diameter, and cardiovascular parameters were assessed in marijuana smoking (Study 1; n=22) and in nonmarijuana smoking (Study 2; n=21) men and women. The results show that in marijuana smokers, low-dose naltrexone blunted the intoxicating effects of a low THC dose (20 mg), while increasing ratings of anxiety at a higher THC dose (40 mg). In nonmarijuana smokers, low-dose naltrexone shifted THC's effects in the opposite direction, enhancing the intoxicating effects of a low THC dose (2.5 mg) and decreasing anxiety ratings following a high dose of THC (10 mg). There were no sex differences in these interactions, although among nonmarijuana smokers, men were more sensitive to the effects of THC alone than women. To conclude, a low, opioid-selective dose of naltrexone blunted THC intoxication in marijuana smokers, while in nonmarijuana smokers, naltrexone enhanced THC intoxication. These data demonstrate that the interaction between opioid antagonists and cannabinoid agonists varies as a function of marijuana use history. Haney, M. *Neuropsychopharmacology*, advance online publication, 8 November 2006.



## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE AND CO-OCCURRING INFECTIONS (HIV/AIDS, HCV)**

### Micronutrient Levels and HIV Disease Status in HIV-Infected Patients on Highly Active Antiretroviral Therapy in the Nutrition for Healthy Living Cohort

Low serum micronutrient levels were common before widespread use of highly active antiretroviral therapy (HAART) and were associated with adverse outcomes. Few data are available on micronutrient levels in subjects taking HAART. This cross-sectional study was conducted to determine the prevalence of low serum retinol, alpha-tocopherol, zinc, and selenium in HIV-infected subjects taking HAART and to assess the association of micronutrient levels with HIV disease status. Participants were HIV-infected subjects on HAART in an ongoing Nutrition for Healthy Living (NFHL) study at Tufts. Retinol, alpha-tocopherol, zinc, and selenium were determined in frozen serum samples from 171 men and 117 women. Low serum levels were defined as retinol <30 µg/dL, selenium <85 µg/L, alpha-tocopherol <500 µg/dL, and zinc <670 µg/L. Association of micronutrient quartiles with CD4 cell count, CD4 count <200 cells/mm, HIV viral load (VL), and undetectable VL was assessed using adjusted multivariate regression. Results indicated that 5% of men and 14% of women had low retinol, 8% of men and 3% of women had low selenium, and 7% of men and no women had low alpha-tocopherol. Forty percent of men and 36% of women had low zinc, however. Subjects in the upper quartiles of zinc had lower log VL levels than those in the lowest quartile (significant for women). Subjects in the upper quartiles of selenium also tended to have lower VL levels compared with those in the lowest quartile. Surprisingly, women in the upper quartiles of retinol had higher log VLs than those in the lowest quartile. There was no significant association of any micronutrient with CD4 cell count or likelihood of CD4 count <200 cells/mm. The level of CD4 cell count influenced the association of retinol with log VL in men, however. In men with CD4 counts >350 cells/mm, those with higher retinol had higher log VLs compared with the lowest quartile, whereas in men with CD4 counts <350, those with higher retinol levels had lower log VLs compared with the lowest quartile. The authors concluded that low retinol, alpha-tocopherol, and selenium are uncommon in HIV-infected subjects on HAART. Zinc deficiency remains common, however. Jones, C.Y., Tang, A.M., Forrester, J.E., Huang, J., Hendricks, K.M., Knox, T.A., Spiegelman, D., Semba, R.D., and Woods, M.N. *J Acquir Immune Defic Syndr.* 43(4), pp. 475-482, December 1, 2006.

### Increased Serum Lipids are Associated with Higher CD4 Lymphocyte Count in HIV-Infected Women

Highly active antiretroviral therapy (HAART) has been associated with dyslipidaemia; however, the roles of immune status and non-HIV-disease risk factors remain unclear. A cross-sectional analysis of fasting lipids was carried out for 231 women, of whom 132 were HIV-infected and 99 were uninfected. The concentrations of total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and apolipoprotein B (apo B) were measured. CD4 lymphocyte count, hepatitis C status, demographics, diet, and anthropometrics were also assessed. A total of 132 women were HIV-infected [30 were antiretroviral-naïve, 68 were on protease inhibitors (PIs), and 34 were on non-PI HAART]. HIV infection was associated with higher triglycerides, lower HDL-C, and, among obese women, higher total cholesterol and LDL-C. Non-PI and PI HAART were each independently associated with higher total cholesterol, LDL-C, and apo B, compared with being ART-naïve. Among HIV-infected women, after adjustment for HAART use, women with a CD4 lymphocyte count > or =500 cells/microL had total cholesterol 41.8 mg/dL (P = 0.002) and LDL-C 28.8 mg/dL (P = 0.01) higher, on average, than women with a CD4 count <200 cells/microL. Women with a CD4 count of 200-499 cells/microL had total cholesterol 26.31 mg/dL higher, on average, than those with a CD4 count <200 cells/microL (P = 0.04), although differences in LDL-C did not reach significance (15.51 mg/dL; P = 0.12). A higher CD4 count was also associated with higher apo B (P < 0.001). Active hepatitis C infection was associated with lower total cholesterol, LDL-C, triglycerides, and apo B. The authors concluded that higher CD4 lymphocyte counts were associated with higher lipid levels, suggesting that immune competence may independently affect the dyslipidaemia seen in the HAART era. In addition, it is important that hepatitis C status be

assessed in studies of dyslipidaemia in the HIV-infected population. Floris-Moore, M., Howard, A.A., Lo, Y., Arnsten, J.H., Santoro, N., and Schoenbaum, E.E. Increased Serum Lipids are Associated with Higher CD4 Lymphocyte Count in HIV-infected Women. *HIV Med.* 7(7), pp. 421-430, 2006.

## **SERVICES RESEARCH**

### Welfare Reform, Employment, and Alcohol and Drug Use among Low-Income Women

In 1996 welfare reform legislation transformed income assistance for needy families by imposing work requirements, time-limited benefits, and explicit provisions allowing states to sanction recipients who fail to meet program requirements. Though they represent a minority of the welfare population, women with substance use disorders (SUDs) experience multiple, and more severe, employment barriers than other Temporary Assistance to Needy Families (TANF) recipients. This review of welfare reform, substance abuse, and employment documents the evidence to date regarding the employment patterns of women with SUDs before and after welfare reform, and proposes several topics for further research. Based on higher rates of unemployment, less work experience, and lower earnings when working, women with SUDs have worse employment records than other TANF recipients. Despite elevated employment barriers, women with SUDs left TANF after 1996 as fast as, or faster than, other women. Since the 1996 welfare reform, women with SUDs have increased their employment and earnings, but by less than similar women without SUDs. Future research should describe how specific state welfare policies relate to employment of low-income women with SUDs, how the well-being of these women and their children changes with employment, and how welfare and employment interact to affect access to health insurance among this population. Meara, E. Welfare Reform, Employment, and Drug and Alcohol Use among Low-Income Women. *Harv Rev Psychiatry*, 14(4), pp. 223-232, 2006.

### Mental Health Problems and Criminal Justice Involvement among Female Street-Based Sex Workers

This paper examines the connections of mental health, victimization, and criminal justice involvement among a sample of 343 street-based female sex workers in Miami, Florida. Using targeted sampling strategies, drug-using sex workers were recruited into an HIV prevention intervention and research program. Data were collected by trained interviewers using standardized questionnaires that focused on drug use, childhood abuse, recent victimization, mental health, and criminal justice involvement. More than half of the participants reported histories of physical (54.5%) or sexual (54.2%) abuse as children, and more than one-third reported violent victimization in the past year. Nearly 32% were classified with moderate or severe anxiety symptoms, 46.2% had symptoms of moderate or severe depression, and 64.6% had symptoms of acute traumatic stress. In addition, 81.9% had prior arrest histories. The intersection of these factors suggests that police and law enforcement agencies must play a substantial role in managing an offender population with impaired mental health functioning. The policy implications of these findings are discussed. Surratt, H. Mental Health Problems and Criminal Justice Involvement Among Female Street-Based Sex Workers. *Law Enforcement Executive Forum*, 6, pp. 121-134, 2006.

### Blood Pressure Levels May Vary in Population because of Genetic, Ethnic and Body Size Factors

Blood pressure data of 2278 Indian boys and 2930 Indian girls in the age group of 3-18 years were analyzed to study the distribution pattern of systolic blood pressure and diastolic blood pressure and to develop reference values to define hypertension. Blood pressure was measured using standardized techniques in all. The first and fifth phases of Korotkoff sounds were taken as indicative of systolic blood pressure and diastolic blood pressure respectively. Height percentiles were computed for each one-year age group. According to percentiles of height 50th, 90th, 95th and 99th percentiles of systolic blood pressure and diastolic blood pressure were estimated for every one-year age. Results indicated that the blood pressure (both systolic and diastolic) tends to increase with age. The stepwise regression analysis revealed that the age and height but not gender, are important determinants of blood pressure. Age and height

specific, 50th, 90th and 95th and 99th percentiles of systolic and diastolic blood pressure were derived and are presented in tabular form. Authors concluded that the blood pressure of children and adolescents can be evaluated using the reference table according to body size. The table provided helps to classify blood pressure as 'normal' or 'pre hypertension' and to define different stages of 'hypertension'. Pushpa, K., KumanPrasanna, K.M., Nagaraj, D., and Thennarasu, K. Blood Pressure Reference Tables for Children and Adolescents of Karnataka. Indian Pediatrics, 43 (June), pp. 491-501, 2006.

## **INTERNATIONAL RESEARCH**

### NIDA-Supported Researchers Identify New Injection Practice among Tanzanian Women

Dr. Mark Williams, University of Texas at Houston and colleagues (Dr. Sheryl McCurdy, University of Texas at Houston; Dr. Gad P. Kilonzo and Dr. M. T. Lesheaberi, University of Muhumbili, Dar Es Salaam, Tanzania) presented their recent epidemiological findings on Tanzanian IDUs and HIV at a conference December 1, 2006 – World AIDS Day – at the University of Muhumbili. The research was supported by a NIDA International Program collaborative research supplement (NOT-02-003) and a subsequent R21 (DA19394). The binational research team reports that heroin injection and risky injection practices are continuing to increase in Dar Es Salaam and spreading outward to neighboring communities. Using modified snowball sampling and outreach, the team recruited 537 heroin IDUs in Dar Es Salaam (318 male, 219 female); 42% of whom tested HIV positive (27% among males, 64% among females). The team observed a new and unusual practice among women IDUs – termed “flashblood” – where IDUs share blood-filled syringes after one has injected heroin. The research has been published in [AIDS Care, June 2005; 17\(Supplement 1\): S65-S76](#); [BMJ 2005; 331: 778-781](#); [Drug and Alcohol Dependence 82 Supplement 1\(2006\): S23-S27](#); and [AIDS Behavior DOI 10.1007/s10461-006-9102-x](#). Participants at the conference included representatives from the University of Muhumbili medical faculty; the Tanzanian Ministry of Labor, Employment, and Youth; the Tanzanian Ministry of Health; other Tanzanian officials; and invited media. The binational research team also met with Tanzanian Deputy Minister of Labor, Employment, and Youth Dr. Emmanuel Nchimbi on October 18, 2006.

# DIRECTOR'S REPORT TO COUNCIL

May 2007

## BASIC NEUROSCIENCE RESEARCH

### Rat Prenatal or Adolescent THC Exposure is Associated with Greater Heroin Intake in Adulthood

Brain cannabinoid and opioid systems are intimately connected. Cannabinoids stimulate release of enkephalin in the nucleus accumbens (NAS). They also stimulate PENK – the precursor gene for this endogenous opioid. Cannabinoid and opioid mu receptors are found on the same VTA neurons. Dr. Yasmin Hurd and colleagues have been conducting NIDA-supported studies to model (1) prenatal effects of clinically relevant gestational THC exposure and (2) adolescent marijuana abuse, to determine effects on the vulnerability for opiate self-administration in adulthood. In the prenatal study, rats were implanted for i.v. THC administration and then bred. THC was administered (.15 mg/kg) from gestational day 5 to postnatal day (PND) two (corresponding to mid-gestation in the human). Results showed that THC rats administered more drug and emitted more responses after stress, and had more drug-seeking behavior during extinction, but resembled controls on reinstatement tests with a heroin “prime” (return to bar-pressing on the drug-associated lever). Other groups were used to measure opioid peptide mRNA expression. The authors report that PENK mRNA in the NAS core and medial shell, and in the amygdala, was significantly increased in THC exposed animals at PND 62, suggesting a hyperactivity of the mesocorticolimbic encephalergic system that may mediate greater sensitivity for heroin reinforcement seen on some measures of these behavioral paradigms. Spano, M.S, Allgren, M., Wang, X. and Hurd, Y.L. Prenatal Cannabis Exposure Increases Heroin Seeking with Allostatic Changes in Limbic Enkephalin Systems in Adulthood. *Biological Psychiatry*, 61, pp. 554-563, 2007. In the adolescent study, THC exposed adolescents took significantly more opiate (greater number of infusions on the active lever, with no differences on an inactive lever) than adults. During dose response testing, they also self-administered significantly more heroin at this dose, and at 60 µg/kg/inf. Interestingly, THC treated animals did not exhibit more drug-seeking behavior during extinction. In a separate group sacrificed at PND 57, THC treatment was associated with significant increases of PENK mRNA expression in the NAC shell. There was also a significant positive correlation between the heroin self-administration and DAMGO-stimulated [<sup>35</sup>S]GTPγS binding in the shell suggesting that THC increases opiate µ receptors in this region, and a significant correlation between heroin self-administration and CB-1 (cannabinoid receptor) binding in the substantia nigra. Ellgren, M., Spano, S.M. and Hurd, Y.L. Adolescent Cannabis Exposure Alters Opiate Intake and Opioid Limbic Neuronal Populations in Adult Rats. *Neuropsychopharmacology*, (Epub ahead of print) May 22, 2006, pp. 1-9. Findings from these studies suggest that developmental exposure to the active pharmacological ingredient in marijuana, THC, may enhance subsequent vulnerability for opiate abuse, and shed light on potential neurobiological mechanisms responsible for this effect.

### Prenatal Marijuana Exposure and Marijuana Use at Age 14

In this longitudinal study conducted at the University of Pittsburgh, a cohort was recruited during the fourth prenatal month, and the mothers and their offspring were assessed at multiple ages from that time on. The assessments involved maternal psychological, social, and environmental factors, demographic status and substance use, and offspring cognitive, behavioral, psychological, and physical development. This report focuses on the association between prenatal marijuana exposure and marijuana use by the offspring at age 14 years. The analyses in this report are based on 563 offspring-mother pairs (74% of the original sample). The sample was half African American, half Caucasian, and mostly of lower socioeconomic status. Overall, at age 14 years, 30% of the adolescents reported using marijuana in the past year, and 7.5% reported using marijuana regularly (i.e., at least three to four times per week). Thirteen additional

adolescents had initiated marijuana use but did not report use in the past year. Based on multivariate models of analysis, the authors conclude that prenatal marijuana exposure (i.e., average daily joints), in addition to other factors, predicts marijuana use at age 14 years. Specifically, they report a marginally significant association between prenatal marijuana exposure and age of onset of marijuana use, and a significant association between prenatal marijuana exposure and frequency of marijuana use at age 14 years. Variables controlled in these analyses include child's current alcohol and tobacco use, pubertal stage, delinquency, peer drug use, family history of drug use, and parental depression, current drug use, and strictness/supervision. Prenatal marijuana use did not predict age of onset or frequency of use for either alcohol or tobacco. The investigators discuss possible mechanisms by which prenatal marijuana exposure may predict marijuana use at age 14, and also discuss limitations on generalizability of the findings. Day, N.L., Goldschmidt, L., and Thomas, C.A. Prenatal Marijuana Exposure Contributes to the Prediction of Marijuana Use at Age 14. *Addiction*, 101, pp. 1313-1322, 2006.

### Prenatal Cocaine Exposure and Child Behavior Outcomes Through Age 7 Years

Investigators from the Maternal Lifestyle Study, a multi-site longitudinal cohort study of development following prenatal exposure to cocaine and other substances, have reported on child behavior problems at ages 3, 5, and 7 years. The Child Behavior Checklist (CBCL) was administered to caregivers at all three ages, and data were reported for internalizing (e.g., social withdrawal, somatic complaints, anxiety), externalizing (e.g., delinquent and aggressive behaviors), and total behavior problems. Between 752 and 917 children were included in data analyses depending on the score category and the assessment age. Longitudinal hierarchical linear models were utilized to investigate relationships between prenatal cocaine exposure and behavior problem trajectories from 3 to 7 years. Statistical analyses included adjusting for a number of other prenatal exposures, and for time-varying covariates such as ongoing caregiver use of substances, demographic factors, family violence, and caregiver psychological distress. The authors report that high prenatal cocaine exposure was associated with trajectories of behavior problems (high exposure was defined as use  $\geq 3$  times per week in the first trimester), independent of, and less than the significant combined effect of prenatal and postnatal tobacco and alcohol exposures. Caregiver depression and family violence were found to have independent negative association with all behavior outcomes. The investigators note that although the analyses are an important step in examining relationships between prenatal cocaine exposure and behavior outcomes, causality is far from being established. In addition, they point out that the findings highlight a need not only for continued prevention and treatment programs directed toward illegal drug use, but also for increased effort toward prevention and treatment of tobacco and alcohol use. Bada, H.M., Das, A., Bauer, C.R. et al. Impact of Prenatal Cocaine Exposure on Child Behavior Problems through School Age. *Pediatrics*, 119, pp. e348-e359, 2007.

### Maternal Depression, Prenatal Cocaine Use, and Infant Neurobehavior

Infant neurobehavior was assessed for 1053 infants at 1 month of age, and was studied in relation to prenatal cocaine use and postpartum maternal depression. The NICU Network Neurobehavioral Scale (NNS) was used to measure infant neurobehavior, and the Addiction Severity Index (ASI) was used to assess present and past psychiatric history. These analyses were carried out within the context of the Maternal Lifestyle Study, a multi-site longitudinal cohort study of development following prenatal exposure to cocaine and other substances. Four groups were derived based on combinations of prenatal cocaine exposure/no prenatal cocaine exposure and current postpartum depression/no current postpartum depression. Analysis of covariance (with covariates birthweight, maternal age, SES, research site, and prenatal nicotine, marijuana, and alcohol) was utilized to examine infant neurobehavior in the four groups. Prenatal cocaine exposure by postpartum depression interactions were significant. A postpartum depression association was found for the non-cocaine-exposed infants (poorer self-regulation and more stress signs, excitability, and arousal than infants in the other groups). The combined prenatal cocaine exposure/current postpartum depression group did not differ on any of the neurobehavioral measures from the no-prenatal cocaine exposure/no current postpartum depression group. The investigators suggest that prenatal cocaine

exposure may buffer or alter the relationship between postpartum depression and infant neurobehavior, with one possible explanation being prenatal cocaine exposure influences on developing monoamine systems. While cautioning that these analyses cannot determine if the observed depression effects are related solely to postpartum depression or if prenatal depression contributes to this relationship, the authors note that the findings do suggest the importance of considering maternal mood in studies of prenatal substance exposure. Salisbury, A.L., Lester, B.M., Seifer, R. et al. Prenatal Cocaine Use and Maternal Depression: Effects on Infant Neurobehavior. *Neurotoxicology and Teratology*, epub ahead of print, December 2006.

#### Prenatal Cocaine Exposure and Infant Regulation at 7 Months of Age

Using heart rate (HR) and respiratory sinus arrhythmia (RSA) as indices of reactivity and regulation during infancy, Drs. Schuetze, Eiden, and Coles report on assessments at 7 months of age in a sample of 154 infants (79 prenatally-exposed to cocaine and 75 not prenatally-exposed to cocaine). Data were collected during baseline and during tasks designed to elicit positive and negative affect. Analyses of covariance were carried out to examine group differences in change scores, with maternal alcohol and cigarette use during pregnancy, maternal age, measures of fetal growth, and gestational age as covariates. The investigators report that there was a significant suppression of RSA during the negative affect task for the non-exposed group but not for the exposed group. The response pattern of RSA suppression from baseline to environmental challenge is noted by the authors as being associated with more optimal state regulation in infancy, decreased behavior problems in preschool aged children, and more adaptive behavior during attention and affect eliciting tasks in preschool and school aged children. Based on their RSA suppression finding and other results, the authors conclude that their findings provide additional support for an association between prenatal cocaine exposure and dysregulation during infancy. Schuetze, P., Eiden, R.D., and Coles, C.D. Prenatal Cocaine and Other Substance Exposure: Effects on Infant Autonomic Regulation at 7 Months of Age. *Developmental Psychobiology*, 49, pp. 276-289, 2007.

#### Types of Violence, Protective Factors, Psychopathology, and Behaviors in Drug-Exposed Youth at 11 Years of Age

In this examination of violence and resilience among youth exposed to cocaine and other substances during pregnancy, four types of violence (community, domestic, violent friends, history of child abuse) were studied relative to the occurrence of several outcomes (delinquency, early drug use, symptoms of depression, diagnosis of conduct disorder or oppositional defiant disorder, diagnosis of ADHD) for 517 children at 11 years of age. Measurement of protective factors involved seven indicators of positive relationships and prosocial behavior to teachers, parents, friends, and peers, as well as indicators of effortful control (inhibitory control and attentional focusing). This work was conducted in the context of the Maternal Lifestyle Study, a multi-site longitudinal study of the development of children prenatally-exposed to cocaine and other substances. Mixed model regression analysis was used for each outcome, and all models were adjusted for research site effects. The results show various patterns of associations between specific types of violence and specific outcomes. For example, all forms of delinquency were associated with having violent friends, symptoms of depression were related to history of abuse, CD/ODD was more likely if exposed to domestic violence, and ADHD was not associated with any type of violence. Associations with protective factors also showed variation by outcome. For example, reduced occurrence of CD/ODD was associated with positive relatedness to others and with effortful control, while reduced school delinquency and reduced depression were related to positive relatedness. The authors conclude that the study provides new evidence on violence and protective factors relative to disruptive forms of psychopathology and behavior, and they comment on implications of the findings for interventions. Lagasse, L.L., Hammond, J., Liu, J., et al. Violence and Delinquency, Early Onset Drug Use, and Psychopathology in Drug-Exposed Youth at 11 Years. *Annals of the New York Academy of Science*, 1094, pp. 313-318, 2006.

### Convergence of HIV Seroprevalence Among Injecting and Non-injecting Drug Users in New York City

HIV infection has historically been higher among injecting drug users because the virus is efficiently transmitted through the sharing of drug-injecting equipment. In this study, researchers sought to compare HIV prevalence among injecting and non-injecting heroin and cocaine users in New York City by analyzing data from 2 separate cross-sectional surveys, both with HIV counseling and testing and drug use and HIV risk behavior questionnaires. Participants included injecting and non-injecting heroin and cocaine users recruited at detoxification and methadone maintenance treatment from 2001-2004 (n = 2121) and through respondent-driven sampling from a research storefront in 2004 (n = 448). In both studies, HIV prevalence was nearly identical among current injectors (injected in the last 6 months) and heroin and cocaine users who had never injected: 13% [95% confidence interval (CI), 12-15%] among current injectors and 12% (95% CI, 9-16%) among never-injectors in the drug treatment program study, and 15% (95% CI, 11-19%) among current injectors and 17% (95% CI, 12-21%) among never injectors in the respondent driven sampling storefront study. The 95% CIs overlapped in all gender and race/ethnicity subgroup comparisons of HIV prevalence in both studies. These findings indicate that the very large HIV epidemic among drug users in New York City may be entering a new phase, in which sexual transmission is increasingly important. Additional prevention programs are needed to address this transition. Des Jarlais, D., Arasteh, K., Perlis, T., Hagan, H., Abdul-Quader, A., Heckathorn, D., McKnight, C., Bramson, H., Nemeth, C., Torian, L., and Friedman, S. Convergence of HIV Seroprevalence Among Injecting and Non-injecting Drug Users in New York City. *AIDS*, 21(2), pp. 231-235, 2007.

### Grandmother and Parent Influences on Child Self-Esteem

This study tests a model of intergenerational influences on childhood self-esteem that proposes paths from grandmothers' drug problems to grandchildren's self-esteem via parents' drug problems and parental adaptive child rearing and from grandmothers' maternal acceptance to grandchildren's self-esteem via parents' unconventionality and adaptive child rearing. This longitudinal study uses data obtained from interviews with a New York City sample of black and Puerto Rican children (N = 149) and 1 of their parents and from mailed questionnaires or comparable interviews with those parents' mothers. Structural equation modeling was used to test the proposed model. The LISREL analysis found that, with 3 exceptions, all of the hypothesized paths were significant. The total effects analysis indicated that parents' adaptive child rearing was the strongest latent construct, a finding that was consistent with this construct's proximal position in the model. This study suggests that mothers' drug problems are not just near-term risks for their children, but also pose long-term risks for their children's future functioning as parents and thereby for their grandchildren. The authors conclude that the relative strength of parents' adaptive child rearing in this intergenerational model indicates that this area should be the focus of therapeutic intervention efforts, but addressing future grandmothers' drug problems may have positive effects on multiple generations. Brook, J., Ning, Y., Balka, E., Brook, D., Lubliner, E., and Rosenberg, G. Grandmother and Parent Influences on Child Self-Esteem. *Pediatrics*, 119(2), pp. 444-451, 2007.

### Women Who Gave Birth as Unmarried Adolescents: Trends in Substance Use from Adolescence to Adulthood

The purpose of this study was to determine whether adolescent childbearing mothers "mature out" of substance use as they transition into adulthood; how their substance use compares to that of typical young women of the same ages; and whether there are different patterns of substance use evident in this vulnerable population. The data come from an ongoing longitudinal study of 240 young women who were unmarried, pregnant, and under age 18 at enrollment. They have been interviewed regularly from pregnancy through 11.5 years postpartum. The data are based on self-reported substance use verified by random urinalysis for drug metabolites. Substance use did not decline during the transition to adulthood nor into early adulthood. With the exception of alcohol, the prevalence of substance use was higher than that of a nationally representative sample of same-aged women. Three distinct patterns of substance use

were identified: licit users (cigarettes and/or alcohol), marijuana users, and "hard" drug users. Based on these findings, the authors suggest that clinicians should routinely assess substance use among young mothers who bore children as teenagers, and make referrals for appropriate treatment. Cigarette smoking is especially a cause for concern, given its widespread use and harmful effects for both mothers and their children. Although only a small proportion (about 5%) of young mothers used hard drugs consistently over time, this group will likely require comprehensive interventions that address multiple issues such as mental health and contextual factors to be effective. Future research should address reasons for continued substance use in this population. Gillmore, M., Gilchrist, L., Lee, J., and Oxford, M. Women who Gave Birth as Unmarried Adolescents: Trends in Substance Use from Adolescence to Adulthood. *J Adolesc Health*, 39(2), pp. 237-243, 2006.

#### Maternal Cigarette Smoking During Pregnancy and Child Aggressive Behavior

This study's objective was to examine the association between maternal smoking during pregnancy and childhood aggressive behavior in African-American and Puerto Rican children, as well as the relationship between maternal unconventional behavior, low maternal affection, and offspring aggression. Participants consisted of African-American and Puerto Rican children (N = 203; mean age = 8.6, SD = 0.87) and their mothers living in an inner city community. An interview consisting of a structured questionnaire was administered to the mothers and their children. Scales with adequate psychometric properties were adapted from previous validated measures. They included maternal smoking during pregnancy, maternal education, unconventionality, and warmth. Controlling for demographic factors, maternal unconventional behavior, and low maternal warmth, maternal smoking during pregnancy was associated with having offspring who were aggressive. Maternal unconventionality and warmth were independently related to childhood aggression. The authors suggest that although causal limitations are noted, it may be that a decrease in smoking during pregnancy is associated with a reduction in aggression in the offspring. Brook, D., Zhang, C., Rosenberg, G., and Brook, J. Maternal Cigarette Smoking during Pregnancy and Child Aggressive Behavior. *Am J Addict*, 15(6), pp. 450-456, 2006.

#### Between Parental and Offspring Psychiatric Disorders

The present study was conducted to investigate the specificity of the association between parental and offspring psychiatric disorders using epidemiological data from a series of parent and offspring interviews. A community-based sample of 593 mothers and their offspring from upstate New York were interviewed during the adolescence and early adulthood of the offspring. The children of parents with generalized anxiety disorder were at specifically elevated risk for anxiety disorders when co-occurring psychiatric disorders were controlled. The associations between parental and offspring antisocial, conduct, depressive, and substance use disorders were characterized by modest specificity. Children of parents with externalizing disorders were nearly as likely to develop internalizing disorders as they were to develop externalizing disorders. Children of parents with internalizing disorders were somewhat, but not significantly, more likely to develop internalizing disorders. These findings support the inference that children of parents with generalized anxiety disorder may be more likely to develop anxiety disorders than they are to develop other psychiatric disorders. However, when co-occurring psychiatric disorders are accounted for, the children of parents with depressive, disruptive, and substance use disorders may be as likely to develop other disorders as they are to develop the same type of disorder that their parents have had. Johnson, J., Cohen, P., Kasen, S., and Brook, J. A Multiwave Multi-Informant Study of the Specificity of the Association between Parental and Offspring Psychiatric Disorders. *Compr Psychiatry*, 47(3), pp. 169-177, 2006.

#### Prescription Drug Abuse and Diversion among Adolescents

The aims of this study were to determine the prevalence of medical use of 4 classes of prescription medications relative to nonmedical use (illicit use) and to assess whether gender differences exist in the



trading, selling, loaning, or giving away of medications. A Web-based survey was administered to 7th- to 12th-grade students residing in 1 ethnically diverse school district in 2005. There were 1086 secondary students, including 586 girls, 498 boys, 484 black students, and 565 white students. Students were asked about their medical and nonmedical use of sleeping, sedative or anxiety, stimulant, and pain medications. Diversion of prescription medication was assessed by determining who asked the student to divert his or her prescription and who received it. Thirty-six percent of students reported having a recent prescription for 1 of the 4 drug classes. A higher percentage of girls reported giving away their medications than boys (27.5% vs. 17.4%, respectively;  $\chi^2(1) = 6.7$ ;  $P = .01$ ); girls were significantly more likely than boys to divert to female friends (64.0% vs. 21.2%, respectively;  $\chi^2(1) = 17.5$ ;  $P < .001$ ) whereas boys were more likely than girls to divert to male friends (45.5% vs. 25.6%, respectively;  $\chi^2(1) = 4.4$ ;  $P = .04$ ). Ten percent diverted their drugs to parents. These findings provide evidence of the need for physicians to discuss the proper use of prescription medications with their patients and their patients' families. Boyd, C., McCabe, S., Cranford, J., and Young, A. Prescription Drug Abuse and Diversion among Adolescents in a Southeast Michigan School District. *Arch Pediatr Adolesc Med*, 161(3), pp. 276-281, 2007.

#### Predictors of Unprotected Sex with Non-cohabitating Primary Partners among Sheltered and Low-income Housed Women in Los Angeles County

This study investigated cross-sectional associations of substance use, relationship abuse and HIV self-protective behavior with unprotected sex among 290 impoverished women with a non-cohabitating primary partner. Unprotected sex was associated with having a physically or psychologically abusive partner among low-income housed women, and having an abusive partner who also drank to intoxication among women living in shelters. Indicators of HIV self-protective behavior were associated with less frequent unprotected sex among sheltered women, even after accounting for abuse and substance use within the relationship. Results suggest the need for HIV-prevention interventions to address the problems of partner substance use and relationship abuse. Tucker, J., Wenzel, S., Elliott, M., and Hambarsoomian, K. Predictors of Unprotected Sex with Non-Cohabiting Primary Partners among Sheltered and Low-Income Housed Women in Los Angeles County. *J Health Psychol*, 11(5), pp. 697-710, 2006.

#### Psychological Correlates of Trading Sex for Money among African American Crack Cocaine Smokers

This article compares demographic characteristics, sexual practices, and psychosocial status among 193 African American female crack cocaine users who currently, previously, or never traded sex for money. Current traders were less likely to have a main sexual partner, more likely to have a casual sexual partner, and more likely to smoke larger quantities of crack. There was a significant trend towards current traders reporting lower self-esteem, greater depression and anxiety, poorer decision-making confidence, more hostility, less social conformity, greater risk taking behaviors, and more problems growing up, compared to previous and never traders. These differences suggest that interventions should address self-esteem, risk-taking practices, depression and anxiety as well as other psychosocial factors. Risser, J., Timpson, S., McCurdy, S., Ross, M., and Williams, M. Psychological Correlates of Trading Sex for Money among African American Crack Cocaine Smokers. *Am J Drug Alcohol Abuse*, 32(4), pp. 645-653, 2006.

#### Assortative Mating Explains Spousal Similarity in Cigarette and Alcohol Use and Dependence

Non-random mating affects population variation for substance use and dependence. Developmentally, mate selection leading to positive spousal correlations for genetic similarity may result in increased risk for substance use and misuse in offspring. Mate selection varies by cohort and thus, assortative mating in one generation may produce marked changes in rates of substance use in the next. This team of researchers used data from female twins and their male spouses to clarify the mechanisms contributing to spousal similarity for cigarette smoking and alcohol consumption. They found that assortative mating significantly influenced regular smoking, regular alcohol use, nicotine dependence and alcohol dependence. The bivariate models for cigarette smoking and alcohol consumption also highlighted the importance of primary

assortative mating on all stages of cigarette smoking and alcohol consumption, with additional evidence for assortative mating across the two stages of alcohol consumption. They concluded that women who regularly used, and subsequently were dependent on cigarettes or alcohol were more likely to marry men with similar behaviors. After mate selection had occurred, one partner's cigarette or alcohol involvement did not significantly modify the other partner's involvement with these psychoactive substances. Agrawal, A., Heath, A., Grant, J., Pergadia, M., Statham, D., Bucholz, K., Martin, N., and Madden, P. Assortative Mating for Cigarette Smoking and for Alcohol Consumption in Female Australian Twins and their Spouses. *Behav Genet*, 36(4), pp. 553-566, 2006.

## **PREVENTION RESEARCH**

### Multidimensional Treatment Foster Care For Girls in the Juvenile Justice System: Two Year Follow-Up of a Randomized Clinical Trial

This study is a 2-year follow-up of girls with serious and chronic delinquency who were enrolled in a randomized clinical trial conducted from 1997 to 2002 comparing multidimensional treatment foster care (MTFC) and group care (N = 81). Girls were referred by juvenile court judges and had an average of over 11 criminal referrals when they entered the study. A latent variable analysis of covariance model controlling for initial status demonstrated maintenance of effects for MTFC in preventing delinquency at the 2-year assessment, as measured by days in locked settings, number of criminal referrals, and self-reported delinquency. A latent variable growth model focusing on variance in individual trajectories across the course of the study also demonstrated the efficacy of MTFC. Older girls exhibited less delinquency over time relative to younger girls in both conditions. Implications for gender-sensitive programming for youths referred from juvenile justice are discussed. Chamberlain, P., Leve, L., and Degarmo, D. Multidimensional Treatment Foster Care for Girls in the Juvenile Justice System: 2-Year Follow-up of a Randomized Clinical Trial. *J Consult Clin Psychol*, 75(1), pp. 187-193, 2007.

### Neighborhood Effects on Prevention Program Efficacy

This study examines how neighborhood characteristics affect program efficacy through an analysis of data from a randomized prevention trial. The prevention program, called "Keepin' it REAL", was administered to a predominantly Mexican American sample of 4,622 middle school students in Phoenix, Arizona, beginning in 1998. The program was designed to extend evidence-based resistance and life-skills prevention approaches to incorporate ethnically appropriate traditional values and practices that promote protection against drug use. Thirty-five middle schools were randomized to one of two culturally grounded prevention conditions or a control condition. Prior research supports the overall efficacy of the prevention program. However, among less linguistically acculturated Latinos, living in poorer neighborhoods and in single-mother families decreased program effectiveness in reducing alcohol use. High neighborhood immigrant composition increased program effectiveness. Unexpectedly, the program was also more effective in neighborhoods with higher rates of crime. Yabiku, S., Kulis, S., Marsiglia, F.F., Lewin, B., Nieri, T., and Hussaini, S. Neighborhood Effects on the Efficacy of a Program to Prevent Youth Alcohol Use. *Subst Use Misuse*, 42, pp. 65-87, 2007.

### Adolescent Predictors of Emerging Adult Sexual Patterns

This study estimates the percentages of young adults who fall into three groups based on the context of sexual transition: (1) those who had vaginal intercourse before marriage (Premaritals), (2) those who postponed sex until after marriage (Postponers), and (3) those who have never had vaginal intercourse (Virgins). The second purpose was to determine adolescent biopsychosocial factors that predict membership in these adult groups. Analyses are based on 11,407 respondents ages 18-27 years who participated in Waves I and III of the National Longitudinal Study of Adolescent Health. Adolescent indicators reflecting sociodemographic, biosocial, experiential, and contextual factors were used to predict

young adult sexual status using multinomial logistic regression models. About 8% of the sample were virgins and 2% were virgins until marriage. Almost 90% had sex before marriage (Premaritals--referent group). Most predictors of status were similar for males and females. Compared with Premaritals, Virgins were younger, non-Black, not advanced in physical maturity relative to peers in adolescence, had higher body mass indexes, were more religious, and perceived parental disapproval of sex during adolescence. Postponers were also more religious than Premaritals but were older. Female Postponers were non-Black and perceived parental disapproval of sex during adolescence. Male Postponers were less likely to have same-gender attractions or no sexual attractions. Findings document premarital sexual activity as the almost universal sexual trajectory into young adulthood for these cohorts and underscore the roles of biosocial factors and conventional institutions in emerging sexual patterns. Halpern, C., Waller, M., Spriggs, A., and Hallfors, D. Adolescent Predictors of Emerging Adult Sexual Patterns. *J Adolesc Health*, 39(6), pp. e1-e10, 2006.

#### Drug Abuse Risk and Protective Factors among Black Urban Adolescent Girls: A Group-randomized Trial of Computer-delivered Mother-daughter Intervention

A group-randomized design tested a mother-daughter intervention in which researchers aimed to increase protective factors in a community sample of Black urban adolescent girls. Girls and their mothers at 2 community agencies were pretested and, by agency, were randomized to either an intervention arm or a control arm. Intervention arm girls and their mothers received a program for improving mother-daughter rapport. Posttest data collected 3 weeks after program delivery revealed that intervention arm mothers and daughters improved more than did control arm mothers and daughters on measures of communication and closeness. At 3-month follow-up, intervention arm mothers, relative to control arm mothers, continued to report better communication with and closeness to their daughters. Girls and mothers in the intervention arm rated the computer program favorably on parameters of enjoyment, comfort, relevance, usefulness of information, improvements to their relationship with one another, and whether they would recommend the computer program to friends. Schinke, S., Di Noia, J., Schwinn, T., and Cole, K. Drug Abuse Risk and Protective Factors among Black Urban Adolescent Girls: A Group-Randomized Trial of Computer-Delivered Mother-Daughter Intervention. *Psychol Addict Behav*, 20(4), pp. 496-500, 2006.

#### Perceived Smoking Environment and Smoking Initiation among Multi-ethnic Urban Girls

The purpose of this study was to examine associations between the perceived smoking environment and smoking initiation among urban multi-ethnic adolescent girls in New York City. Self-report surveys completed in grades 7, 8, and 9 assessed girls' (n = 858) smoking initiation, and perceived smoking environment (family smoking, friends' smoking, smoking norms, and cigarette availability). Carbon monoxide breath samples were collected from girls using a variation of the bogus pipeline procedure. Differences were found in smoking prevalence with white girls reporting the highest prevalence of smoking at baseline and greatest increase in smoking prevalence from seventh to eighth grade. Black girls reported an initial increase in smoking prevalence from seventh to eighth grade followed by a decrease from eighth to ninth grade. Family smoking, friends' smoking, smoking norms, and cigarette availability were all associated with smoking initiation at eighth grade but only friends' smoking was associated with smoking initiation at ninth grade. Few ethnic differences were found in risk factors at baseline and racial/ethnic group did not modify associations between risk and smoking initiation. Urban adolescent girls of different racial/ethnic backgrounds had similar perceptions of the smoking environment. Despite the similarity of risk factors across racial/ethnic groups, urban white girls are at increased risk to initiate smoking. Preventive interventions that target girls' perceived smoking environment during early adolescence should be effective across ethnic groups. Nichols, T., Birnbaum, A., Birnel, S., and Botvin, G. Perceived Smoking Environment and Smoking Initiation among Multi-Ethnic Urban Girls. *J Adolesc Health*, 38(4), pp. 369-375, 2006.

### Perceived Physical Maturity, Age of Romantic Partner, and Adolescent Risk Behavior

Early pubertal timing and advanced physical maturity for age confer elevated risk for problem behaviors for both boys and girls. However, examinations of possible biological and social mediators have been limited. Using more than 4,000 adolescents under age 15 who participated in Waves I and II of the National Longitudinal Study of Adolescent Health (Add Health), authors examined the relationship between perceived physical maturity and membership in risk behavior clusters, and tested whether having a romantic partner mediates the maturity/risk behavior relationship. Results of multinomial regression models indicated that for both boys and girls, advanced physical maturity was associated with membership in higher risk clusters, and that having a romantic partner plays an important mediating role in this association. For females, the additional impact of having an older partner, versus any partner at all, was substantial and particularly important for the highest risk clusters. The role of partner age could not be tested for males. Because romantic partners elevate risk for young adolescent males and females, there is a need to identify and understand facets and developmental functions of adolescent romantic relationships that play a role in substance use and sexual decisions. Halpern, C., Kaestle, C., and Hallfors, D. Perceived Physical Maturity, Age of Romantic Partner, and Adolescent Risk Behavior. *Prevention Science*, 8(1), pp. 1-10, 2006.

### Adolescent Girls Offending and Health-Risking Sexual Behavior: The Predictive Role of Trauma

Several studies have highlighted high levels of risk for girls who have been exposed to traumatic experiences, but little is known about the exact relationship between traumatic experiences and problems with delinquency and health-risking sexual behavior (e.g., precipitatory and/or exacerbatory roles). However, numerous short- and long-term detrimental effects have been linked to trauma, delinquency, and health-risking sexual behavior. The utility of diagnostic and experiential trauma measures in predicting the greatest risk for poor outcomes for delinquent girls was examined in this study. Results indicate that the experiential measures of trauma (cumulative and composite trauma scores) significantly predicted adolescent offending and adolescent health-risking sexual behavior, whereas the diagnostic measures of trauma (full and partial diagnostic criteria) did not. Smith, D., Leve, L.D., and Chamberlain, P. Adolescent Girls' Offending and Health-Risking Sexual Behavior: The Predictive Role of Trauma. *Child Maltreat*, 11, pp. 346-353, 2006.

### The Relationship between Cultural Practices and Commonly Used Markers of Acculturation

The current study was conducted to ascertain the validity of two commonly used markers of acculturation (nativity and years in the receiving culture). Relationships between these markers and a bidimensional measure of acculturation were examined in a convenience sample of Hispanic immigrant adolescents and their caregivers in Miami. Nativity was examined using adolescent-reported data; approximately half of the youth were U.S.-born and half foreign-born, but all of the caregivers were foreign-born. Years in the receiving culture was examined using both adolescent and caregiver data. Results indicated that nativity was significantly associated with adoption of receiving-culture practices, with a small to moderate effect size. Years in the receiving culture was significantly associated with adoption of receiving-culture practices only for adolescent girls and for female caregivers who immigrated as youth. Neither nativity nor years in the receiving culture explained even moderate amounts of variance in retention or loss of culture-of-origin practices. Schwartz, S.J., Pantin, H. and Sullivan, S. Nativity and Years in the Receiving Culture as Markers of Acculturation in Ethnic Enclaves. *J Cross Cult Psychol*, 37(3), pp. 345-353, 2006.

### Research on the Caretaking of Children of Incarcerated Parents: Findings and Their Service Delivery Implications

This paper reviews research findings on caretaking-related problems associated with the absence of parents from the home following incarceration. It focuses on the impact of incarceration on the welfare and

adjustment of urban African American children and on the assumption of caretaking responsibilities by other caretakers, principally maternal grandmothers. Noting the complex situational difficulties involved and the potential burdens associated with surrogate parenting in general, and with this population in particular, the service-provider implications of this parenting arrangement are considered in this review. Findings indicate that problems associated with incarceration of parents tend to be intergenerational and vary considerably in complexity and severity. To the extent that they impact the children involved, these issues should be addressed in coordinated service delivery focusing on prevention. Hanlon, T.E., Carswell, S.B., and Rose, M. Research on the Caretaking of Children of Incarcerated Parents: Findings and Their Service Delivery Implications. *Child and Youth Services Review*, 29(3), pp. 348-362, 2006.

### Sex Differences in Overt Aggression and Delinquency

Given the recent debate over whether differential pathways to overt aggression and delinquency exist between boys and girls, this study examined sex differences in overt aggressive and delinquent acts along with potential differences in precursors (anger, self-control, family disruption) to antisocial behaviors among a sample of urban minority adolescents ( $N = 1559$ ). Overall the sample was 54% girls, 47% African American, 27% Latino/Hispanic, 5% Asian American, 7% Caucasian, and 13% biracial or other race/ethnicity. Almost all of the students (85%) attended public schools. Using a longitudinal design with data from 6th to 7th grade, results showed that girls had greater increases in rates of aggression relative to boys. Delinquency increased over time for both boys and girls, with boys consistently engaging in more delinquency. Girls and boys did not differ on the level of risk factors experienced except for a greater increase in anger over time for girls relative to boys. Across sex, anger and self-control predicted increases in both overt aggression and delinquency; family disruption also predicted increases in delinquency. Implications for subsequent studies on developmental process and preventive interventions are discussed. Nichols, T.R., Graber, J.A., Brooks-Gunn, J., and Botvin, G.J. Sex Differences in Overt Aggression and Delinquency among Urban Minority Middle School Students. *Applied Developmental Psychology*, 27, pp. 78-91, 2006.

### Latino Students Perceptions of School Environment

This study describes results from an investigation of Latino students attending a Hispanic Education Summit (HES) in North Carolina. Findings from data gathered from 275 middle and high school students are presented ( $n = 142$  female;  $n = 121$  male). Self-report data assessed level of acculturation, as well as students' perceptions with regard to a variety of issues, including school programs, barriers to participation in programs, problems in the school environment, and academic aspirations. Results revealed that students reported few perceived barriers to school and aspirations. However, there was a significant relationship between acculturation level and the frequency with which students reported selected barriers and future life goals. Results indicated that low-acculturated students more often reported language-related problems as barriers to school involvement. Also reported by those students in the low-acculturation group were perceived discrimination, parental lack of time as a barrier, and low or no community involvement. These results indicate that high acculturation provides some students with a greater sense of belonging to their community and fewer barriers, including perceived discrimination. Gender differences were found with regard to acculturation level, perception of barriers, and academic aspirations. Specifically, with the exception of lack of interest, females reported more barriers than males and were rated as low in acculturation more frequently than males. Females also reported higher levels of academic aspirations, desires to do well in school, and a desire to be successful more frequently than males. Being female seems to promote resiliency with regard to academic aspirations for Latinos/as. These results lend support to previous research findings that females' higher value of academic achievement is related to being less acculturated or less vulnerable to assimilation of adversarial attitudes and behaviors responsible for academic failure. Overall this study suggests that there is not a linear relationship between acculturation and academic aspirations but, rather, this relationship may be mediated by a variety of factors including students' beliefs and attitudes, family cohesion, parental monitoring, parental attitudes concerning

education, cultural identity, perceived stereotypes, and discrimination. Future studies examining acculturation would benefit from a framework that clearly captures the complex dynamics of acculturation and how this phenomenon affects academic achievement and the overall adjustment of Latino immigrant students into their environment. Valencia, E.Y., and Johnson, V. Latino Students in North Carolina: Acculturation, Perceptions of School Environment, and Academic Aspirations. *Hispanic Journal of Behavioral Sciences*, 28(3), pp. 350-367, 2006.

#### Adding MEMS Feedback to Behavioral Smoking Cessation Therapy Increases Compliance with Bupropion: A Replication and Extension Study

This study was conducted to replicate and extend initial positive findings on the usefulness of a Medication Event Monitoring System (MEMS) to assess pill-taking behavior and enhance compliance with Bupropion for smoking cessation. Participants were 55 women aged 20-65, smoking a minimum of 10 cigarettes per day. All participants received MEMS bottles containing Bupropion-SR (150 mg) to be taken twice daily for 7 weeks, then randomized into one of two conditions, Usual Care (UC) or Enhanced Therapy (ET). In the UC condition, participants received individual cognitive behavioral therapy for smoking cessation. In the ET condition, weekly smoking cessation therapy sessions included additional 10 min of MEMS feedback and counseling using CBT techniques. Compliance outcomes included total doses taken and number of doses taken within the prescribed time interval. Results indicated significantly higher compliance over time for the Enhanced Therapy group. Smoking abstinence rates did not differ between the two groups, but pooled sample analysis showed a significant association between level of medication compliance and abstinence status at treatment weeks 3 and 6. Findings recommend incorporating MEMS-based compliance interventions into smoking pharmacotherapy trials. Mooney, M.E., Sayre, S.L., Hokanson, P.S., Stotts, A.L., and Schmitz, J.M., *Addictive Behaviors*, 32, pp. 875-880, 2007.

#### Attrition in a Multi-Component Smoking Cessation Study for Females

Attrition is a major challenge faced by researchers when implementing clinical trials. Investigators conducted this study to determine which baseline smoking-related, demographic and psychological participant characteristics were associated with attrition. Data were from a clinical trial evaluating exercise as an adjunctive treatment for nicotine gum among female smokers (N=246). There were a number of significant demographic predictors of attrition. Participants with at least one child living at home were at increased risk of both early and late dropout. Non-Whites were at increased risk of early dropout, while not having a college degree put one at increased risk of late dropout. Age was found to be a protective factor in that the older a participant was, the less likely she was to drop out in the early stages of the trial. With respect to psychological variables, weight concerns and guilt increased risk of attrition. In terms of smoking-related variables, mean cigarettes per day was not a significant predictor of attrition, although length of longest prior quit attempt was a significant predictor of early dropout when age was removed from the regression. Leeman, R.F., Quiles, Z.N., Molinelli, L.A., Medaglia Terwal, D., Nordstrom, B.L., Garvey, A.J. and Kinnunen, T. *Tobacco Induced Diseases*, 3, pp. 59-71, 2006.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

#### Mood Disorders Affect Drug Treatment Success of Drug-dependent Pregnant Women

This study examined the impact of co-occurring Axis I disorders on drug treatment outcomes of drug-dependent pregnant women. Participants (N =106) were women who met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for opioid dependence and were receiving methadone. Based on DSM-IV Axis I criteria, participants were categorized into three groups: (1) absence of mood/anxiety disorder (ND, n = 29), (2) primary mood disorder (MD, n = 39), or (3) primary anxiety disorder (AD, n = 38). Demographically, the groups were similar. The MD group was significantly more likely to be positive for drugs while in treatment compared with both the ND and AD groups. The MD and

AD groups had more psychosocial impairment and higher incidence of suicidal ideation compared with the ND group. Interestingly, the AD group spent more days in treatment compared with the ND or MD group. These findings highlight the need to treat co-occurring Axis I disorders, particularly given the higher relapse risk for those with mood disorders. [Fitzsimons, H.E., Tuten, M., Vaidya, V., and Jones, H.E.](#) Mood Disorders Affect Drug Treatment Success of drug-dependent pregnant women. *J Subst Abuse Treat.* 32(1), pp. 19-25, 2007. Epub 2006 October 13, 2006.

## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE AND CO-OCCURRING INFECTIONS (HIV/AIDS, HCV)**

### Needle Exchange Program Utilization and Entry into Drug User Treatment: Is There a Long-Term Connection in Baltimore, Maryland?

This study examined the relationship between Needle Exchange Program (NEP) utilization and treatment entry in Baltimore, Maryland. The sample was composed of 440 drug injectors with disadvantaged backgrounds. Face-to-face interviews, focusing on HIV risk behaviors, drug use, and health, were conducted between June 1997 and June 2002. Multivariate logistic analyses revealed that entering treatment was associated with NEP utilization, being female, and being HIV-positive. Cocaine sniffers/snorters were less likely to enter treatment. These findings highlight the importance of NEPs in linking injectors to treatment. They also suggest that treatment programs should be prepared and capable of addressing co-occurring problems, like HIV and mental illness. Study limitations are noted. [Latkin, C., Davey, M., and Hua, W.](#) Needle Exchange Program Utilization and Entry into Drug User Treatment: Is There a Long-Term Connection in Baltimore, Maryland? *Subst Use Misuse*, 41(14), pp. 1991-2001, 2006.

## **CLINICAL TRIALS NETWORK RESEARCH**

### Substance Abuse Treatment Entry, Retention, and Outcome in Women: A Review of the Literature

A search of the English language literature from 1975 to 2005 using Medline and PsycInfo databases found 280 relevant articles. Ninety percent of the studies investigating gender differences in substance abuse treatment outcomes were published since 1990, and of those, over 40% were published since the year 2000. Only 11.8% of these studies were randomized clinical trials. A convergence of evidence suggests that women with substance use disorders are less likely, over the lifetime, to enter treatment compared to their male counterparts. Once in treatment, however, gender is not a significant predictor of treatment retention, completion, or outcome. Gender-specific predictors of outcome do exist, and individual characteristics and treatment approaches can differentially affect outcomes by gender. While women-only treatment is not necessarily more effective than mixed-gender treatment, some greater effectiveness has been demonstrated by treatments that address problems more common to substance-abusing women or that are designed for specific subgroups of this population. There is a need to develop and test effective treatments for specific subgroups such as older women with substance use disorders, as well as those with co-occurring substance use and psychiatric disorders such as eating disorders. Future research on effectiveness and cost-effectiveness of gender-specific versus standard treatments, as well as identification of the characteristics of women and men who can benefit from mixed-gender versus single-gender treatments, would advance the field. [Greenfield, S.F., Brooks, A.J., Gordon, S.M., Green, C.A., Kropp, F., McHugh, R.K., Lincoln, M., Hien, D., and Miele, G.M.](#) Substance Abuse Treatment Entry, Retention, and Outcome in Women: A Review of the Literature. *Drug Alcohol Depend.* 86(1), pp. 1-21, 2007. Epub June 8, 2006.

## **INTERNATIONAL RESEARCH**

### Naltrexone With or Without Fluoxetine for Preventing Relapse to Heroin Addiction in St. Petersburg, Russia

INVEST Fellow: Anton Beshpalov, Russia, 1994-1995

This randomized placebo-controlled trial tested the efficacy of oral naltrexone with or without fluoxetine for preventing relapse to heroin addiction and for reducing HIV risk, psychiatric symptoms, and outcome. All patients received drug counseling with parental or significant-other involvement to encourage adherence. Patients totaling 414 were approached, 343 gave informed consent, and 280 were randomized (mean age, 23.6 +/- 0.4 years). At 6 months, two to three times as many naltrexone patients as naltrexone placebo patients remained in treatment and had not relapsed, odds ratio (OR) = 3.5 (1.96-6.12),  $p < .0001$ . Overall, adding fluoxetine did not improve outcomes, OR = 1.35 (0.68-2.66),  $p = .49$ ; however, women receiving naltrexone and fluoxetine showed a trend toward a statistically significant advantage when compared to women receiving naltrexone and fluoxetine placebo, OR = 2.4 (0.88-6.59),  $p = .08$ . HIV risk, psychiatric symptoms, and overall adjustment were markedly improved among all patients who remained on treatment and did not relapse, regardless of group assignment. More widespread use of naltrexone could be an important addition to addiction treatment and HIV prevention in Russia. Krupitsky, E.M., Zvartau, E.E., Masalov, D.V., Tsoy, M.V., Burakov, A.M., Egorova, V.Y., Didenko, T.Y., Romanova, T.N., Ivanova, E.B., Beshpalov, A.Y., Verbitskaya, E.V., Neznanov, N.G., Grinenko, A.Y., O'Brien, C.P. and Woody, G.E. *J Subst Abuse Treat.* 31(4), pp. 319-328, 2006. Epub July 24, 2006.

## **FORMER HUBERT H. HUMPHREY DRUG ABUSE RESEARCH FELLOWS**

### Predictors of HIV Sero-status Among Drug Injectors at Three Ukraine Sites

HHH Fellow: Sergey Dvoryak, Ukraine, 1999-2000

The objective of this study was to assess the HIV serostatus of injection drug users (IDU) in Ukraine, as well as associations between serostatus and selected demographic and risk factors. IDU were recruited from the streets in Kiev, Odessa and Makeevka/Donesk. Participants were interviewed using an HIV risk behavior assessment and tested for HIV with a finger-stick rapid test. Multiple logistic regression was used to identify determinants of HIV infection. Of the 891 IDUs surveyed, one-third came from each site and 22% were female. Their mean age was 29 years and on average they had been injecting for slightly more than 10 years. Seven hundred and seventy-eight of the total sample did not know their HIV status when first interviewed; they are the participants in this investigation. Overall, 33% tested positive for HIV, including 34% in Kiev, 51% in Odessa and 17% in Makeevka/Donesk. Independent predictors of HIV included injecting a sedative/opiate mixture, female sex, having sex with a person who was HIV positive or whose HIV status was unknown and injecting daily. HIV-negative IDU were significantly younger than those infected, they were more likely to be from Makeevka/Donesk and they were more likely to have been sexually active. Rates of HIV infection among IDU vary considerably across Ukraine, although even in the site with the lowest rate nearly one in five was infected. The extent of drug and sex-related risk behaviors calls for interventions to reduce the spread of HIV and other infectious diseases. Booth, R.E., Kwiatkowski, C.F., Brewster, J.T., Sinitsyna, L. and Dvoryak, S. *AIDS.* 20(17), pp. 2217-2223, 2006.

### Obstetric and Neonatal Outcomes in Women Who Live in an Urban Resettlement Area of Delhi, India: A Cohort Study

HHH Fellow: Arun Kumar Sharma, India, 2004-2005

The aim of the present research was to study the pregnancy outcome, namely mode and place of delivery, attendant at birth and perinatal mortality in an urban resettlement area of Delhi, India, and to determine factors that affect the outcome. Methods: All the pregnant women (n = 909) in the area were enrolled and followed until 7 days after delivery. The authors calculated the crude and adjusted odds ratios for



predictors of pregnancy related obstetric and neonatal outcomes, using logistic regression analysis. A total of 884 (97.3%) women could be followed up. Approximately two-thirds of deliveries took place at home. Primigravida, more educated mothers and mothers with non-cephalic presentation or complications were more likely to deliver in a health facility ( $P < 0.05$ ). Most deliveries (97%) were vaginal, 2.5% were cesarean and 0.5% forceps deliveries. Primigravida mothers, mothers with short stature, mothers with non-cephalic presentation or complications had cesarean and forceps delivery more often ( $P < 0.05$ ). A perinatal mortality rate of 74.5 per 1000 live births was observed. Presentation of the fetus and complications in the mother remained important factors. The authors conclude that the majority of deliveries in the under-privileged sections in urban Delhi take place at home and the perinatal mortality remains high. Chhabra, P., Sharma, A.K. and Tupil, K.A. *J Obstet Gynaecol Res.* 32(6), pp. 567-573, 2006.

# DIRECTOR'S REPORT TO COUNCIL

September 2007

## **BASIC NEUROSCIENCES RESEARCH**

### Prenatal Cocaine Exposure and the Developing Brain

Children exposed to cocaine during gestation have a higher incidence of neurobehavioral deficits. The neurochemical bases of these deficits have not been determined but the pharmacology of cocaine and the nature of abnormalities suggest that disruptions in catecholaminergic systems may be involved. In a recent study, NIDA-supported researchers report that prenatal cocaine exposure resulted in lasting changes to the regulation and responsivity of rat locus coeruleus norepinephrine (NE) neurons. From these findings, the researchers speculate that a similar dysregulation of locus coeruleus NE neurons may occur in children exposed to cocaine during gestation, and this may explain, at least partly, the increased incidence of cognitive deficits that have been observed in these subjects. This study was conducted in pregnant rats that received intravenous injection of cocaine twice daily between gestational days 10 and 20 and the progeny was tested as juveniles. The researchers also observed that the locus coeruleus NE system was more responsive to stimuli, such as exposure to a mild stressor, in rats exposed to prenatal cocaine compared to rats exposed to saline solution. Elsworth, J.D., Morrow, B.A., Nguyen, V.T., Mitra, J., Picciotto, M.R., and Roth, R.H. Prenatal Cocaine Exposure Enhances Responsivity of Locus Coeruleus Norepinephrine Neurons: Role of Autoreceptors. *Neuroscience* 147, pp. 419-427, 2007.

### Elevated Vulnerability of Male Adult to Drug Abuse after Prenatal Exposure to Cocaine Seen in Animal Model

It is estimated that for children born in the US 20% have been exposed to drugs of abuse in utero. Young adults who had in-utero drug exposure are more likely to abuse substances and show persistent affective and behavioral deficits; however, the biological bases of such deficits are not well understood. A team of NIDA supported researchers at Harvard University and Cornell University show that in animal models cocaine exposure during brain development changed dopaminergic neuron responses to cocaine in mice and increased their drug seeking behavior. Using brain stimulation-reward (BSR) method, Barry Kosofsky and colleagues report that the reinforcing effect of cocaine is greatly increased in adult male mice who were exposed to cocaine in utero. In pharmacological studies, these researchers demonstrate that a dopamine D1-receptor agonist has a similar effect as cocaine on these mice, indicating the involvement of limbic forebrain dopaminergic neural circuit in the BSR shift. Furthermore, they observed that a dopamine D2-receptor agonist had a biphasic effect on the threshold of BSR. Thus, the low doses increased the BSR threshold, but higher doses decrease the threshold. Similarly, they observed enhanced potency of the D2 agonist in the male adult mice that showed enhanced cocaine potency, which suggests adaptations in dopamine receptors may, in part, account for the changes in the rewarding potency of cocaine in adulthood after prenatal cocaine exposure. These results also provide biological evidence of developmental changes in the brain as consequences of early exposure to drugs of abuse. Malanga, C.J., Riday, T.T., Carlezon, W.A., and Kosofsky, B.E. Prenatal Exposure to Cocaine Increases the Rewarding Potency of Cocaine and Selective Dopaminergic Agonists in Adult Mice. *Biological Psychiatry*, 63(2), pp. 214-221, 2008.

## **BASIC BEHAVIORAL RESEARCH**

### Low Dose Nicotine Pretreatment Increases Cocaine Reward in Adolescent but not Adult Rats

Prior animal behavioral studies have shown that compared to adult rats, adolescent rats exhibit greater sensitivity to nicotine's stimulant and rewarding effects and lesser sensitivity to nicotine's negative effects. In the present study, Dr. Frances Leslie and colleagues at the University of California at Irvine sought to determine if nicotine pretreatment differentially modulates cocaine self-administration in adolescent and adult rats. Male and female rats, aged postnatal day P28 and P86, were treated twice daily with nicotine (0.03 ug/kg, i.v.) or saline daily for 4 days. At P32 and P90, the rats were tested for 5 consecutive days for acquisition of cocaine (0.2 or 0.5 mg/kg) self-administration. There were no main effects of sex or cocaine dose. In the first hour of acquisition, there was more cocaine self-administration by the adolescent nicotine-pretreatment group than by adolescent saline-pretreated animals or by adult nicotine and saline groups. Nicotine pretreatment also significantly enhanced cocaine self-administration in the adolescent, but not adult rats, across the first four of five sessions of cocaine self-administration. In a separate similar experiment with adolescent rats, nicotine pretreatment failed to enhance acquisition of sucrose operant responding, suggesting that nicotine's enhancement of cocaine self-administration does not merely reflect a generalized increase in appetitive responding. The authors conclude these findings suggest "that brief treatment with low doses of nicotine in early adolescence, but not adulthood, may cross-sensitize the brain to cocaine reward" (p.70). McQuown, S.C., Belluzzi, J.D., and Leslie, F.M. Low Dose Nicotine Treatment during Early Adolescence Increases Subsequent Cocaine Reward. *Neurotoxicology and Teratology*, 29, pp. 66-73, 2007.

### Sex Differences in Adolescent-onset vs Adult-onset Nicotine Self-administration

Dr. Ed Levin and colleagues at Duke University previously reported higher levels of nicotine self-administration in adolescent female rats than in adult female rats. This enhancement of nicotine self-administration in adolescence was still observed when animals were tested as adults (Levin et al. *Psychopharmacology*, 169, pp. 141-149, 2003). To complement this previous study, Dr. Levin and his colleagues have now conducted a parallel study in males. They found that male adolescent rats, like female adolescent rats, self-administered more nicotine on a per kilogram basis than adults. Additionally, they found two important sex differences. First, males were more vulnerable to this adolescent enhancement effect than females: compared to adult onset nicotine self-administration, the adolescent enhancement was two-fold in females, but three-fold in males. Second, unlike the female rats that persisted in higher rates of self-administration when they became adults, male rats exhibit adult-like levels of nicotine self-administration after the adolescent period. Thus, male rats appear to be more vulnerable than females to the adolescent enhancement effect, but only females exhibited a persistence of this enhancement into adulthood. Levin, E.D., Lawrence, S.S., Petro, A., Horton, K., Rezvani, A.H., Seidler, F.J., and Slotkin, T.A. Adolescent vs. Adult-onset Nicotine Self-administration in Male Rats: Duration of Effect and Differential Nicotinic Receptor Correlates. *Neurotoxicology and Teratology*, 29, pp. 458-465, 2007.

### Self-Control, Symptomatology and Substance Use in 9 yr Old Children

NIDA researcher, Rick Gibbons and colleagues, tested a theoretical model of how self-control constructs are related to psychological symptomatology and variables that predispose to involvement versus noninvolvement in substance use: willingness to use, affiliation with peers who use, and efficacy for resisting use. Data were obtained from a sample of 332 children, mean age = 9.3 years, who were interviewed in their homes. Overall, self-control constructs were significantly related to symptomatology or well-being. Moreover, the results showed significant pathways from symptomatology measures to predisposing factors plus a direct effect from poor self-control to lower resistance efficacy. The study was conducted with a diverse sample of children, and the results were obtained with control for relevant demographic characteristics, including ethnicity and parental education. The results may have implications

for preventive interventions. The results suggest that self-control training components can be included in prevention programs focused on adolescent problem behaviors. The results for predisposing factors suggest that prevention programs for younger children can target perceptions of substance users and resistance efficacy, as there is evidence that both processes can be altered through family- or school-based interventions. Furthermore, prevention research may be designed to examine the implications of more distal factors (e.g., neighborhood disadvantage, racial discrimination), as well as more proximal factors such as peer affiliations. Finally, the present results suggest that cognitive and motivational processes are more salient for young boys, whereas social processes are more salient for young girls. These gender differences need to be replicated, but results of this type need exploration because of their implications for targeted prevention programs. Wills, T.A., Ainette, M.G., Mendoza, D., Gibbons, F.X., and Brody, G.H. Self-Control, Symptomatology, and Substance Use Precursors: Test of a Theoretical Model in a Community Sample of 9-Year-Old Children. *Psychology of Addictive Behaviors*, 21, pp. 205-215, 2007.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Demographic and Psychosocial Characteristics of Mothers Using Methamphetamine During Pregnancy: Preliminary Results from the Infant Development, Environment, and Lifestyle Study (IDEAL)

The psychological characteristics and caretaking environments of 131 women enrolled in the first longitudinal study of prenatal methamphetamine (MA) exposure and child development were examined. Preliminary results from this study found that prenatal MA use was associated with lower maternal perceptions on quality of life, greater likelihood of substance use among family and friends, increased risk for ongoing legal difficulties, and a markedly increased likelihood of developing a substance abuse disorder. Preliminary findings also suggest that MA using women are more likely to have multiple, intertwined psychosocial risks that may result in maladaptive parenting and caregiving. These factors may impact the developmental outcomes of affected children. Derauf, C., LaGasse, L.L., Smith, L.M., Grant, P., Shah, R., Arria, A., Huestis, M., Haning, W., Strauss, A., Della Grotta, S., Liu, J., and Lester, B.M. Demographic and Psychosocial Characteristics of Mothers Using Methamphetamine during Pregnancy: Preliminary Results of the Infant Development, Environment, and Lifestyle study (IDEAL). *The American Journal of Drug and Alcohol Abuse*, 33(2), pp. 281-289, 2007.

### Impact of Prenatal Cocaine Exposure on Attention and Response Inhibition

This study examined the influence of prenatal cocaine exposure on attention and response inhibition measured by continuous performance tests (CPTs) at ages 5 and 7 years. Participants included 219 cocaine-exposed and 196 non-cocaine-exposed children enrolled prospectively at birth and assessed comprehensively through age 7 years in the longitudinal Miami Prenatal Cocaine Study. Deficits in attention and response inhibition were estimated in relation to prenatal cocaine exposure using generalized estimating equations within the general linear model. Results indicate cocaine-associated increases in omission errors at ages 5 and 7 as well as increases in response times for target tasks (i.e., slower reaction times) and decreased consistency in performance at age 7. There were no demonstrable cocaine-associated deficits in commission errors. Estimates did not change markedly with statistical adjustment for selected prenatal and postnatal covariates. Evidence supports cocaine-associated deficits in attention processing through age 7 years. Accornero, V.H., Amado, A.J., Morrow, C.E., Xue, L., Anthony, J.C., Bandstra, E.S. Impact of Prenatal Cocaine Exposure on Attention and Response Inhibition as Assessed by Continuous Performance Tests. *Journal of Developmental and Behavioral Pediatrics*, 28(3), pp. 195-205, 2007.

### Children's Language Trajectories Relative to Prenatal Cocaine Exposure

In this ongoing longitudinal study at Case Western Reserve University, language development was assessed at 1, 2, 4, and 6 years of age, and performance was analyzed for two groups of children based on cocaine exposure in utero (209 exposed, 189 not exposed). The groups were compared on receptive, expressive, and total language scores across time. Multiple potentially confounding and moderating factors were included in the analyses. A relationship between prenatal cocaine exposure and language development was seen over time for receptive, expressive, and total language scores, with cocaine exposure related to poorer performance. Analyses also indicated that prenatal tobacco exposure was related to lower receptive language scores, and that environmental factors were associated with language scores. The authors note that their findings are consistent with and extend the findings of other longitudinal studies of prenatal cocaine exposure and language development. In addition, it was noted that both the cocaine-exposed and nonexposed children declined in language performance over time, a result believed to be related to factors common to both groups (such as low SES, education, and poverty), and also consistent with findings from another prenatal cocaine exposure cohort study. Lewis, B.A., Kirchner, H.L., Short, E.J., Minnes, S., Weishampel, P., Satayathum, S., and Singer, L.T. Prenatal Cocaine and Tobacco Effects on Children's Language Trajectories. *Pediatrics*, 120(1), pp. e78-e85, 2007.

### Prenatal Cocaine Exposure and Physical Growth Patterns to Age 8 Years

This report focuses on longitudinal growth patterns in a cohort of children observed from birth until 8 years of age following prenatal exposure to cocaine. Birth weight, length, and head circumference were recorded. Weight, length or height, and head circumference were assessed at 6, 12, 24, 48, 72, and 96 months of age. Analyses were reported for 202 primarily African American/ Caribbean children. Ninety of these children were classified as prenatally unexposed to cocaine, 38 as having heavier cocaine exposure (top quartile of meconium concentration for cocaine metabolites, and/or top quartile days of self-reported use during the entire pregnancy), and 74 as having lighter exposure. Prenatal cocaine and prenatal alcohol exposure were independently associated with lower weight, length, and head circumference at birth. The relationships between prenatal cocaine exposure and longitudinal growth patterns to 8 years of age were analyzed using multiple linear regression models, including covariates of gestational age, gender, ethnicity, age at assessment, current caregiver, birth mother's use of alcohol, marijuana, and tobacco during the pregnancy, and maternal pre-pregnancy weight and height indicators. The association of prenatal cocaine exposure and growth did not persist beyond the neonatal period. The authors report that although the rate of change in growth parameters for cocaine-exposed children (heavier exposure compared to unexposed, and lighter exposure compared to unexposed) exceeded those of unexposed children in the first two years and then lagged up to age 4, the negative association with cocaine ultimately largely dissipated by school age. The authors also note that their findings agree with school-age results from another cohort of children prenatally exposed to cocaine, and differ in some ways from the findings for two other study cohorts, adding that ongoing examination of growth patterns in their cohort as well as in cohorts from other studies will continue to clarify the potential impact of in utero cocaine exposure on growth patterns to school age and beyond. Lumeng, J.C., Cabral, H.J., Gannon, K., Heeren, T., and Frank, D.A. Pre-natal Exposures to Cocaine and Alcohol and Physical Growth Patterns to Age 8 Years. *Neurotoxicology and Teratology*, 29(4), pp. 446-457, 2007.

### Visuospatial Working Memory in School-Aged Children Exposed in Utero to Cocaine

Among the neurocognitive impairments reported as associated with prenatal cocaine exposure, slower response time, and less efficient learning in school-aged children are common to findings from several laboratories. This study by Dr. Linda Mayes and her colleagues presents performance data on a spatial working memory task in 75 prenatally cocaine exposed (CE) and 55 nondrug-exposed (NDE) 8- to 10-year-old children. Children were administered a novel neuropsychological measure of immediate- and short-

term memory for visuospatial information, the Groton Maze Learning Test (GMLT), a computer-based hidden maze learning test that consists of a "timed chase test" (a simple measure of visuomotor speed), eight learning trials followed by a delayed recall trial after an 8-minute delay and a reverse learning trial. Performance is expressed as correct moves per second and number of errors per trial. Across all trials, the cocaine-exposed group showed significantly slower correct moves per second and made significantly more errors. There were no significant main effects for amounts of alcohol, tobacco, or marijuana exposure. After an 8-minute delay and compared to the eighth trial, cocaine-exposed children showed less consolidation in learning compared to nonexposed children. When asked to complete the maze in reverse, cocaine-exposed children showed a greater decrement in performance (decreased correct moves per second and increased errors) compared to the eighth learning trial. Children exposed in utero to cocaine exhibit a possible impairment in procedural learning and diminished efficiency in creating and accessing an internal spatial map to master the hidden maze. Mayes, L., Snyder, P.J., Langlois, E., and Hunter, N. Visuospatial Working Memory in School-aged Children Exposed in Utero to Cocaine. *Child Neuropsychology*, 13(3), pp. 205-218, 2007.

#### Multivariate Examination of Brain Abnormality Using Structural and Functional MRI with Adolescents Prenatally-Exposed to Cocaine

This article presents a methodological framework for extracting regional brain features simultaneously from both structural and functional images as a means for detecting brain abnormalities, and reports on the application of this method with a sample of 25 adolescents who had been exposed to cocaine in utero and a socioeconomically-matched comparison group of 24 non-exposed adolescents. High-resolution 3D structural MRI and arterial spin labeling perfusion MRI were the imaging modalities used. The procedure involved a regional statistical feature extraction approach to capture discriminative features from voxel-wise morphometric and functional representations of brain images. This feature extraction method was used in conjunction with a hybrid feature selection method and a nonlinear support vector machine for the classification of brain abnormalities. The investigators conclude that the method is capable of accurately detecting spatially distributed and complex patterns of brain alterations associated with prenatal cocaine exposure in an adolescent sample. Fan, Y., Rao, H., Hurt, H., Giannetta, J., Korczykowski, M., Shera, D., Avants, B.B., Gee, J.C., Wang J., and Shen, D. Multivariate Examination of Brain Abnormality Using both Structural and Functional MRI. *Neuroimage*, 36(4), pp. 1189-1199, 2007.

#### Abnormal Cortical Thickness and Brain-Behavior Correlation Patterns in Individuals with Heavy Prenatal Alcohol Exposure

Quantitative magnetic resonance imaging (MRI) studies in children with fetal alcohol spectrum disorders (FASDs) have shown regional patterns of dysmorphology, most prominent in parietal and posterior temporal cortices. Various methods of image analysis have been employed in these studies, but abnormalities in cortical thickness have not yet been mapped over the entire cortical surface in individuals with FASD. Further, relationships between cognitive dysfunction and cortical thickness measures have not yet been explored. In this study Dr. Elizabeth Sowell and her colleagues applied cortical pattern matching algorithms and techniques for measuring cortical thickness in millimeters to the structural brain MRI images of 21 subjects with heavy prenatal alcohol exposure (8-22 years, mean age 12.6 years), and 21 normally developing control subjects (8-25 years, mean age 13.5 years). Dissociable cognitive measures, of verbal recall and visuospatial functioning, were correlated with cortical thickness, and group by test score interactions were evaluated for predicting cortical thickness. Significant cortical thickness excesses of up to 1.2 mm were observed in the FASD subjects in large areas of bilateral temporal, bilateral inferior parietal, and right frontal regions. Significant group by test score interactions were found in right dorsal frontal regions for the verbal recall measure and in left occipital regions for the visuospatial measure. These results are consistent with earlier analyses from this and other research groups and, for the first time,

show that cortical thickness is also increased in right lateral frontal regions in children with prenatal alcohol exposure. Further, the significant interactions show for the first time that brain-behavior relationships are altered as a function of heavy prenatal alcohol exposure. Sowell, E.R., Mattson, S.N., Kan, E., Thompson, P.M., Riley, E.P., and Toga, A.W. Abnormal Cortical Thickness and Brain-Behavior Correlation Patterns in Individuals with Heavy Prenatal Alcohol Exposure. *Cerebral Cortex*, 18(1), pp. 136-144, 2008.

#### fMRI of Verbal Learning in Children with Heavy Prenatal Alcohol Exposure

Dr. Elizabeth Sowell and her colleagues examined functional MRI activation patterns corresponding to verbal paired associate learning in a group of 11 children (between 8 and 13 years of age) with heavy prenatal alcohol exposure compared with 16 typically-developing children (between 7 and 15 years old). Among the typically developing children, prominent activation was observed in the left medial temporal lobe, left dorsal frontal lobe and bilateral posterior temporal cortices during learning and recall. Analyses revealed significantly less activation in left medial and posterior temporal regions and significantly more activation in right dorsal frontal cortex in the alcohol-exposed children relative to controls, even when group differences in memory test performance were statistically controlled. These results may indicate an increased reliance on frontal memory systems in the children with heavy prenatal alcohol exposure, perhaps compensating for dysfunctional medial temporal memory systems. These findings are consistent with neuropsychological and structural imaging studies, and provide the first evidence for brain activation abnormalities, independent of group performance differences, during verbal learning and recall in children with heavy prenatal alcohol exposure. Sowell, E.R., Lu, L.H., O'Hare, E.D., McCourt, S.T., Mattson, S.N., O'Connor, M.J., and Bookheimer, S.Y. Functional Magnetic Resonance Imaging of Verbal Learning in Children with Heavy Prenatal Alcohol Exposure. *NeuroReport*, 18(7), pp. 635-639, 2007.

#### Magnetic Resonance and Spectroscopic Imaging in Prenatal Alcohol-Exposed Children: Preliminary Findings in the Caudate Nucleus

This study was designed to identify and compare the neuroanatomical and neurochemical abnormalities that are associated with prenatal exposure to alcohol in both fetal alcohol syndrome (FAS)-diagnosed children and those diagnosed with fetal alcohol effects (FAE). MR data of three age-, gender- and race-balanced small groups of children (age range 9.6 to 12.7 years), FAS-diagnosed, FAE-diagnosed, and non-exposed controls, were compared. Effects of prenatal alcohol exposure, regardless of diagnosis, were found in the caudate nucleus. Specifically, a significantly smaller caudate nucleus was found for the FAS and FAE participants compared to the controls. In addition, the metabolite ratio of N-acetyl-aspartate to creatine (NAA/Cr), an indicator of neuronal function, in left caudate nucleus of both the FAS and FAE participants was elevated compared to the control group. Analysis of absolute concentrations revealed that the increase in the ratio of NAA/Cr was due to an increase in NAA alone. Although its exact function in the CNS is unknown, NAA is believed to be a neuronal marker due to its exclusive localization to neurons. Some also speculate a role for NAA in myelination. Elevated NAA in the prenatal alcohol-exposed participants could indicate a lack of normal programmed cell death, dendritic pruning and/or myelination during development. The present study demonstrates that prenatal alcohol-exposed children, with or without facial dysmorphism, have abnormal brain anatomy and chemistry. Corteses, B.M., Moore, G.J., Bailey, B.A., Jacobson, S.W., Delaney-Black, V., and Hannigan, J.H. Magnetic Resonance and Spectroscopic Imaging in Prenatal Alcohol-exposed Children: Preliminary Findings in the Caudate Nucleus. *Neurotoxicology and Teratology*, 28(5), pp. 597-606, 2006.

#### Smoking During Teenage Pregnancies and Behavioral Problems in Offspring

In this paper, Cornelius and colleagues at the University of Pittsburgh report on relationships between prenatal tobacco exposure (PTE) and school-age child behavior in a cohort of 357 offspring of teenage mothers. PTE was defined as any exposure across pregnancy for some of the analyses, and exposure within each trimester in other analyses. Interviews were conducted with the mothers at the fourth or fifth prenatal

month visit and within 24-36 hours after delivery. Child exposure to environmental tobacco smoke (ETS) was assessed by urinary cotinine. Average age of the offspring in the analyses was 6.4 years. PTE (any exposure across pregnancy) was a significant predictor ( $p < .01$ ) of increased activity (Routh Activity Scale) when controlling for other prenatal substance exposure, demographics, maternal psychological characteristics, home environment, and ETS. When controlling for the same factors, PTE (in each of the three trimesters) significantly ( $p < .01$ ) predicted increased activity, and PTE (in the second trimester) significantly ( $p < .05$ ) predicted attention problems (SNAP). ETS was not a significant predictor of behavioral outcomes when PTE was taken into account. The researchers indicate that their finding of an association of PTE with higher activity levels in exposed offspring agrees with results from animal and other human studies, and adds new evidence of the strength of this association given the extent of control for covariates in this study. Cornelius, M.D., Goldschmidt, L., DeGenna, N., and Day, N.L. Smoking during Teenage Pregnancies: Effects on Behavioral Problems in Offspring. *Nicotine and Tobacco Research*, 9(7), pp. 739-750, 2007.

#### Gender-Specific Effects of Prenatal and Adolescent Exposure to Tobacco Smoke on Auditory and Visual Attention

Smoking during pregnancy results in elevated risks of cognitive and auditory processing deficits and of smoking in the offspring. Preclinical studies have revealed that nicotine exposure in the prenatal and/or adolescent period results in a sex-specific pattern of reduction in cortical cholinergic markers. This study was designed to examine gender-specific effects of exposure to smoking in adolescents on auditory and visual attention. The sample consisted of 181 adolescent smokers and nonsmokers who had previously been exposed to maternal smoking or had not. The results demonstrated that both auditory and visual attention performance accuracy was decreased in females who were exposed to tobacco smoke during prenatal or adolescent development; however, the greatest deficits on these tasks were seen in female smokers who had also been exposed to tobacco smoke in the prenatal period (combined exposure). The pattern was somewhat different in males in that combined exposure resulted in greater deficits during the auditory attention conditions versus the visual processing tasks. Functional neuroimaging was conducted in a subset of 63 subjects while they were engaged in auditory and visual attentional tasks. In those adolescents with prenatal or adolescent exposure, activation of brain regions that support auditory attention was greater relative to controls with no exposure to tobacco smoke. The results of the functional imaging data suggest that reduced cortical cholinergic neurotransmission resulting from prenatal exposure or adolescent exposure to tobacco smoke results in a loss of efficiency in cortical regions that support auditory attention. This study supports the need for effective smoking prevention programs for women of childbearing age and for adolescents. Jacobsen, L., Slotkin, T., Mencl, W., Frost, S., and Pugh, K. Gender-Specific Effects of Prenatal and Adolescent Exposure to Tobacco Smoke on Auditory and Visual Attention. *Neuropsychopharmacology*, 32(12), 2453-2464, 2007.

#### The Adolescent Trials Network for HIV/AIDS Interventions: A Case Study of Developing Adolescent Health Community-Researcher Partnerships in Fifteen U.S. Communities

This article describes the partner selection process in 15 U.S. communities developing community-researcher partnerships for the Connect to Protect (C2P): Partnerships for Youth Prevention Interventions, an initiative of the Adolescent Trials Network for (HIV/AIDS) Interventions. Each site generated an epidemiological profile of urban youth in their community, selected a focus population and geographic area of youth at risk for HIV, conducted a series of successive structured interviews, and engaged in a process of relationship-building efforts culminating in a collaborative network of community agencies. Sites chose as their primary target population young women who have sex with men ( $n = 8$  sites), young men who have sex with men ( $n = 6$ ), and intravenous drug users ( $n = 1$ ). Of 1162 agencies initially interviewed, 281 of 335 approached (84%) agreed to join the partnership (average 19/site). A diverse array of community agencies were represented in the final collaborative network; specific characteristics included: 93% served the sites' target population, 54% were predominantly youth oriented, 59% were located in the geographical



area of focus, and 39% reported provision of HIV/STI (sexually transmitted infection) prevention services. Relationship-building activities, development of collaborative relationships, and lessons learned, including barriers and facilitators to partnership, are also described. Study findings address a major gap in the community partner research literature. Health researchers and policymakers need an effective partner selection framework whereby community-researcher partnerships can develop a solid foundation to address public health concerns. Straub, D.M., Deeds, B.G., Willard, N., Castor, J., Peralta, L., Francisco, V.T., Ellen, J., and the Adolescent Trials Network for HIV/AIDS Interventions. Partnership Selection and Formation: A Case Study of Developing Adolescent Health Community-Researcher Partnerships in Fifteen U.S. Communities. *Journal of Adolescent Health*, 40(6), 489-498, 2007.

#### Prototypical Images in Condom Scripts among AIDS-Bereaved Adolescents

Twenty-five HIV-negative late adolescents (13 women and 12 men) who had lost a parent to AIDS generated vignettes in which the characters were deciding whether to use a condom (condom scripts). Two clinically trained judges rated the interpersonal tone of the condom scripts on 17 semantic differential scales. Three other clinically trained raters described script characters' attributes by selecting from a list of 36 terms. Multidimensional scaling (MDS) and individual differences hierarchical classes analyses (INDCLAS) were used to inductively derive a typology of condom scripts. Two dimensions emerged from MDS analysis: incompatibility and inequality. Condom scripts culminating in unprotected sex depicted situations in which partners held unequal influence. INDCLAS results suggested a prototype for equal-influence condom scripts - excited male and assertive, powerful female, and for unequal-influence (unprotected sex) condom scripts - powerful, disengaged male and permissive female. These results inform the development of theoretical models and HIV prevention program materials. Reich, W.A. and Rubin, R.M. Prototypical Images in Condom Scripts among AIDS-bereaved Adolescents. *AIDS Education and Prevention*, 19(1), pp. 82-94, 2007.

#### Predictors of Repeat Pregnancy among HIV-1 Infected Women

In the Women and Infants Transmission Study (WITS), a prospective cohort study of HIV-infected pregnant women at six US mainland and Puerto Rican sites, changes in the HIV-1 epidemic have included higher income, better education, and better-controlled HIV disease among more recently enrolled women. Because these changes may alter the reproductive patterns of these women, an awareness of these women's current reproductive behaviors is essential. Predictors of repeat pregnancy among HIV-1-infected women enrolled in the Women and Infants Transmission Study (WITS) were investigated. Women enrolled in WITS without a history of sterilization were included. Using bivariate and multivariate analyses, predictors of a repeat pregnancy were modeled. Changes in risk factors for repeat pregnancy over time were examined and important predictors of repeat pregnancy were determined. Of 2246 eligible women, 22% had more than one WITS-enrolled pregnancy. In bivariate analyses, risk of repeat pregnancy was associated with younger age, lower educational status, higher CD4%, and lower viral loads. There was little change in risk factors for repeat pregnancy over time. HIV-1-infected women who are younger and healthier are more likely to have more than one pregnancy. Factors associated with repeat pregnancy among HIV-1-infected women have remained stable over time. Awareness of these factors will better equip healthcare providers to address the reproductive needs of HIV-1-infected women. Bryant, A.S., Leighty, R.M., Shen, X., Read, J.S., Brouwers, P., Turpin, D.B., LaRussa, P.S., Pacheco-Acosta, E., Paul, M.E., Vajaranant, M., Tuomala, R.E. and the Women and Infants Transmission Study. Predictors of Repeat Pregnancy among HIV-1 Infected Women. *Journal of Acquired Immune Deficiency Syndrome*, 44(1), pp. 87-92, 2007.

## **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

### Twin Study of Stimulant Use/Abuse and Associations with Cannabis

This paper explores the magnitude of, and extent of overlap between, genetic, shared environmental and non-shared environmental influences on lifetime stimulant use and on stimulant abuse/dependence symptoms. It further explores the associations between stimulant use and cannabis use and the extent to which these associations can be attributed to common or correlated genetic and environmental influences. Data came from self report on lifetime stimulant use, DSM-IV abuse/dependence symptoms and corresponding measures of cannabis involvement collected from a sample of 6265 male and female Australian twins born between 1964 and 1971. Results showed that approximately one in five study participants reported lifetime stimulant use while 5% reported experiencing at least one symptom of abuse/dependence. Multivariate genetic model fitting indicated moderate genetic influences on stimulant use (40%) and symptoms (65%) while there was no evidence of sex differences in the magnitude of these influences. Despite moderate overlap, 65% of the genetic influence on stimulant abuse/dependence was specific to these symptomatologic outcomes. There were also strong genetic and shared environmental correlations between the factors associated with stimulant use and those associated with cannabis use. The authors conclude that there is evidence for both overlapping and distinct genetic factors contributing to stimulant use vs. abuse/dependence, which may have implications for opportunities for intervention, for example if those leading to initiation are in the personality realm and those leading to abuse/dependence are more metabolic. Moreover, the overlap in familial (genetic and environmental) risk factors for both stimulant and cannabis use suggests some degree of non-specificity in the risk for using these substances, although more study is needed. Lynskey, M., Grant, J., Li, L., Nelson, E., Bucholz, K., Madden, P., Statham, D., Martin, N., and Heath, A. Stimulant Use and Symptoms of Abuse/Dependence: Epidemiology and Associations with Cannabis Use--A Twin Study. *Drug Alcohol Depend*, 86(2-3), pp. 147-153, 2007.

### Male-Female Differences in the Risk of Progression from First Use to Dependence upon Cannabis, Cocaine, and Alcohol

The authors extend prior reports about the risk of dependence on specific drugs by providing developmental-specific risk estimates for progression from first use to meeting criteria for DSM-III-R dependence upon cannabis, cocaine, or alcohol, as well as male-female differences. The data are from the National Comorbidity Survey, with a national probability sample of persons 15-44 years old in the United States, which included many respondents who used cannabis, cocaine and alcohol on at least one occasion (n=3558, 1337, and 6149, for cannabis, cocaine, and alcohol, respectively). Survival analysis procedures provided cumulative risk estimates of progression from first use to dependence upon each drug. The estimated risk of cannabis dependence among male cannabis users was 1% in the first year after first use, and reached a peak at 4% per year 2 years later, before declining. In contrast, the estimated risk of cannabis dependence among female cannabis users remained at 1% per year for 3 years, without the peak. For both male and female cocaine users, the estimated risk for developing cocaine dependence was 5 to 6% within the first year after first use. Thereafter, the estimated risk declined from the peak value, with a somewhat faster decline for females in the next 3 years after first use. For alcohol, the estimated risk period extended for many years after the first drink, with female drinkers becoming alcohol dependent at a rate of about 1% per year; with somewhat higher risk for male drinkers. For both male and female drinkers, the period of risk for developing alcohol dependence extended for a span of more than 20 years since first use; for cannabis and cocaine, the estimated period of risk was much shorter. There are male-female differences in the risk of becoming cannabis dependent during the first several years after initiation of cannabis use, less pronounced male-female differences for alcohol, and relatively smaller male-female differences for cocaine. These results should interest scientists whose focus is upon the origins of male-female differences in the occurrence of drug dependence. Wagner, F., and Anthony, J. Male-Female Differences in the Risk

of Progression from First Use to Dependence upon Cannabis, Cocaine, and Alcohol. *Drug Alcohol Depend*, 86(2-3), pp. 191-198, 2007.

#### Gender Differences in Criteria for Cannabis Abuse and Dependence

This study explored whether gender contributes to heterogeneity in the latent construct for abuse and dependence of cannabis, and furthermore, whether after accounting for differences in the mean scores of abuse and dependence across genders, there is any evidence for heterogeneity in the individual abuse and dependence criteria. The authors utilized data on criteria for cannabis abuse and dependence from the NESARC (National Epidemiological Survey on Alcohol and Related Conditions), a large, nationally representative sample including 8172 lifetime cannabis users. Analyses used factor analyses and modeling to examine dimensionality and gender heterogeneity. Results supported a unidimensional construct for cannabis abuse/dependence combined, rather than separate entities, which has also been found in prior research. The authors also identified two abuse (legal and hazard) and two dependence (quit and problems) criteria which showed significant gender heterogeneity; the abuse criteria exhibited higher thresholds in women and the dependence criteria in men. They concluded that the criteria that serve as indicators of DSM-IV cannabis abuse and dependence do not function identically in men and women and that certain criteria (e.g. hazardous use) require further refinement. These findings have important implications for the revision of the DSM criteria for abuse and dependence, both for questioning a distinction between abuse and dependence and for considering gender-sensitive diagnostic criteria in research and clinical settings. Agrawal, A., and Lynskey, M. Does Gender Contribute to Heterogeneity in Criteria for Cannabis Abuse and Dependence? Results from the National Epidemiological Survey on Alcohol and Related Conditions. *Drug Alcohol Depend*, 88(2-3), pp. 300-307, 2007.

#### Grandmother and Parent Influences on Child Self-Esteem

This study tests a model of intergenerational influences on childhood self-esteem that proposes paths from grandmothers' drug problems to grandchildren's self-esteem via parents' drug problems and parental adaptive child rearing and from grandmothers' maternal acceptance to grandchildren self-esteem via parents' unconventionality and adaptive child rearing. This longitudinal study uses data obtained from interviews with a New York City sample of black and Puerto Rican children (N = 149) and 1 of their parents and from mailed questionnaires or comparable interviews with those parents' mothers. Structural equation modeling was used to test the proposed model. The LISREL analysis found that, with 3 exceptions, all of the hypothesized paths were significant. The total effects analysis indicated that parents' adaptive child rearing was the strongest latent construct, a finding that was consistent with this construct's proximal position in the model. This study suggests that mothers' drug problems are not just near-term risks for their children, but also pose long-term risks for their children's future functioning as parents and thereby for their grandchildren. The authors conclude that the relative strength of parents' adaptive child rearing in this intergenerational model indicates that this area should be the focus of therapeutic intervention efforts, but addressing future grandmothers' drug problems may have positive effects on multiple generations. Brook, J., Ning, Y., Balka, E., Brook, D., Lubliner, E., and Rosenberg, G. Grandmother and Parent Influences on Child Self-Esteem. *Pediatrics*, 119(2), pp. 444-451, 2007.

#### Injecting and Sexual Risk Correlates of HBV and HCV Seroprevalence among New Drug Injectors

This study examines injecting and sexual risk correlates of hepatitis B (HBV) and hepatitis C (HCV) seroprevalence among new injecting drug users (IDUs) (age 18-30 years, injecting  $\leq$  6 years or 300 lifetime drug injections). Participants were interviewed/serotested (HIVab, HBVcAb, HCVab) in New York City, February 1999–February 2003. Gender-stratified, multivariate logistic regression was conducted. Participants (N= 259) were: 68% male; 81% white. Women were more likely to test HCV seropositive (42% versus 27%) and men HBV seropositive (24% versus 12%); HIV seroprevalence was low (3%). Among both men and women, HBV seropositivity was associated with ever selling sex, and HCV

seropositivity with ever having had infected (HIV, HBV or HCV) sex partners (among those ever sharing injecting equipment). Among women only, HBV seropositivity was associated with ever having had infected sex partners (regardless of ever sharing injecting equipment), and HCV seropositivity with  $\geq 300$  lifetime drug injections. Among men only, HCV seropositivity was associated with  $\geq 40$  lifetime number of sex partners (among those never sharing injecting equipment). In this new IDU sample, HBV and HCV seroprevalence differed by gender and were considerably higher than HIV seroprevalence. The findings suggest that early interventions, targeting injecting and sexual risks and including HBV vaccination, are needed among new IDUs to prevent HBV, HCV and, potentially, HIV epidemics. Neaigus, A., Gyamathy, A., Miller, M., Frajzyngier, V., Zhao, M., Friedman, S., and Des Jarlais, D. Injecting and Sexual Risk Correlates of HBV and HCV Seroprevalence among New Drug Injectors. *Drug Alcohol Depend*, 89(2-3), pp. 234-243, 2007.

#### Comorbid Mental Disorders Associated with Nicotine Dependence in Pregnant Women

Dr. Renee Goodwin and colleagues investigated the association between mental disorders and cigarette use and nicotine dependence among pregnant women in the United States. Using a face-to-face general population survey, the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions, 1516 women reporting a pregnancy in the past year were assessed for cigarette smoking and nicotine dependence, as well as DSM-IV-defined mood and anxiety disorders and personality disorders. They found that among pregnant women, 21.7% reported cigarette use and 12.4% met the criteria for nicotine dependence. Among pregnant women with cigarette use, 45.1% met criteria for at least one mental disorder, and among those with nicotine dependence, 57.5% met criteria for at least one other mental disorder. After adjusting for demographics and comorbidity, nicotine dependence during pregnancy significantly predicted any mental disorder (odds ratio [OR] 3.3, 95% confidence interval [CI] 2.1-5.1), any mood disorder (OR 2.5, 95% CI 1.5-4.0), major depression (OR 2.07, 95% CI 1.3-3.4), dysthymia (OR 6.2, 95% CI 2.9-13.1), and panic disorder (OR 3.1, 95% CI 1.6-6.1) in the past year. No significant associations were found between nondependent cigarette use and mental disorders. These results suggest an association between mental disorders and nicotine dependence among pregnant women in the United States, a finding with implications for treatment and service provision. Goodwin, R., Keyes, K., and Simuro, N. Mental Disorders and Nicotine Dependence among Pregnant Women in the United States. *Obstet Gynecol*, 109(4), pp. 875-883, 2007.

#### Peer and Parental Influences on Longitudinal Trajectories of Smoking among African Americans and Puerto Ricans

The purpose of this study was to identify distinct trajectories of smoking behavior during a period extending from adolescence (mean age = 14 years) to young adulthood (mean age = 26 years) among African American and Puerto Rican adolescents/young adults, to examine ethnic and gender differences in group membership, and to assess the ability of peer and parental smoking to distinguish among trajectory groups. A community-based sample of 451 African American and Puerto Rican adolescents was interviewed four times during adolescence and in early adulthood, covering a span of 12 years. For both ethnic/racial groups, four distinct trajectories were identified: Nonsmokers, maturing-out smokers, late-starting smokers, and early-starting continuous smokers. Compared with Puerto Ricans, African Americans were over-represented in the nonsmoking group, whereas Puerto Ricans were over-represented in the early-starting continuous group. Females were more likely than males to be early-starting continuous smokers than late starters. Adolescents who were exposed to peer and parental smoking in early adolescence were more likely to belong to trajectory groups characterized by higher levels of smoking. These findings show that exposure to peer and parental smoking in early adolescence constitutes a risk factor for engaging in elevated levels of smoking behavior at an early age and for continued smoking into adulthood for urban African Americans and Puerto Ricans. To be most effective, smoking prevention programs should address peer group and family influences on adolescent smoking. Brook, J., Pahl, K., and

Ning, Y. Peer and Parental Influences on Longitudinal Trajectories of Smoking among African Americans and Puerto Ricans. *Nicotine Tob Res*, 8(5), pp. 639-651, 2006.

#### Women Who Gave Birth as Unmarried Adolescents: Trends in Substance Use from Adolescence to Adulthood

The purpose of this study is to determine whether adolescent childbearing mothers “mature out” of substance use as they transition into adulthood, how their substance use compares to that of typical young women of the same ages, and whether there are different patterns of substance use evident in this vulnerable population. The data come from an ongoing longitudinal study of 240 young women who were unmarried, pregnant, and under age 18 at enrollment. They have been interviewed regularly from pregnancy through 11.5 years postpartum. The data are based on self-reported substance use verified by random urinalysis for drug metabolites. Substance use did not decline during the transition to adulthood nor into early adulthood. With the exception of alcohol, the prevalence of substance use was higher than that of a nationally representative sample of same-aged women. Three distinct patterns of substance use were identified: licit users (cigarettes and/or alcohol), marijuana users, and "hard" drug users. From these findings, the authors suggest that clinicians routinely assess substance use among young mothers who bore children as teenagers, and make referrals for appropriate treatment. Cigarette smoking is especially a cause for concern, given its widespread use and harmful effects for both mothers and their children. Although only a small proportion (about 5%) of young mothers used hard drugs consistently over time, this group will likely require comprehensive interventions that address multiple issues such as mental health and contextual factors to be effective. Future research should address reasons for continued substance use in this population. Gillmore, M., Gilchrist, L., Lee, J., and Oxford, M. Women Who Gave Birth as Unmarried Adolescents: Trends in Substance Use from Adolescence to Adulthood. *J Adolesc Health*, 39(2), pp. 237-243, 2006.

#### Twentieth Century Rises in Adult Cigarette Use in the U.S. Parallel Rises in Asthma in Children

The prevalence of asthma has increased at least 3-fold during the past several decades. However, the reason for this increase remains unknown. Renee Goodwin of Columbia University examined one possible factor that may be affecting the increase in prevalence of asthma among youth in the United States from 1900 to 2003. She hypothesized that (1) there has been a marked increase in smoking during the past century, (2) this increase in smoking has resulted in a substantial increase in exposure to environmental tobacco smoke among children, and (3) increased exposure to environmental tobacco smoke has contributed to the increase in childhood asthma. Using a sample of 4,500 children from the National Health Interview Survey, data on the incidence of asthma were aggregated and compared on an ecologic level with data on cigarette consumption from the American Lung Association. Her results suggest a parallel increase in the rates of cigarette use among adults and asthma in children. These findings show an increase in cigarette use during the past 4 birth cohorts, with subsequent leveling off at a population level with a progressively more prominent increase in cigarette use among women in the United States. She notes that future studies will be needed to confirm these ecological trends with community-level analyses in a variety of geographic regions. Goodwin, R. Environmental Tobacco Smoke and the Epidemic of Asthma in Children: The Role of Cigarette Use. *Ann Allergy Asthma Immunol*, 98(5), pp. 447-454, 2007.

#### Maternal Cigarette Smoking During Pregnancy and Child Aggressive Behavior

This study's objective was to examine the association between maternal smoking during pregnancy and childhood aggressive behavior in African-American and Puerto Rican children, as well as the relationship between maternal unconventional behavior, low maternal affection, and offspring aggression. Participants consisted of African-American and Puerto Rican children (N = 203; mean age = 8.6, SD = 0.87) and their mothers living in an inner city community. An interview consisting of a structured questionnaire was administered to the mothers and their children. Scales with adequate psychometric properties were adapted

from previous validated measures. They included maternal smoking during pregnancy, maternal education, unconventionality, and warmth. Controlling for demographic factors, maternal unconventional behavior, and low maternal warmth, maternal smoking during pregnancy was associated with having offspring who were aggressive. Maternal unconventionality and warmth were independently related to childhood aggression. The authors suggest that although causal limitations are noted, it may be that a decrease in smoking during pregnancy is associated with a reduction in aggression in the offspring. Brook, D., Zhang, C., Rosenberg, G., and Brook, J. Maternal Cigarette Smoking during Pregnancy and Child Aggressive Behavior. *Am J Addict*, 15(6), pp. 450-456, 2006.

#### Long-Term Effects of Child Abuse and Neglect on Alcohol Use and Excessive Drinking in Middle Adulthood

The purpose of this study was to determine the long-term effects of child abuse and neglect on alcohol use in middle adulthood. Individuals with documented cases of childhood physical and sexual abuse and/or neglect ( $n = 500$ ) and matched controls ( $n = 396$ ) from a metropolitan county in the Midwest were followed and interviewed in middle adulthood. Outcomes were Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised, diagnoses of alcohol abuse or dependence in young adulthood (age 29) and excessive drinking in middle adulthood (age 40). Women with documented histories of child abuse or neglect reported higher past-year typical quantity ( $p < .01$ ) and past-month number of days drinking eight or more drinks ( $p < .05$ ) than nonabused/nonneglected women. Controlling for parental alcohol/drug problems, the effect of child maltreatment on excessive drinking in middle adulthood was not significant for women. For women, the final structural equation model revealed an indirect path through alcohol diagnosis in young adulthood ( $p < .05$ ) to excessive drinking in middle adulthood ( $p < .001$ ) but no direct path from child abuse and neglect to excessive drinking in middle adulthood. For men, there were no significant paths from child abuse and neglect to alcohol diagnosis in young adulthood or excessive drinking in middle adulthood. For men and women, parental alcohol/drug problems had a significant indirect effect on the offspring's drinking in middle adulthood ( $p < .001$ ) through young adult alcohol diagnosis ( $p < .001$ ). In conclusion, consequences of abuse and neglect persist into middle adulthood for women, through continuation of earlier alcohol problems, suggesting the need for interventions throughout the life course. The influence of parental alcohol and drug problems warrants further attention. Widom, C., White, H., Czaja, S., and Marmorstein, N. Long-Term Effects of Child Abuse and Neglect on Alcohol Use and Excessive Drinking in Middle Adulthood. *J Stud Alcohol Drugs*, 68(3), pp. 317-326, 2007.

#### A Multiwave Multi-Informant Study of the Specificity of the Association between Parental and Offspring Psychiatric Disorders

The present study was conducted to investigate the specificity of the association between parental and offspring psychiatric disorders using epidemiological data from a series of parent and offspring interviews. A community-based sample of 593 mothers and their offspring from upstate New York were interviewed during the adolescence and early adulthood of the offspring. The children of parents with generalized anxiety disorder were at specifically elevated risk for anxiety disorders when co-occurring psychiatric disorders were controlled. The associations between parental and offspring antisocial, conduct, depressive, and substance use disorders were characterized by modest specificity. Children of parents with externalizing disorders were nearly as likely to develop internalizing disorders as they were to develop externalizing disorders. Children of parents with internalizing disorders were somewhat, but not significantly, more likely to develop internalizing disorders. These findings support the inference that children of parents with generalized anxiety disorder may be more likely to develop anxiety disorders than they are to develop other psychiatric disorders. However, when co-occurring psychiatric disorders are accounted for, the children of parents with depressive, disruptive, and substance use disorders may be as likely to develop other disorders as they are to develop the same type of disorder that their parents have had. Johnson, J., Cohen, P., Kasen, S., and Brook, J.A. Multiwave Multi-Informant Study of the

Specificity of the Association between Parental and Offspring Psychiatric Disorders. *Compr Psychiatry*, 47(3), pp. 169-177, 2006.

### Predictors of Resilience in Abused and Neglected Children Grown-Up: The Role of Individual and Neighborhood Characteristics

This paper examines individual, family, and neighborhood level predictors of resilience in adolescence and young adulthood and describes changes in resilience over time from adolescence to young adulthood in abused and neglected children grown up. The sample includes documented cases of childhood physical and sexual abuse and neglect (n=676) from a Midwestern county area during the years 1967-1971 and information from official records, census data, psychiatric assessments, and self-reports were obtained through 1995. Analyses involve logistic regressions, replicated with Mplus to test for possible contextual effects. Almost half (48%) of the abused and neglected children in adolescence and nearly one-third in young adulthood were resilient. Over half of those who were resilient in adolescence remained resilient in young adulthood, whereas 11% of the non-resilient adolescents were resilient in young adulthood. Females were more likely to be resilient during both time periods. Being white, non-Hispanic decreased and growing up in a stable living situation increased the likelihood of resilience in adolescence, but not in young adulthood. Stressful life events and a supportive partner promoted resilience in young adulthood. Neighborhood advantage did not exert a direct effect on resilience, but moderated the relationship between household stability and resilience in adolescence and between cognitive ability and resilience in young adulthood. In conclusion, ecological factors appear to promote or interfere with the emergence and stability of resilience following childhood maltreatment. DuMont, K., Widom, C., and Czaja, S. Predictors of Resilience in Abused and Neglected Children Grown-Up: The Role of Individual and Neighborhood Characteristics. *Child Abuse Negl*, 31(3), pp. 255-274, 2007.

### Growth Trajectories of Sexual Risk Behavior in Adolescence and Young Adulthood

Adolescence and young adulthood (ages 18-25 years) are periods of development and change, which include experimentation with and adoption of new roles and behaviors. Researchers investigated longitudinal trajectories of sexual risk behaviors across these time periods and how these trajectories may be different for varying demographic groups. They developed multilevel growth models of sexual risk behavior for a predominantly African American sample (n=847) that was followed for 8 years, from adolescence to young adulthood and investigated differences in growth parameters by race/ethnicity and gender and their interactions. The final model included linear and quadratic terms for both adolescence and young adulthood, indicating acceleration of sexual risk behaviors during adolescence and a peak and deceleration during young adulthood. African American males exhibited the highest rate of sexual risk behavior in ninth grade, yet had the slowest rate of growth. Compared with their White peers, African American males and females exhibited less sexual risk behavior during young adulthood. These results suggest that youths of different races/ethnicities and genders exhibit varying sexual risk behavior trajectories. Fergus, S., Zimmerman, M., and Caldwell, C. Growth Trajectories of Sexual Risk Behavior in Adolescence and Young Adulthood. *Am J Public Health*, 97(6), pp. 1096-1101, 2007.

### Gender Differences in Injection Risk Behaviors at the First Injection Episode

This study sought to examine gender differences in drug injection equipment sharing at injecting initiation. Young injecting drug users in New York City (February 1999-2003) were surveyed about injection risk behaviors and circumstances at initiation. Analyses were gender-stratified and excluded participants who initiated alone. Multiple logistic regression estimated adjusted odds ratios. Participants (n=249) were 66% male and 82% White. Mean initiation age was 19.2; mean years since initiating was 3.0. Women were significantly more likely to cite social network influence as a reason for initiating, to have male and sex partner initiators, and to share injecting equipment than men. Among women, sharing any injection equipment was associated with initiation by a sex partner and having  $\geq 2$  people present. Among men,

being injected by someone else predicted sharing any injection equipment, while using a legally obtained syringe was protective. Social persuasion stemming from sexual and/or social relationships with IDUs may increase women's risk of sharing injection equipment at initiation, and consequently, their early parenteral risk of acquiring blood-borne infections. Effective interventions should focus on likely initiators, especially women in injecting-discordant sex partnerships, and IDUs (potential initiators). Frajzyngier, V., Neaigus, A., Gyarmathy, V., Miller, M., and Friedman, S. Gender Differences in Injection Risk Behaviors at the First Injection Episode. *Drug Alcohol Depend*, 89(2-3), pp. 145-152, 2007.

#### An Examination of Pathways from Childhood Victimization to Violence: The Role of Early Aggression and Problematic Alcohol Use

Using prospective data from a cohort design study involving documented cases of child abuse and neglect and a matched control group, the researchers examine two potential pathways between childhood victimization and violent criminal behavior: early aggressive behavior and problematic drinking. Structural equation models, including controls for race/ethnicity, socioeconomic status, parental alcoholism, and parental criminality, revealed different pathways for men and women. For men, child maltreatment has direct and indirect (through aggressive behavior and problematic alcohol use) paths to violence. For women, problematic alcohol use mediates the relationship between childhood victimization and violence, and, independent of child maltreatment, early aggression leads to alcohol problems, which lead to violence. Interventions for victims of childhood maltreatment need to recognize the role of early aggressive behavior and alcohol problems as risk factors for subsequent violence. Widom, C., Schuck, A., and White, H. An Examination of Pathways from Childhood Victimization to Violence: The Role of Early Aggression and Problematic Alcohol Use. *Violence Vict*, 21(6), pp. 675-690, 2006.

#### Childhood Victimization and Illicit Drug Use in Middle Adulthood

Using a prospective cohort design, the authors examined in this study whether childhood victimization increases the risk for illicit drug use and related problems in middle adulthood. Court-documented cases of childhood physical and sexual abuse and neglect and matched controls (N = 892) were first assessed as young adults (mean age = 29 years) during 1989-1995 and again in middle adulthood (mean age = 40 years) during 2000-2002. In middle adulthood, abused and neglected individuals were about 1.5 times more likely than controls to report using any illicit drug (in particular, marijuana) during the past year and reported use of a greater number of illicit drugs and more substance-use-related problems compared with controls. The current results reveal the long-term impact of childhood victimization on drug use in middle adulthood. These new results reinforce the need for targeted interventions with abused and neglected children, adolescents, and adults, and particularly for women. Widom, C., Marmorstein, N., and White, H. Childhood Victimization and Illicit Drug Use in Middle Adulthood. *Psychol Addict Behav*, 20(4), pp. 394-403, 2006.

#### Consistency between Adolescent Reports and Adult Retrospective Reports of Adolescent Marijuana Use: Explanations of Inconsistent Reporting Among an African American Population

This study examines the consistency of marijuana self-reports from adolescence and adulthood and what characterizes inconsistent reporting among a cohort of African American first graders followed longitudinally from age 6 to 32 (N=599, 51% female). Self-reported lifetime adolescent marijuana use (ages 16-17) and retrospective reports at age 32 were combined to categorize respondents as consistent reporters of nonuse (22%), consistent reporters of use (42%), adult recanters (19%), adolescent under reporters (8%), and inconsistent reporters of age of initiation (9%). Overall, about 64% of the population were consistent in their reports of adolescent marijuana use from adolescence to age 32. Multivariate logistic regression analyses found that recanters reported less marijuana use as adolescents, lower parental supervision during adolescence, lower deviant behavior as an adult, and stronger anti-drug values as adults than did consistent reporters. Adolescent under reporters reported less assault behaviors and less alcohol



use as adolescents and had lower first grade math achievement than consistent reporters. Family background, depression, criminal arrests, and the field conditions of the interview were not related to inconsistent reporting. Ensminger, M., Juon, H., and Green, K. Consistency between Adolescent Reports and Adult Retrospective Reports of Adolescent Marijuana Use: Explanations of Inconsistent Reporting Among an African American Population. *Drug Alcohol Depend*, 89(1), pp. 13-23, 2007.

#### Pubertal Maturation and Risk for Alcohol Use and Abuse

This study sought to examine the impact of various aspects of puberty on risk of using alcohol and developing alcohol use disorder (AUD). Data came from the Great Smoky Mountains Study, a longitudinal study of a representative sample of 1420 youth aged 9-13 at recruitment. Participants were interviewed annually to age 16. A parent was also interviewed. Information was obtained about use of a range of drugs including alcohol, drug abuse and dependence, other psychiatric disorders, life events, and a wide range of family characteristics. Pubertal hormones were assayed annually from blood samples, and morphological development was assessed using a pictorial measure of Tanner stage. The authors found that, controlling for age, Tanner stage predicted alcohol use and AUD in both boys and girls. The effect of morphological development was strongest in those who matured early. Early pubertal maturation predicted alcohol use in both sexes, and AUD in girls. The highest level of excess risk for alcohol use was seen in early maturing youth with conduct disorder and deviant peers. Lax supervision predicted alcohol use in early maturing girls, while poverty and family problems were predictive in early maturing boys. The authors conclude that, among the many biological, morphological, and social markers of increasing maturation, the visible signs of maturity are important triggers of alcohol use and AUD, especially when they occur early and in young people with conduct problems, deviant peers, problem families and inadequate parental supervision. These findings may help target those at greatest risk for early onset and progression of alcohol use and disorders. Costello, E., Sung, M., Worthman, C., and Angold, A. Pubertal Maturation and the Development of Alcohol Use and Abuse. *Drug Alcohol Depend*, 88, Suppl 1, pp. S50-S59, 2007.

#### Predictors of Drinking Immediacy Following Daily Sadness: An Application of Survival Analysis to Experience Sampling Data

Previous studies of daily assessments show modest mood-drinking covariation as a function of gender and coping motives; however previous analyses also assume a fixed interval across all individuals in the onset of drinking following negative mood. The current study used survival analysis and experience sampling methods to test whether gender and coping motives predicted shorter sadness-to-drinking intervals among those with greater alcohol-related drinking consequences. A sample of 85 college students (46% male; 78% Caucasian) completed daily assessments over 28 days. Survival analyses showed that women drank more on days following elevated sadness when they reported being motivated to drink to cope and having experienced alcohol-related consequences. For men, the two groups showing greater drinking risk following days of elevated sadness did not report alcohol-related consequences, with those reporting the presence of coping motives showing the greatest risk. Implications of these findings for self-medication mechanisms are discussed. Hussong, A. Predictors of Drinking Immediacy Following Daily Sadness: An Application of Survival Analysis to Experience Sampling Data. *Addict Behav*, 32(5), pp. 1054-1065, 2007.

#### Predictors of Unprotected Sex with Non-Cohabiting Primary Partners among Sheltered and Low-Income Housed Women in Los Angeles County

This study investigated cross-sectional associations of substance use, relationship abuse and HIV self-protective behavior with unprotected sex among 290 impoverished women with a non-cohabiting primary partner. Unprotected sex was associated with having a physically or psychologically abusive partner among low-income housed women, and having an abusive partner who also drank to intoxication among women living in shelters. Indicators of HIV self-protective behavior were associated with less frequent unprotected sex among sheltered women, even after accounting for abuse and substance use within the

relationship. Results suggest the need for HIV-prevention interventions to address the problems of partner substance use and relationship abuse. Tucker, J., Wenzel, S., Elliott, M., and Hambarsoomian, K. Predictors of Unprotected Sex with Non-Cohabiting Primary Partners among Sheltered and Low-Income Housed Women in Los Angeles County. *J Health Psychol*, 11(5), pp. 697-710, 2006.

#### Gender-specific Correlates of Sex Trade among Homeless and Marginally Housed Individuals in San Francisco

Sex exchange is a well-established risk factor for HIV infection. Little is known about how correlates of sex trade differ by biologic sex and whether length of homelessness is associated with sex trade. The researchers conducted a cross-sectional study among a sample of 1,148 homeless and marginally housed individuals in San Francisco to assess correlates of exchanging sex for money or drugs. Key independent variables included length of homelessness; use of crack, heroin or methamphetamine; HIV status; and sexual orientation. Analyses were restricted by biologic sex. In total, 39% of women and 30% of men reported a lifetime history of sex exchange. Methamphetamine use and greater length of homelessness were positively associated with a history of sex trade among women, while heroin use, recent mental health treatment, and homosexual or bisexual orientation were significantly associated with sex trade for men. Crack use was correlated with sex trade for both genders. Correlates of sex trade differ significantly according to biologic sex, and these differences should be considered in the design of effective HIV prevention programs. The researchers' findings highlight the critical need to develop long-term services to improve housing status for homeless women, mental health services for homeless men, and drug treatment services for homeless adults involved in sex work. Weiser, S., Dilworth, S., Neilands, T., Cohen, J., Bangsberg, D., and Riley, E. Gender-Specific Correlates of Sex Trade among Homeless and Marginally Housed Individuals in San Francisco. *J Urban Health*, 83(4), pp. 736-740, 2006.

#### Ethnic Pride and Self-control Related to Protective and Risk Factors

The purpose of this study was to test a theoretical model of how ethnic pride and self-control are related to risk and protective factors. A community sample of 670 African American youth (mean age = 11.2 years) were interviewed on measures of cigarette smoking, alcohol use, and sexual behavior (lifetime to past month). Structural modeling analyses indicated parenting was related to self-control and self-esteem, and racial socialization was related to ethnic pride. Self-control and self-esteem variables were related to levels of deviance-prone attitudes and to perceptions of engagers in, or abstainers from, substance use and sexual behavior. The proximal factors (behavioral willingness, resistance efficacy, and peer behavior) had substantial relations to the criterion variables. Participant gender and parental education also had several paths in the model. Results were generally similar for the 2 outcome behaviors. In this population, self-esteem and self-control are related to parenting approaches and have pathways to attitudes and social perceptions that are significant factors for predisposing to, or protecting against, early involvement in substance use and sexual behavior. Wills, T., Murry, V., Brody, G., Gibbons, F., Gerrard, M., Walker, C., and Ainette, M. Ethnic Pride and Self-Control Related to Protective and Risk Factors: Test of the Theoretical Model for the Strong African American Families Program. *Health Psychol*, 26(1), pp. 50-59, 2007.

#### Racial/Ethnic and Socioeconomic Status Differences in Overweight and Health-Related Behaviors among American Students: National Trends 1986-2003

This article reports long-term trends by race/ethnicity and socioeconomic status (SES) in the percent of American students who are overweight and who engage in three health-related behaviors hypothesized to be associated with overweight. Data are from the Monitoring the Future annual surveys, using nationally representative samples of eighth, 10th, and 12th grade students. Participants include 62,156 eighth and 64,899 10th graders who completed the 1993-2003 surveys and 35,107 12th graders who completed the questionnaire form containing the measures pertaining to this study in the 1986-2003 surveys. Trends are

presented separately by gender and grade level for different racial/ethnic and SES subgroups, in: (a) percent overweight (body mass index  $\geq$  85th percentile), (b) percent who always or almost always eat breakfast, (c) percent who regularly exercise vigorously, and (d) average hours of weekday television viewing. The prevalence of overweight and of engaging in less healthy behaviors is considerably greater among youth from racial/ethnic minority backgrounds, of lower socioeconomic status, and in higher grades. Trends in overweight and these behaviors are found to vary substantially by gender, racial/ethnic group, socioeconomic status, and grade level. The study findings show well-established and persistent differences in the percent of racial/ethnic minority and low SES youth who are overweight and who's dietary and exercise habits are less healthy. Documentation of these problems may lead to research and policy agendas that will contribute both to understanding and to the reduction of these important health disparities. Delva, J., O'Malley, P., and Johnston, L. Racial/Ethnic and Socioeconomic Status Differences in Overweight and Health-Related Behaviors among American Students: National Trends 1986-2003. *J Adolesc Health*, 39(4), pp. 536-545, 2006.

### Learning Disabilities and Intellectual Functioning in School-Aged Children with Prenatal Cocaine Exposure

Risk for developing a learning disability (LD) or impaired intellectual functioning by age 7 was assessed in full-term children with prenatal cocaine exposure drawn from a cohort of 476 children born full term and enrolled prospectively at birth. Intellectual functioning was assessed using the Wechsler Intelligence Scale for Children-Third Edition (Wechsler, 1991) short form, and academic functioning was assessed using the Wechsler Individual Achievement Test (WIAT; Wechsler, 1993) Screener by examiners blind to exposure status. LDs were categorized based on ability-achievement discrepancy scores, using the regression-based predicted achievement method described in the WIAT manual. The sample in this report included 409 children (212 cocaine-exposed, 197 non-cocaine-exposed) from the birth cohort with available data. Cumulative incidence proportions and relative risk values were estimated using STATA software (Statacorp, 2003). No differences were found in the estimate of relative risk for impaired intellectual functioning (IQ below 70) between children with and without prenatal cocaine exposure (estimated relative risk = .95; 95% confidence interval [CI] = 0.65, 1.39;  $p = .79$ ). The cocaine-exposed children had 2.8 times greater risk of developing a LD by age 7 than non-cocaine-exposed children (95% CI = 1.05, 7.67;  $p = .038$ ; IQ  $\geq$  70 cutoff). Results remained stable with adjustment for multiple child and caregiver covariates, suggesting that children with prenatal cocaine exposure are at increased risk for developing a learning disability by age 7 when compared to their non-cocaine-exposed peers. Morrow, C., Culbertson, J., Accornero, V., Xue, L., Anthony, J., and Bandstra, E. Learning Disabilities and Intellectual Functioning in School-Aged Children with Prenatal Cocaine Exposure. *Dev Neuropsychol*, 30(3), pp. 905-931, 2006.

### Examination of the Nicotine Metabolite Ratio in a Multiethnic/Multiracial Sample

The recent development of a noninvasive measure of nicotine metabolism, the nicotine metabolite ratio (trans-3 hydroxycotinine/cotinine), makes it possible to examine the association between rate of nicotine metabolism and smoking behavior in the general population. Dr. Denise Kandel and colleagues examined group differences in the ratio measured in urine and the association between the ratio and multiple measures of smoking behavior and nicotine dependence in a large, nationally representative sample of young adults. The sample included 900 daily smokers aged 18-26 years from wave III (2001-2002) of the National Longitudinal Survey of Adolescent Health. Nicotine dependence was measured by using the Fagerström Test for Nicotine Dependence. Females had higher nicotine metabolite ratios than males; Whites and Hispanics had higher nicotine metabolite ratios than African Americans or Asians. This finding is consistent with those from laboratory studies of older smokers based on intravenous infusion of nicotine. No significant association was found between the nicotine metabolite ratio and number of cigarettes smoked per day or nicotine dependence. The availability of a noninvasive measure makes possible systematic testing of causal hypotheses generated by laboratory studies in the general population. Kandel, D., Hu, M., Schaffran, C., Udry, J., and Benowitz, N. Urine Nicotine Metabolites and Smoking

Behavior in a Multiracial/Multiethnic National Sample of Young Adults. *Am J Epidemiol*, 165(8), pp. 901-910, 2007.

#### Self-Control, Symptomatology, and Substance Use Precursors

The authors tested a theoretical model of how self-control constructs are related to psychological symptomatology and variables that predispose to involvement versus noninvolvement in substance use: willingness to use, affiliation with peers who use, and efficacy for resisting use. Data were obtained from a sample of 332 children (mean age = 9.3 years) who were interviewed in households. Structural equation modeling showed that good self-control was related to more positive well-being and less externalizing symptomatology, whereas poor self-control was related to more externalizing and to more internalizing symptomatology. Externalizing had paths to willingness and peer use, well-being had inverse paths to these variables, and poor self-control had a direct effect to lower resistance efficacy. Multiple-group analyses indicated gender differences in paths from symptomatology to predisposing factors. Implications for understanding vulnerability to substance use are discussed. Wills, T., Ainette, M., Mendoza, D., Gibbons, F., and Brody, G. Self-Control, Symptomatology, and Substance Use Precursors: Test of a Theoretical Model in a Community Sample of 9-year-old Children. *Psychol Addict Behav*, 21(2), pp. 205-215, 2007.

#### A Study of Latino Adolescent Health Behaviors and Weight in the United States of America

The authors examined, by gender, differences in being overweight among adolescents of Mexican, Puerto Rican, and other Latin American heritage who live in the United States of America, and investigated the relationships between these differences and socioeconomic status, health-related behaviors, and family characteristics. The study analyzed data from nationally representative samples of Latino 8th and 10th graders in the Monitoring the Future study from 1991 to 2004 (N = 11 265). Investigators found a higher proportion of Mexican-American girls were overweight than other Latin American girls, both before and after adjusting for many confounders. For both genders, being overweight was inversely associated with socioeconomic status and frequency of vigorous exercise, and positively associated with the amount of television viewing. No family characteristic variable examined was associated with overweight. Time spent exercising and time spent watching television are two potentially modifiable risk factors that, if targeted, may result in important reductions in overweight. The findings indicate the need to identify gender- and culturally-appropriate interventions that can increase physical activity and reduce sedentary activities among Latino adolescents, particularly in families of low socioeconomic status. Delva, J., O'Malley, P., and Johnston, L. Health-Related Behaviors and Overweight: A Study of Latino Adolescents in the United States of America. *Rev Panam Salud Publica*, 21(1), pp. 11-20, 2007.

### **PREVENTION RESEARCH**

#### The Role of Gender and Acculturation on Drug-related Outcomes for "Keepin' it REAL" Prevention Program

This study examined whether the efficacy of the Keepin' it REAL school-based prevention program was moderated by gender, ethnicity, and acculturation. Data came from a randomized trial in Phoenix AZ middle schools involving 4622 mostly Latino 7th graders. Youth participated in the prevention program that involved 10 classroom lessons and 5 videos developed based on extensive input from youth. Previous research on the program has demonstrated its efficacy with regard to slowing initiation of drug use. In the current study, using multi-level mixed models, results for the total sample showed no gender differences in program effects on recent substance use. However, the program was more effective in fostering anti-drug norms among boys than among girls. Subgroup analyses indicated that there were more beneficial program effects for less acculturated boys than less acculturated girls. Specifically, there was less alcohol and cigarette use and stronger anti-drug norms post intervention for less acculturated boys in the intervention

group than their female counterparts. It is notable that less acculturated Latino boys had higher baseline substance use rates and stronger pro-drug norms than less acculturated Latino girls, and the lower risk of use for less acculturated girls may have attenuated the potential for program effects. The results of this study, while generally verifying the efficacy of gender-inclusive prevention strategies, suggest that efforts may be strengthened by attending to the special risks and resilience of certain subgroups of female and male youth. Kulis, S., Yabiku, S.T., Marsiglia, F.F., Nieri, T., and Crossman, A. Differences by Gender, Ethnicity, and Acculturation in the Efficacy of the Keepin' it REAL Model Prevention Program. *J Drug Educ*, 37(2), pp. 123-144, 2007.

#### Effects of Iowa Strengthening Families Program on Internalizing Symptoms and Polysubstance Use in Adolescence

This study evaluated effects of the Iowa Strengthening Families Program, a family-focused universal preventive intervention, on growth patterns of adolescent internalizing (anxiety and depressive symptoms) and monthly polysubstance use (alcohol, tobacco, marijuana, inhalants, and other illicit drugs), as well as the association between internalizing and polysubstance growth factors. The sample consisted of rural Midwestern adolescents (N=383), followed from sixth through twelfth grade. Compared to the control group, the intervention group adolescents showed a slower rate of increase in internalizing symptoms and polysubstance use. Intervention effects on internalizing symptoms were similar for boys and girls; however, girls demonstrated a higher overall level and a greater rate of increase across time. The intervention slowed the rate of increase in polysubstance use significantly more for girls than for boys, although overall levels of use were lower in the intervention group for both genders. Associations between internalizing and polysubstance use growth factors were found for girls, but not for boys, suggesting gender differences in psychosocial development. Trudeau, L., Spoth, R., Randall, G.K., and Azevedo, K. Longitudinal Effects of a Universal Family-Focused Intervention on Growth Patterns of Adolescent Internalizing Symptoms and Polysubstance Use: Gender Comparisons. *Journal of Youth and Adolescence*, 36(6), pp. 725-740, 2007.

#### School-Level Influences on Discipline Referrals in First Grade

School discipline referrals (SDRs) may be useful in the early detection and monitoring of disruptive behavior problems to inform prevention efforts in the school setting, yet little is known about the nature and validity of SDRs in the early grades. For this descriptive study, SDR data were collected on a sample of first grade students who were at risk for developing disruptive behavior problems (n = 186) and a universal sample (n = 531) from 20 schools. Most SDRs were given for physical aggression and the predominant consequence was time out. As expected, boys and at-risk students were more likely to receive an SDR and to have more SDRs than were girls and the universal sample. A large difference between schools regarding the delivery of SDRs was found. A zero-inflated Poisson model clustered by school tested the prediction of school-level variables. Students in schools that had a systematic way of tracking SDRs were more likely to receive one. Also, schools with more low-income students and larger class sizes gave fewer SDRs. SDRs predicted teacher ratings, and to a lesser extent, parent ratings of disruptive behavior at the end of first grade. Thus, practitioners and researchers should examine school-level influences whenever first grade discipline referrals are used to measure problem behavior for the purpose of planning and evaluating interventions. Rusby, J.C., Taylor, T.K., and Foster, E.M. A Descriptive Study of School Discipline Referrals in First Grade. *Psychol Sch*, 44(4), pp. 333-350, 2007.

#### HIV Risk Reduction is Affected by Beliefs about HIV Treatment Efficacy

This study describes the sexual behavior of HIV-positive women within new versus more established relationships and determines whether beliefs about HIV antiretroviral therapy (ART) impact these behaviors. The Women's Interagency HIV Study is a longitudinal cohort study of HIV among women in the United States. Sexually active HIV-positive women (N = 1,090) completed interviews on beliefs and

behaviors at 6-month intervals. Data were analyzed for the period between April 2002 and March 2003. Of 1,517 sexual partners reported, 32% were newly acquired within the previous 6 months. As compared with more established sexual relationships, newer partnerships were characterized by greater condom use consistency (odds ratio = 1.8, 95% confidence interval = 1.4-2.3). Holding beliefs that ART is protective for HIV transmission impacted the relationship between partner type and condom use. In established relationships, 63% reported consistent condom use if they believed that ART is not protective, whereas 54% reported consistent condom use if they believed that ART is protective. These findings highlight the importance of ongoing support for sexual risk reduction among women with HIV-infection and for strategies that reduce the strength of relationships between ART beliefs and sexual risk behavior. Wilson, T.E., Feldman, J., Vega, M.Y., Ghandi, M., Richardson, J., Cohen, M.H., McKaig, R., Ostrow, D., Robison, E., and Gange, S.J. Acquisition of New Sexual Partners among Women with HIV Infection: Patterns of Disclosure and Sexual Behavior within New Partnerships. *AIDS Educ Prev*, 19(2), pp. 151-159, 2007.

### Racial and Gender Differences in Adolescent Sexual Attitudes and Associations with Coital Debut

Delay of sexual debut is an important strategy in reducing the risk of negative adolescent health outcomes. Race and gender are known to be related to sexual behavior and outcomes, but little is known about how these characteristics affect sexual attitudes. This article examines differences in coital and pregnancy attitudes by gender and race, the influence of attitudes on transition to first coitus for each subgroup, and implications for prevention. Data are from Waves I and II of the National Longitudinal Study of Adolescent Health, limited to Non-Hispanic White and African American adolescents (n = 6652). The authors' factor analyzed attitude items, and examined effects of race, gender, and their interaction, controlling for sexual debut at Wave I. Next, sexual debut over time was predicted by attitudes for virgins (n = 3281) separately for each subgroup, controlling for covariates. Results showed that compared with boys, girls perceived less positive benefits from sex and more shame and guilt with sex, but had fewer negative perceptions about pregnancy. Compared with White boys, African American boys perceived less shame and guilt about sex; girls did not differ by race. Higher perceived benefits of sex increased the likelihood of sexual debut among African American girls. Perceived shame and guilt lowered the likelihood for White boys and girls. It was concluded that reinforcing protective attitudes through gender and race-specific programs may delay sexual intercourse, but more research is needed. Specifically, it will be important to examine whether there is an optimal coital age after which negative health outcomes are attenuated, and whether this differs by gender and race. Cuffee, J., Hallfors, D., and Waller, M. Racial and Gender Differences in Adolescent Sexual Attitudes and Longitudinal Associations with Coital Debut. *J Adolesc Health*, 41(1), pp. 19-26, 2007.

### Mothers' Relational Schemas Predict Adolescent Antisocial Behavior

Relational schemas, as described and measured in this study, refer to automatic, unconscious response tendencies that reflect the nature of one's relationship to another person. In this research, these are measured through interpreting speech samples where a mother (biological, step, or adoptive) is describing her relationship with a target adolescent. These samples were assessed using the Family Affective Attitude Rating Scale for coding 5-minute speech samples. The internal consistency and validity of positive relational schema and negative relational schema scales were also evaluated. Data were collected from a multiethnic subsample of early-starting antisocial (n = 20) and successful (n = 20) urban adolescents and their families, using direct observations of parent-adolescent interactions, 5-minute speech samples, and questionnaires. The negative relational schema and positive relational schema scales were internally consistent, correlated reliably with critical and positive dimensions of 5-minute speech samples expressed emotion and with observed parent-adolescent interactions, and discriminated between antisocial and successful adolescents. The negative relational schema scale accounted for unique variance in adolescent antisocial behavior when controlling for previous problem behavior and observed coercion. A significant interaction was also found between negative relational schema rating and observed parent-adolescent

dynamics when escalations in adolescent problem behavior were added to the model. Relational schema narratives provided unique information in the prediction of adolescent antisocial behavior and should be considered in the assessment of family dynamics and the design of interventions to prevent and treat adolescent behavior problems. Bullock, B., and Dishion, T. Family Processes and Adolescent Problem Behavior: Integrating Relationship Narratives into Understanding Development and Change. *J Am Acad Child Adolesc Psychiatry*, 46(3), pp. 396-407, 2007.

### Substance Use and Risk for Suicide

This study examined the association between onset of substance use and risk factors related to suicide. 1252 adolescents in two urban school districts completed surveys as part of a large, randomized controlled prevention effectiveness trial. Risk factors measured included depressive symptoms, suicide ideation, suicide ideation specifically with alcohol and/or drug use, endorsement of suicide as a personal option, and suicide attempt. Results from multivariate models controlling for current substance use and demographic characteristics indicated that earlier onset of hard drug use among boys was associated with all five suicide risk factors. In comparison, among girls, earlier onset of regular cigarette smoking, getting drunk, and hard drug use was associated with some suicide risk factors. The findings confirm the importance of screening for substance use in early adolescence. The association between early substance use and suicide risk factors differed by gender; both research and intervention efforts need to incorporate gender differences. Cho, H., Hallfors, D., and Iritani, B. Early Initiation of Substance Use and Subsequent Risk Factors Related to Suicide Among Urban High School Students. *Addict Behav*, 32(8), pp. 1628-1639, 2007.

### Effects of Prenatal and Postnatal Parental Substance Use on Child Maltreatment

Parental substance use is a well-documented risk for children. However, little is known about specific effects of prenatal and postnatal substance use on child maltreatment and foster care placement transitions. In this study, the authors' unpacked unique effects of (a) prenatal and postnatal parental alcohol and drug use and (b) maternal and paternal substance use as predictors of child maltreatment and foster care placement transitions in a sample of 117 maltreated foster care children. Models were tested with structural equation path modeling. Results indicated that prenatal maternal alcohol use predicted child maltreatment and that combined prenatal maternal alcohol and drug use predicted foster care placement transitions. Prenatal maternal alcohol and drug use also predicted postnatal paternal alcohol and drug use, which in turn predicted foster care placement transitions. Findings highlight the potential integrative role that maternal and paternal substance use has on the risk for child maltreatment and foster care placement transitions. Smith, D., Johnson, A., Pears, K., Fisher, P., and DeGarmo, D. Child Maltreatment and Foster Care: Unpacking the Effects of Prenatal and Postnatal Parental Substance Use. *Child Maltreat*, 12(2), pp. 150-160, 2007.

### Physical Environmental Influences on Early Externalizing Behaviors

Research on the development of externalizing behaviors during early childhood has focused on child and parenting factors. Fewer studies have investigated effects of aversive features of the micro-level physical environment, such as overcrowding and chaos in the home, and the macro-level environment, such as neighborhood quality. This study extends research on physical environmental factors by examining their association with children's early externalizing behaviors, and exploring how maternal monitoring may serve as a protective factor in such contexts. One hundred twenty male toddlers at high risk for developing early externalizing behaviors, participating in an ecologically-based family preventive intervention were followed from ages 2 to 5 years. Direct longitudinal associations were found for micro-level environmental factors beginning at age 2 and for neighborhood risk beginning at age 3. Maternal monitoring served as a protective factor for child externalizing behaviors in the context of neighborhood risk. Implications for prevention research and the development of early externalizing behaviors are discussed. Supplee, L.H., Unikel, E., and Shaw, D.S. Physical Environmental Adversity and the Protective Role of Maternal

Monitoring in Relation to Early Child Conduct Problems. *Journal of Applied Developmental Psychology*, 28(2), pp. 166-183, 2007.

#### Ethnic Identity as a Predictor of Substance Use Norms and Behaviors

This paper explores whether ethnicity and three ethnic identity instruments are useful in predicting substance use outcomes among three samples of ethnically diverse middle school youth. Participants were 7th and 8th grade youth attending a multiethnic school in an urban low-income community who were subsampled from participants in a larger prevention research study. More than half of the participants in the research were of Hispanic origin. Results suggest that age, gender, and/or racial/ethnic group membership influenced the strength of ethnic identity. In addition, age, sex, and strength of ethnic identity influenced substance use norms and behaviors. In each case where effects were significant, a stronger sense of ethnic identity as measured by two of the instruments predicted more negative attitudes toward and less use of alcohol, cigarettes, and marijuana. Holley, L.C., Kulis, S., Marsiglia, F.F., and Keith, V.M. Ethnicity versus Ethnic Identity: What Predicts Substance Use Norms and Behaviors. *Journal of Social Work Practice in the Addictions*, 6(3), pp. 53-79, 2006.

#### Quality of Parent-Child Interaction Predicts Child Problem Behaviors

This article reports on two exploratory studies where the hypothesis is tested that there will be an inverse relationship between the quality of parent-child interactions and adolescent problem behaviors. Study 1 involves survey data from Midwestern parents of boys (n=377) and girls (335) between the ages of 11 and 13 years. Study 2, conducted to replicate the findings of Study 1, was similarly constructed with parents of boys (n=279) and girls (n=269). The quality of parent child interactions latent construct was formed from indicators of effective child management and parent-child affective quality, both self-reported by parents. Child problem behaviors were assessed with indicator measures of aggressive and oppositional behavior, school-related problems, and problematic peer relations. Multisample latent variable structural equation modeling confirms that a higher level of parent-child interaction quality was associated with a lower level of problem behaviors. This relationship was significant for parent-reported behavior, for both boys and girls, in both Study 1 and Study 2. The amount of variance explained indicated a moderate relationship between these variables and is consistent with earlier studies indicating that parent-child interaction quality is associated with problem behaviors among rural dwelling early adolescents. Spoth, R., Neppl, T., Goldberg-Lillehoj, C., Jung, T., and Ramisetty-Mikler, S. Gender-Related Quality of Parent-Child Interactions and Early Adolescent Problem Behaviors: Exploratory Study with Midwestern Samples. *Journal of Family Issues*, 27(6), pp. 826-849, 2006.

#### Cross-sectional Study of Female Students Reporting Anabolic Steroid Use

The objective of this article was to determine the characteristics of female US high school students reporting anabolic steroid use. This paper reports findings from cross-sectional assessments collected as part of the 2003 Centers for Disease Control and Prevention national school-based Youth Risk Behavior Survey database. The data come from a nationally representative sample of US high schools, and the focus was on Female students in grades 9 through 12 (n = 7544). Participants' self-reported anabolic steroid use was compared with other health-related behaviors and with sports participation. Prior or ongoing anabolic steroid use was reported by 5.3% of female high school students. Those adolescent girls had a marked increase in other health-compromising behaviors, including past 30-day use of alcohol (odds ratio [OR], 8.83; 95% confidence interval [CI], 5.49-14.20), cigarettes (OR, 5.14; 95% CI, 3.14-8.42), marijuana (OR, 7.91; 95% CI, 5.20-12.04), cocaine (OR, 10.78; 95% CI, 6.18-18.81), and diet pills (OR, 4.86; 95% CI, 2.98-7.93). They were more likely to carry a weapon (OR, 7.54; 95% CI, 4.83-11.76), have had sexual intercourse before age 13 years (OR, 2.90; 95% CI, 1.58-5.33), and have had feelings of sadness or hopelessness almost every day for at least 2 consecutive weeks (OR, 4.13; 95% CI, 2.57-7.22). They were less likely to play school-sponsored team sports (OR, 0.52; 95% CI 0.34-0.80). Steroid users participating



in sports shared the same problem behaviors as steroid users not participating in team athletics. Self-reported anabolic steroid use is not confined to adolescent girls in competitive athletics and is an indicator of adolescent girls with a marked increase in a cluster of other health-harming behaviors. Elliot, D.L., Cheong, J., Moe, E.L., and Goldberg, L. Cross-Sectional Study of Female Students Reporting Anabolic Steroid Use. *Arch Pediatr Adolesc Med*, 161(6), pp. 572-577, 2007.

#### A Review of Research on Caretaking of Children of Incarcerated Parents

This paper reviews the literature for research findings on caretaking-related problems associated with the absence of parents from the home following incarceration. It focuses on the impact of incarceration on the welfare and adjustment of urban African American children and on the assumption of caretaking responsibilities by other caretakers, principally maternal grandmothers. Noting the complex situational difficulties involved and the potential burdens associated with surrogate parenting in general, and with this population in particular, the service-provider implications of this parenting arrangement are considered in this review. Findings indicate that problems associated with incarceration of parents tend to be intergenerational and vary considerably in complexity and severity. To the extent that they impact the children involved, these issues should be addressed in coordinated service delivery focusing on prevention. Hanlon, T.E., Carswell, S.B., and Rose, M. Research on the Caretaking of Children of Incarcerated Parents: Findings and Their Service Delivery Implications. *Children and Youth Services Review*, 29(3), pp. 348-362, 2007.

#### The Role of Delinquency and Depressed Mood in Late Adolescent Substance Use

This study examines the extent to which delinquency and depressed mood, measured at ages 11, 12, 13, 14, and 16, predict problem substance use at age 18. This study also examines mediation of these effects through alcohol use at age 16 across gender. Participants were 429 rural youths (222 girls and 207 boys) and their families who participated in Project Family, a prevention research study. Problem substance use was defined through both youth and parent responses to survey items reflecting problems with alcohol and drug use. Both delinquency and depressed mood appeared to play a role in the development of problem substance use, but their effects may be moderated by gender and may vary throughout adolescence. Indirect positive effects of delinquency on problem substance use were observed for boys, while direct positive effects of depressed mood were observed for girls. These findings have potential implications for specific targets of early prevention and how these may differ for boys and girls. Mason, W., Hitchings, J., and Spoth, R. Emergence of Delinquency and Depressed Mood Throughout Adolescence as Predictors of Late Adolescent Problem Substance Use. *Psychol Addict Behav*, 21(1), pp. 13-24, 2007.

### **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

#### Delay Discounting Predicts Postpartum Relapse to Cigarette Smoking Among Pregnant Women

Investigators conducted this study to examine whether delay discounting (DD), a measure of impulsivity, predicts treatment outcome among cigarette smokers. More specifically, the authors examined whether baseline discounting for hypothetical monetary rewards predicted smoking status at 24 weeks postpartum among women who discontinued smoking during pregnancy. Participants were 48 pregnant women who participated in a clinical trial examining the use of incentives to prevent postpartum relapse. Several sociodemographic characteristics (being younger, being less educated, and reporting a history of depression) assessed at study entry were associated with increased baseline DD, but in multivariate analyses only DD predicted smoking status at 24 weeks postpartum. Greater baseline DD was a significant predictor of smoking status at 24 weeks postpartum. DD was reassessed periodically throughout the study and did not significantly change over time among those who eventually resumed smoking or those who sustained abstinence. The results extend the association of DD with risk for substance abuse to pregnant and recently postpartum cigarette smokers and demonstrate a significant relationship between DD and

treatment outcome. Yoon, J.H., Higgins, S.T., Sugerbaker, R.J., Thomas, C.S., and Badger, G.J. Delay Discounting Predicts Postpartum Relapse to Cigarette Smoking Among Pregnant Women. *Experimental and Clinical Psychopharmacology*, 15 (2), pp. 176-186, 2007.

#### If Substance Abuse Is a Chronic, Relapsing Condition, Substance Abuse Treatment May Need to Be Chronic and Addressing Relapse Too

Drs. Suniya Luthar of Columbia University, Nancy Suchman of Yale University, and Michelle Altomare published the results of a randomized clinical trial testing Relational Psychotherapy Mothers' Group (RPMG) for substance-abusing, methadone-maintained mothers with young children. A total of 60 mothers participated in RPMG and 67 participated in recovery training (RT). At 6 months after starting treatment, women in the RPMG group showed greater improvements in child maltreatment and cocaine abuse, and children of women in RPMG reported greater improvements in emotional adjustment than did other children. However, these treatment gains were not sustained once treatment was discontinued. These results lend support to the notion of substance abuse as a chronic, relapsing condition that may best be treated by ongoing monitoring and intervention. Luthar, S.S., Suchman, N.E., and Altomare, M. Relational Psychotherapy Mother's Group: A Randomized Clinical Trial for Substance Abusing Mothers. *Development and Psychopathology*, 19, pp. 243-261, 2007.

### **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

#### Women and Men Do Not Appear to Differ in Response to the Discriminative-Stimulus Effects of d-Amphetamine

The results of animal and human laboratory studies are mixed regarding gender differences in response to stimulant drugs. This study performed a retrospective analysis of six studies conducted by this team that used identical procedures and methods. Thirteen women and 14 men learned to discriminate 15 mg of oral d-amphetamine, then the effects of a range of doses of d-amphetamine (0, 2.5, 5, 10, and 15 mg) alone and in combination with other drugs, were assessed. In these studies, d-amphetamine functioned as a discriminative stimulus and dose-dependently increased drug-appropriate responding. Women and men did not differ in their ability to discriminate d-amphetamine, but differed on participant-ratings of high (women < men), nausea (women > men) and sluggish (women < men); women also experienced greater increases in diastolic pressure than men following the administration of higher d-amphetamine doses (10 and 15 mg). Changes in menstrual cycle and hormone levels were not evaluated in the current study. Because the study results may have been confounded by the training procedures, future research should use other behavioral arrangements (e.g. drug self-administration) to determine if women and men respond differently to the effects of d-amphetamine. Vansickel, A.R., Lile, J.A., Stoops, W.W., and Rush, C.R. Similar Discriminative-Stimulus Effects of d-Amphetamine in Women and Men. *Pharmacology, Biochemistry and Behavior*, 87, pp. 289-296, 2007.

#### Biochemical and Virologic Parameters in Patients Co-infected with Hepatitis C and HIV versus Patients with Hepatitis C Mono-infection

Previous studies of patients with hepatitis C virus (HCV) infection looking at the effect of human immunodeficiency virus (HIV) co-infection on biochemical parameters and HCV RNA level have shown conflicting results. Accurate characterization of the effect of HIV is important for evaluation and treatment of HCV in co-infected persons. The authors studied 315 HCV mono-infected and 75 HCV-HIV co-infected subjects to determine the effect of HIV on biochemical parameters and HCV RNA and to determine the predictors of elevated serum alanine aminotransferase (ALT) levels and HCV RNA levels. The co-infected subjects were more likely to be African-American (55% vs 26%,  $P < 0.0005$ ), have used injection drugs (68% vs 60%,  $P = 0.02$ ), have detectable HCV RNA (84% vs 70.5%,  $P = 0.018$ ), have HCV RNA levels  $>6 \log_{10}$  IU/mL (60% vs 38%,  $P = 0.001$ ), and have lower mean serum ALT levels (50.4

IU/mL vs 73.7 IU/mL,  $P = 0.006$ ). In multivariable analyses, the following factors predicted an ALT level  $>50$  IU/mL:  $\log_{10}$  HCV RNA (OR, 1.15; 95% CI, 1.00 to 1.32); HIV co-infection (OR, 0.48; 95% CI, 0.25 to 0.89); and having ever been treated for HCV (OR, 1.92; 95% CI, 1.16 to 3.18). The only significant predictor of HCV RNA level  $>6 \log_{10}$  IU/mL was HIV co-infection (OR, 2.75; 95% CI, 1.46 to 5.15). Significant predictors of having a detectable HCV RNA level were female sex (OR, 3.81; 95% CI, 1.18 to 12.25); HIV co-infection (2.45; 95% CI, 1.14 to 5.26); and ever being treated for HCV (OR, 1.96; 95% CI, 1.10 to 3.48). The authors conclude that HCV-HIV co-infected persons have higher HCV RNA levels but lower serum ALT levels than HCV mono-infected patients. Criteria for performing liver biopsy and treating HCV infection in co-infected patients may need to be revisited. Butt, A.A., Tsevat, J., Ahmad, J., Shakil, A.O., and Mrus, J.M. *Am J Med Sci.* 333(5), pp. 271-275, 2007.

#### Sexual and Other Noninjection Risks for HBV and HCV Seroconversions among Noninjecting Heroin Users

Many heroin users do not inject drugs but may still be at risk of infection with Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), and Hepatitis C Virus (HCV), via sexual or other non-injection related activity. Non-injecting heroin users (NIUs) in New York City who were recruited and prospectively followed during March 1996-February 2003 were tested for anti-HIV, anti-hepatitis B core antigen, and anti-HCV and were interviewed about their sexual and other non-injecting risk. A seroconversion is represented by the first positive test result after the last negative test result. Hazard ratios (HRs) ( $P < .05$ ) were estimated by use of Cox proportional hazards regression. Of 253 HIV-negative participants, 2 seroconverted (0.29/100 person-years at risk [pyar]); of 184 HBV-negative participants, 16 (3.3/100 pyar); and, of 219 HCV-negative participants, 16 (2.7/100 pyar). Independent predictors of seroconversion were, for HBV, being a female who engages in unprotected receptive anal sex (HR, 6.8), having short-term sex partners (HR, 6.2), and being a male with male sex partners (HR, 5.7); for HCV, being a male who receives money/drugs for sex (HR, 5.6) and sharing non-injecting crack-use equipment (HR, 4.5). These findings suggest that NIUs are at considerable risk of HBV infection via high-risk sex; and, for HCV, via high-risk sexual activity and the sharing of non-injecting crack-use equipment. Interventions for NIUs should seek to reduce high-risk sexual activity and the sharing of non-injecting drug-use equipment. Neaigus, A., Gyarmathy, V., Zhao, M., Miller, M., Friedman, S., and Des Jarlais, D. *Sexual and Other Non-injection Risks for HBV and HCV Seroconversions among Non-injecting Heroin Users.* *J Infect Dis*, 195(7), pp. 1052-1061, 2007.

#### HIV Risk Behaviors among Rural Stimulant Users: Variation by Gender and Race/Ethnicity

Data were examined from a community sample of rural stimulant users ( $n = 691$ ) in three diverse states to identify gender and racial/ethnic differences in HIV risk behaviors. Bivariate and logistic regression analyses were conducted with six risk behaviors as dependent variables: injecting drugs, trading sex to obtain money or drugs, trading money or drugs to obtain sex, inconsistent condom use, multiple sex partners, and using drugs with sex. Controlling for state, income, age, heavy drinking, and type of stimulant used, men had lower odds than women for trading sex to obtain money or drugs (adjusted odds ratio [AOR] = 0.4, confidence interval [CI] = 0.28-0.59;  $p < .0001$ ), greater odds than women for trading money or drugs to obtain sex (AOR = 44.4, CI = 20.30-97.09;  $p < .0001$ ), greater odds than women of injecting drugs (adjusted odds ratio (AOR) = 1.6, CI = 1.11-2.42;  $p = .01$ ), and lower odds than women of using condoms inconsistently (AOR = 0.6, CI = 0.35-0.92;  $p = .02$ ); African Americans had lower odds than Whites of injecting drugs (AOR = .08, CI = 0.04-0.16;  $p < .0001$ ), greater odds than Whites for trading sex to obtain money or drugs (AOR = 1.7, CI = 1.01-2.85;  $p = .04$ ) and for trading money or drugs to obtain sex (AOR = 2.9, CI = 1.53-5.59;  $p = .001$ ), and greater odds than Whites of using drugs with sex (AOR = 3.9, CI = 1.47-10.09;  $p = .006$ ). These findings indicate HIV prevention efforts should be tailored to address gender and racial/ethnic differences in risk behaviors among rural stimulant users. Booth, B.M., Wright, P.B., Stewart, K.E., Fischer, E.P., Carlson, R.G., Falck, R., Wang, J., and Leukefeld, C.G. *HIV Risk Behaviors*

among Rural Stimulant Users: Variation by Gender and Race/Ethnicity. *AIDS Educ Prev*, 12(2), pp. 137-150, 2007.

#### Effects of Pregnancy on Nicotine Self-administration and Nicotine Pharmacokinetics in Rats

Dr. Pentel's group at Minneapolis Medical Research Foundation developed an animal model of smoking during pregnancy by initially characterizing nicotine self-administration (NSA) in pregnant rats. In addition, they also began to explore the effects of pregnancy on nicotine pharmacokinetics in rats. NSA decreased over the course of pregnancy with NSA significantly lower in the third trimester compared to nonpregnant controls. NSA remained suppressed for up to 10 days into lactation. Locomotor behavior was also significantly suppressed during the second and third trimesters and throughout lactation. Nicotine elimination was slower in pregnant females compared to nonpregnant females only in the third trimester. In conclusion, NSA, locomotor behavior, and nicotine elimination in rats are decreased during late pregnancy. The present study is the first to characterize NSA during pregnancy in animals, providing a potential model of maternal smoking in humans. Lesage, M.G., Keyler, D.E., Burroughs, D., and Pentel, P.R. Effects of Pregnancy on Nicotine Self-administration and Nicotine Pharmacokinetics in Rats. *Psychopharmacology (Berl)*, 194(3), pp. 413-421, 2007.

#### Maternal Separation Alters Drug Intake Patterns in Adulthood in Rats

Dr. Kuhar's group at Emory University, Atlanta, Georgia, examined the effects of maternal separation and drug intake patterns in adulthood in rats. Maternal separation/handling (MS/H) is an animal model of early life stress that causes profound neurochemical and behavioral alterations in pups that persist into adulthood. Many recent studies have used the MS/H model to study changes in drug effects in adulthood that are linked to behavioral treatments and stressors in the perinatal period. The drug effects focused on in this review are the reinforcing properties of the abused drugs, cocaine and alcohol. A striking finding is that variations in maternal separation and handling cause changes in ethanol and cocaine self-administration. Further, these changes indicate that various manipulations in the perinatal period can have long lasting effects of interest to biochemical pharmacologists. This article reviewed recent studies on ethanol and cocaine self-administration using the MS/H model and the neurochemical alterations that may play a role in the effects of MS/H on ethanol and cocaine self-administration. Studying the MS/H model can provide important clues into the vulnerability to drug abuse and perhaps identify a crucial window of opportunity for therapeutic intervention. Moffett, M.C., Vicentic, A., Kozel, M., Plotsky, P., Francis, D.D. and Kuhar, M.J. Maternal Separation Alters Drug Intake Patterns in Adulthood in Rats. *Biochem Pharmacology*, 73(3), pp. 321-330, 2007.

### **SERVICES RESEARCH**

#### Smoking Cessation via the Internet: a Randomized Clinical Trial of an Internet Intervention as Adjuvant Treatment in a Smoking Cessation Intervention

Internet interventions for smoking cessation are ubiquitous. Yet, to date, there are few randomized clinical trials that gauge their efficacy. To address this question, the authors performed a randomized clinical trial (N= 284, n= 140 in the treatment group, n= 144 in the control group) of an Internet smoking cessation intervention. Smokers were randomly assigned to receive either bupropion plus counseling alone, or bupropion and counseling in addition to 12 weeks of access to the Comprehensive Health Enhancement Support System for Smoking Cessation and Relapse Prevention (CHESS SCRIP; a Web site which provided information on smoking cessation as well as support). It was found that access to CHESS SCRIP was not significantly related to abstinence at the end of the treatment period (OR= 1.13, 95% CI 0.66-2.62) or at 6 months post quit (OR= 1.48, 95% CI 0.66-2.62). However, the number of times participants used CHESS SCRIP per week was related to abstinence at both ends of treatment (OR= 1.79, 95% CI 1.25-2.56) and at the 6-month follow-up (OR= 1.59, 95% CI 1.06-2.38). Participants with access to CHESS SCRIP logged in

an average of 33.64 times (SD=30.76) over the 90-day period of access. Rates of CHESS SCRIP use did not differ by ethnicity, level of education or gender (all  $p > .05$ ). In sum, results suggest that participants used CHESS SCRIP frequently and that CHESS SCRIP use was related to success in smoking cessation. Japuntich, S., Zehner, M., Smith, S., Jorenby, D., Valdez, J., Fiore, M., Baker, T., and Gustafson, D. Smoking Cessation via the Internet: a Randomized Clinical Trial of an Internet Intervention as Adjuvant Treatment in a Smoking Cessation Intervention. *Nicotine Tob Res*, 8 Suppl 1, pp. S59-S67, 2006.

#### Organizational, but Not Client, Factors Associated with Substance Abuse Treatment Cost

This study uses data from the Alcohol and Drug Services Survey (ADSS) to estimate the statistical associations between organizational and client characteristics on per client and per day costs of outpatient substance abuse treatment. Variables examined include facility ownership, average length of stay, and visits per enrollment day, and client characteristics such as gender, age, and primary drug of abuse. The authors found several organizational characteristics were statistically significant in the model estimating cost per episode, including log of point prevalence client count (-0.53,  $p < .01$ ), log of average length of stay (0.73,  $p < .01$ ), log of visits per enrollment day (0.45,  $p < .01$ ), log of labor cost index (0.50,  $p < .01$ ), proportion of counselor time spent in direct counseling (-0.52,  $p < .01$ ), and location outside a metropolitan area (-0.19,  $p < .05$ ). None of the client variables are statistically significant in this model. These findings suggest there exists increasing returns to scale in outpatient substance abuse treatment indicating that mergers of substance abuse treatment programs may be economically beneficial. Beaston-Blaakman, A., Shepard, D., Horgan, C., and Ritter, G. Organizational and Client Determinants of Cost in Outpatient Substance Abuse Treatment. *J Ment Health Policy Econ*, 10(1), pp. 3-13, 2007.

### **CLINICAL TRIALS NETWORK RESEARCH**

#### AIDS Research in the NIDA Clinical Trials Network: Emerging Results

Prevention and treatment of HIV/AIDS among drug users continue to be vexing problems. Scientifically validated interventions have been developed to prevent and treat HIV/AIDS among substance users. The Clinical Trials Network (CTN) of the National Institute on Drug Abuse (NIDA) is conducting multi-site clinical trials, with emerging results that address both prevention and treatment of HIV/AIDS. This is a report of preliminary results from several of those trials, presented at a workshop of the College on Problems of Drug Dependence. Lawrence Brown surveyed over 120 CTN clinics and reports on the state of the clinics in treating HIV/AIDS and other infectious diseases. Robert Booth summarized preliminary data from over 600 participants in a multi-site trial of HIV and hepatitis C virus (HCV) interventions in drug detoxification settings. Donald Calsyn reported preliminary results from an effectiveness trial of a gender-specific, action-oriented, safer-sex group intervention for 575 men in drug treatment programs. Susan Tross reported on a similar study focusing on 515 women in 12 clinics. Yong Song presented the perspective of treatment programs in conducting clinical trials. Jacques Normand added comments from the perspective of the Director of the NIDA AIDS research program. Sorensen, J.L., Brown, L., Calsyn, D., Tross, S., Booth, R.E., Song, Y., and Normand, J. AIDS Research in the NIDA Clinical Trials Network: Emerging Results. *News & Views Section Drug Alcohol Depend.* 89(2-3), pp. 310-313, 2007.

### **INTERNATIONAL RESEARCH**

### **FORMER NIDA INVEST DRUG ABUSE RESEARCH FELLOWS**

### Drug Use Opportunities and the Transition to Drug Use among Adolescents from the Mexico City Metropolitan Area

Benjet, C., Borges, G., Medina-Mora, M.E., Blanco, J., Zambrano, J., Orozco, R., Fleiz, C., Rojas, E. Drug Alcohol Depend. 2007 Mar 21; [Epub ahead of print]

INVEST Fellow: Guilherme Borges, Mexico, 1997-1998

The earliest stage of drug involvement is being presented with the opportunity to use drugs. During adolescence these opportunities increase. Because of the scarcity of data for the Mexican population, the aim is to estimate the prevalence of drug use opportunities among Mexican adolescents, the prevalence of drug use among those who were presented with the opportunity, and the socio-demographic correlates of both. A multistage probability survey was carried out among 12-17 year olds from Mexico City. Adolescents were administered the adolescent version of the World Mental Health Composite International Diagnostic Interview. The response rate was 71% (n=3005). Descriptive and logistic regression analyses were performed considering the multistage and weighted sample design. Twenty-nine percent have had the opportunity to try illicit drugs; of those presented with an opportunity, 18% have done so. Males, older adolescents, school drop-outs, and those whose parent has had drug problems are more likely to have been exposed to drug use opportunities while more religious adolescents are less likely. Given the chance to try drugs, older adolescents and school drop-outs are more likely to do so and those with high parental monitoring and religiosity are less likely. These results suggest that less substance use among females in Mexico may be due in part to fewer opportunities to use since females were equally likely to use drugs given the opportunity. Given the increase in opportunity among older adolescents, preventive efforts should start by age 12 and with special attention to adolescents who have dropped out of school. PMID: 17382489 [PubMed - as supplied by publisher]

### Prophylactic Role for Complementary and Alternative Medicine in Perinatal Programming of Adult Health

Hodgson, D.M., Nakamura, T., and Walker, A.K. Forsch Komplementarmed. Apr; 14(2), pp. 92-101, 2007. Epub 2007 Apr 23

INVEST Fellow: Tamo Nakamura, Australia, 2002-2003

The health status of an individual in adulthood is proposed to be determined by events occurring in the prenatal and early postnatal period. A common early life event proven to have long lasting effects on the developing fetus is stress, including pain. Exposure of fetal and neonatal infants to repetitive psychological (e.g., maternal stress) or physiological (e.g., pain, infection, and noise) stress during this period is proposed to alter mechanisms involved in the regulation of stress, immunological maturation, pain perception, and cognition. Such changes, which persist into adulthood, may occur via alterations in the development of the hypothalamic-pituitary-adrenal (HPA) axis. This process is typically referred to as 'perinatal programming'. Ontogenic alterations in the development of the HPA-axis have been related to a number of adult pathologies such as cardiovascular disease, type 2 diabetes, asthma, as well as psychopathologies such as anxiety and depression. In this review, the effectiveness of complementary and alternative medicine (CAM), such as music, dietary supplements, massage and aromatherapy, in reducing perinatal stress in mothers and infants is examined. An emphasis is placed on these therapies as preventative measures which may be of value to individuals at risk of developing disease profiles associated with the consequences of adverse perinatal programming. The widening interest in perinatal programming and CAM suggests the potential for CAM to become a valuable tool in offsetting negative adult health outcomes resulting from perinatal programming associated with adverse gestational early life environments.

### Parenting Interventions for Drug-Dependent Mothers and Their Young Children: The Case for an Attachment-Based Approach

Suchman, N., Pajulo, M., Decoste, C., and Mayes, L. *Fam Relat. Apr*; 55(2), pp. 211-226, 2006.  
INVEST Fellow: Marjaterittu Pajulo, Finland, 2003-2004

Maternal substance abuse is the most common factor involved when children come to the attention of the child welfare system. Although there is a clear need for clinical trials to evaluate parenting interventions for drug-dependent women, few studies to date have systematically examined the efficacy of interventions for this population. The authors first review six published reports of outpatient interventions that aimed to enhance the caregiving skills of substance-abusing mothers caring for children between birth and 5 years of age. After discussing implications of these preliminary studies, they then describe an attachment-based intervention that addresses these implications and has demonstrated preliminary feasibility in a pilot trial.

### Body Mass Index and the Prevalence of Metabolic Syndrome among Children and Adolescents in Two Mexican Populations

Halley Castillo, E., Borges, G., Talavera, J.O., Orozco, R., Vargas-Alemanm C., Huitron-Bravom G., Diaz-Montiel, J.C., Castanon, S., and Salmeron, J. *J Adolesc Health. Jun*; 40(6), pp. 521-526, 2007. Epub 2007 Mar 21, 2007.

INVEST Fellow: Guilherme Borges, Mexico, 1997-1998

The purpose of this study was to report the prevalence of metabolic syndrome (MS) among children and adolescents living in central Mexico, and its association with body mass index (BMI). In a sample of 1366 subjects from 7 to 24-years-old, a self-administered questionnaire was used to determined demographic characteristics. The definition of pediatric MS was determined using analogous criteria to Adult Treatment Panel III (ATPIII) as  $\geq 3$  of the following: concentration of triglycerides  $\geq 100$  mg/dL, HDL cholesterol  $< 45$  mg/dL for males and  $< 50$  mg/dL for females, waist circumference  $\geq 75$ th percentile (sex specific), glucose concentration  $\geq 110$  to  $< 126$  mg/dL, and systolic or diastolic blood pressure  $\geq 90$ th percentile (age, height, and sex specific). Most of the sample was in the 10-14- (32.4%) and the 15-19-year (35.4%) age groups, mostly females (57%), and 31% of this young sample was overweight (mean BMI = 21.6 kg/m<sup>2</sup>). About 1 in every 5 participants had full criteria for MS (19.2%, 95% confidence interval [CI]: 16.4-22.1 among females, and 20.2%, 95% CI: 17.1-23.7 among males), and only 1 in every 10 was free of any MS component. The most common component was a low HDL level, observed in 85.4% of the sample. Unfavorable fat distribution, as indicated by a large waist circumference, was present in 27.9% of the sample. About 66% of those 10-14-year-olds with a large BMI were positive for MS. MS and overweight are major problems for youth in Mexico. Immediate and comprehensive actions at home and schools are needed if Mexico wants to avoid the heavy burden that this disorder will have for its population in the near future.

## **FORMER HHH DRUG ABUSE RESEARCH FELLOWS**

### Brazilian Female Crack Users Show Elevated Serum Aluminum Levels

Pechansky, F., Kessler, F.H., Diemen, L., Bumaguin, D.B., Surratt, H.L., and Inciardi, J.A.  
*Rev Bras Psiquiatr. Mar*; 29(1), pp. 39-42, 2007.

HHH Fellow: Flavio Pechansky, Brazil, 1993-1994

There is no information in the literature on the impact of crack smoking using crushed aluminum cans as makeshift pipes, a common form of crack use in Brazil. Since aluminum intake is associated with neurological damage, the authors measured serum aluminum levels in crack smokers. The objective of this study was to ascertain the levels of aluminum in crack users who smoke on makeshift aluminum pipes. 71 female crack smokers, their mean age being 28.0 (+/- 7.7), provided information about their drug use, and had blood samples tested for serum aluminum level. 56 (79%) subjects smoked crack from crushed can pipes, while 15 (21%) smoked from other containers. Fifty-two (73.2%) out of the 71 subjects presented a serum aluminum level of 2 microg/l and 13 (18.3%) had a serum aluminum level of 6 microg/l cut-off

point, which is above the reference value. When compared to non-drug users matched by their mean age and gender, they had similar median values and interquartile ranges for serum aluminum level [3 (2-4.6) for crack smokers; 2.9 (1.6-4.1) for controls], but with different means and standard deviations (4.7 +/- 4.9 and 2.9 +/- 1.7, respectively). Crack smokers have high serum aluminum level, but the authors are unsure of its complete association with aluminum cans. Further studies are needed. If such association is proven true in future research, further issues will be raised in dealing with this important disorder, including proper planning and evaluation of public health policies in this area.

#### Drug Consumption among Sexual Offenders against Females

Baltieri, D.A., and de Andrade, A.G. *Int J Offender Ther Comp Criminol.*, 52(1), pp. 62-80, 2007.

HHH Fellow: Arthur Guerra de Andrade, Brazil, 1991-1992

This article aims to evaluate the role of drug consumption among sexual offenders against females. Three groups of participants (N =133) comprising sexual offenders against girls, pubertal females, and women were examined with reference to history of drug and/or alcohol use, impulsivity level, sexual addiction, and recidivism risk. Sexual offenders against women were found to have significantly more difficulties with drug use, higher impulsivity level, and to be younger than the sexual offenders against girls and pubertal females. The combination of drug consumption and higher level of impulsivity may contribute to sexual aggression against adult females.

#### Alcohol and Drug Consumption among Sexual Offenders

Baltieri, D.A., and de Andrade, A.G. *Forensic Sci Int.*, 175(1), pp. 31-35, 2007.

HHH Fellow: Arthur Guerra de Andrade, Brazil, 1991-1992

The purpose of this study was to evaluate the role of alcohol and drug consumption between sexual offenders against boys and girls. It was an observational, retrospective and cross-sectional study carried out by the Ambulatory for the treatment of sexual disorders of ABC Medical College, Santo André, São Paulo, Brazil (ABSEx). The sample comprised 104 convicts, over 18 years old, sentenced only for sexual crimes against children (below 11 years old). Alcohol and drug consumption, sexual abuse history, sexual impulsivity, and risk of recidivism were evaluated. The sexual offenders against boys showed higher alcohol consumption problems than sexual offenders against girls ( $\chi^2=19.76$ , 1d.f.,  $p<0.01$ ). The severity of alcohol consumption was also significantly higher in the sexual offenders against non-related boys than in the sexual offenders against non-related girls ( $p=0.037$ , ANOVA). After adjustment for other variables, such as monthly income before the penalty and alcohol consumption at the moment of the crime, the alcohol consumption severity in sexual offenders against boys was significantly higher than in sexual offenders against girls (OR=1.05, CI 1.01-1.08,  $p<0.01$ ). Alcohol use or abuse is associated with the perpetration of sexual aggression. The role of alcohol consumption seems to be greater in sexual offenders against boys than in girls and this can contribute to criminal recidivism.



# DIRECTOR'S REPORT

February 2008

## BASIC BEHAVIORAL RESEARCH

### Sex Differences in THC's Effects on Spatial Learning in Adult and Adolescent Rats

In 2006 Dr. Scott Swartzwelder and colleagues at Duke University reported effects of 2.5, 5.0, and 10.0mg/kg THC on learning in male adolescent and adult rats in the Morris water maze (Cha et al., 2006). The researchers found that THC disrupts both spatial and non-spatial learning more powerfully in adolescent rats than in adults at all dose levels. Dr. Swartzwelder and his colleagues have now published results from three studies that extend findings of this initial report. In the first study, effects of 5.0 mg/kg THC on spatial learning in the Morris Water maze were studied in male and female adolescent and adult rats over 5 daily test sessions. In males, spatial learning was impaired in adolescents on all test days, but was not impaired on any of the test days in adults. Among females, adolescents exhibited impairment on all test days, but adults were impaired only during the first two sessions. Thus, THC impairment was more potent in adolescents than adults and more potent in adult females than adult males. To assess the effects of chronic THC on subsequent learning, in a second experiment, separate groups of male and female adolescent and adults rats were treated with 5.0 mg/kg THC for 21 days and tested 28 days later in the Morris Water maze. Chronic THC treatment did not produce learning deficits in any of the groups. The third experiment was a THC dose-response study (2.5, 5.0, and 10.0mg/kg THC) using adolescent and adult female rats, conducted to parallel the initial experiment in males (Cha et al., 2006). Each dose was tested for 5 days. Consistent with the earlier outcome in males, THC produced a dose-response impairment in spatial learning. Although there was no overall age effect on spatial learning, there were differences in the dose-response function between adolescents and adults, suggesting a greater dose sensitivity in adolescents. Additionally, assessment of spatial memory indicated impairment in adolescents but not adults. These outcomes have important implications for future research on THC and other abused drugs. Animal model research in drug abuse has largely been conducted on adult males. The results of the present study join a growing body of drug abuse research showing that outcomes observed in adult males do not always generalize to females and to adolescents, highlighting the limitations of research conducted with only adult male subjects. Cha, Y.M., Jones, K.H., Kuhn, C.M., Wilson, W.A., and Swartzwelder, H.S. Sex Differences in the Effects of Delta (9)-tetrahydrocannabinol on Spatial Learning in Adolescent and Adult Rats. *Behavioral Pharmacol.* 18, pp. 563-569, 2007.

### Sex Chromosome Complement Regulates Habit Formation

Gonadal hormones can cause sex differences via their brain organization effects during development and via their activational effects in puberty and adulthood. Other sex differences, however, are not due to gonadal hormones, but rather the direct action of the chromosome complement. Recent development of the 'four core genotype' mouse model permits dissociation of gonadal sex and chromosomal sex by comparison of males and females that are gonadally and chromosomally either congruent or incongruent. The two incongruent cases are (1) chromosomal XY males with deletion of the testis-determining Sry gene and are therefore gonadally female and (2) chromosomal XX females with insertion of the Sry gene and are therefore gonadally male. Dr. Jane Taylor and colleagues at Yale and UCLA have used this four core genotype mouse model to study the role of chromosomal sex versus gonadal sex on habit formation. In the first phase of their study, mice were trained to nose-poke in one of three apertures for a food pellet delivery. Following either moderate training (9 days) or extended training (15 days), food pellets were devalued in a conditioned taste aversion procedure in which food pellets were paired with injections of the emetic lithium chloride. The mice were then retested in the instrumental procedure. In past studies using this habit formation procedure, devaluation decreases instrumental performance prior to habit formation, but after habit formation, instrumental performance is unaffected by devaluation. Dr. Taylor and her

colleagues found that XX mice that previously received moderate instrumental training, showed operant performance following devaluation that was insensitive to changes in reinforcer value, indicating formation of a habit. XY mice subjected to devaluation, however, exhibited poorer performance than those not subjected to devaluation of the reinforcer, indicating that XY mice had not yet acquired habit formation. This outcome was independent of gonadal phenotype and was independent of gonadectomy vs. sham-operated status, indicating that the effects did not depend on organizational or activational functions of gonadal hormones. Following extended instrumental training, XX mice exhibited better instrumental performance (more correct nose-pokes) than XY mice. After devaluation, XX and XY mice were equally insensitive to changes in reward value of the reinforcer, indicating that with extended training, all mice had developed an instrumental habit. The authors speculate that sex differences in habit formation, as determined by the sex chromosome complement, could have implications for studying and understanding sex differences in drug addiction. Quinn, J.J., Hitchcott, P.K., Umeda, E.A., Arnold, A.P. and Taylor, J.R. Sex Chromosome Complement Regulates Habit Formation. *Nature Neurosci.* 10, pp. 1398-1400, 2007.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Predictors of Neonatal Abstinence Syndrome Severity in Methadone-Exposed Newborns

Investigators at Johns Hopkins University examined potential predictors of Neonatal Abstinence Syndrome (NAS), which is made up of symptoms reflecting dysfunction in autonomic and central nervous systems. Although infants born to mothers who experienced methadone-maintenance during pregnancy frequently show evidence of NAS, the signs and symptoms of NAS vary widely among infants. This study attempted to investigate some possible reasons behind such variation, with a focus on maternal vagal tone, a measure that reflects autonomic nervous system homeostasis, stress vulnerability, and self-regulation. Specifically, the investigators examined whether vagal tone responsivity to methadone administration in pregnant women provides insight into the pathophysiology and expression of NAS in the newborn. The expectation was that newborns born to mothers who show greater autonomic dysregulation, as reflected by increased levels of vagal suppression relative to methadone maintenance, would exhibit more severe NAS. At 36 weeks of gestation, electrocardiogram monitoring was carried out for 50 methadone-maintained pregnant women, at the times of trough and peak maternal methadone levels. NAS expression was related to maternal vagal activity; maternal vagal tone suppression and activation were associated with NAS symptomatology and treatment. NAS expression was not related to histories of maternal substance use or methadone maintenance, or to psychotropic medication exposure. The authors discuss potential mechanisms for interpretation of their findings. Jansson, L.M., DiPietro, J.A., Elko, A., and Velez, M. Maternal Vagal Tone Change in Response to Methadone is Associated with Neonatal Abstinence Syndrome Severity in Exposed Neonates. *Journal of Maternal, Fetal and Neonatal Medicine*, 20(9), pp. 677-685, 2007.

### Prenatal and Adolescent Exposure to Tobacco Smoke Modulates the Development of White Matter Microstructure

Smoking during pregnancy is related to elevated risks of cognitive and auditory processing deficits. Preclinical studies have revealed that disruption in neurodevelopment by exposure to nicotine is likely linked to the disruption of the trophic actions of acetylcholine at nicotinic acetylcholine receptors. This study utilized diffusion tensor anisotropy and anatomical magnetic resonance images to examine white matter microstructure in 67 adolescent smokers and nonsmokers with and without prenatal exposure to maternal smoking. Auditory attention was assessed in all subjects. Adolescents with prenatal and/or adolescent exposure demonstrated increases in regional white matter fractional anisotropy (FA) primarily in anterior cortical and subcortical regions. Increased FA of regions of the internal capsule that contain auditory thalamocortical and corticofugal fibers was associated with adolescent smoking. Performance on the auditory performance task in smokers was positively correlated with FA of the posterior limb of the left internal capsule, but not in nonsmokers. The magnitude of tobacco exposure during adolescence was

positively related to the FA of the genu of the corpus callosum further supporting the notion that the effects of nicotine on white matter maturation may be particularly significant during this developmental period. The results suggest that nicotine may disrupt the development of auditory corticofugal fibers which ultimately leads to reduced efficiency in the neurocircuitry that supports auditory processing. Jacobsen, L., Picciotto, M., Heath, C., Frost, S., Tsou, K., Dwan, R., Jackowski, M., Constable, R., and Menel, W. Prenatal and Adolescent Exposure to Tobacco Smoke Modulates the Development of White Matter Microstructure. *The Journal of Neuroscience*, 27(49) pp. 13491-13498, 2007.

### Marijuana Use and HIV-Related Risk Factors

This study examined the role of early and current marijuana use as it relates to sexually transmitted infection (STI) risk in a sample of young women who had been pregnant teenagers. Pregnant adolescents (N= 279), ages 12-18, were recruited from an urban prenatal clinic as part of a study that was developed to evaluate the long-term effects of prenatal substance exposure. Six years later, they were asked about their substance use and sexual history. The association of early and late marijuana use to two HIV-related risk factors -- lifetime sexual partners and STIs --was examined, and then structural equation modeling (SEM) was used to illustrate the associations among marijuana use, number of sexual partners, and STIs. Bivariate analyses revealed a dose-response effect of early and current marijuana use on STIs in young adulthood. Early and current marijuana use also predicted a higher number of lifetime sexual partners. Using SEM, the effect of early marijuana use on STIs was mediated by lifetime number of sexual partners. African-American race, more externalizing problems, and a greater number of sexual partners were directly related to more STIs. Adolescent pregnancy, early marijuana use, mental health problems, and African-American race were significant risk factors for STIs in young adult women who had become mothers during adolescence. Pregnant teenage girls should be screened for early drug use and mental health problems, because they may benefit the most from the implementation of STI/HIV screening and skill-based STI and HIV prevention programs. DeGenna, N.M., Cornelius, M.D., and Cook, R.L. Marijuana Use and Sexually Transmitted Infections in Young Women Who Were Teenage Mothers. *Women's Health Issues*, 17(5), pp. 300-309, 2007.

## **CLINICAL NEUROSCIENCE RESEARCH**

### PET Study Reveals Minimal Gender Differences or Menstrual Cycle Effects on Nicotinic Acetylcholine Receptors

The effects of sex and hormones on brain chemistry and neurotransmission are not well-characterized, and are of increasing importance as evidence emerges of sex differences in behavioral symptoms and treatment response in neuropsychiatric disorders. The nicotinic acetylcholine receptor (nAChR) system has been implicated in a variety of psychiatric disorders, including tobacco smoking, for which there is strong evidence supporting sex differences in behaviors and response to smoking cessation treatments. Kelly Cosgrove, Julie Staley, and colleagues at Yale examined the availability of nAChR containing the  $\beta_2$  subunit in healthy men and women nonsmokers, and the influence of menstrual phase among women. Regional brain activity was higher (39%–54%) in women than in men. When regional brain activity was normalized to total plasma parent to correct for individual differences in radiotracer metabolism (VT'), differences of 10%–16% were observed, with women greater than men. In contrast, when regional brain activity was normalized to free plasma parent (VT), there was less than a 4% difference by sex in regional brain  $\beta_2$ -nAChR availability. These sex differences in kBq/cm<sup>3</sup> and VT' resulted from significantly higher levels of total plasma parent, free fraction (f1), and free plasma parent in women than in men nonsmokers. No differences in plasma measures or brain  $\beta_2$ -nAChR availability were observed across the menstrual cycle for any outcome measure. Overall, these findings demonstrate no significant difference in brain  $\beta_2$ -

nAChR availability between men and women nonsmokers or across the menstrual cycle. Importantly, these findings demonstrate the need to control for sex differences in radiotracer metabolism and plasma protein binding. Cosgrove, K.P., Mitsis, E.M., Bois, F., Frohlich, E., Tamagnan, G.D., Krantzler, E., Perry, E., Maciejewski, P.K., Epperson, C.N., Allen, S., O'Malley S., Mazure, C.M., Seibyl, J.P., van Dyck, C.H., and Staley, J.K. 123I-5-IA-85380 SPECT Imaging of Nicotinic Acetylcholine Receptor Availability in Nonsmokers: Effects of Sex and Menstrual Phase. *J. Nucl. Med.*, 48(10), pp. 1633-1640, 2007.

## **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

### A Twin Study of Delinquent Peer Affiliation

This study used genetic epidemiologic approaches to evaluate whether the association between delinquent peer affiliation and conduct problems may occur because of shared genetic liability. Data came from 553 monozygotic and 558 dizygotic (same sex and opposite sex) twin pairs, over half female, aged 11 to 18 years, recruited from community based samples in Colorado, assessed through self-report for delinquent peer affiliation and conduct problems. The authors investigated whether genes contribute to both delinquent peer affiliation and the correlation between delinquent peer affiliations and conduct problems. Modeling found that delinquent peer affiliation was influenced by genetic, shared environmental and non-shared environmental factors; genetic factors also contributed to the correlation between delinquent peer affiliations and conduct problems, providing evidence for genotype-environment correlation. The magnitude of the genetic variance of conduct problems was contextually dependent on levels of delinquent peer affiliation and was greater at higher levels of delinquent peer affiliation. Thus, this study adds to the growing literature showing that many putative environmental risks for drug abuse correlate with individuals "genotypes". Button, T., Corley, R., Rhee, S., Hewitt, J., Young, S., and Stallings, M. Delinquent Peer Affiliation and Conduct Problems: A Twin Study. *J. Abnorm. Psychol.*, 116(3), pp. 554-564, 2007.

### Externalizing Symptoms among Children of Alcoholic Parents: Entry Points for an Antisocial Pathway to Alcoholism

The authors examined heterogeneity in risk for externalizing symptoms in children of alcoholic parents (COA), as it may inform the search for entry points into an antisocial pathway to alcoholism. That is, they tested whether the number of alcoholic parents in a family, the comorbid subtype of parental alcoholism, and the gender of the child predicted trajectories of externalizing symptoms over the early life course, as assessed in high-risk samples of children of alcoholic parents and matched controls. Data from the Michigan Longitudinal Study provided 596 children from 338 families, and Adolescent/Adult Family Development Project 454 adolescents and their parents, both with COA and matched controls assessed over multiple waves. Through integrative analyses of these independent, longitudinal studies, they showed that children with either an antisocial alcoholic parent or 2 alcoholic parents were at greatest risk for externalizing symptoms. Moreover, children with a depressed alcoholic parent did not differ from those with an antisocial alcoholic parent in reported symptoms. These findings were generally consistent across mother, father, and adolescent reports of symptoms; child gender and child age (ages 2-17); and the 2 independent studies examined. Multi-alcoholic and comorbid-alcoholic families may thus convey a genetic susceptibility to dysregulation along with environments that both exacerbate this susceptibility and provide few supports to offset it. Hussong, A., Wirth, R., Edwards, M., Curran, P., Chassin, L., and Zucker, R. Externalizing Symptoms among Children of Alcoholic Parents: Entry Points for an Antisocial Pathway to Alcoholism. *J. Abnorm. Psychol.*, 116, pp. 529-542, 2007.

### State Anti-Tobacco Advertising and Smoking Outcomes by Gender and Race/Ethnicity

Investigators examined overall and gender- and racial/ethnic-specific relationships between exposure to state-sponsored anti-tobacco televised advertising and smoking-related outcomes among US middle and high school students using five years of cross-sectional nationally representative data. Nationally

representative 8th, 10th, and 12th grade student sample data for 1999-2003 were merged with commercial ratings data on mean potential audience exposure to network and cable television anti-tobacco advertising across the 74 largest US designated market areas, resulting in a final sample size for analysis of 122,340. Associations between state-sponsored anti-tobacco televised advertising exposure and youth smoking-related beliefs and behaviors' were modeled while controlling for relevant individual and environmental factors as well as other televised tobacco-related advertising. Authors found higher potential for exposure to state anti-tobacco advertising within the previous four months was generally associated with decreasing odds of current smoking across groups. In addition, such exposure was related, to varying degrees, with decreased perceptions that most/all friends smoked, stronger five-year intentions not to smoke, and increased perceived harm of smoking. These relationships appeared possibly to be weaker for Asian students. The results from these analyses indicate that state anti-tobacco advertising significantly relates to beneficial outcomes -- especially regarding current smoking behaviour -- among US youth as a whole. Terry-McElrath, Y., Wakefield, M., Emery, S., Saffer, H., Szczypka, G., O'Malley, P., Johnston, L., Chaloupka, F., and Flay, B. State Anti-tobacco Advertising and Smoking Outcomes by Gender and Race/ethnicity. *Ethn. Health*, 12(4), pp. 339-362, 2007.

#### Gender Differences in Social Network Influence among Injection Drug Users: Perceived Norms and Needle Sharing

Whereas substantial research has linked perceived norms and HIV sexual risk behavior, less attention has been given to the relationship between perceived norms and injection drug practices. This study investigated the relationship between needle sharing and perceived norms in a sample of injection drug users. Data were collected through face-to-face interviews with 684 injectors from the STEP Into Action (STEP) project in Baltimore, Maryland. Logistic regression was used to assess the associations between perceived norms (descriptive and injunctive norms) and needle sharing. Results were stratified by gender. Descriptive norms were significantly related to needle sharing among males (AOR = 1.58, 95%CI = 1.20-2.40) and females (AOR = 1.78; 95%CI = 1.24-2.55). Whereas injunctive norms were significantly associated with needle sharing among men (AOR = 1.30 95%CI = 1.05-1.61), this association was not significant among women (AOR = 0.99; 95%CI = 0.74-1.31). These findings suggest the utility of peer education interventions that promote norms regarding risk reduction among injection drug users. The data also provide support for gender-specific HIV prevention interventions. Davey-Rothwell, M., and Latkin, C. Gender Differences in Social Network Influence among Injection Drug Users: Perceived Norms and Needle Sharing. *J. Urban Health*, 84(5), pp. 691-703, 2007.

#### HCV Synthesis Project: Preliminary Analyses of HCV Prevalence in Relation to Age and Duration of Injection

Early acquisition of hepatitis C virus (HCV) infection appears to affect a substantial proportion of IDUs--between 20 percent and 90 percent. Analyzing the range of HCV prevalence estimates in new injectors may help identify factors that can be modified to reduce HCV transmission. The HCV Synthesis Project is a meta-analysis of studies of HCV epidemiology and prevention in drug users worldwide. In this preliminary analysis, researchers examined data from 127 studies of IDUs that reported HCV prevalence in relation to age or year since onset of drug injection, analyzing heterogeneity and calculating summary statistics where appropriate. Six studies reported gender-specific HCV prevalence rates among young or new injectors; the group mean prevalence was 47 percent for men and 44 percent for women (NS). Group mean age for HCV-negatives was 24.7 years (range 24-28) and 26.1 years (range 21-31) for HCV-positives (n=8 studies). Data were examined from 13 studies that compared HCV prevalence among young injectors to older injectors using 5-year age categories; substantial variation was present within these categories such that measures of central tendency were not calculated. Similarly, among studies reporting HCV prevalence among IDUs in relation to 1-year intervals of duration of injection (<1 year, <2 years, and <3 years), considerable variability was observed. Notably, there were studies in each category that reported prevalence of 70 percent or higher among recent-onset drug injectors. These findings confirm previous

studies reporting high risk of acquiring HCV shortly after onset of injection; thus, HCV prevention programmes must emphasize methods to reach new injectors. Future research should (1) report data on time to infection in depth, (2) provide detailed information on study methodology, and (3) characterize the research setting with respect to underlying factors that affect injection practices and networks. This will permit synthesis of a greater number of studies and may lead to the identification of factors that impede HCV transmission. Hagan, H., Des Jarlais, D., Stern, R., Lelutiu-Weinberger, C., Scheinmann, R., Strauss, S., and Flom, P. HCV Synthesis Project: Preliminary Analyses of HCV Prevalence in Relation to Age and Duration of Injection. *Int. J. Drug Policy*, 18(5), pp. 341-351, 2007.

## **PREVENTION RESEARCH**

### Effects of a Nurse Visiting Program with African American Mothers and Infants on Age 9 Outcomes

This study examined the effect of prenatal and infancy home visits by nurses on mothers' fertility and children's functioning 7 years after the program ended at child age 2. A randomized, controlled trial in a public system of obstetric and pediatric care was conducted. A total of 743 primarily black women <29 weeks gestation, with previous live births and at least 2 socio-demographic risk characteristics (unmarried, <12 years of education, unemployed), were randomly assigned to receive nurse home visits or comparison services. Primary outcomes consisted of intervals between births of first and second children and number of children born per year; mothers' stability of relationships with partners and relationships with the biological father of the child; mothers' use of welfare, food stamps, and Medicaid; mothers' use of substances; mothers' arrests and incarcerations; and children's academic achievement, school conduct, and mental disorders. Secondary outcomes were the sequelae of subsequent pregnancies, women's employment, experience of domestic violence, and children's mortality. Nurse-visited women had longer intervals between births of first and second children, fewer cumulative subsequent births/year, and longer relationships with current partners. From birth through child age 9, nurse-visited women used welfare and food stamps for fewer months. Nurse-visited children born to mothers with low psychological resources, compared with control-group counterparts, had better grade-point averages and achievement test scores in math and reading in grades 1-3. Nurse-visited children, as a trend, were less likely to die from birth through age 9, an effect accounted for by deaths that were attributable to potentially preventable causes. By child age 9, the program reduced women's rates of subsequent births, increased the intervals between the births of first and second children, increased the stability of their relationships with partners, facilitated children's academic adjustment to elementary school, and seems to have reduced childhood mortality from preventable causes. Olds, D., Kitzman, H., Hanks, C., Cole, R., Anson, E., Sidora-Arcoleo, K. et al. Effects of Nurse Home Visiting on Maternal and Child Functioning: Age-9 Follow-up of a Randomized Trial. *Pediatrics*, 120(4), pp. e832-e845, 2007.

### An Acute Post-Sexual Assault Intervention to Prevent Drug Abuse

Sexual assault and rape routinely produce extreme distress and negative psychological reactions in victims. Further, past research suggests that victims are at increased risk of developing substance use or abuse post-rape. The post-rape forensic medical exam may itself exacerbate peritraumatic distress because it includes cues that may serve as reminders of the assault, thereby potentiating post-assault negative sequelae. To address these problems, a two-part video intervention was developed to take advantage of the existing sexual assault forensic exam infrastructure, and to specifically (a) minimize anxiety/discomfort during forensic examinations, thereby reducing risk of future emotional problems, and (b) prevent increased substance use and abuse following sexual assault. Updated findings with a sample of 268 sexual assault victims participating in the forensic medical exam and completing one or more follow-up assessments at: (1) less than 3 months post-assault; (2) 3 to 6 months post-assault; or (3) 6 months or longer post-assault indicated that the video was associated with significantly lower frequency of marijuana use at each time point, among women who reported use prior to the assault. Resnick, H.S., Acierno, R., Amstadter, A. B.,

Self-Brown, S., and Kilpatrick, D.G. An Acute Post-Sexual Assault Intervention to Prevent Drug Abuse: Updated Findings. *Addictive Behaviors*, 32, pp. 2032-2045, 2007.

### Randomized Controlled Evaluation of an Early Intervention to Prevent Post-Rape Psychopathology

A randomized between-group design was used to evaluate the efficacy of a video intervention to reduce post-traumatic stress disorder (PTSD) and other mental health problems, implemented prior to the forensic medical examination conducted within 72 h post-sexual assault. Participants were 140 female victims of sexual assault (68 video/72 non video) aged 15 years or older. Assessments were targeted for 6 weeks (Time 1) and 6 months (Time 2) post-assault. At Time 1, the intervention was associated with lower scores on measures of PTSD and depression among women with a prior rape history relative to scores among women with a prior rape history in the standard care condition. At Time 2, depression scores were also lower among those with a prior rape history who were in the video relative to the standard care condition. Small effects indicating higher PTSD and Beck Anxiety Inventory (BAI) scores among women without a prior rape history in the video condition were observed at Time 1. Accelerated longitudinal growth curve analysis indicated a video X prior rape history interaction for PTSD, yielding four patterns of symptom trajectory over time. Women with a prior rape history in the video condition generally maintained the lowest level of symptoms. Resnick, H., Acierno, R., Waldrop, A., King, L., King, D., Danielson, C., Ruggiero, K., and Kilpatrick, D. Randomized Controlled Evaluation of an Early Intervention to Prevent Post-Rape Psychopathology. *Behav. Res. Ther.*, 45(10), pp. 2432-2447, 2007.

### Adolescent Friendship Interactions and Deviant vs. Normative Developmental Pathways

Interpersonal dynamics within friendships were observed in a sample of 120 (60 male, 60 female) ethnically diverse 16- and 17-year-old adolescents characterized as “persistently antisocial”, “adolescent-onset”, and normative. Group definitions were based on antisocial behavior scores from a survey of antisocial behavior and substance use developed by Dishion and Kavanagh and administered at four points in time to adolescents starting at age 11-12. Persistently antisocial adolescents were defined as those who had above average scores compared to those within their gender group and had greater than the median antisocial score at all assessment points. “Adolescent-onset” youth comprised participants whose antisocial behaviors increased from below the median in earlier waves of the survey to above the median in later waves. The normative group included participants with the lowest sum antisocial behavior scores of the group who also had below median antisocial behavior scores during all waves. Dyadic mutuality, i.e., talk that is mutually responsive, reciprocal, and harmonious, and deviant talk, i.e., inappropriate talk and talk about violating community or societal rules, were coded from videotaped friendship interactions. Persistently antisocial adolescents demonstrated lower levels of dyadic mutuality compared with adolescent-onset and normative adolescents. Persistently antisocial and adolescent-onset adolescents spent more time in deviant talk than did normative adolescents. Across groups, girls were rated as more mutual and coded less in deviant talk than boys. Furthermore, friendship dyads that engaged in high levels of deviant talk and were mutual in their interactions reported the highest rates of antisocial behavior, Piehler, T., and Dishion, T. Interpersonal Dynamics within Adolescent Friendships: Dyadic Mutuality, Deviant Talk, and Patterns of Antisocial Behavior. *Child Dev.*, 78(5), pp. 1611-1624, 2007.

## **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

### Behavioral Incentives Improve Outpatient Treatment Participation/Retention for Pregnant Drug Abusers

Treating pregnant drug abusers poses unique challenges; compared with non-pregnant drug users they leave treatment more often and their attendance is often unreliable. This study examined the utility of providing 2 weeks of vouchers exchangeable for goods and services on an escalating schedule to motivate participation in a program comprised of seven days of residential and thirty days of outpatient treatment. Ninety-one pregnant women were assigned to either a standard treatment condition (ST) or a voucher reinforcement

condition (VR) in which vouchers were earned for treatment program attendance. Voucher values began at \$5.00 and increased by \$5.00 for each day the participant attended up to a maximum value of \$70.00 for 2 weeks. If a participant missed a single session they forfeited their voucher that day. Participant voucher value reset to \$5.00 if more than one session was missed. VR assignment did not impact early treatment dropout; one third of participants in both groups left treatment against medical advice (AMA). Among those who did not leave AMA, those assigned to VR attended more treatment days than those in ST. Additionally, those assigned to VR were more likely to attend treatment consistently (12-14 full days) as opposed to the typical pattern of attendance for ST (only 4 or 6 full days). When all participants were categorized as either consistent or inconsistent attenders, consistent early attendance predicted better attendance in the 30 days following the intervention. Within five days of the voucher treatment ending, no consistent early attenders dropped out of treatment. However, 25% of inconsistent treatment attenders dropped out during the five days post-intervention. These findings are significant for several reasons. First, although inpatient treatment participation was not differentially impacted by vouchers, the voucher program begun during the inpatient treatment period appeared to have an important effect on pregnant women making the transition to outpatient treatment. Additionally, critics contend that voucher effects do not last after the treatment ends but in this case the voucher effect was sustained post-treatment. More research is needed to determine what if any effect vouchers can have on pregnant women entering treatment to reduce dropout AMA rates. Svikis, D., Silverman K, Haug, N., Stitzer, M., Keyser-Marcus, L. Behavioral Strategies to Improve Treatment Participation and Retention by Pregnant Drug-dependent Women. *Substance Use Misuse*, 42(10), pp. 1527-1535, 2007.

#### Bupropion and Cognitive-Behavioral Therapy for Smoking Cessation in Women

Dr. Schmitz and colleagues at the University of Texas Health Science Center at Houston conducted this study to examine the independent and interactive effects of medication (bupropion 300 mg/day vs. placebo) and psychotherapy (cognitive-behavioral therapy [CBT] vs. supportive therapy [ST]) in women in a two level factorial design. In addition to testing the hypothesis that bupropion with CBT would be the most effective of all the treatments, medication compliance and its role in the efficacy of bupropion was examined. Participants were 154 women who smoked more than 10 cigarettes/day. Compliance with study medication was assessed using Medication Event Monitoring Systems (MEMS) over 7 weeks of treatment. Psychological interventions were delivered in 60-min weekly group sessions. Longitudinal analysis of abstinence outcomes from end of treatment (EOT) through 12 months after treatment revealed a significant interaction of medication and therapy. Higher abstinence rates at EOT and 3, 6, 9, and 12-month follow-ups were observed when bupropion was delivered concurrently with CBT (44%, 24%, 30%, 23%, 17%) rather than with ST (18%, 1%, 8%, 5%, 2%). The bupropion-CBT combination, however, was not clearly superior to placebo, regardless of therapy assignment. Higher rates of medication compliance were positively predictive of abstinence, and this effect was most evident in the placebo condition. Findings provide only modest support for CBT as the preferred type of intensive therapy in conjunction with bupropion in women. Schmitz, J.M., Stotts, A.L., Mooney, M.E., DeLaune, K.A., and Moeller, F.G. Bupropion and Cognitive-Behavioral Therapy for Smoking Cessation in Women. *Nicotine & Tobacco Research*, 9, pp. 699-709, 2007.

#### Incremental Validity of Anxiety Sensitivity in Terms of Motivation to Quit, Reasons for Quitting, and Barriers to Quitting Among Community-Recruited Daily Smokers

Dr. Zvolensky and colleagues at the University of Vermont conducted the present investigation to examine the relationships between anxiety sensitivity and motivation to quit smoking, barriers to smoking cessation, and reasons for quitting smoking among 329 adult daily smokers. As expected, after covarying for the theoretically relevant variables of negative affectivity, gender, Axis I psychopathology, nonclinical panic attack history, number of cigarettes smoked per day, and current levels of alcohol consumption, it was found that anxiety sensitivity was significantly incrementally related to level of motivation to quit smoking as well as current barriers to quitting smoking. Partially consistent with the hypotheses, after accounting



for the variance explained by other theoretically relevant variables, it was found that anxiety sensitivity was significantly associated with self-control reasons for quitting smoking (intrinsic factors) as well as immediate reinforcement and social influence reasons for quitting (extrinsic factors). These findings set the stage for additional research targeted at disentangling the specific mechanisms that underlie these documented associations between anxiety sensitivity and smoking, and should help guide the future development for specialized intervention programs for smokers with anxiety vulnerabilities. Zvolensky, M.J., Vujanovic, A.A., Bonn Miller, M.O., Bernstein, A., Yartz, A.R., Gregor, K.L., McLeish, A.C., Marshall, E.C., and Gibson, L.E. Incremental Validity of Anxiety Sensitivity in Terms of Motivation to Quit, Reasons for Quitting, and Barriers to Quitting Among Community-Recruited Daily Smokers. *Nicotine & Tobacco Research*, 9, Pp. 965-975, 2007.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

### Bupropion for Methamphetamine Dependence, Clinical Trial

Bupropion was tested for efficacy in increasing weeks of abstinence in methamphetamine-dependent patients, compared to placebo. This was a double-blind placebo-controlled study, with 12 weeks of treatment and a 30-day follow-up. Five outpatient substance abuse treatment clinics located west of the Mississippi participated in the study. One hundred and fifty-one treatment-seekers with DSM-IV diagnosis of methamphetamine dependence were consented and enrolled. Seventy-two participants were randomized to placebo and 79 to sustained-release bupropion 150 mg twice daily. Patients were asked to come to the clinic three times per week for assessments, urine drug screens, and 90-min group psychotherapy. The primary outcome was the change in proportion of participants having a methamphetamine-free week. Secondary outcomes included: urine for quantitative methamphetamine, self-report of methamphetamine use, subgroup analyses of balancing factors and comorbid conditions, addiction severity, craving, risk behaviors for HIV, and use of other substances. The generalized estimating equation regression analysis showed that, overall, the difference between bupropion and placebo groups in the probability of a non-use week over the 12-week treatment period was not statistically significant ( $p < 0.09$ ). Mixed model regression was used to allow adjustment for baseline factors in addition to those measured (site, gender, level of baseline use, and level of symptoms of depression). This subgroup analysis showed that bupropion had a significant effect compared to placebo, among male patients who had a lower level of methamphetamine use at baseline ( $p < 0.0001$ ). Comorbid depression and attention-deficit/hyperactivity disorder did not change the outcome. These data suggest that bupropion, in combination with behavioral group therapy, was effective for increasing the number of weeks of abstinence in participants with low-to-moderate methamphetamine dependence, mainly male patients, regardless of their comorbid condition. Elkashef, A.M., Rawson, R.A., Anderson, A. L., Li, S.H., Holmes, T., Smith, E. V., Chiang, N., Kahn, R., Vocci, F., Ling, W., Pearce, V.J., McCann, M., Campbell, J., Gorodetzky, C., Haning, W., Carlton, B., Mawhinney, J., and Weis, D. Bupropion for the Treatment of Methamphetamine Dependence. *Neuropsychopharmacology*, 33(5), pp. 1162-70, 2007.

### Buprenorphine and Norbuprenorphine in Hair of Pregnant Women and Their Infants after Controlled Buprenorphine Administration

Buprenorphine is under investigation as a pharmacotherapeutic agent for treating opioid dependence in pregnant women. The investigators hypothesized that there would be a relationship between the cumulative maternal dose of buprenorphine during pregnancy and the concentration of buprenorphine and norbuprenorphine in maternal and infant hair. This study examined buprenorphine and norbuprenorphine concentrations in hair obtained from 9 buprenorphine-maintained pregnant women and 4 of their infants. Specimens were analyzed by liquid chromatography-tandem mass spectrometry with limits of quantification of 3.0 pg/mg. All maternal hair specimens were washed with methylene chloride before analysis, and when sufficient amounts of maternal hair were available, specimens also were analyzed without washing. Infant hair specimens were not washed. Buprenorphine concentrations were significantly

greater in unwashed hair than washed hair ( $P = 0.031$ ). Norbuprenorphine concentrations were significantly greater than buprenorphine concentrations in both maternal ( $P = 0.0097$ ) and infant hair ( $P = 0.0033$ ). There were statistically significant associations between the cumulative maternal dose of buprenorphine administered and the concentrations of buprenorphine (washed,  $P < 0.0001$ ; unwashed,  $P = 0.0004$ ), norbuprenorphine (washed,  $P < 0.0001$ ; unwashed,  $P = 0.0005$ ), and buprenorphine plus norbuprenorphine (washed,  $P < 0.0001$ ; unwashed,  $P = 0.0005$ ) for both washed and unwashed maternal hair specimens. There was a significant positive association between concentrations of buprenorphine and norbuprenorphine in maternal hair (washed,  $P < 0.0001$ ; unwashed,  $P = 0.0003$ ), a trend for this association in infant hair ( $P = 0.08$ ), and an association between buprenorphine concentrations in maternal unwashed hair and infant hair ( $P = 0.0002$ ). The buprenorphine: norbuprenorphine ratio increased in distal segments. Buprenorphine treatment during gestation provides an opportunity for monitoring drug disposition in maternal and fetal tissues under controlled conditions. Goodwin, R.S., Wilkins, D.G., Averin, O., Choo, R.E., Schroeder, J.R., Jasinski, D.R. et al. Buprenorphine and Norbuprenorphine in Hair of Pregnant Women and Their Infants after Controlled Buprenorphine Administration. *Clin. Chem.*, 53(12), pp. 2136-43, 2007.

### Opioid Antagonism of Cannabinoid Effects: Differences between Marijuana Smokers and Nonmarijuana Smokers

The objective of this study was to test a lower, more opioid-selective dose of naltrexone (12 mg) in combination with THC. The influence of marijuana-use history and sex was also investigated. Naltrexone (0, 12 mg) was administered 30 min before oral THC (0-40 mg) or methadone (0-10 mg) capsules, and subjective effects, task performance, pupillary diameter, and cardiovascular parameters were assessed in marijuana smoking (Study 1;  $n=22$ ) and in nonmarijuana smoking (Study 2;  $n=21$ ) men and women. The results show that in marijuana smokers, low-dose naltrexone blunted the intoxicating effects of a low THC dose (20 mg), while increasing ratings of anxiety at a higher THC dose (40 mg). In nonmarijuana smokers, low-dose naltrexone shifted THC's effects in the opposite direction, enhancing the intoxicating effects of a low THC dose (2.5 mg) and decreasing anxiety ratings following a high dose of THC (10 mg). There were no sex differences in these interactions, although among nonmarijuana smokers, men were more sensitive to the effects of THC alone than women. To conclude, a low, opioid-selective dose of naltrexone blunted THC intoxication in marijuana smokers, while in nonmarijuana smokers, naltrexone enhanced THC intoxication. These data demonstrate that the interaction between opioid antagonists and cannabinoid agonists varies as a function of marijuana use history. Haney, M. Opioid Antagonism of Cannabinoid Effects: Differences between Marijuana Smokers and Nonmarijuana Smokers. *Neuropsychopharmacology*, 32, pp. 1391-1403, 2007.

### Gender Differences with High-dose Naltrexone in the Patients with Co-occurring Cocaine and Alcohol Dependence

This is a randomized, double-blind, placebo-controlled clinical trial that evaluated the efficacy of a higher-than-typical daily dose of naltrexone (150 mg/day), taken for 12 weeks, in 164 patients ( $n = 116$  men and  $n = 48$  women) with co-occurring cocaine and alcohol dependence. Patients were stratified by gender and then randomly assigned to either naltrexone or placebo, and to either cognitive-behavioral therapy or a type of medical management. The two primary outcomes were cocaine use and alcohol use. Significant Gender x Medication interactions were found for cocaine use via urine drug screens (three way, with time) and self-reports (two way) for drug severity (two way) and alcohol use (two way). The type of psychosocial treatment did not affect outcomes. Thus, 150 mg/day naltrexone added to a psychosocial treatment resulted in reductions in cocaine and alcohol use and drug severity in men, compared to higher rates of cocaine and alcohol use and drug severity in women. Pettinati, H., Kampman, K., Lynch, K., Suh, J., Dackis, C., Oslin, D. et al. Gender Differences with High-dose Naltrexone in the Patients with Co-occurring Cocaine and Alcohol Dependence. *J. Subst. Abuse Treat*, 34, pp. 378-390, 2008.

## Nicotine Replacement and Behavioral Therapy for Smoking Cessation in Pregnancy

This study examines whether adding nicotine replacement therapy (NRT) to cognitive-behavioral therapy (CBT) for pregnant smokers increases rates of smoking cessation. An open-label randomized trial (Baby Steps, n=181) of CBT-only versus CBT+NRT (choice of patch, gum, or lozenge; 1:2 randomization) was used. Data were collected from 2003 through 2005; analyses were conducted in 2006 and 2007. Outcomes were biochemically validated self-reported smoking status at 7 weeks post-randomization, 38 weeks gestation, and 3 months postpartum. Women in the CBT+NRT arm were almost three times more likely than women in the CBT-only arm to have biochemically validated cessation at both pregnancy time points (after 7 weeks: 24% vs 8%, p=0.02; at 38 weeks gestation: 18% vs 7%, p=0.04), but not at 3 months postpartum (20% vs 14%, p=0.55). Recruitment was suspended early by an Independent Data and Safety Monitoring Board when an interim analysis found a higher rate of negative birth outcomes in the CBT+NRT arm than in the CBT-only arm. In the final analysis, the difference between the arms in rate of negative birth outcomes was 0.09 (p=0.26), when adjusted for previous history of preterm birth. The addition of NRT to CBT promoted smoking cessation in pregnant women. This effect did not persist postpartum. More data are needed to determine safety parameters and to confirm the efficacy of NRT use during pregnancy. Pollak, K.I., Oncken, C.A., Lipkus, I.M., Lyna, P., Swamy, G.K., Pletsch, P.K. et al. Nicotine Replacement and Behavioral Therapy for Smoking Cessation in Pregnancy. *Am. J. Prev. Med.*, 33, pp. 297-305, 2007.

## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE & CO-OCCURRING INFECTIONS (HIV/AIDS, HCV)**

### **HIV/AIDS-RELATED**

#### Factors Affecting Reproductive Hormones in HIV-infected, Substance-using Middle-aged Women

The objective of this study was to determine whether reproductive hormone levels are affected by human immunodeficiency virus (HIV) and drug use. HIV-infected and uninfected women (N=429), median age 45, were interviewed on menstrual frequency, demographic and psychosocial characteristics, and drug use behaviors. Serum was obtained on cycle days 1 to 5 in women reporting regular menses. Premenopausal, early menopausal, and late menopausal transition and postmenopausal stages were assigned based on menstrual history. Serum was assayed for follicle-stimulating hormone (FSH), estradiol (E2), luteinizing hormone (LH), prolactin, thyroid-stimulating hormone, and inhibin B. Body mass index, HIV serostatus, and CD4+ counts were measured. Factors associated with hormone concentrations were assessed using uni- and multivariable analyses. Hormone concentrations were compared within menstrual status categories using nonparametric comparisons of means. In this cross-sectional analysis, LH and FSH increased, and E2 and inhibin B were significantly lower in women of older age and more advanced menopausal status. Increased body mass index was strongly associated with decreased LH. Opiate use was significantly associated with lower inhibin B and E2 and increased prolactin. Poorer self-rated health was statistically significantly associated with lower LH and FSH, but increased education was associated with higher LH and FSH. Among HIV-seropositive women, opiate users had detectably lower FSH and LH than nonusers, and use of highly active antiretroviral therapy was significantly related to higher LH, FSH, and E2, whereas cocaine use was associated with lower E2. Authors conclude that age and menopausal status are strongly related to reproductive hormones. Body mass index and use of opiates, cocaine, and highly active antiretroviral therapy as well as educational attainment and perceived health can significantly modify reproductive hormones during the menopausal transition and need to be considered when interpreting hormone levels in middle-aged women. Santoro, N., Lo, Y., Moskaleva, G., Arnsten, J.H., Floris-Moore, M., Howard, A.A., Adel, G., Zeitlian, G., Schoenbaum, E.E. *Menopause*, 14(5), pp. 859-865, 2007.

## **HEPATITIS C OR DUAL INFECTIONS OF HIV AND HCV**

### Factors Affecting Serum Concentrations of Hepatitis C Virus (HCV) RNA in HCV genotype 1-Infected Patients with Chronic Hepatitis

The serum concentration of hepatitis C virus (HCV) RNA is usually stable (4 to 8 log(10) IU/ml) in untreated patients with chronic hepatitis C. While this baseline HCV RNA concentration ([HCV RNA](BL)) is predictive of a sustained virologic response to treatment, its determinants are only partially identified. The authors therefore analyzed the baseline characteristics of 2,472 HCV genotype 1-infected patients to identify correlations with gender, age, race, weight, body mass index (BMI), HCV acquisition mode, HCV subtype, alanine aminotransferase concentration, or histopathologic changes in the liver. After separation of the data according to four [HCV RNA](BL) groups (< or =5.0, >5.0 to 5.6, >5.6 to 5.9, and >5.9 log(10) IU/ml), the authors determined that increasing [HCV RNA](BL) correlated ( $P < 0.05$ ) with increasing proportions of patients who were male, >40 years of age, or heavier (a weight of >85 kg or a BMI of >27 kg/m<sup>2</sup>). Histologic activity index (HAI) data were available for 1,304 of these patients: increasing [HCV RNA](BL) correlated with higher fibrosis and necrosis-inflammation scores. As a continuous variable, [HCV RNA](BL) correlated with age, gender, weight (continuous or < or =85 versus >85 kg), BMI (continuous or < or =27 versus >27 kg/m<sup>2</sup>), subtype, fibrosis score, and necrosis-inflammation score; however, multiple-regression analysis yielded  $P$  values of <0.1 only for age, gender, BMI (< or =27 versus >27 kg/m<sup>2</sup>), and fibrosis score. While these findings are suggestive of a role for these factors in maintenance of the pretreatment state of HCV infection, the multiple-regression model accounted for only < or =4.6% of the [HCV RNA](BL) differences between individuals ( $R^2 = 0.046$  for 1,304 patients with HAI scores; 0.043 for all 2,472 patients). Ticehurst, J., Hamzeh, F., Thomas, D. J. Clin. Microbiol. 45, pp. 2426-2433, 2007.

### Co-morbid Medical and Psychiatric Illness and Substance Abuse in HCV-infected and Uninfected Veterans

Comorbidities may affect the decision to treat chronic hepatitis C virus (HCV) infection. The authors undertook this study to determine the prevalence of these conditions in HCV-infected persons compared with HCV-uninfected controls. Demographic and comorbidity data were retrieved for HCV-infected and -uninfected subjects from the VA National Patient Care Database using ICD-9 codes. Logistic regression was used to determine the odds of comorbid conditions in the HCV-infected subjects. HCV-uninfected controls were identified matched on age, race/ethnicity and sex. Authors identified 126,926 HCV-infected subjects and 126,926 controls. The HCV-infected subjects had a higher prevalence of diabetes, anemia, hypertension, chronic obstructive pulmonary disease (COPD)/asthma, cirrhosis, hepatitis B and cancer, but had a lower prevalence of coronary artery disease and stroke. The prevalence of all psychiatric comorbidities and substance abuse was higher in the HCV-infected subjects. In the HCV-infected persons, the odds of being diagnosed with congestive heart failure, diabetes, anemia, hypertension, OPD/asthma, cirrhosis, hepatitis B and cancer were higher, but lower for coronary artery disease and stroke. After adjusting for alcohol and drug abuse and dependence, the odds of psychiatric illness were not higher in the HCV-infected persons. The prevalence and patterns of comorbidities in HCV-infected veterans are different from those in HCV-uninfected controls. The association between HCV and psychiatric diagnoses is at least partly attributable to alcohol and drug abuse and dependence. These factors should be taken into account when evaluating patients for treatment and designing new intervention strategies. Butt, A., Khan, U., McGinnis, K. Et al. J. Viral Hepat.14, pp. 890-896, 2007.

### Biochemical and Virologic Parameters in Patients Co-infected with Hepatitis C and HIV versus Patients with Hepatitis C Mono-infection

Previous studies of patients with hepatitis C virus (HCV) infection looking at the effect of human immunodeficiency virus (HIV) co-infection on biochemical parameters and HCV RNA level have shown conflicting results. Accurate characterization of the effect of HIV is important for evaluation and treatment

of HCV in coinfecting persons. Authors studied 315 HCV mono-infected and 75 HCV-HIV co-infected subjects to determine the effect of HIV on biochemical parameters and HCV RNA and to determine the predictors of elevated serum alanine aminotransferase (ALT) levels and HCV RNA levels. The co-infected subjects were more likely to be African-American (55% vs 26%,  $P < 0.0005$ ), have used injection drugs (68% vs 60%,  $P = 0.02$ ), have detectable HCV RNA (84% vs 70.5%,  $P = 0.018$ ), have HCV RNA levels  $> 6 \log_{10}$  IU/mL (60% vs 38%,  $P = 0.001$ ), and have lower mean serum ALT levels (50.4 IU/mL vs 73.7 IU/mL,  $P = 0.006$ ). In multivariable analyses, the following factors predicted an ALT level  $> 50$  IU/mL:  $\log_{10}$  HCV RNA (OR, 1.15; 95% CI, 1.00 to 1.32); HIV co-infection (OR, 0.48; 95% CI, 0.25-0.89); and having ever been treated for HCV (OR, 1.92; 95% CI, 1.16 to 3.18). The only significant predictor of HCV RNA level  $> 6 \log_{10}$  IU/mL was HIV co-infection (OR, 2.75; 95% CI, 1.46-5.15). Significant predictors of having a detectable HCV RNA level were female sex (OR, 3.81; 95% CI, 1.18-12.25); HIV co-infection (2.45; 95% CI, 1.14-5.26); and ever being treated for HCV (OR, 1.96; 95% CI, 1.10 to 3.48). HCV-HIV co-infected persons have higher HCV RNA levels but lower serum ALT levels than HCV mono-infected patients. Criteria for performing liver biopsy and treating HCV infection in co-infected patients may need to be revisited. Butt, A., Tsevat, J., Ahmad, J., et al., *Am. J. Med. Sci.* 333, pp. 271-275, 2007.

## **SERVICES RESEARCH**

### Violence and HIV Risk among Incarcerated Women

The association between history of violence and risk for HIV infection among incarcerated women was examined. Specifically, physical violence and rape were considered as they relate to unprotected sex with male primary and non primary (male or female) sexual partners among a sample of HIV negative female inmates ( $n = 1,588$ ) housed in Connecticut's sole correctional facility for women between November 1994 and October 1996. A supplement to the mandatory Connecticut Department of Correction Inmate Medical Screening/Health History was used to collect information on each woman's background, history of violence, and unprotected sex practices. Multivariate logistic regression was used to determine the associations between violence and unprotected sex by partner type. Experiencing any violence was found to be significantly associated with increased odds of unprotected sex with one's primary partner, even after controlling for race, history of sex work, drug use, employment status, and having other non primary partners. Of particular importance was having a history of physical violence. History of violence was not significantly associated with unprotected sex with non primary partners. These findings demonstrate the considerable vulnerability of incarcerated women to violence and suggest that this history is associated with increased unprotected sex practices, especially with male primary partners. HIV prevention interventions among women should take experiences of violence into account. Conversely, violence prevention and interventions aimed at coping with violence can be a part of the HIV prevention agenda for incarcerated women. Future longitudinal research can confirm the relationships of violence to HIV risk in women. Ravi, A., Blankenship, K., and Altice, F. *The Association between History of Violence and HIV Risk: A Cross-Sectional Study of HIV-Negative Incarcerated Women in Connecticut.* *Womens Health Issues*, 17(4), pp. 210-216, 2007.

### Gender Differences in Housing Patterns and Homelessness

Homeless individuals experience high rates of morbidity and mortality, yet many homeless studies include small percentages of female participants. The authors therefore sought to determine correlates of homelessness separately for men and women in a sample of individuals visiting free food programs. Between August 2003 and April 2004, 324 individuals were recruited from San Francisco free food programs and interviewed regarding housing, sociodemographics, health, drug use, sex trade, and incarceration. Over one-half of women and almost three-fourths of men reported homelessness in the prior year. Among women, white race, younger age, not living with minor children, engaging in sex trade and recent incarceration were strongly associated with homelessness; however, only incarceration maintained the strong association in adjusted analysis (OR = 7.16, CI = 3.83-13.4). Among men, heavy alcohol use,

drug use, years spent living in San Francisco and monthly income were strongly associated with homelessness; however, only years living in San Francisco (OR = 0.28, CI = 0.19-0.42) and monthly income maintained strong association in adjusted analysis (OR = 0.27, CI = 0.13-0.57). Housing patterns and the strongest correlates of homelessness among individuals visiting free food programs differ by sex. These results suggest the need to characterize homelessness and develop effective homeless interventions separately for men and women. Riley, E., Weiser, S., Sorensen, J., Dilworth, S., Cohen, J., and Neilands, T. Housing Patterns and Correlates of Homelessness Differ by Gender Among Individuals Using San Francisco Free Food Programs. *J. Urban Health*, 84(3), pp. 415-422, 2007.

### Cultural Competence among Healthcare Providers

Mandates for culturally competent substance abuse and mental health services call for behavioral health providers to recognize and engage cultural issues. These efforts to incorporate culture typically focus on client culture, but provider views of culture can also influence the provision of services. Analysis of 42 semi-structured interviews with behavioral health providers suggests that culture is considered by many to be an obstacle to help seeking and treatment of substance-abusing youth. Although some providers do not highlight cultural issues, others conceptualize culture in terms of (a) generalized Hispanic cultural attributes, (b) male-dominant gender roles, and (c) the culture of poverty. Recommendations for provider training on cultural issues focus on ways they might critically consider their ideas about culture. Quintero, G., Lillioth, E., and Willging, C. Substance Abuse Treatment Provider Views of "Culture": Implications for Behavioral Health Care in Rural Settings. *Qual. Health Res.*, 17(9), pp. 1256-1267, 2007.

### Violence against Homeless Women

Research on violence against homeless women has focused mainly on individual rather than community-level risk factors. Using an ecological conceptual framework, the researchers estimated the independent association of community characteristics with sexual and physical assault in a probability sample of 974 homeless women. Participants were interviewed at 66 assistance programs in Los Angeles County, California in 1997. Individual responses were linked to community-level data from land use files and the U.S. Census by the facility ZIP codes. Multivariate logistic regression analysis showed that women using service providers in closer proximity to Skid Row had higher odds of physical assault (OR=1.48; 95% CI=1.03, 2.14). A number of individual characteristics were also associated with violent victimization. To reduce violence against homeless women, ensuring the safety of locations for shelters and other assistance programs should be a planning priority for local housing authorities. Heslin, K., Robinson, P., Baker, R., and Gelberg, L. Community Characteristics and Violence against Homeless Women in Los Angeles County. *J. Health Care Poor Underserved*, 18(1), pp. 203-218, 2007.

### Gender-specific Substance Abuse Treatment for Women Promotes Continuity of Care

Research has stressed the value of providing specialized services to women and suggests the importance of treatment duration. This quasiexperimental retrospective study reports on the continuity of care for women with children who were admitted to long-term residential substance abuse treatment. Women were admitted to 7 agencies offering specialized, women's only treatment (SP, n = 747) or to 9 agencies that provided standard mixed-gender treatment (ST, n = 823). Client and treatment data were gathered from administrative sources. Women in SP programs (37%) were more likely than those in ST programs (14%) to continue care. Multivariate analyses revealed that SP clients who completed treatment with longer stays were most likely to continue care. The findings show that specialized treatment for women promotes continuing care and demonstrate the importance of treatment completion. Claus, R.E., Kissin, W., Krupski, A., Campbell, K., and Stark, K. Does Gender-Specific Substance Abuse Treatment for Woman Promote Continuity of Care. *J. Subst. Abuse Treat.*, 32, pp. 29-39, 2007.

### Children Are Important Sources of Social Support for Women in Addiction Treatment

The authors examined the status of children and the types of support available from children as reported by women in substance abuse treatment. Their findings indicate that children are viewed as sources of social support to women in addiction treatment. Children were viewed as providing as much sobriety support to respondents as that provided by adult network members. In addition, both children living with the respondent and children in the care of others were viewed as providers of specific types of social support. These study findings indicate that treatment providers need to be aware of the extent to which women clients may rely on support from children. Focusing only on adult relationships misses the fact that children may be a strong source of support for women in treatment, particularly for women in residential treatment, where the need for support may be greater. Tracy, E., and Martin, T. Children's Roles in The Social Networks of Women in Substance Abuse Treatment. *J. Subst. Abuse Treat.*, 32(1), pp. 81-88, 2007.

### Older Women Have Better Long-Term Addiction Treatment Outcomes than Older Men

This study examined participants at seven-year follow-up to assess long-term outcomes of older women (n = 25) and men (n = 59) ages 55 and over in an outpatient addiction program. It measured demographic characteristics, alcohol and drug use, psychiatric symptoms, Addiction Severity Index, treatment length, and outcomes. At seven years, 76.0% of women reported abstinence in the prior 30 days versus 54.2% of men (p = 0.05). Logistic regression analysis revealed that longer treatment stay predicted abstinence. Findings indicate that older women have better long-term addiction outcome than older men, but treatment length is more significant than gender in predicting outcome. Satre, D., Blow, F., Chi, F., and Weisner, C. Gender Differences in Seven-year Alcohol and Drug Treatment Outcomes among Older Adults. *Am. J. Addict.*, 16(3), pp. 216-221, 2007.

### Measuring Offender Attributes and Engagement in Treatment Using the Client Evaluation of Self and Treatment

Monitoring drug abuse treatment delivery and progress requires the use of reliable and valid instruments to measure client motivation, psychosocial and cognitive functioning, and other treatment process dynamics. As part of the Criminal Justice Drug Abuse Treatment Studies (CJDATS) protocol to examine client performance indicators for corrections-based treatment populations, this study examined psychometric properties of the 108-item TCU Criminal Justice Client Evaluation of Self and Treatment (CJ CEST), which is composed of 15 scales across 3 major domains. Treatment Motivation includes scales on desire for help; treatment readiness; treatment needs; and pressures for treatment. Psychosocial Functioning includes scales on depression; anxiety; self-esteem; decision-making; hostility; and risk-taking. Treatment Engagement includes scales on treatment participation; treatment satisfaction; counseling rapport; peer support; and social support. The sample included 3,266 offenders from 26 corrections-based treatment programs located in 6 states. Overall, the client assessment demonstrated good reliabilities at individual and program levels, and in test-retest administrations. Additionally, evidence for construct validity was favorable, based on confirmatory factor analyses. All but 4 scales had conventionally acceptable fit indices; the remaining 4 scales (desire for help; treatment readiness; decision making; risk taking) had acceptable GFIs, but other indices indicated possible multidimensionality. Multilevel analyses were used to examine program level variation, after controlling for client-level attributes (e.g., age, race, time in treatment). Over 20% of treatment readiness and counseling rapport was at the program level, but only 5-7% of offender anxiety and hostility. Differences were also found between male-only and female-only programs (all but 3 programs). Women were more motivated and involved in their treatment, and had stronger social support systems. Finally, bivariate correlations were examined between CJ CEST scales and criminal thinking scales (using the CTU Criminal Thinking Scales), after removing program differences. Less criminal thinking was found with higher overall motivation, psychosocial functioning, and engagement. In conclusion, the CJ CEST is a brief yet comprehensive instrument that effectively and efficiently measures client needs and functioning at intake. It also is appropriate for use during treatment to

monitor client progress over time. Garner, B.R., Garner, K.K., Flynn, M.P., Morey, J.T., and Simpson, D.D. Measuring Offender Attributes and Engagement in Treatment Using the Client Evaluation of Self and Treatment. *Criminal Justice & Behavior*, 34(9), pp. 1113-1130, 2007.

### Self-rated Health and its Determinants among Adults in Syria: A Model from the Middle East

Self-rated health (SRH) has been widely used to research health inequalities in developed western societies, but few such studies are available in developing countries. Similar to many Arab societies, little research has been conducted in Syria on the health status of its citizens, particularly in regards to SRH. This Study aims to investigate and compare determinants of SRH in adult men and women in Aleppo, Syria. The authors performed a cross-sectional survey of adults 18 to 65 years old residing in Aleppo, Syria (2,500,000 inhabitants) in 2004. The study involved 2038 household representatives (45.2% men, age range 18-65 years, response rate 86%). SRH was categorized as excellent, normal, and poor. Odds ratios for poor and normal SRH, compared to excellent, were calculated separately for men and women using logistic regression. It was found that women were more likely than men to describe their health as poor. Men and women were more likely to report poor SRH if they were older, reported two or more chronic health problems, or had high self perceived functional disability. Important gender-specific determinants of poor SRH included being married, low socioeconomic status, and not having social support for women, and smoking with low physical activity for men. The authors conclude that women were more likely than men to describe their health as poor. The link with age and pre-existing chronic conditions seems universal and likely reflects natural aging process. Determinants of SRH differed between men and women, possibly highlighting underlying cultural norms and gender roles in the society. Understanding the local context of SRH and its determinants within the prevailing culture will be important to tailor intervention programs aimed at improving health of the Syrian and similar Arab societies. Asfar, T., Ahmad, B., Rastam, S., Mulloli, T., Ward, K., and Maziak, W. Self-Rated Health and its Determinants among Adults in Syria: A Model from the Middle East. *MC Public Health*, 7, pp. 177-186, 2007.

### Measuring Offender Progress in Treatment Using the Client Assessment Inventory

The accurate and reliable assessment of client psychological and cognitive change during correctional substance abuse treatment has gained increasing importance during the past decade as criminal justice systems seek to evaluate and understand those treatment elements associated with long-term change. The 103-item Client Assessment Inventory (CAI) is a self-report instrument for measuring client change during treatment, using 14 subscales across four cognitive and behavioral domains. The Developmental dimension includes subscales on maturity; responsibility; and values. The Socialization dimension includes subscales on drug/criminal lifestyle; maintaining images; work attitude; and social skills. The Psychological dimension includes subscales on cognitive skills; emotional skills; and self-esteem/self-efficacy. The program participation dimension includes subscales on philosophy/understands program rules; engagement; attachment/investment; and role model. The reliability and internal consistency of the CAI, as adapted for use in criminal justice settings, were examined with data gathered from 1,170 offenders. The research addressed the utility of the CAI for different subpopulations of offenders (e.g., race/ethnicity, gender) across a variety of correctional treatment settings. Total CIA demonstrated high reliability ( $\alpha = .96$ ). Subscale alphas ranged from .42 to .90; with work attitudes and maintaining image demonstrating low unidimensionality ( $\alpha$ s = .42 and .53). Female clients were significantly higher on 9 of 14 subscales, after controlling for ethnicity, treatment program, and treatment retention. A sub-sample ( $n=165$ ) were retested after 1 week. Total CAI test-retest reliability was  $\text{Kappa} = .68$ ; subscale  $\text{Kappa}$ 's ranged from .31 to .54. Validity of the instrument was evaluated using time in treatment at CAI administration, which ranged from 2 weeks to 15 mos. Longer time in treatment was associated with significantly higher scores on 13 of 14 scales. Overall, the data support the use of the CAI as a consistent, reliable, and easily administered instrument for measuring client performance and progress in treatment in both therapeutic community (TC) and non-TC correctional treatment settings. Sacks, J.Y., McKendrick,



K., and Kressel, D. Measuring Offender Progress in Treatment Using The Client Assessment Inventory. *Criminal Justice and Behavior*, 64(9), pp. 1131-1142, 2007.

#### Gender Differences in Treatment Engagement among a Sample of Incarcerated Substance Abusers

This article examines gender differences in treatment engagement, psychosocial variables, and criminal thinking among a sample of male and female substance abusers (N = 2,774) enrolled in 20 prison-based treatment programs in five different states as part of the National Institute on Drug Abuse-funded Criminal Justice Drug Abuse Treatment Studies cooperative agreement. Results indicate that inmates in female treatment programs report more psychosocial dysfunction, less criminal thinking, and higher engagement than in male facilities, and there is a more negative relationship between psychosocial variables and treatment engagement (compared to male programs). Only one subscale of criminal thinking had a significant gender interaction, with males having a significantly stronger relationship between cold-heartedness and low treatment engagement. Implications for treatment interventions with a gender-specific focus are discussed. Staton-Tindall, M., Garner, B.R., Morey, J.S., Leukefeld, C., Krietemeyer, J., Saum, C.A., and Oser, C.B. Gender Differences in Treatment Engagement among a Sample of Incarcerated Substance Abusers. *Criminal Justice and Behavior*, 34(9), pp. 1143-1156, 2007.

#### An Assessment of Criminal Thinking among Incarcerated Youths in Three States

The Texas Christian University Criminal Thinking Scales (CTS) instrument has been shown to predict outcomes for institutionalized adult offenders. This article examines responses among male (n = 151) and female (n = 52) incarcerated adolescents, and they were compared to norms for incarcerated adult offenders. The results indicated that the adolescent sample had higher scores on four scales (Entitlement, Justification, Personal Irresponsibility, and Power of Orientation) but not on Criminal Rationalization. Scores did not differ by gender or ethnicity of respondents. The results provide convergent validity indicating that the scores for adolescents were correlated with prior history of criminal behavior, substance use, family dysfunction, and Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition diagnoses of conduct disorder and oppositional defiant disorder. Thus, the CTS may provide useful diagnostic information to help identify youth with a constellation of problem behaviors that predict poor outcomes following incarceration. It also may prove helpful in accounting for individual variations in response to treatment for incarcerated adolescents who receive treatment during reentry back into the community. Dembo, R., Turner, C. W., and Jainchill, N. An Assessment of Criminal Thinking among Incarcerated Youths in Three States. *Criminal Justice and Behavior*, 34(9), pp. 1157-1167, 2007.

#### Application of Gelberg-Andersen Behavioral Model

The Gelberg-Andersen Behavioral Model for Vulnerable Populations was applied to predict health services utilization (HSU) in 875 homeless US women. Structural models assessed the impact of predisposing (demographics, psychological distress, alcohol/drug problems, and homelessness severity), enabling (health insurance, source of care, barriers) and need (illness) variables on HSU (preventive care, outpatient visits, and hospitalizations). Homelessness severity predicted illness, barriers and less insurance. Distress predicted more barriers, illness and less outpatient HSU. Drug problems predicted hospitalizations. Barriers predicted more illness and less outpatient HSU. Health and homelessness indicators were worse for White women. Better housing, access to care and insurance would encourage appropriate HSU. Stein, J., Andersen, R., and Gelberg, L. Applying the Gelberg-Andersen Behavioral Model for Vulnerable Populations to Health Services Utilization in Homeless Women. *J. Health Psychol.*, 12(5), pp. 791-804, 2007.

## **CLINICAL TRIALS NETWORK RESEARCH**

### Treatment Programs in the National Drug Abuse Treatment Clinical Trials Network

Drug abuse treatment programs and university-based research centers collaborate to test emerging therapies for alcohol and drug disorders in the National Drug Abuse Treatment Clinical Trials Network (CTN). Programs participating in the CTN completed Organizational Surveys (n=106 of 112; 95% response rate) and Treatment Unit Surveys (n=348 of 384; 91% response rate) to describe the levels of care, ancillary services, patient demographics, patient drug use and co-occurring conditions. Analyses describe the corporations participating in the CTN and provide an exploratory assessment of variation in treatment philosophies. A diversity of treatment centers participate in the CTN; not for profit organizations with a primary mission of treating alcohol and drug disorders dominate. Compared to National Survey of Substance Abuse Treatment Services (N-SSATS), programs located in medical settings are over-represented and centers that are mental health clinics are under-represented. Outpatient, methadone, long-term residential and inpatient treatment units differed on patients served and services provided. Larger programs with higher counselor caseloads in residential settings reported more social model characteristics. Programs with higher social model scores were more likely to offer self-help meetings, vocational services and specialized services for women. Conversely, programs with accreditation had less social model influence. The CTN is an ambitious effort to engage community-based treatment organizations into research and more fully integrate research and practice. McCarty, D., Fuller, B., Kaskutas, L.A., Wendt, W.W., Nunes, E.V., Miller, M., Forman, R., Magruder, K.M., Arfken, C., Copersino, M., Floyd, A., Sindelar, J., and Edmundson, E. Treatment programs in the National Drug Abuse Treatment Clinical Trials Network. *Drug Alcohol Depend.* 92(1-3), pp. 200-207, 2008

## **INTERNATIONAL RESEARCH**

### **PUBLICATIONS BY FORMER NIDA INVEST DRUG ABUSE RESEARCH FELLOWS**

#### Gender Differences in the Relationship between Alcohol and Violent Injury: An Analysis of Cross-national Emergency Department Data

INVEST Fellow: Guilherme Borges, Mexico, 1997-1998

The objectives of the present study were twofold: (1) to determine whether gender differences exist in the roles of drinking in the event (i.e., self-reported drinking before the injury and estimated blood alcohol concentration [BAC] captured after injury) and drinking pattern (i.e., heavy episodic drinking) in explaining violent versus nonviolent injuries and (2) to assess whether these gender differences vary by country. Emergency department data were analyzed from 30 hospitals in 15 countries, as part of the Emergency Room Collaborative Alcohol Analysis Project and the World Health Organization Collaborative Study of Alcohol and Injuries. Interaction effects between gender and alcohol were tested in the prediction of violent versus nonviolent injury for each country. The bivariate analyses revealed significantly larger effects of drinking-in-the-event variables for men than for women in three countries (i.e., 6 hours before the injury in Argentina and having a positive BAC in Belarus and Spain). In the multivariate analyses, restricted to countries with sufficient sample sizes (i.e., Mexico, South Africa, and the United States), no significant gender differences were found between the drinking-in-the-event variables and violent injury. In the bivariate and multivariate analyses, a significant interaction effect between gender and heavy episodic drinking was found in the United States, indicating that heavy episodic drinking predicted violent injury for women but not for men. Although the results are preliminary, treatment and prevention programs may need to target both genders equally or perhaps even focus more on heavy-drinking women, particularly in the United States. Wells, S., Thompson, J.M., Cherpitel, C., Macdonald, S., Marais, S., and Borges, G. *J. Stud. Alcohol Drugs*, 68(6), pp. 824-833, 2007.

### Age and Gender Effects on Olanzapine and Risperidone Plasma Concentrations in Children and Adolescents

INVEST Fellow: Gerald Zernig, Austria, 1993-1994

Risperidone and olanzapine are second-generation antipsychotics that are increasingly used in child and adolescent psychiatry. So far, little is known about plasma concentrations and concentration-to-dose (C/D) ratios of these agents in children and adolescents compared to adults. This study investigated whether age and gender influence risperidone and olanzapine plasma concentration by determining risperidone and olanzapine plasma levels by tandem mass spectrometry in 162 Caucasian patients (98 risperidone and 64 olanzapine). For risperidone and 9-hydroxyrisperidone, the C(total)/D ratio was almost identical in both age groups (10-18 and 19-45 years, respectively). In the younger age group, females exhibited significantly higher total plasma levels than males while receiving similar doses of risperidone. For olanzapine, in adolescents significantly higher C/D ratios were detected by an average of 43% (after adjustment for weight: 34%) compared to adults. This study demonstrates an age effect for olanzapine but not for risperidone resulting in higher olanzapine plasma levels in younger patients. For risperidone, the authors found a gender effect as female adolescent patients had significantly higher risperidone plasma concentrations than male adolescent patients. Future prospective studies are necessary to clarify whether the prescribed dosage should be different in young and older patients. Aichhorn, W., Marksteiner, J., Walch, T., Zernig, G., Hinterhuber, H., Stuppaeck, C., and Kemmler, G. J. *Child Adolesc. Psychopharmacol.* 17(5), pp. 665-674, 2007.

### Study on the Association between Vaginal Douching and Sexually Transmitted Diseases among Female Sex Workers in a County of Yunnan Province

INVEST Fellow: Lan Zhang, China, 2004-2005

The objective of the present study was to explore the epidemic characteristics of vaginal douching, human immunodeficiency virus (HIV) and other sexually transmitted diseases(STD) among female sex workers (FSWs) in Yunnan province. FSWs were recruited to be investigated on their demographic data, drug abuse and sexual behavior, HIV/AIDS knowledge and procreation health status. Venous blood were collected to test for HIV, herpes simplex virus 2 (HSV-2) and syphilis while urine specimen was for morphine, cervical secretion for Gonorrhoea and Chlamydia trachomatis, and vaginal secretion for Trichomonas. A total number of 833 blood specimen were collected, in which 84 specimen were confirmed to be HIV positive with a prevalence rate of 10.1%. The prevalence rates of syphilis and HSV-2 were 8.2% and 68.4% respectively. 832 vaginal and cervical secretion specimens were collected with the prevalence rates of Gonorrhoea, Chlamydia trachomatis and Trichomonas were 11.5%, 28.2% and 11.9% respectively. In multivariate logistic analysis, the factors associated with vaginal douching were: being Han nationality, locations of sex work at middle/high level, ever heard of HIV/AIDS, emerged hypogastric pain last year, the number of sex work location  $\geq 4$ . Vaginal douching was shown a risk factor for HIV and some STD. Wang, H.B., Wang, N., Ma, J.G., Wang, G.X., Chang, D.F., Ding, G.W., Xu, J.J., Zhang, G.L., Dong, R.L., Zhang, L., Wu, Z.L., and Zheng, X.W. *Zhonghua Liu Xing Bing Xue Za Zhi.* 28(6), pp. 558-561, 2007. [Article in Chinese]

## **PUBLICATIONS BY FORMER NIDA HUBERT H. HUMPHREY FELLOWS**

### Alcohol and Drug Use among University Students: Gender Differences

HHH Fellows: Arthur Guerra de Andrade, Brazil, 1991-1992, and Vladimir Stempliuk, Brazil, 2003-2004  
This study compared the pattern of alcohol, legal and illegal drugs use among students of the Universidade de São Paulo (Brazil) in 1996 and 2001. Samples of 2,564 (1996) and 2,837 (2001) students answered a questionnaire proposed by the World Health Organization, which characterizes the consumption of alcohol, legal and illegal drugs in lifetime, in the last 12 months and in the last 30 days. Men showed a significant increase in lifetime use of tobacco (44.8% to 50.9%), marijuana (33.7% to 39.5%) and hallucinogens (6.6%

to 14.1%) between 1996 and 2001. No significant change was observed among women between 1996 and 2001 in tranquilizer use. Concerning the consumption reported in the last 12 months, both genders displayed significant increases in the consumption of marijuana (22.3% to 27.1% for men and 12.9% to 16.9% for women), amphetamines (1.9% to 5.0% for men and 3.4% to 5.6% for women), and inhalants (9.8% to 15.7% for men and 5.4% to 10.6% for women). The greatest gender difference was observed in consumption reported in the last 30 days with significant increases in male use of tobacco (19.6% to 23.5%), marijuana (15.8% to 20.5%), amphetamines (1.1% to 3.2%), and inhalants (4.0% to 7.9%). Substance use reported in the last 30 days remained stable among women between the 2 surveys. Rates of substance use among university students increased. These gender differences in substance consumption should be taken into account in the development of preventive and treatment strategies for undergraduate university students. Wagner, G.A., Stempluk, Vde A., Zilberman, M.L, Barroso, L.P., and de Andrade, A.G. Rev. Bras. Psiquiatr. 29(2), pp. 123-129, 2007.

### Gender Differences in Sex Risk Behaviors among Ukraine Injection Drug Users

HHH Fellow: Sergiy Dvoryak, Ukraine, 1999-2000

The objective of this study was to assess gender differences in drug and sex risk behaviors and evaluate predictors of HIV-related sex risk behaviors among heterosexual injection drug users (IDUs) in Ukraine. Street-recruited IDUs from Kiev, Odessa, and Makeevka/ Donesk, Ukraine. From June 2004 through November 2006, outreach workers recruited 1557 IDUs, including 526 from Kiev, 494 from Odessa, and 537 from Makeevka/Donesk. Participants were administered a standardized computer-assisted interview assessing HIV-related drug and sex risk behaviors, self-efficacy for practicing safe sex, and HIV knowledge. Overall, 80% of the participants were sexually active in the 30-day period before their interview. They also engaged in high-risk sex behaviors during this brief 30-day window: 53% reported anal or vaginal sex without a condom, 27% had sex with more than 1 partner, 41% had an IDU sex partner, and 37% had an HIV-positive sex partner or a partner whose HIV status they did not know. Overall, women were at higher risk than men and were more likely to have been told they were HIV-positive. The extremely high HIV prevalence rate in Ukraine and in this cohort, combined with their recent high-risk sex behaviors, forecasts not only a continuance of the epidemic in the region but an escalation. Booth, R.E., Lehman, W.E., Brewster, J.T., Sinitsyna, L., and Dvoryak, S. J. Acquir. Immune Defic. Syndr. July 19, 2007 (e-pub ahead of print).

## **INTRAMURAL RESEARCH**

### **PRECLINICAL PHARMACOLOGY SECTION BEHAVIORAL NEUROSCIENCE RESEARCH BRANCH**

#### Sex-dependent Metabolic, Neuroendocrine, and Cognitive Responses to Dietary Energy Restriction and Excess

Females and males typically play different roles in survival of the species and would be expected to respond differently to food scarcity or excess. To elucidate the physiological basis of sex differences in responses to energy intake, IRP scientists maintained groups of male and female rats for 6 months on diets with usual, reduced [20% and 40% caloric restriction (CR), and intermittent fasting (IF)], or elevated (high-fat/high-glucose) energy levels and measured multiple physiological variables related to reproduction, energy metabolism, and behavior. In response to 40% CR, females became emaciated, ceased cycling, underwent endocrine masculinization, exhibited a heightened stress response, increased their spontaneous activity, improved their learning and memory, and 44 maintained elevated levels of circulating brain-derived neurotrophic factor. In contrast, males on 40% CR maintained a higher body weight than the 40% CR females and did not change their activity levels as significantly as the 40% CR females. Additionally, there was no significant change in the cognitive ability of the males on the 40% CR diet. Males and females exhibited similar responses of circulating lipids (cholesterols/triglycerides) and energy-regulating

hormones (insulin, leptin, adiponectin, ghrelin) to energy restriction, with the changes being quantitatively greater in males. The high-fat/high-glucose diet had no significant effects on most variables measured but adversely affected the reproductive cycle in females. Heightened cognition and motor activity, combined with reproductive shutdown, in females may maximize the probability of their survival during periods of energy scarcity and may be an evolutionary basis for the vulnerability of women to anorexia nervosa. Martin, B., Pearson, M., Kebejian Golden, E., Keselman, A., Bender, M., Carlson, O., Egan, J., Ladenheim, B., Cadet, J.L., Becker, K.G., Wood, W., Duffy, K., Vinayakumar, P., Muudsley, S. and Mattson, M.P. *Endocrinology* 148(9), pp. 4318-4333, 2007.

# DIRECTOR'S REPORT TO COUNCIL

May 2008

## **BASIC BEHAVIORAL RESEARCH**

### Sex Differences and Hormonal Factors in the Acquisition and Maintenance of Cocaine Self-administration in Adolescent Rat

Previous research has reported that females more rapidly acquire self-administration than males, that a greater percentage of females acquire self-administration, and that females exhibit greater motivation for cocaine as assessed via a progressive ratio (PR) schedule. Additionally, cocaine self-administration in females is modulated by estrogen, whereas testosterone has not been found to play a role in cocaine self-administration in males. Dr. Wendy Lynch compared these behavioral outcomes in male and female rats during adolescence. Replicating prior findings with adult rats, female adolescents acquired cocaine self-administration more rapidly than males, a greater percentage of females than males acquired self-administration, and females received more infusions than males under the PR schedule. In females, serum estradiol concentration, but not progesterone concentration, was positively correlated with number of infusions obtained under the PR schedule, and for four of the five rats it accounted for 50% of the variance in number of infusions. Additionally, number of infusions varied with the estrus cycle. In males however, serum testosterone was unrelated to the number of infusions. In a parallel control study, Dr. Lynch compared acquisition of lever-pressing for sucrose reinforcement and subsequent behavior under a PR schedule in adolescent males versus females, in order to assess potential sex differences in general learning and motivation. She found that males and females did not differ in the rate of acquisition, nor did they differ in the number of pellets received under the PR schedule. This research suggests that the observed sex differences in cocaine self-administration in adults, as well as the modulation by estrogen and the estrus cycle, are reflective of sex differences and underlying mechanisms that are present in adolescents. The contribution of the organization and activational effects of gonadal hormones in these sex differences remains to be understood. Lynch, W.J. Acquisition and Maintenance of Cocaine Self-Administration in Adolescent Rats: Effects of Sex and Gonadal Hormones. *Psychopharmacology*, 197, pp. 237-246, 2008.

### Personality and Gender Moderate Amphetamine's Effects on Risk Taking

Dr. Harriet de Wit and her colleagues examined how gender and personality (temperament) moderate the effects of d-amphetamine on risk taking, measured by performance on the BART (Balloon Analogue Risk Task). Previous research indicates that stimulant drugs can either increase or decrease impulsive behavior, depending upon a number of factors including gender and variation in personality traits related to reward and punishment sensitivity. The present study assessed personality using the Multidimensional Personality Questionnaire Brief Form, because this questionnaire is an empirically derived measurement instrument that assesses three orthogonal factors related to reward sensitivity, behavioral impulsivity, and negative affect. These include the personality dimensions of Agentic Positive Emotionality (AgPEM), which is thought to reflect individual differences in the function of ascending VTA dopamine projections that modulate behavioral approach and incentive motivation; Constraint (CON), which measures impulsive spontaneity and approach-versus-avoidance of physical harm, which could be relevant to drug-induced changes in the relative frequency of impulsive choices versus successful impulse control; and Negative Emotionality (NEM), which measures anxiety proneness, interpersonal alienation and aggression, which could be relevant to drug-induced changes in aggressive impulsive behavior. Forty healthy men and women, aged 18 to 35, completed the BART after ingesting placebo or d-amphetamine (10, 20 mg). There were three main findings. First, for male participants, there were strong, positive correlations between the personality trait of AgPEM and amphetamine-induced increases in risk taking on the BART risk task.

Second, there was evidence of discriminant validity, as correlations between AgPEM and drug-induced risk behavior were significantly greater than correlations with trait CON and trait NEM in the same participants. Third, 20 mg d-amphetamine significantly decreased risk behavior in men with scores in the lower half of the distribution for AgPEM, and significantly increased risk behavior in men with scores in the upper half of the distribution on AgPEM. The drug did not affect risk taking in women. Overall, the current findings suggest that the personality trait of AgPEM could constitute a preexisting risk factor (neural, metabolic, or behavioral characteristics) for amphetamine-induced changes in risk-taking in healthy young adult males, and could affect behavioral responses to stimulant drugs when used recreationally or therapeutically. White, T.L., Lejuez, C.W., and de Wit, H. Personality and Gender Differences in Effects of d-Amphetamine on Risk Taking. *Experimental and Clinical Psychopharmacology*, 15, pp. 599-609, 2007.

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Prenatal Cocaine Exposure, Gender, and Preadolescent Substance Use and Other Health Risk Behaviors

Dr. Michael Lewis and his colleagues examined prenatal cocaine exposure, gender, and environmental risk as predictors of self-reported substance use, aggression, and a disregard for safety precautions on the Youth Risk Behavior Survey in a sample of 10.5 year olds (n = 154, including 60 who were prenatally exposed to cocaine). Gender tended to moderate the effects of prenatal cocaine exposure because exposure effects were found for boys but not girls. Boys who were prenatally exposed to cocaine reported engaging in more high-risk behavior. In examining individual outcomes, cocaine exposed boys had the highest scores for aggression, substance use, and a disregard for safety precautions, although these differences were significant only for the composite health risk behavior measure. The findings extend earlier work showing that prenatal cocaine exposure places boys at risk for problems of inhibitory control, emotional regulation, and antisocial behavior. Research is needed to examine whether the effects of prenatal cocaine on health risk behaviors persist into adolescence, when such behaviors tend to increase. Bennett, D., Bendersky, M., and Lewis, M. Preadolescent Health Risk Behavior as a Function of Prenatal Cocaine Exposure and Gender. *Journal of Behavioral Pediatrics*, 28(6), pp. 467- 472, 2007.

### Longitudinal Analysis of the Effects of Prenatal Cocaine Exposure on Growth

Dr. Gale Richardson and her colleagues at the University of Pittsburgh investigated the effects of prenatal cocaine exposure on offspring growth from 1 through 10 years of age using a repeated-measures growth-curve model. Cross-sectional analyses showed that children exposed to cocaine during the first trimester (n = 99) were smaller on all growth parameters at 7 and 10 years, but not at 1 or 3 years, than the children who were not exposed to cocaine during the first trimester (n = 125). The longitudinal analyses indicated that the growth curves for the 2 groups diverged over time: children who were prenatally exposed to cocaine grew at a slower rate than children who were not exposed. These analyses controlled for other factors associated with child growth. This is the first study of the long-term effects of prenatal cocaine exposure to conduct longitudinal growth-curve analyses using four time points in childhood. Children who were exposed to cocaine during the first trimester grew at a slower rate than those who were not exposed. These findings indicate that prenatal cocaine exposure has a lasting effect on child development. Richardson, G.A., Goldschmidt, L., and Larkby, C. Effects of Prenatal Cocaine Exposure on Growth: A Longitudinal Analysis. *Pediatrics*, 120(4), pp. e1017-1027, 2007.

### fMRI and Working Memory in Adolescents with Prenatal Cocaine Exposure

This fMRI study examined prefrontal cortex activation during task performance on an n-back task with 34 adolescents, 17 who were exposed to cocaine and 17 who were not exposed. Five functionally derived regions of interest (ROI) were defined; in addition, 2 a priori anatomical ROIs were generated for Brodmann regions 10 and 46. Groups had similar performance on the n-back task ( $P \geq .4$ ), with both showing a fewer number of correct responses on the 2-back than the 1-back ( $P < .001$ ), indicating increased

demands on working memory with greater task difficulty. In functionally derived ROIs, imaging results showed increased activation for both groups in the 2-back versus the 1-back condition. In anatomical ROIs, both groups showed greater activation in the 2-back versus the 1-back condition, with activation in the non-exposed group proportionally greater for the left prefrontal region ( $P = .05$ ). In this sample of adolescents, participants who were exposed to cocaine and participants who were not exposed were similar in performance on an executive function task and in fMRI activation patterns during task performance. Hurt, H., Giannetta, J.M., Korczykowski, M., Hoang, A., Tang, K.Z., Betancourt, L., Brodsky, N.L., Shera, D.M., Farah, M.J., and Detre, J.A. Functional Magnetic Resonance Imaging and Working Memory in Adolescents with Gestational Cocaine Exposure. *Journal of Pediatrics*, 152(3), pp. 371-377, 2008.

### Smoking During Teenage Pregnancies and Offspring Behavioral Problems

Dr. Nancy Day and her colleagues at the University of Pittsburgh prospectively examined the relationship between prenatal tobacco exposure (PTE) and child behavior in a birth cohort of 357 offspring of teenage mothers. PTE was defined as any exposure across pregnancy and, in separate analyses, exposure within each trimester. Outcomes included measures of behavior problems, activity, and attention. On average, the children were 6.4 years of age, 48% were females, and 69% were Black. Data on maternal tobacco and other substance use were collected prenatally and postnatally: 46% of the mothers smoked in the first trimester and 58% smoked 6 years later. Child urinary cotinine measured exposure to environmental tobacco smoke (ETS). PTE predicted significantly increased offspring activity; impulsivity; and aggression, externalizing, and total behavior problems in step 1. PTE remained a significant predictor of increased activity when maternal psychological characteristics, home environment, and ETS were added. The results were similar when PTE was examined by trimesters, although later pregnancy tobacco exposure predicted the most behavioral outcomes. In the final model, PTE (all three trimesters) and PTE (second trimester) were significant predictors of increased activity and attention problems, respectively. Other predictors of child behavior included maternal anxiety, depression, hostility, and home environment. ETS was not a significant predictor of child behavior when PTE was considered. Smoking during pregnancy among adolescents is a significant predictor of increased activity and attention problems in their offspring after controlling for covariates in the prenatal and current environments. Smoking cessation interventions are recommended for this population to avoid the effects of PTE on the offspring of pregnant adolescents. This is particularly important because these mothers will likely become pregnant again and many will increase their level of tobacco use as they mature. Cornelius, M.D., Goldschmidt, L., DeGenna, N., and Day, N.L. Smoking during Teenage Pregnancies: Effects on Behavioral Problems in Offspring. *Nicotine and Tobacco Research*, 9(7), pp. 739-750, 2007.

### Volumetric MRI Study of Brain in Children with Intrauterine Exposure to Cocaine, Alcohol, Tobacco, and Marijuana

This study used volumetric MRI to study brain volumes of thirty-five 10- to 14-year-old children with ( $n=14$ ) and without ( $n=21$ ) intrauterine exposure to cocaine, alcohol, cigarettes, or marijuana. Volumetric MRI was performed to determine the effect of prenatal drug exposure on volumes of cortical gray matter; white matter; subcortical gray matter; cerebrospinal fluid; and total parenchymal volume. Head circumference was also obtained. Analyses of each individual substance were adjusted for demographic characteristics and the remaining 3 prenatal substance exposures. Regression analyses adjusted for demographic characteristics showed that children with intrauterine exposure to cocaine had lower mean cortical gray matter and total parenchymal volumes and smaller mean head circumference than comparison children. After adjustment for other prenatal exposures, these volumes remained smaller but lost statistical significance. Similar analyses conducted for prenatal ethanol exposure adjusted for demographics showed significant reduction in mean cortical gray matter; total parenchymal volumes; and head circumference, which remained smaller but lost statistical significance after adjustment for the remaining 3 exposures. Notably, prenatal cigarette exposure was associated with significant reductions in cortical gray matter and total parenchymal volumes and head circumference after adjustment for demographics that retained



marginal significance after adjustment for the other 3 exposures. Finally, as the number of exposures to prenatal substances grew, cortical gray matter and total parenchymal volumes and head circumference declined significantly with smallest measures found among children exposed to all 4. These data suggest that intrauterine exposures to cocaine, alcohol, and cigarettes are individually related to reduced head circumference; cortical gray matter; and total parenchymal volumes as measured by MRI at school age. Adjustment for other substance exposures precludes determination of statistically significant individual substance effect on brain volume in this small sample; however these substances may act cumulatively during gestation to exert lasting effects on brain size and volume. Rivkin, M.J., Davis, P.E., Lemaster, J.L., Cabral, H.J., Warfield, S.K., Mulkern, R.V., Robson, C.D., Rose-Jacobs, R., and Frank, D.A. Volumetric MRI Study of Brain in Children with Intrauterine Exposure to Cocaine, Alcohol, Tobacco, and Marijuana. *Pediatrics*, 121(4), pp. 741-750, 2008.

#### Methadone Maintenance and Breastfeeding in the Neonatal Period

In a sample of methadone-maintained breastfeeding women and a matched group of formula-feeding women, this study evaluated concentrations of methadone in breast milk among breastfeeding women and concentrations of methadone in maternal and infant plasma in both groups. Eight methadone-maintained (dose: 50-105 mg/day), lactating women provided blood and breast milk specimens on days 1, 2, 3, 4, 14, and 30 after delivery, at the times of trough and peak maternal methadone levels. Eight matched formula-feeding subjects provided blood samples on the same days. Infant blood samples for both groups were obtained on day 14. Urine toxicological screening between 36 weeks of gestation and 30 days after the birth confirmed that subjects were not using illicit substances in the perinatal period. Concentrations of methadone in breast milk were low (range: 21.0-462.0 ng/mL) and not related to maternal dose. There was a significant increase in methadone concentrations in breast milk over time for all 4 sampling times. Concentrations of methadone in maternal plasma were not different between groups and were unrelated to maternal dose. Concentrations of methadone in infant plasma were low (range: 2.2-8.1 ng/mL) in all samples. Infants in both groups underwent neurobehavioral assessments on days 3, 14, and 30; there were no significant effects of breastfeeding on neurobehavioral outcomes. Fewer infants in the breastfed group required pharmacotherapy for neonatal abstinence syndrome, but this was not a statistically significant finding. Results contribute to the recommendation of breastfeeding for methadone-maintained women. Jansson, L.M., Choo, R., Velez, M.L., Harrow, C., Schroeder, J.R., Skakleya, D.M., and Huestis, M.A., Methadone Maintenance and Breastfeeding in the Neonatal Period. *Pediatrics*, 121(1), pp. 106-114, 2008.

#### Impact of Prenatal Cocaine Exposure on Attention and Response Inhibition as Assessed by Continuous Performance Tests

This longitudinal study examined the influence of prenatal cocaine exposure on attention and response inhibition measured by continuous performance tests (CPTs) at ages 5 and 7 years. The sample included 415 children from the Miami Prenatal Cocaine Study (219 cocaine-exposed, 196 non-cocaine-exposed as determined by maternal self-report and infant bioassays). Children were enrolled prospectively at birth and assessed comprehensively through age 7 years. Deficits in attention and response inhibition were estimated in relation to prenatal cocaine exposure using generalized estimating equations within the general linear model. Results indicate cocaine-associated increases in omission errors at ages 5 and 7 as well as increases in response times for target tasks (i.e., slower reaction times) and decreased consistency in performance at age 7. There were no demonstrable cocaine-associated deficits in commission errors. Estimates did not change markedly with statistical adjustment for selected prenatal and postnatal covariates. Evidence supports cocaine-associated deficits in attention processing through age 7 years. Accornero, V.H., Amado, A.J., Morrow, C.E., Xue, L., Anthony, J.C., and Bandstra, E.S. Impact of Prenatal Cocaine Exposure on Attention and Response Inhibition as Assessed by Continuous Performance Tests. *Journal of Developmental Behavioral Pediatrics*, 28(3), pp. 195-205, 2007.

### P3 Components of the Event-Related Potential and Marijuana Dependence in Southwest California Indians

Marijuana use and abuse is very high in Native Americans; however, little is known about neurobiological measures that are associated with marijuana addiction in this population. This study utilized event-related potentials to examine the responses to a facial recognition task in an adult sample of 317 Southwest California (SWC) Indians with (1) no drug dependence diagnosis; (2) marijuana use, but not other drug dependence diagnosis; and (3) marijuana dependence, as well as other drug dependence diagnosis. After taking age, gender, and the presence of a lifetime diagnosis of alcohol dependence into consideration; an increased latency in the P350 and P450 component peaks was found in those individuals with a diagnosis of marijuana dependence and also marijuana dependence co-morbid with other drug dependence. The amplitudes of these late component peaks were not associated with a diagnosis of marijuana dependence. Women appeared to be more impacted by a marijuana dependence diagnosis in that the P450 latencies were longer in females than in males which may be indicative of greater toxicity. The findings suggest that marijuana dependence may be associated with delays in the evaluation and identification of emotional stimuli in SWC Indians. Further longitudinal studies will be necessary to determine whether pre-disposing or co-morbid factors are a possible cause of the P300 latency effects in this high risk and understudied ethnic group. Ehlers, C., Gilder, D., and Phillips, E. P3 Components of the Event-Related Potential and Marijuana Dependence in Southwest California Indians. *Addiction Biology*, 13(11), pp. 130-142, 2008.

### **CLINICAL NEUROSCIENCE RESEARCH**

#### Presence of a Social Stressor Inhibits the Ability to Learn from Bad Choices in a Gambling Task in Men More than in Women

Antoine Bechara and colleagues at University of Southern California used neuropsychological testing to investigate whether decision making during a task is disrupted by an emotional stressor unrelated to the task. Drug-dependent individuals typically encounter a variety of social stressors, some of which are self-initiated. Two groups of healthy volunteers played the Iowa Gambling Task, with one group anticipating having to give a public speech. Those who anticipated having to give a speech took longer to learn to make advantageous choices. In addition, a gender interaction was present later in the game. Stressed female participants exhibited more explicit knowledge and more advantageous performance than stressed males. These results indicate that effects of anticipatory stress on decision making are complex and depend on both the nature of the task and the individual. Preston, S.D., Buchanan, T.W., Stansfield, R.B., and Bechara, A. Effects of Anticipatory Stress on Decision Making In a Gambling Task. *Behavioral Neuroscience*, 121(2), pp. 257-263, 2007.

#### Emotional Stimuli and Context Moderate Effects of Nicotine on Specific but Not Global Affects

David Gilbert and colleagues at the University of Southern Illinois investigated how nicotine interacts with the emotional and cognitive modulation of attention. The study involved the presence or absence of emotionally positive and negative stimuli and attentional choice to avoid attending to emotionally negative stimuli. Two groups of habitual smokers (32 per group) performed attentional tasks in which they either had the freedom to look back and forth at 2 simultaneously presented pictures or viewed single pictures without attentional choice. Blocks of pictures contained one of 4 combinations of picture types: a) emotionally negative + neutral, b) negative + positive, c) positive + neutral, or d) neutral + neutral. Participants wore a nicotine patch on one day and a placebo patch on a second day. Nicotine reduced anxiety most when negative pictures were presented in combination with neutral pictures, but it had no effect on anxiety when negative pictures were presented in combination with positive pictures and when negative pictures were not presented. In contrast, nicotine only reduced depressive affect when the participant had attentional choice between positive and negative pictures. Nicotine also enhanced positive affect and reduced negative affect as measured by the Positive and Negative Affect Schedule, but these effects were not moderated by task manipulations. Nicotine tended to enhance eye-gaze orientation to

emotional pictures versus neutral pictures in women, but it had no significant effect on eye-gaze in men. Overall, the findings support the view that nicotine's ability to reduce specifically negative affect is moderated by overall emotional context and attentional freedom. Gilbert, D.G., Riise, H., Dillon, A., Huber, J., Rabaanovich, N.E., and Sugai, C. *Exp. Clin. Psychopharmacol.*, 16(1), pp. 33-42, 2008.

### Interactions between Genotype and Retrospective ADHD Symptoms Predict Lifetime Smoking Risk in a Sample of Young Adults

Joseph McClernon and colleagues at Duke University investigated whether ADHD symptoms interact with candidate gene variation to predict smoking risk. Attention-deficit/hyperactivity disorder (ADHD) symptoms are associated with an increased risk of smoking, and genetic studies have identified similar candidate genes associated with both ADHD and smoking phenotypes. Participants were a subsample of individuals from the National Longitudinal Study of Adolescent Health (Add Health), a nationally representative sample of adolescents followed from 1995 to 2002. The sample analyzed included a subset from Add Health of 1,900 unrelated individuals with genotype data. Multiple logistic regression was used to examine relationships between self-reported ADHD symptoms, genotype, and lifetime history of regular smoking. Polymorphisms in the Dopamine D2 receptor gene and, the MAO-A gene (females only) interacted with retrospective reports of ADHD symptoms in contributing to risk for smoking. Trends were observed for interactions between the Dopamine D4 receptor gene and the MAO-A gene (males only) and ADHD symptoms to predict smoking risk. No main effect for any of these polymorphisms was observed. No main effects or interactions with CYP2A6, DAT, and SLC6A4 genes were found. These findings suggest that genotypes associated with catecholamine neurotransmission interact with ADHD symptoms to predict lifetime smoking risk in a sample of young adults. McClernon, F.J., Fuemmeler, B.F., Kollins, S.H., Kail, M.E., and Ashley-Koch, A.E. *Nicotine Tob. Res.*, 10(1), pp. 117-127, 2008.

## **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

### Specificity of Genetic Factors for Dependence on Licit and Illicit Drugs

Although genetic risk factors have been found to contribute to dependence on both licit and illicit psychoactive substances, we know little of how these risk factors interrelate. This study sought to clarify the structure of genetic and environmental risk factors for symptoms of dependence on cannabis, cocaine, alcohol, caffeine, and nicotine in males and females. Four thousand eight hundred sixty-five adult members of male-male and female-female pairs from the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders were assessed for lifetime symptoms of abuse of and dependence on cannabis, cocaine, alcohol, caffeine, and nicotine by structured interview. Controlling for greater symptom prevalence in males, genetic and environmental parameters could be equated across sexes. Two models explained the data well. The best-fit exploratory model contained 2 genetic factors and 1 individual environmental factor contributing to all substances. The first genetic factor loaded strongly on cocaine and cannabis dependence; the second, on alcohol and nicotine dependence. Nicotine and caffeine had high substance-specific genetic effects. A confirmatory model, which also fit well, contained 1 illicit drug genetic factor--loading only on cannabis and cocaine--and 1 licit drug genetic factor loading on alcohol, caffeine, and nicotine. However, these factors were highly intercorrelated ( $r = +0.82$ ). Large substance-specific genetic effects remained for nicotine and caffeine. The authors conclude that the pattern of genetic and environmental risk factors for psychoactive substance dependence was similar in males and females, and that genetic risk factors for dependence on common psychoactive substances cannot be explained by a single factor. Rather, two genetic factors--one predisposing largely to illicit drug dependence, the other primarily to licit drug dependence--are needed. Furthermore, a large proportion of the genetic influences on nicotine and particularly caffeine dependence appear to be specific to those substances. Kendler, K., Myers, J., and Prescott, C. *Specificity of Genetic and Environmental Risk Factors for Symptoms of Cannabis, Cocaine, Alcohol, Caffeine, and Nicotine Dependence. Arch. Gen. Psychiatry*, 64(11), pp. 1313-1320, 2007.

### Neighborhood Income and Income Distribution and the Use of Cigarettes, Alcohol, and Marijuana

Evidence about the relationship between contextual variables and substance use is conflicting. Relationships between neighborhood income and income distribution and the prevalence and frequency of substance use in 59 New York City (NYC) neighborhoods were assessed while accounting for individual income and other socio-demographic variables. Measures of current substance use (in the 30 days prior to the survey) were obtained from a random-digit-dial phone survey of adult residents of NYC and data from the 2000 U.S. Census to calculate median neighborhood income and income distribution (assessed using the Gini coefficient). Among 1355 respondents analyzed (female=56.2%, mean age=40.4), 23.9% reported cigarette, 40.0% alcohol, and 5.4% marijuana use in the previous 30 days. In ecologic assessment, neighborhoods with both the highest income and the highest income maldistribution had the highest prevalence of drinking alcohol (69.0%) and of smoking marijuana (10.5%) but not of cigarette use; there was no clear ecologic association between neighborhood income, income distribution, and cigarette use. In multilevel multivariable models adjusting for individual income, age, race, sex, and education, high neighborhood median income and maldistributed neighborhood income were both significantly associated with a greater likelihood of alcohol and marijuana use but not of cigarette use. Both high neighborhood income and maldistributed income also were associated with greater frequency of alcohol use among current alcohol drinkers. These observations suggest that neighborhood income and income distribution may play more important roles in determining population use of alcohol and marijuana than individual income, and that determinants of substance use may vary by potential for drug dependence. Further research should investigate specific pathways that may explain the relationship between neighborhood characteristics and use of different substances. Galea, S., Ahern, J., Tracy, M., and Vlahov, D. Neighborhood Income and Income Distribution and the Use of Cigarettes, Alcohol, and Marijuana. *Am. J. Prev. Med.*, 32 (6 Suppl), pp. S195-S202, 2007.

### Study Describes Current Patterns of Extra-Medical Drug Use

In 1994, epidemiological patterns of extra-medical drug use in the United States were estimated from the National Comorbidity Survey. This paper describes such patterns based upon more recent data from the National Comorbidity Survey Replication (NCS-R). The NCS-R was a nationally representative face-to-face household survey of 9282 English-speaking respondents, aging 18 years and older, conducted in 2001-2003 using a fully structured diagnostic interview, the WHO Composite International Diagnostic Interview (CIDI) Version 3.0. The estimated cumulative incidence of alcohol use in the NCS-R was 92%; tobacco, 74%; extra-medical use of other psychoactive drugs, 45%; cannabis, 43% and cocaine, 16%. Statistically robust associations existed between all types of drug use and age, sex, income, employment, education, marital status, geography, religious affiliation and religiosity. Very robust birth cohort differences were observed for cocaine, cannabis, and other extra-medical drug use, but not for alcohol or tobacco. Trends in the estimated cumulative incidence of drug use among young people across time suggested clear periods of fluctuating risk. These epidemiological patterns of alcohol, tobacco, and other extra-medical drug use in the United States in the early 21st century provide an update of NCS estimates from roughly 10 years ago, and are consistent with contemporaneous epidemiological studies. New findings on religion and religiosity, and exploratory data on time trends, represent progress in both concepts and methodology for such research. These estimates lead to no firm causal inferences, but contribute to a descriptive epidemiological foundation for future research on drug use and dependence across recent decades, birth cohorts, and population subgroups. Degenhardt, L., Chiu, W., Sampson, N., Kessler, R., and Anthony, J. Epidemiological Patterns of Extra-Medical Drug Use in the United States: Evidence from the National Comorbidity Survey Replication, 2001-2003. *Drug Alcohol Depend.*, 90 (2-3), pp. 210-223, 2007.

### Misperceptions of Non-medical Prescription Drug Use Among College Students

This study compared undergraduate students' perceived versus actual prevalence rates of non-medical use of marijuana, prescription opioids and prescription stimulants. In 2005, a randomly selected sample of

3639 college students self-administered a Web survey regarding their substance use behaviors and attitudes (68% response rate). Analysis showed that the majority of undergraduate students overestimated the prevalence of non-medical use of prescription stimulants (70.2%) and prescription opioids (69.9%) and marijuana use (50.5%) among peers on their campus. The mean difference between perceived versus actual past-year use was considerably greater for non-medical use of prescription stimulants (mean difference=12.2, 95% CI=11.7-12.7) and prescription opioids (mean difference=8.8, 95% CI=8.3-9.2) than marijuana (mean difference=2.9, 95% CI=2.2-3.6). Multivariate regression analysis revealed overestimation of non-medical use of prescription drugs was significantly associated with gender and medical use of prescription drugs. The authors conclude that the study results provide strong evidence of misperception of non-medical prescription drug use among college students and suggest that future research and prevention efforts should assess the impact of correcting misperceived norms on reducing non-medical prescription drug use. McCabe, S. E. Misperceptions of Non-medical Prescription Drug Use: A Web Survey of College Students. *Addict. Behav.*, 33, pp. 713-724, 2008.

#### Association between Early Onset of Non-medical Use of Prescription Drugs and Subsequent Prescription Drug Use and Dependence

This study examined the associations between early onset of non-medical use of prescription drugs (NMUPD) (i.e. sedatives, tranquilizers, opioids, stimulants) and the development of prescription drug abuse and dependence in the United States. Data were collected from structured diagnostic interviews using the National Institute on Alcohol Abuse and Alcoholism (NIAAA) Alcohol Use Disorder and Associated Disabilities Interview Schedule: Diagnostic and Statistical Manual version IV (DSM-IV). National prevalence estimates were derived from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC, n = 43,093). NESARC included a nationally representative cross-sectional sample of civilian non-institutionalized adults aged 18 years or older in the United States, of whom 52% were women, 71% white, 12% Hispanic, 11% African American, 4% Asian and 2% Native American or of other racial background. Analyses revealed that a higher percentage of individuals who began using prescription drugs non-medically at or before 13 years of age were found to have developed prescription drug abuse and dependence as compared with those individuals who began using at or after 21 years of age. Multivariate logistic regression analyses indicated that the odds of developing any life-time prescription drug abuse among non-medical users was reduced by approximately 5% with each year non-medical use was delayed [adjusted odds ratio (AOR) = 0.95, 95% CI = 0.94, 0.97], and that the odds of developing any lifetime prescription drug dependence were reduced by about 2% with each year onset was delayed (AOR = 0.98, 95% CI = 0.96, 1.00) when controlling for relevant covariates. The authors conclude that early onset of NMUPD was a significant predictor of prescription drug abuse and dependence. These findings reinforce the importance of developing prevention efforts to reduce NMUPD and diversion of prescription drugs among children and adolescents. McCabe, S., West, B., Morales, M., Cranford, J., and Boyd, C. Does Early Onset of Non-medical Use of Prescription Drugs Predict Subsequent Prescription Drug Abuse and Dependence? Results from a National Study. *Addiction*, 102(12), pp. 1920-1930, 2007.

#### Non-prescribed Use of Pain Relievers Among Adolescents in the United States

This study examined gender-specific prevalences, patterns, and correlates of non-prescribed use of pain relievers (mainly opioids) in a representative sample of American adolescents (N=18,678). Data were drawn from the public use data file of the 2005 U.S. National Survey on Drug Use and Health, a survey of non-institutionalized American household residents. Patterns of non-prescribed use of prescription pain relievers were examined, and logistic regression procedures were conducted to identify correlates of non-prescribed use. Analysis showed that approximately one in 10 adolescents aged 12-17 years reported non-prescribed use of pain relievers in their lifetime (9.3% in males and 10.3% in females). The mean age of first non-prescribed use was 13.3 years, which was similar to the mean age of first use of alcohol and marijuana but older than the age of first inhalant use. Among all non-prescribed users, 52% reported having used hydrocodone products (Vicodin, Lortab, Lorcet, and Lorcet Plus, and hydrocodone), 50% had

used propoxyphene (Darvocet or Darvon) or codeine (Tylenol with codeine), and 24% had used oxycodone products (OxyContin, Percocet, Percodan, and Tylox). Approximately one quarter (26%) of all non-prescribed users had never used other non-prescribed or illicit drugs. There were gender variations in correlates of non-prescribed use. These findings indicate that use of non-prescribed pain relievers occurs early in adolescence. The authors suggest that research is needed to understand whether early use of non-prescribed pain relievers is related to later drug use. Wu, L., Pilowsky, D., and Patkar, A. Non-Prescribed Use of Pain Relievers among Adolescents in the United States. *Drug Alcohol Depend.*, 94(1-3), pp. 1-11, 2008.

### Specificity of Psychosocial Risk Factors for Child Psychiatric Disorders

Most psychosocial risk factors appear to have general rather than specific patterns of association with common childhood and adolescence disorders. However, previous research has typically failed to 1) control for comorbidity among disorders, 2) include a wide range of risk factors, and 3) examine sex by developmental stage effects on risk factor-disorder associations. This study tests the specificity of putative psychosocial risk factors while addressing these criticisms. Eight waves of data from the Great Smoky Mountains Study (N = 1,420) were used, covering children in the community age 9-16 years old. Youth and one parent were interviewed up to seven times using the Child and Adolescent Psychiatric Assessment, providing a total of 6,674 pairs of interviews. A wide range of putative neighborhood, school, peer, family, and child risk factors, and common and comorbid youth disorders were assessed. The authors found that a majority of putative risk factors were specific to one disorder or one disorder domain. A unique or "signature set" of putative risk factors was identified for each disorder. Several putative risk factors were associated with a disorder in preadolescent males, preadolescent females, adolescent males, or adolescent females only. They conclude that there is a need to define risk factors and disorders narrowly, to control comorbidity and other risk factors, and to consider developmental patterns of specificity by sex. This may augment efforts in the prevention arena. Shanahan, L., Copeland, W., Costello, E., and Angold, A. Specificity of Putative Psychosocial Risk Factors for Psychiatric Disorders in Children and Adolescents. *J. Child. Psychol. Psychiatry*, 49(1), pp. 34-42, 2008.

### The Formation of a Socioeconomic Disparity: A Case Study of Cocaine and Marijuana Use in the 1990s'

Around 1990, the reputation of cocaine use changed from glamorous to undesirable, and at the same time, a socioeconomic disparity in cocaine use emerged. This study examined (1) whether the socioeconomic disparity was created by differential incidence, differential cessation, or both, (2) whether a socioeconomic disparity also developed in marijuana use, and (3) whether disparities formed across race, Hispanic ethnicity, and/or gender. The analyses center on 6544 respondents aged 14-21 in 1979 in the National Longitudinal Survey of 1979 that provided information on past-year use of powder cocaine and marijuana use before and after 1990--specifically, in 1984, 1988, 1992, 1994, and 1998. Both differential incidence and differential cessation across education contributed to the formation of the socioeconomic disparity in cocaine use, although differential cessation played a more influential role in this cohort. A socioeconomic disparity in marijuana use also came about around the same time. No emerging disparities by race, Hispanic ethnicity, or gender were observed. This case study suggests that the redefinition of a health behavior as unhealthy will result in a socioeconomic disparity in the behavior across socioeconomic strata as a result of both differential incidence and cessation, but disparities will not necessarily form by race, ethnicity, or gender. Miech, R., and Chilcoat, H. The Formation of A Socioeconomic Disparity: A Case Study of Cocaine and Marijuana Use in the 1990s. *Am. J. Prev. Med.*, 32 (6 Suppl), pp. S171-s176, 2007.

### Rapid Increase in the Diagnosis of Youth Bipolar Disorder

Although bipolar disorder may have its onset during childhood, little is known about national trends in the diagnosis and management of bipolar disorder in young people. The purpose of this study was to present national trends in outpatient visits with a diagnosis of bipolar disorder and to compare the treatment

provided to youth and adults during those visits. Investigators compared rates of growth between 1994-1995 and 2002-2003 in visits with a bipolar disorder diagnosis by individuals aged 0 to 19 years vs those aged 20 years or older. For the period of 1999 to 2003, we also compare demographic, clinical, and treatment characteristics of youth and adult bipolar disorder visits. Patient visits from the National Ambulatory Medical Care Survey (1999-2003) with a bipolar disorder diagnosis (n = 962) were assessed drawn from outpatient visits to physicians in office-based practice. Visits with a diagnosis of bipolar disorder by youth (aged 0-19 years) and by adults (aged > or = 20 years) were assessed. The study indicated the estimated annual number of youth office-based visits with a diagnosis of bipolar disorder increased from 25 (1994-1995) to 1003 (2002-2003) visits per 100,000 population, and adult visits with a diagnosis of bipolar disorder increased from 905 to 1679 visits per 100,000 population during this period. In 1999 to 2003, most youth bipolar disorder visits were by males (66.5%), whereas most adult bipolar disorder visits were by females (67.6%); youth were more likely than adults to receive a comorbid diagnosis of attention-deficit/hyperactivity disorder (32.2% vs 3.0%, respectively;  $P < .001$ ); and most youth (90.6%) and adults (86.4%) received a psychotropic medication during bipolar disorder visits, with comparable rates of mood stabilizers, antipsychotics, and antidepressants prescribed for both age groups. There has been a recent rapid increase in the diagnosis of youth bipolar disorder in office-based medical settings. This increase highlights a need for clinical epidemiological reliability studies to determine the accuracy of clinical diagnoses of child and adolescent bipolar disorder in community practice. Moreno, C., Laje, G., Blanco, C., Jiang, H., Schmidt, A., and Olfson, M. National Trends in the Outpatient Diagnosis and Treatment of Bipolar Disorder in Youth. *Arch. Gen. Psychiatry*, 64(9), pp. 1032-1039, 2007.

#### The Impact of Sociodemographic Factors and Psychiatric Disorders on Maternal Smoking during Pregnancy

Maternal smoking during pregnancy increases birth complication risk and has long-term developmental consequences for child development. This study investigated the relative importance of sociodemographic factors and psychiatric disorders for smoking among 453 pregnant women in the National Epidemiological Survey on Alcohol and Related Conditions. Women with less than a high school education and those with current-year nicotine dependence had the highest risk of smoking (90.5%), compared with women with a college degree and without nicotine dependence (3.9%). More effective and accessible interventions for nicotine dependence among pregnant smokers are needed. Gilman, S., Breslau, J., Subramanian, S., Hitsman, B., and Koenen, K. Social Factors, Psychopathology, and Maternal Smoking during Pregnancy. *Am. J. Public Health*, 98(3), pp. 448-453, 2008.

#### Getting Into Ecstasy: Comparing Moderate and Heavy Young Adult Users

In this article, the authors examine factors associated with initial and present Ecstasy use among young adults. Face-to-face structured interviews were conducted in Atlanta, Georgia among 261 active Ecstasy users. The median age at which respondents first heard of Ecstasy was 16 years, whereas the median age of first Ecstasy use was 18 years. Initial Ecstasy use frequently involved polydrug use, including alcohol (50.4%). In terms of their current use, 47.5% of respondents were considered heavy Ecstasy users (using on 10 or more separate occasions in the last 90 days). White respondents, those who used more than one pill during their initial use, and those who used again within one month after their initial use were more likely to be current heavy Ecstasy users. Women, those who waited a longer time between initial and subsequent Ecstasy use, and those who considered themselves in the upper SES bracket were less likely to be current heavy Ecstasy users. A better understanding of initial and current Ecstasy use patterns, including polydrug use, is essential for effective prevention and intervention efforts. Sterk, C., Theall, K., and Elifson, K. Getting Into Ecstasy: Comparing Moderate and Heavy Young Adult Users. *J. Psychoactive Drugs*, 39(2), pp. 103-113, 2007.

## Social Anxiety and Risk for Alcohol and Cannabis Dependence

Social anxiety disorder (SAD) is highly comorbid with alcohol use disorders (AUDs) and cannabis dependence. However, the temporal sequencing of these disorders has not been extensively studied to determine whether SAD serves as a specific risk factor for problematic substance use. The present study examined these relationships after controlling for theoretically-relevant variables (e.g., gender, other Axis I pathology) in a longitudinal cohort over approximately 14 years. The sample was drawn from participants in the Oregon Adolescent Depression Project., who were originally recruited as adolescents from high schools in 1987-89, at a mean age of 16.6 years. The sample, half female, was followed at ages 24 and 30; the final data point was collected from 816 participants, 59% women, 59% Caucasian. After excluding those with substance use disorders at baseline, SAD at study entry was associated with 6.5 greater odds of cannabis dependence (but not abuse) and 4.5 greater odds of alcohol dependence (but not abuse) at follow-up after controlling for relevant variables (e.g., gender, depression, conduct disorder). The relationship between SAD and alcohol and cannabis dependence remained even after controlling for other anxiety disorders. Other anxiety disorders and mood disorders were not associated with subsequent cannabis or alcohol use disorder after controlling for relevant variables. Among the internalizing disorders, SAD appears to serve as a unique risk factor for the subsequent onset of cannabis and alcohol dependence. Buckner, J., Schmidt, N., Lang, A., Small, J., Schlauch, R., and Lewinsohn, P. Specificity of Social Anxiety Disorder as a Risk Factor for Alcohol and Cannabis Dependence. *J. Psychiatr. Res.*, 42(3), pp. 230-239, 2008.

## Correlates of Cannabis Initiation in Young Women

As rates of cannabis use have increased in young women over the last decade, the authors sought to characterize the potential correlates of onset of cannabis use during emerging adulthood. Using data from 1065 females (collected 1994-2005) who participated in both the baseline (ages 16-23) and follow-up wave (ages 20-29) of interviews of the Missouri Adolescent Female Twin Study, they examined the associations between correlates from the peer, parental and individual domains and new onsets of cannabis use, using logistic regression. Univariate models revealed that initiation of cannabis use was associated with alcohol and cigarette use at baseline, peer attitude towards alcohol/cigarette/cannabis use, peer substance use and other aspects of impulse-disinhibited behavior. However, multivariate stepwise modeling retained only the significant influences of alcohol use at baseline and peer attitudes towards cannabis as correlates of cannabis initiation. The authors concluded that having peers with favorable attitudes towards alcohol, cigarette and cannabis use is an important correlate of initiation of cannabis use in women, and that prevention and intervention efforts need to take this into account when developing drug resistance training programs for adolescents. Agrawal, A., Lynskey, M., Bucholz, K., Madden, P., and Heath, A. Correlates of Cannabis Initiation in a Longitudinal Sample of Young Women: The Importance of Peer Influences. *Prev. Med.*, 45(1), pp. 31-34, 2007.

## Race/Ethnicity and Gender Differences in Drug Use and Abuse among College Students

This study examined race/ethnicity and gender differences in drug use and abuse for substances other than alcohol among undergraduate college students. A probability-based sample of 4,580 undergraduate students at a Midwestern university completed a cross-sectional Web-based questionnaire that included demographic information and several substance use measures. Male students were more likely to report drug use and abuse than female students. Hispanic and White students were more likely to report drug use and abuse than Asian and African American students prior to coming to college and during college. Results of multiple logistic regression analysis for past 12-month illicit use of prescription drugs or illicit drugs revealed that after controlling for race, there was no statistically significant effect of gender. With respect to race, results using African Americans as the reference group showed that, controlling for gender, the odds of past 12-month drug use were statistically significantly higher among Whites (OR=1.86) and Hispanics (OR=2.14). The authors conclude that the findings of the present study reveal several important



racial/ethnic differences in drug use and abuse that need to be considered when developing collegiate drug prevention and intervention efforts. McCabe, S., Morales, M., Cranford, J., Delva, J., McPherson, M., and Boyd, C. Race/Ethnicity and Gender Differences in Drug Use and Abuse among College Students. *J. Ethn. Subst. Abuse*, 6(2), pp. 75-95, 2007.

#### Intimate Partner Violence Perpetration against Main Female Partners among HIV-Positive Male Injection Drug Users

Intimate partner violence (IPV) against women is a serious public health and social problem and is associated with a host of adverse health outcomes and behaviors, including HIV risk behaviors, among women who are victimized. Historically, research has focused on correlates of IPV victimization among women; thus, there is less information on the role of men in perpetrating IPV, particularly among men at risk for transmitting HIV to their female partners. The authors assessed the self-reported prevalence and correlates of perpetration and threat of perpetration of physical and/or sexual IPV against a main female partner among 317 HIV-positive men who were current injection drug users (IDUs). More than 40% of men reported perpetrating physical (39%) and/or sexual (4%) violence against their main female partners in the past year. Multivariate analyses revealed that low education, homelessness, psychologic distress, and unprotected sex with main and nonmain HIV-negative female partners were positively associated with IPV perpetration against main female partners. These findings reveal that IPV perpetration is prevalent among HIV-positive male IDUs and associated with sexual HIV transmission risk behaviors. IPV assessment and treatment among HIV-positive men in HIV care is recommended as a way to prevent IPV perpetration and victimization and to reduce potential HIV transmission. Frye, V., Latka, M., Wu, Y., Valverde, E., Knowlton, A., Knight, K., Arnsten, J., and O'Leary, A. Intimate Partner Violence Perpetration against Main Female Partners among HIV-Positive Male Injection Drug Users. *J. Acquir. Immune Defic. Syndr.*, 46 Suppl. 2, pp. S101-S109, 2007.

#### Blood Contamination in Children's Saliva: Prevalence, Stability, and Impact on the Measurement of Salivary Cortisol, Testosterone, and Dehydroepiandrosterone

The prevalence, stability, and impact of blood contamination in children's saliva on the measurement of three of the most commonly assayed hormones were examined. Participants were 363 children (47% boys; ages 6-13 years) from economically disadvantaged families who donated saliva samples on 2 days in the morning, midday, and late afternoon. Samples (n=2178) were later assayed for cortisol (C), testosterone (T), and dehydroepiandrosterone (DHEA). To index the presence of blood (and its components) in saliva, samples were assayed for transferrin. Transferrin levels averaged 0.37 mg/dl (SD=0.46, range 0.0-5.5, Mode=0), and were: (1) highly associated within individuals across hours and days, (2) positively correlated with age, (3) higher for boys than girls, (4) higher in PM than AM samples, and (5) the highest (>1.0 mg/dl) levels were rarely observed in samples donated from the same individuals. Transferrin levels were associated with salivary DHEA and C, but less so for T. As expected, the relationships were positive, and explained only a small portion of the variance. Less than 1% of the statistical outliers (+2.5 SDs) in salivary hormone distributions had correspondingly high transferrin levels. The researchers conclude that blood contamination in children's saliva samples is rare, and its effects on the measurement of salivary hormones is small. Guidelines and recommendations are provided to steer investigators clear of this potential problem in special circumstances and populations. Granger, D., Cicchetti, D., Rogosch, F., Hibel, L., Teisl, M., and Flores, E. Blood Contamination in Children's Saliva: Prevalence, Stability, and Impact on the Measurement of Salivary Cortisol, Testosterone, and Dehydroepiandrosterone. *Psychoneuroendocrinology*, 32(6), pp. 724-733, 2007.

### Puberty is associated with Changes in the Form and Frequency of Self-Harm

A cross-sectional survey of 12- to 15-year-olds in 300 secondary schools in the U.S. state of Washington in February-April 2002 and the Australian state of Victoria was conducted to ascertain the association between pubertal stage and deliberate self-harm. A total of 3,332 students in grades 7 and 9 provided complete data on episodes of deliberate self-harm in the previous 12 months and pubertal stage. Pubertal stage was assessed with the Pubertal Development Scale. The prevalence of deliberate self-harm was 3.7% with a more than twofold higher rate in females. Late puberty was associated with a more than fourfold higher rate of self-harm (odds ratio 4.6, 95% confidence interval 1.5-14) after adjustment for age and school grade level. In contrast age had a protective association (odds ratio 0.7, confidence interval 0.4-1.0). The sharpest rises in prevalence across puberty were for self-laceration and self-poisoning in females. Higher rates of depressive symptoms, frequent alcohol use, and initiation of sexual activity largely accounted for the association between self-harm and pubertal stage in multivariate models. Puberty is associated with changes in the form and frequency of self-harm. For adolescents with a gap between puberty and brain development, risk factors such as early sexual activity and substance abuse may be particularly potent. Patton, G., Hemphill, S., Beyers, J., Bond, L., Toumbourou, J., McMorris, B., and Catalano, R. Pubertal Stage and Deliberate Self-harm in Adolescents. *J. Am. Acad. Child Adolesc. Psychiatry*, 46(4), pp. 508-514, 2007.

### Sexual Abstinence in Adolescence Predicts Adult Mental Health Differentially for Males and Females

Investigators examined whether adolescent sexual abstinence predicts better adult mental health. 1,917 adolescents, recruited from middle schools at age 13, were surveyed at ages 13, 18, 23, and 29. In bivariate analyses, adolescent sexual abstinence was associated with better mental health at age 29 for females, but not males; three adolescent factors, educational prospects, family bonding, and unconventionality were investigated as explanatory variables of this relationship. The abstinence-mental health relationship was nonsignificant when educational prospects was included in multivariate models, and marginally significant when family bonding and unconventionality were included; all three explanatory factors accounted for significant proportions of the variance in adult mental health. Girls who are uninvolved in school, have weak family backgrounds, and exhibit unconventionality may have poor adult mental health, whether or not they abstain from sex in adolescence. Interventions that strengthen adolescents' connections to families and schools may reduce risk for long-term mental health problems. Bogart, L., Collins, R., Ellickson, P., and Klein, D. Association of Sexual Abstinence in Adolescence with Mental Health in Adulthood. *J. Sex Res.*, 44(3), pp. 290-298, 2007.

### Adolescent Work Related to Slight Decreases in Problem Behavior

Researchers have found mixed support for documenting whether work is protective or harmful during adolescence. This study of 592 African American youth (53% female;  $M = 14.8$  years,  $SD = .60$ ) examined the association between work and problem behaviors. Youth were followed from mid-adolescence to young adulthood over eight Waves (90% response rate over the first four Waves and a 68% response rate across all eight Waves). Investigators explored three competing operationalizations of work: work history (never worked, worked), work intensity (no work, 20 h or less, and 21 h or over), and work trajectories (never worked, episodic work, stopped working, late starter, and consistent worker). Non-working youth reported higher marijuana use during young adulthood than their working counterparts. Nonworkers reported lower self-acceptance during young adulthood than those working greater number of hours per week. Differences in work trajectories for cigarette use, depression, and anxiety during adolescence imply that when and for how long youth work are also important factors to explore. The findings lend tentative support to the work benefits perspective and suggest that the association between work and problem behaviors may depend in part on how work is measured. Bauermeister, J. A., Zimmerman, M. A., Barnett, T. E., and Caldwell, C. H. Working in High School and Adaptation in the Transition to Young Adulthood among African American Youth. *J. Youth Adolescence*, 36, pp. 877-890, 2007.

### Individual Action and Community Context: the Health Intervention Project

HIV risk-reduction efforts have traditionally focused on the individual. The need for including the role of the social context and community is being recognized. Social capital provides social relationships and potential resources that may hinder or trigger risk or protective health behaviors, especially for individuals with limited economic means. Sixty-five adult inner-city female drug users, who were included in a woman-focused HIV risk-reduction intervention trial, participated in in-depth interviews in Atlanta, Georgia, between 2002 and 2004. The interviews focused on the women's individual behavioral changes during the 6 months since completion of the intervention as well as on the impact of community conditions. Topics discussed were sexual and drug use behaviors, social relationships, social capital, and community physical and social infrastructure. The data were analyzed using the constant comparison methods. The respondents indicated that poor physical and social infrastructure led to alienation and negatively affected their behavioral change efforts. Social capital and social support mediated these negative influences. Drug-related violence was especially debilitating in their efforts to reduce HIV risk associated with crack cocaine or injection drug use and associated sexual behavior. Environmental conditions and opportunity structures played salient roles in the women's success. Individual actions and community context must be considered simultaneously when facilitating and assessing behavioral interventions. Sterk, C., Elifson, K., and Theall, K. Individual Action and Community Context: the Health Intervention Project. *Am. J. Prev. Med.*, 32(6 Suppl), pp. S177-S181, 2007.

### Cigarette Smoking Rates in an Adolescent Treatment Sample at Eight-Year Follow Up

This study examined the relationship between cigarette smoking and alcohol use outcomes over an 8-year period following treatment for adolescent alcohol and other drug (AOD) use disorders. A sample of 166 adolescents were recruited during inpatient AOD abuse treatment. Included were 123 (74% of the full sample) participants, of whom 41% were female, 81% identified themselves as White and who averaged 15.9 years of age (SD = 1.3) when entering treatment. Using interviews conducted at the time of treatment and 2-, 4-, 6- and 8-years post-treatment, the investigators found that 26% of participants had quit smoking for > 1 year at the 8-year assessment, while 44% reported persistent smoking over time. Overall smoking rates decreased significantly over time. Those with the highest alcohol involvement trajectory reported significantly greater likelihood of persistent smoking as well as higher current smoking and cigarette consumption across time points. The investigators reported that the significant declines observed in smoking from adolescence into young adulthood were contrary to expectations, indicating that this behavior may be less stable than previously thought among adolescent AOD abusers. Smoking involvement over time was greater within the highest alcohol use trajectory, consistent with previous evidence for a positive relationship between these behaviors'. However, when compared with the general population smoking rates remained very high regardless of alcohol involvement. Thus, individuals treated for AOD abuse as adolescents remained at elevated risk for tobacco related disease regardless of post-treatment AOD use outcomes. Myers, M., Doran, N., and Brown, S. Is Cigarette Smoking Related to Alcohol Use During the 8 Years Following Treatment for Adolescent Alcohol and Other Drug Abuse? *Alcohol Alcohol*, 42(3), pp. 226-233, 2007.

### Adult Smokers in Colombia: Who Isn't Giving It Up?

Without ongoing surveillance systems to assess tobacco product demand and exposure levels, many low and middle income countries monitor smoking via periodic cross-sectional surveys. In this article, the authors provide updated estimates for the prevalence of adult smoking in Colombia and contribute additional information useful for tobacco control initiatives. Data are from the 2003 Colombian National Study of Mental Health (NSMH). A national probability sample of 4426 adults (age 18-65) was assessed via a computer-assisted interview. An estimated 49% of the adult population had smoked at least once in their lifetimes; one in three adults (31%) had smoked regularly. Nearly half of regular smokers had been able to quit (44%; 95% CI=40-48). Several personal and smoking-related characteristics were associated

with failing to quit: being a younger age, employed as compared to being a homemaker, and a history of daily use. Quitters and non-quitters were equivalent with respect to sex, educational status, and age of smoking onset. These findings may help guide tobacco control activities in Colombia and other low and middle income countries. Storr, C., Cheng, H., Posada-Villa, J., Aguilar-Gaxiola, S., and Anthony, J. Adult Smokers in Colombia: Who Isn't Giving It Up? *Addict Behav.*, 33(3), pp. 412-421, 2008.

#### Depressive Symptomatology in Young Adults with a History of MDMA Use: A Longitudinal Analysis

Research suggests that methylenedioxymethamphetamine (MDMA)/ ecstasy can cause serotonin depletion as well as serotonergic neurodegradation that may result in depression. This longitudinal study used the Beck Depression Inventory (BDI-II) to assess depressive symptomatology every six months over a two-year period among a community sample of young adult MDMA/ecstasy users (n = 402). Multilevel growth modeling was used to analyze changes in BDI scores. Between baseline and 24 months, the mean BDI score declined from 9.8 to 7.7. Scores varied significantly across individuals at baseline and declined at a rate of 0.36 points every six months. Persons with higher baseline scores were more likely to have their scores decrease over time. Several factors were significantly associated with score levels, independent of time: gender - men's scores were lower than women's; ethnicity - whites' scores were lower than those of non-whites; education - persons with at least some university education had scores that were lower than those without any college experience; benzodiazepines - current users' scores were higher than non-users; opioids - current users' scores were higher than non-users; and cumulative ecstasy use - people who had used MDMA more than 50 times had scores that were higher than persons who had used the drug less often. The results reported here show low levels of depressive symptoms among a sample that, after 24 months, consisted of both current and former MDMA users. The low and declining mean scores suggest that for most people MDMA/ecstasy use does not result in long-term depressive symptomatology. Falck, R., Jichuan Wang, and Carlson, R. Depressive Symptomatology in Young Adults with a History of MDMA Use: A Longitudinal Analysis. *J. Psychopharmacol.*, 22(1), pp. 47-54, 2008.

#### An Investigation of a Personal Norm of Condom-Use Responsibility among African American Crack Cocaine Smokers

The purpose of this study was to investigate the unique contribution of a personal norm of condom-use responsibility to the formation of intentions to reduce risks for HIV by using male condoms during vaginal sex. Data were collected from 402 male and 157 female heterosexual African American crack cocaine smokers in Houston, Texas, US. Two structural equation models of the intention to use a condom with the last sex partner were estimated. One model included measures of condom-use attitudes, subjective norms and condom-use self-efficacy. A second model included these three measures and a fourth measure of a personal norm of condom-use responsibility. Separate models were estimated for men and women. The addition of a personal norm of condom-use responsibility provided a significantly better fit to the data than did models including only outcome expectations, subjective norms and self-efficacy. Results also showed distinctly different underlying cognitive structures of condom-use intention for men and women. A personal norm of condom-use responsibility had a strong direct effect on men's intentions to use condoms with the last sex partner. Other variables appeared to have no direct effect on men's intentions. Women's intentions were strongly influenced by a personal norm and social subjective norms. Situational self-efficacy and outcome expectations had weaker, yet significant, effects on women's intentions. These findings suggest promising directions for the development of sexual risk reduction interventions that emphasize the effect of condom-use responsibility on men's intentions to use condoms. Williams, M., Bowen, A., Ross, M., Timpson, S., Pallonen, U., and Amos, C. An Investigation of a Personal Norm of Condom-Use Responsibility among African American Crack Cocaine Smokers. *AIDS Care*, 20(2), pp. 225-234, 2008.

### An Examination of Perceived Norms and Exchanging Sex for Money or Drugs among Women Injectors in Baltimore, MD

Injection drug users who exchange sex for money or drugs may serve as a bridge group for transmitting HIV between injectors and non-injectors. While many individual characteristics have been linked to exchanging sex, little attention has been given to the influence of social network members. The present study assessed the relationship between exchanging sex and perceptions of peers' sex exchange behaviour and attitude toward sex exchange. The sample was composed of 267 women heroin and cocaine injectors in Baltimore, MD, USA. The results indicate that women who believed that their friends exchanged sex were more than twice as likely to exchange sex in the past 90 days (95% CI: 1.49-2.70). Participants who thought their peers disapproved of sex exchange were 20% less likely to exchange sex (95% CI: 0.67-0.95). These findings suggest the need for peer education interventions that promote norms about safer behaviours. Davey-Rothwell, M., and Latkin, C. An Examination of Perceived Norms and Exchanging Sex for Money or Drugs among Women Injectors in Baltimore, MD. *Int. J. STD AIDS*, 19(1), pp. 47-50, 2008.

### Income Generating Activities of People who Inject Drugs

Injection drug users (IDU) commonly generate income through prohibited activities, such as drug dealing and sex trade work, which carry significant risk. However, little is known about the IDUs who engage in such activities and the role of active drug use in perpetuating this behavior. Researchers evaluated factors associated with prohibited income generation among participants enrolled in the Vancouver Injection Drug Users Study (VIDUS) using logistic and linear regression. They examined which sources of income respondents would eliminate if they did not require money to pay for drugs. Among 275 IDUs, 145 (53%) reported engaging in prohibited income generating activities in the past 30 days. Sex work and drug dealing accounted for the greatest amount of income generated. Non-aboriginal females were the group most likely to report prohibited income generation. Other variables independently associated with prohibited income generation include daily heroin injection (AOR=2.3) and daily use of crack cocaine (AOR=3.5). Among these individuals, 68 (47%) indicated they would forgo these earnings if they did not require money for illegal drugs, with those engaged in sex trade work (62%) being most willing to give up their illegal source of income. These findings suggest that the costs associated with illicit drugs are compelling IDUs, particularly those possessing markers of higher intensity addiction, to engage in prohibited income generating activities. These findings also point to an opportunity to explore interventions that relieve the financial pressure of purchasing illegal drugs and reduce engagement in such activities, such as low threshold employment and expansion of prescription and substitution therapies. Debeck, K., Shannon, K., Wood, E., Li, K., Montaner, J., and Kerr, T. Income Generating Activities of People who Inject Drugs. *Drug Alcohol Depend.*, 91(1), pp. 50-56, 2007.

### Gender Differences in Drug Use and Sexual Risk Behaviors among Non-Injecting Heroin Users in Puerto Rico

During the 1990s non-injected heroin use (NIHU) increased notably in several countries. However, few studies have actually examined the drug-using practices and other problem behaviors of NIHUs. In this study, researchers compared male and female NIHUs from Puerto Rico across a number of domains. Recruitment proceeded through visits to drug-copping areas and the local hangouts in their vicinity. Subjects were eligible if they were 18 to 25 years old, had never injected any drugs, and had recently used heroin or cocaine. Study participants were administered a computer-assisted personal interview. Of the 412 NIHUs recruited at the time of this study, 74 (18.0%) were females. Female NIHUs were more likely to report sexual assaults and more likely to manifest severe symptomatology of PTSD than male NIHUs (35.1% vs. 3.6%,  $p<.01$ , and 40.5% vs. 25.7%,  $p=.01$ , respectively). Females were less likely to report a source of emotional support than males (86.5% vs. 95.3%,  $p<.01$ ). Close to one in four of the females (23.0%) reported a history of sexually transmitted infections, compared to three percent of the males

( $p < .01$ ). HIV seroprevalence among females was 4.3% compared to 0.6% among males ( $p = .01$ ). These findings suggest that female heroin users have a host of different needs compared to male heroin users. Given the scarcity of existing programs for female drug users in Puerto Rico, designing supportive systems that effectively address the specific needs of drug-using women should become a high-priority public health issue. Sosa-Zapata, I., Colón, H., Robles, R., and Cabassa, M. Gender Differences in Drug Use and Sexual Risk Behaviors among Non-Injecting Heroin Users in Puerto Rico., *P.R. Health Sci. J.*, 26(3), pp. 205-211, 2007.

#### Potential Risk Factors for Injecting among Mexican American Non-Injecting Heroin Users

Researchers examined potential risk factors for initiating, resuming, and transitioning to injecting in a prospective cohort study of 300 Mexican American non-injecting heroin users (NIUs) with distinct injecting histories (i.e., never vs. former injectors). Participants were recruited using multiple sampling approaches, including respondent driven sampling and outreach. The majority of participants were male (77%) and the average age was 22 years (females were significantly older, at 23 years, compared to males, at 21 years,  $p < .001$ ). NIUs with an injecting history were more likely to use heroin with an IDU, and women were significantly more likely than men to have an IDU sex partner. The young age of the study sample and length of use of non-injecting heroin (for many, more than 4 years of use) suggest the NIU population is at high risk for transitioning to injection drug use. The study also found the cultural characteristic of "fatalism" -- a belief that one's fate is determined by destiny and is inevitable -- among study participants. Former injectors reported that they expected one day to acquire or transmit an infectious disease, including HIV, HBV, or HCV. Attitudes about injecting, perceived vulnerability for infections, fatalism, and length of time using non-injection heroin were found to be important factors for predicting resumption of injecting among former IDUs. These findings bring to light culturally unique risk factors for injecting that may be incorporated into interventions appropriate to the cultural and social context of the Mexican American community. Valdez, A., Neaigus, A., and Cepeda, A. Potential Risk Factors for Injecting among Mexican American Non-Injecting Heroin Users. *J. Ethn. Subst. Abuse*, 6(2), pp. 49-73, 2007.

#### The Impact of Education and Race/Ethnicity Differences on Alcohol Dependence

This study attempts to clarify social inequalities in alcohol dependence by investigating SES and race-ethnicity effects on the development of alcohol dependence following first alcohol use. The literature has shown that while lower socioeconomic status (SES) is related to higher risk for alcohol dependence, minority race-ethnicity is often associated with lower risk. Cross-sectional data from the National Epidemiologic Survey on Alcohol and Related Conditions ( $n = 43,093$ ). Survival analysis was used to model alcohol dependence onset according to education, race-ethnicity and their interaction. Compared with non-Hispanic whites, age-adjusted and sex-adjusted risks of alcohol dependence were lower among Blacks and Hispanics and higher among American Indians. Individuals without a college degree had higher risks of alcohol dependence than individuals with a college degree or more; however, the magnitude of risk varied significantly by race-ethnicity; odds ratios for less than a college degree were 1.12, 1.46, 2.24, 2.35 and 10.99 among Hispanics, whites, Blacks, Asians, and American Indians, respectively. There was no association between education and alcohol dependence among Hispanics. Race-ethnicity differences in the magnitude of the association between education and alcohol dependence suggest that aspects of racial-ethnic group membership mitigate or exacerbate the effects of social adversity. Gilman, S., Breslau, J., Conron, K., Koenen, K., Subramanian, S., and Zaslavsky, A. Education and Race-Ethnicity Differences in the Lifetime Risk of Alcohol Dependence. *J. Epidemiol. Community Health*, 62(3), pp. 224-230, 2008.

### Family and School Associations of Emotional Distress for Asian-American Sexual Minority Youth

This study examined family and school correlates of emotional distress among Asian-American sexual minority youth in the Midwestern United States. Responses from 91 predominantly Asian-American youth who participated in a state-wide, school-based census survey, the 2001 Minnesota Student Survey (MSS), and reported recent same-gender sexual activity were analyzed. The students ranged in age from 13-19 years and 37% of respondents were female. Results showed that sexual minority youth who perceived lower levels of family caring and those with negative perceptions of school climate reported lower self-esteem, which was associated with greater emotional distress. These results highlight the importance of safe and caring environments, and culturally sensitive support for Asian-American sexual minority adolescents. Homma, Y., and Saewyc, E. The Emotional Well-Being of Asian-American Sexual Minority Youth in School. *J. LGBT Health Res.*, 3(1), pp. 67-78, 2007.

### Challenges to HIV Prevention among Men Who Have Sex with Transgender Women

Although transgender women are acknowledged as a priority population for HIV prevention, there is little knowledge regarding men who have sex with transgender women (MSTGWs). MSTGWs challenge conventional sexual orientation categories in public health and HIV prevention research, and warrant increased attention from the public health community. This study utilized qualitative techniques to assess how MSTGWs describe their sexual orientation identities, and to explore the correspondence between men's identities and sexual behaviors with transgender women. The investigators conducted in-depth semi-structured individual interviews with 46 MSTGWs in San Francisco. They observed a diversity in the ways participants identified and explained their sexual orientation, and found no consistent patterns between how men described their sexual orientation identity versus their sexual behavior and attraction to transgender women. Findings from this qualitative study question the utility of category-based approaches to HIV prevention with MSTGWs and offer insights into developing HIV interventions for these men. Operario, D., Burton, J., Underhill, K., and Sevelius, J. Men Who Have Sex with Transgender Women: Challenges to Category-Based HIV Prevention. *AIDS Behav.*, 12(1), pp. 18-26, 2008.

### Fast Track Randomized Controlled Trial to Prevent Externalizing Psychiatric Disorders: Findings From Grades 3 to 9

This study tests the efficacy of the Fast Track Program in preventing antisocial behavior and psychiatric disorders among groups varying in initial risk. Schools within four sites (Durham, NC; Nashville, TN; Seattle, WA; and rural central Pennsylvania) were selected as high-risk institutions based on neighborhood crime and poverty levels. After screening 9,594 kindergarteners in these schools, 891 highest risk and moderate-risk children (69% male and 51% African American) were randomly assigned by matched sets of schools to intervention or control conditions. The 10-year intervention (begun in 1991 with three yearly cohorts) included parent behavior-management training, child social-cognitive skills training, reading tutoring, home visiting, mentoring, and a universal classroom curriculum. Outcomes included criterion counts and psychiatric diagnoses after grades 3, 6, and 9 for conduct disorder, oppositional defiant disorder, attention-deficit/hyperactivity disorder, any externalizing disorder, and self-reported antisocial behavior. Grade 9 outcomes were assessed between 2000 and 2003, depending upon cohort. Significant interaction effects between intervention and initial risk level were found at each age but most strongly after grade 9. Assignment to intervention had a significant positive effect in lowering criterion count scores and diagnoses for conduct disorder, attention-deficit/hyperactivity disorder, and any externalizing disorder, and lowering antisocial behavior scores, but only among those at highest risk initially. Prevention of serious antisocial behavior can be efficacious across sex, ethnicity, and urban/rural residence, but screening is essential. Bierman, K.L., Coie, J.D., Dodge, K.A., Foster, E.M., Greenberg, M.T., Lochman, J.E., McMahon, R.J., and Pinderhughes, E.E. Fast Track Randomized Controlled Trial to Prevent Externalizing Psychiatric Disorders: Findings from Grades 3 to 9. *J. Am. Acad. Child Adolesc. Psychiatry*, 46(10), pp. 1250-1262, 2007.

### Cueing Prenatal Providers to Counsel Pregnant Women with Behavioral Health Risks

This study examined the impact of the Health in Pregnancy (HIP) computer program on prenatal providers' counseling about behavioral risks with patients, in particular risk for intimate partner violence (IPV) during pregnancy. English-speaking women 18 years or older, less than 26-weeks pregnant, and receiving prenatal care at one of five participating clinics in the San Francisco area, were randomized in parallel groups in a controlled trial. Participants reporting one or more risks were randomized to intervention or control in stratified blocks. Providers received summary "cueing sheets" alerting them to their patient's risk(s) and suggesting counseling statements. Thirteen percent (37/286) of the sample reported current IPV. Provider cueing resulted in 85% of the IPV-intervention group reporting discussions with their provider, compared to 23.5% of the control group ( $p < 0.001$ ). Thus IPV discussions were influenced strongly by cueing providers. Provider cueing may be an effective and appropriate adjunct to routine risk counseling in prenatal care. Calderón, S., Gilbert, P., Jackson, R., Kohn, M., and Gerbert, B. Cueing Prenatal Providers Effects on Discussions of Intimate Partner Violence. *Am. J. Prev. Med.*, 34(2), pp. 134-137, 2008.

### Brief Interventions for College Students Can Influence Multiple Health Behaviors

This study examined the effects of brief image-based interventions, including a multiple behavior health contract, a one-on-one tailored consultation, and a combined consultation plus contract intervention, for impacting multiple health behaviors of students in a university health clinic. A total of 155 college students attending a major southern university were recruited to participate in a study evaluating a health promotion program titled Project Fitness during the fall 2005 and spring 2006. The majority of the participating students were female (66%), with a mean age of 19 years. The sample was diverse, with a slight majority being Caucasian (52%), followed by Hispanic (14%), African American (11%), and Asian youth (7%). Participants were randomly assigned to one of three treatments as they presented at the clinic: 1) a multiple behavior health contract, 2) a one-on-one tailored consultation, or 3) a combined consultation plus contract intervention. Baseline and 1-month post-intervention data were collected using computer-assisted questionnaires in a quiet office within the student health clinic. Omnibus repeated-measures analyses of variance were significant for drinking driving behaviors,  $F(2,136) = 4.43$ ,  $p = .01$ , exercise behaviors,  $F(5,140) = 6.12$ ,  $p = .00$ , nutrition habits,  $F(3,143) = 5.37$ ,  $p = .00$ , sleep habits,  $F(2,144) = 5.03$ ,  $p = .01$ , and health quality of life,  $F(5,140) = 3.09$ ,  $p = .01$ , with improvements on each behavior across time. Analysis of group-by-time interaction effects showed an increase in the use of techniques to manage stress,  $F(2,144) = 5.48$ ,  $p = .01$ , and the number of health behavior goals set in the last 30 days,  $F(2,143) = 5.35$ ,  $p = .01$ , but only among adolescents receiving the consultation, or consultation plus contract. Effect sizes were consistently larger across health behaviors, and medium in size, when both consult and contract were used together. Brief interventions using a positive goal image of fitness, and addressing a number of health habits using a contract and consultation strategy alone, or in combination, have the potential to influence positive changes in multiple health behaviors of college students attending a university primary health care clinic. Werch, C., Bian, H., Moore, M., Ames, S., DiClemente, C., and Weiler, R. Brief Multiple Behavior Interventions in a College Student Health Care Clinic. *J. Adolesc. Health*, 41(6), pp. 577-585, 2007.

### Diet Initiation Predicts Smoking Initiation among Adolescent Females

This study was aimed at examining the relation between dieting and smoking initiation among adolescents. Prospective data from a nationally representative study were used. Specifically, the study used two waves (1994 to 1996) of the National Longitudinal Study of Adolescent Health. The sample included 7795 non-Latino Caucasian and non-Latino African-American adolescents. Dieting status was the independent variable and trying smoking and initiation of regular smoking were the dependent variables. Covariates included age, ethnicity, overweight status, false self-perception about being overweight, and availability of cigarettes at home. Logistic regression and latent transition analyses were used. Females had a higher prevalence of dieting (55%) when compared with males (25%). Dieting initiation was a significant



predictor for initiation of regular smoking among females (OR = 1.94,  $p = .010$ ), but not among males. Inactive dieting was a significant predictor among males (OR = 1.74,  $p = .031$ ), but not among females. Compared to nondieters, initiating and consistent female dieters reported a higher probability of transitioning to having tried regular smoking, although results from logistic regression suggested that the association between consistent dieting and initiation of regular smoking was not significant. This analysis suggests that there is a positive relation between initiating dieting and initiating regular smoking among females, but among males it is the inactive dieters who show a positive relationship. Results illustrate the importance of examining the association between dieting and the initiation of regular smoking. Maldonado-Molina, M., Komro, K., and Prado, G. Prospective Association between Dieting and Smoking Initiation among Adolescents. *Am. J. Health Promot.*, 22(1), pp. 25-32, 2007.

### Systemic Factors that Influence Screening for Prenatal Behavioral Risks

This study examined how systemic factors might facilitate or impede providers' ability to screen for and intervene on prenatal behavioral risks. Eight focus groups of 60 prenatal care providers were convened to explore methods for assessing and counseling pregnant women about tobacco, alcohol, and illicit drug use. Because practice setting was often mentioned as either an inducement or barrier to risk prevention, a re-analysis of focus group transcripts to examine systemic factors was conducted. Results indicated that practice setting strongly influenced providers' behavior, and settings differed by continuity of care, availability of resources, and organized support for risk prevention. The most striking contrasts were found between private practice and a large HMO. Thus, each setting had features that facilitated prevention counseling. Understanding such systemic factors could lead to improved risk prevention practices during pregnancy across all health care settings. Gilbert, P., Herzig, K., Thakar, D., Vilorio, J., Bogetz, A., Danley, D., Jackson, R., and Gerbert, B. How Health Care Setting Affects Prenatal Providers' Risk Reduction Practices: A Qualitative Comparison of Settings. *Women Health*, 45(2), pp. 41-57, 2007.

### Measuring Community-Wide Prevention Collaboration

This study assesses a measure of community-wide collaboration on prevention-specific activities (i.e., prevention collaboration) in context of the theory of community change used in the Communities That Care prevention system. Using data from a sample of 599 community leaders across 41 communities, the measure was examined with regard to its factor structure, associations with other concurrent community-level measures, and prediction by individual- and community-level characteristics. Results of multilevel confirmatory factor analysis provide evidence for the construct validity of the measure and indicate significant ( $p < .05$ ) associations with concurrent validity criteria. Female community leaders reported significantly higher levels of prevention collaboration and community leaders sampled from religious organizations reported lower levels of prevention collaboration than did their respective counterparts. Although no community-level characteristics were associated significantly with prevention collaboration, community clustering accounted for 20-28% of the total variation in the measure. Findings support the use of this measure in assessing the importance of collaboration in community-based prevention initiatives. Brown, E., Hawkins, J., Arthur, M., Abbott, R., and Van Horn, M. Multilevel Analysis of a Measure of Community Prevention Collaboration. *Am. J. Community Psychol.*, 41(1-2), pp. 115-126, 2008.

### Drinking By High School Seniors: Implications for Prevention

The transition from high school to college provides a potentially critical window to intervene and reduce risky behavior among adolescents. This study examined high school seniors' motivations (e.g., social, coping, enhancement) for alcohol use and patterns of use. Latent class analysis was used to examine the relationship between different patterns of drinking motivations and behaviors in a sample of 12th graders ( $N = 1,877$ ) from the 2004 Monitoring the Future survey. A person-centered approach was used to identify types of motivations that cluster together within individuals and relates membership in these profiles to drinking behaviors. Results suggest four profiles of drinking motivations for both boys and girls, including

Experimenters, Thrill-seekers, Multi-reasoners, and Relaxers. Early initiation of alcohol use, past year drunkenness, and drinking before 4 P.M. were associated with greater odds of membership in the Multi-reasoners class as compared to the Experimenters class. Although the strength of these relationships varied for boys and girls, findings were similar across gender suggesting that the riskiest drinking behavior was related to membership in the Multi-reasoners class. These findings can be used to inform prevention programming. Specifically, targeted interventions that tailor program content to the distinct drinking motivation profiles described above may prove to be effective in reducing risky drinking behavior among high school seniors. Coffman, D., Patrick, M., Palen, L., Rhoades, B., and Ventura, A. Why Do High School Seniors Drink? Implications for a Targeted Approach to Intervention. *Prev. Sci.*, 8(4), pp. 241-248, 2007.

#### Sexual Behavior during Emerging Adulthood

Emerging adults ( $M = 18.99$  years,  $SD = .50$ ) completed cross-sectional questionnaires ( $N = 943$ ) and targeted follow-up telephone surveys ( $N = 202$ ) across the transition to college. Gender, personal goals (dating, friendship, academic), and past sexual behavior were examined as predictors of reasons to have and not to have sex. Men rated Self-focused reasons to have sex as more important; women rated Partner-focused reasons to have sex and Ethical reasons not to have sex as more important. Importance of Pregnancy/ STD reasons not to have sex did not differ by gender. Before college entrance, sexual history and personal goals predicted endorsement of reasons for/against sex. Personal goals predicted first intercourse during freshman year. Limitations of the study include the single university sample and use of closed-ended self-report measures. Personal goals and reasons for/against sex are associated with sexual behavior and should be addressed in programs designed to promote sexual health among emerging adult college students. Patrick, M., Maggs, J., and Abar, C. Reasons to Have Sex, Personal Goals, and Sexual Behavior during the Transition to College. *J. Sex Res.*, 44(3), pp. 240-249, 2007.

#### Relation of Executive Function to Risk Behaviors in Female College Students

Relations among executive function, behavioral approach sensitivity, emotional decision making, and risk behaviors (alcohol use, drug use, and delinquent behavior) were examined in single female college students ( $N = 72$ ). Hierarchical multiple regressions indicated a significant Approach Sensitivity x Working Memory interaction in which higher levels of alcohol use were associated with the combination of greater approach tendency and better working memory. This Approach Sensitivity x Working Memory interaction was also marginally significant for drug use and delinquency. Poor emotional decision making, as measured by a gambling task, was also associated with higher levels of alcohol use, but only for individuals low in inhibitory control. Findings point to the complexity of relations among aspects of self-regulation and personality and provide much needed data on neuropsychological correlates of risk behaviors in a nonclinical population. Patrick, M.E., Blair, C., and Maggs, J.L. Executive Function, Approach Sensitivity, and Emotional Decision Making as Influences on Risk Behaviors in Young Adults. *J. Clin. Exp. Neuropsychol.*, 30(4), pp. 449-462, 2008.

#### Four Developmental Trajectories of Adolescent Physical Aggression

Latent growth mixture modeling was used to identify discrete patterns of physical aggression from Grades 7 to 11 among a sample of 1,877 youth (952 boys and 925 girls). These middle school students were participating in a field trial designed to test the effects of a drug prevention program. This study included only those students who were randomly assigned to the control condition schools. Students completed annual paper-and-pencil surveys in school at Grades 7 through 11. Four trajectory classes adequately explained the development of physical aggression in both boys and girls: Low/No Aggression; Persistent High Aggression; Desisting Aggression, characterized by decreasing risk throughout adolescence; and Adolescent Aggression, characterized by low early risk that increases until Grade 9, levels out, and then declines in late adolescence. Girls were less likely than boys were to be in any trajectory besides the

Low/No Aggression trajectory. Parental supervision, deviant peer association, academic orientation, impulsivity, and emotional distress at Grade 7 were all strongly associated with trajectory class membership. These associations did not differ by gender. These findings strongly suggest that the processes involved in the development of physical aggression in adolescence operate similarly in boys and girls. Martino, S., Ellickson, P., Klein, D., McCaffrey, D., and Edelen, M. Multiple Trajectories of Physical Aggression among Adolescent Boys and Girls. *Aggress. Behav.*, 34(1), pp. 61-75, 2008.

#### Indirect Measures of Alcohol-related Cognitions Predict Use

Recently there has been increased interest in the role of implicit cognitive processes in the development of addictive behaviors. In this study, the authors compared 3 indirect measures of alcohol-related cognitions in the prospective prediction of alcohol use in at-risk adolescents. Implicit alcohol-related cognitions were assessed in 88 Dutch at-risk adolescents ranging in age from 14 to 20 years (51 males, 37 females) by means of varieties of word association tasks, Implicit Association Tests, and Extrinsic Affective Simon Tasks adapted for alcohol use. Alcohol use and alcohol-related problems were measured with self-report questionnaires at baseline and after 1 month. Results showed that the indirect measures predicted unique variance in prospective alcohol use after controlling for the direct measure of alcohol-related cognitions and background variables. The results indicate that the word association tasks were the best indirect measure of alcohol-related cognitions. These indirect measures appear to assess cognitive motivational processes that affect behavior in ways not reflected by direct measures of alcohol-related cognitions. Thush, C., Wiers, R., Ames, S., Grenard, J., Sussman, S., and Stacy, A. Apples and Oranges? Comparing Indirect Measures of Alcohol-Related Cognition Predicting Alcohol Use in At-Risk Adolescents. *Psychol. Addict. Behav.*, 21(4), pp. 587-591, 2007.

#### Response Inconsistencies for Sex and Drug Use Behaviors among South African High School Students

This study aims to describe patterns of inconsistent reports of sexual intercourse among a sample of South African adolescents. Consistency of reported lifetime sexual intercourse was assessed using five semiannual waves of data. Odds ratios related inconsistent reporting to demographic variables and potential indicators of general and risk-behavior-specific reliability problems. Participants were high school students from Mitchell's Plain, a low-income township near Cape Town, South Africa. Students (N = 2,414) were participating in a research trial of a classroom-based leisure, life skill, and sexuality education program. The sample for the present study was restricted to participants who reported lifetime sexual intercourse in at least one of the first four survey assessments (n = 713). This subsample was mostly male (69%) and "colored" (mix of African, Asian, and European ancestry) and had a mean age at baseline of 14 years. Of the sexually active participants in the sample, nearly 40% reported being virgins after sexual activity had been reported at an earlier assessment. Inconsistent reporting could not be predicted by gender or race or by general indicators of poor reliability (inconsistent reporting of gender and birth year). However individuals with inconsistent reports of sexual intercourse were more likely to be inconsistent reporters of substance use. These results suggest that researchers need to undertake efforts to deal specifically with inconsistent risk behavior data. These may include modification of data collection procedures and use of statistical methodologies that can account for response inconsistencies. Palen, L., Smith, E., Caldwell, L., Flisher, A., Wegner, L., and Vergnani, T. Inconsistent Reports of Sexual Intercourse among South African High School Students. *J. Adolesc. Health*, 42(3), pp. 221-227, 2008.

### **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

#### Craving, Withdrawal, and Smoking Urges on Days Immediately Prior to Smoking Relapse

Dr. Allen and colleagues at the University of Minnesota conducted this study to identify temporal patterns of standardized symptom scores (for craving, withdrawal, and smoking urges) that would either refute or support the assumption that these factors are key contributors to relapse in smokers. Data were analyzed

from 137 female smokers, aged 18-40 years, who completed 30 days of a protocol for a longitudinal smoking cessation trial. All subjects were followed post quit date, regardless of their subsequent smoking status. Measures of craving, withdrawal and smoking urges were completed at baseline and daily for 30 days, beginning on their quit date. A total of 26 women quit smoking and 11 relapsed. A consistent symptom severity pattern was observed, in which craving, withdrawal, and smoking urges increased leading up to the day of relapse and then subsided quickly. These findings suggest an association between patterns of symptom intensity and relapse. The authors conclude that frequent symptom monitoring might be clinically important for relapse prevention. Allen, S.S., Bade, T., Hatsukami, D., and Center, B. Craving, Withdrawal, and Smoking Urges on Days Immediately Prior to Smoking Relapse. *Nicotine & Tobacco Research*, 10(1), pp. 35-45, 2008.

#### Cigarette Smoking in Opioid-Using Patients Presenting for Hospital-Based Medical Services

The authors examined cigarette smoking practices in 126 out-of-treatment opioid users presenting at a hospital for non-psychiatric medical services. In general, the study found the prevalence of smoking (92%) to be comparable to that reported in methadone treatment samples. Nineteen percent preferred unfiltered cigarettes. Women were more likely to smoke menthol cigarettes; men were more likely to smoke unfiltered cigarettes. Caucasians tended to smoke more than other ethnicities and exhibited greater dependence. The authors conclude that opioid users are a particularly high-risk group for continued smoking and they highlight the need for treatment programs to include smoking cessation interventions. Haas, A.L., Sorensen, J.L., Hall, S.M., Lin, C., Delucchi, D., Sporer, K., and Chen, T. Cigarette Smoking in Opioid-Using Patients Presenting for Hospital-Based Medical Services. *The American Journal on Addictions*, 17, pp. 65-69, 2008.

#### Older Versus Younger Treatment-Seeking Smokers

The purpose of this study was to describe treatment seeking smokers aged 50 years or older and compare them with younger smokers (aged <50) presenting to the same smoking treatment facility during the same time period. The subjects (n=810) were participating in one of two studies: one was limited to smokers aged 50 years or older; the other was open to smokers aged 18 years or older. As predicted, smokers aged 50+ were more tobacco dependent, had better psychological functioning, and had poorer physical functioning than those aged <50. Contrary to predictions, no differences were found in motivation to quit cigarette smoking or in alcohol use. Women aged 50+ were less likely to report marijuana use than women aged <50, and less likely than men to receive a positive diagnosis for alcohol abuse. Despite higher scores on measures of tobacco dependence, older smokers were less likely to be diagnosed as tobacco dependent or as having tobacco withdrawal using DSM-IV criteria. Rates of alcohol abuse and dependence were high in both age groups, but were higher for smokers aged <50. Hall, S.M., Humflet, G.L., Gorecki, J.A., Munoz, R.F., Reus, V.I., and Prochaska, J.J. Older Versus Younger Treatment-Seeking Smokers: Differences in Smoking Behavior, Drug and Alcohol Use, and Psychosocial and Physical Functioning. *Nicotine & Tobacco Research*, 10(3), pp. 463-470, 2008.

#### Message Framing for Smoking Cessation

Research on message framing tests whether or not gain-framed messages (i.e., emphasizing the benefits of quitting smoking) are more persuasive in promoting cessation than loss-framed messages (i.e., emphasizing the costs of continuing to smoke). The authors conducted this study to examine how gender differences in perceptions of risk of quitting smoking influence the effects of framed interventions. Participants were 249 adult smokers (129 females, 120 males) in a clinical trial of message framing for smoking cessation with bupropion. The results showed that women reported a higher perceived risk of cessation than men. Participants who anticipated high risks associated with quitting smoking reported fewer days to relapse. Further, females in the gain-framed condition who reported low perceived risks of cessation had a greater number of days to relapse, as opposed to females in the loss-framed condition. These findings suggest that

message framing interventions for smoking cessation should consider the influence of gender and risk perceptions associated with quitting on the effectiveness of framed interventions. Toll, B.A., O'Malley, S.S., Mazure, C.M., Latimer, A., McKee, S.A. Message Framing for Smoking Cessation: The Interaction of Risk Perceptions and Gender. *Nicotine & Tobacco Research*, 10(1), pp. 195-200, 2008.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

### Treatment of Opioid-Dependent Pregnant Women: Clinical and Research Issues

This article addresses common questions that clinicians face when treating pregnant women with opioid dependence. Guidance, based on both research evidence and the collective clinical experience of the authors, which include investigators in the Maternal Opioid Treatment: Human Experimental Research (MOTHER) project, is provided to aid clinical decision making. The MOTHER project is a double-blind, double-dummy, flexible-dosing, parallel-group clinical trial examining the comparative safety and efficacy of methadone and buprenorphine for the treatment of opioid dependence in pregnant women and their neonates. The article begins with a discussion of appropriate assessment during pregnancy and then addresses clinical management stages including maintenance medication selection, induction, and stabilization; opioid agonist medication management before, during, and after delivery; pain management; breast-feeding; and transfer to aftercare. Lastly, other important clinical issues including managing co-occurring psychiatric disorders and medication interactions are discussed. Jones, H.E., Martin, P.R., Heil, S.H., Kaltenbach., Selby, P., Coyle, M.G., Stine, S.M., O'Grady, K.E., Arria, A.M., and Fischer, G. Treatment of Opioid-Dependent Pregnant Women: Clinical and Research Issues. *J. Substance Abuse Treat.*, Jan 11, 2008.

### Opioid Use Disorder in the United States: Insurance Status and Treatment Access

In the United States, insurance status and rates of treatment for individuals with opioid use disorder are unknown. This study employed a cross-sectional survey: 2002-2004 National Survey on Drug Use and Health (NSDUH). Bivariate and multivariate associations between demographics, treatment and insurance status and presence or absence of opioid use disorder were investigated. On unadjusted analysis, young respondents, respondents of Hispanic ethnicity (OR 1.5; 95% CI 1.1-2.2), unemployed respondents (OR 2.6; 95% CI 1.8-3.8) and respondents with Medicaid (OR 4.5; 95% CI 2.5-8.3) or lack of insurance (OR 3.2; 95% CI 1.8-5.9) were more likely to have opioid use disorder. On unadjusted analysis among those with any substance use disorder, 12-16 year olds were more likely to have opioid use disorder (OR 3.4; 95% CI 2.0-5.8) than a non-opioid substance use disorder, as were women (OR for men 0.6; 95% CI 0.5-0.7) and unemployed respondents (OR 1.5; 95% CI 1.02-2.1). Only 15.2% of those with past-year opioid use disorder received treatment in the past year. Respondents treated for opioid use had higher rates of Medicaid ( $p<0.01$ ), Medicare ( $p<0.01$ ) and other public assistance ( $p=0.01$ ) compared with those treated for other substances. Treatments for opioid use were more likely to be hospital ( $p=0.04$ ) and inpatient rehabilitation ( $p=0.02$ ) settings compared to treatment for other substance use. Among those with opioid use disorder, not being employed was independently associated with receiving treatment (AOR 3.5; 95% CI 1.4-8.5). The authors conclude that in the U.S., high rates of unemployment, Medicaid and uninsurance among those with opioid use disorder and low rates of treatment suggest that efforts to expand treatment must include policy strategies to help reach a population with significant barriers to treatment access. Becker, W.C., Fiellin, D.A., Merrill, J.O., Schulman, B., Finkelstein, R., Olsen, Y. et al. Opioid Use Disorder in the United States: Insurance Status and Treatment Access. *Drug Alcohol Depend.*, 94, pp. 207-213, 2008.

### Therapeutic Drug Monitoring of Nortriptyline in Smoking Cessation: A Multistudy Analysis

Multiple, controlled clinical trials support the efficacy of nortriptyline as a smoking cessation agent. Although therapeutic plasma nortriptyline concentrations (PNCs) are known for the treatment of

depression, little is known about PNCs in smoking cessation treatment. PNCs from three randomized, placebo-controlled smoking cessation trials (N=244) were analyzed both separately and pooled. PNCs normalized for dose and weight were associated with cigarettes per day and race, but not with sex or age. Greater smoking was associated with decreased normalized PNCs. In addition, both Asian and black populations had significantly higher normalized PNCs than the white populations. Weak and inconsistent associations between PNCs and self-reported side effects were observed. PNCs were linearly related to end of treatment and long-term biochemically verified smoking abstinence. Maximum therapeutic effects were observed over a range of plasma concentrations somewhat lower than those found effective for the treatment of depression. Mooney, M.E., Reus, V.I., Gorecki, J., Hall, S.M., Humfleet, G.L., Munoz, R.F. et al. Therapeutic Drug Monitoring of Nortriptyline in Smoking Cessation: A Multistudy Analysis. *Clin. Pharmacol. Ther.*, 83, pp. 436-442, 2008.

## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE & CO-OCCURRING INFECTIONS (HIV/AIDS, HCV)**

### Impact of Drug Abuse Treatment Modalities on Adherence to ART/HAART Among a Cohort of HIV Seropositive Women

Methadone maintenance is associated with improved adherence to antiretroviral therapies among HIV-positive illicit drug users; however, little information exists on whether adherence is associated with different drug abuse treatment modalities. Using longitudinal data from the Women's Interagency HIV Study, the authors evaluated the relationship between drug abuse treatment modality and adherence to antiretroviral therapies. In prospective analyses, individuals who reported accessing any drug abuse treatment program were more likely to report adherence to antiretroviral regimens  $>$  or  $=$  95% of the time (AOR = 1.39, 95% CI = 1.01-1.92). Involvement in either a medication-based or medication-free program was similarly associated with improved adherence. Drug abuse treatment programs, irrespective of modality, are associated with improved adherence to antiretroviral therapies among drug users. Concerted efforts to enroll individuals with drug use histories in treatment programs are warranted to improve HIV disease outcomes. Kapadia, F., Vlahov, D., Wu, Y., Cohen, M.H., Greenblatt, R.M., Howard, A.A., Cook, J.A., Goparaju, L., Golub, E., Richardson, J., and Wilson, T.E. Impact of Drug Abuse Treatment Modalities on Adherence to ART/HAART Among a Cohort of HIV Seropositive Women. *Am. J. Drug Alcohol Abuse*, 34(2), pp.161-170, 2008.

### Attribution of Menopause Symptoms in Human Immunodeficiency Virus-Infected or At-Risk Drug-Using Women

The objective of this study was to examine the relationship of human immunodeficiency virus (HIV) and attribution of menopausal symptoms. Peri- and postmenopausal women participating in a prospective study of HIV-infected and at-risk midlife women (the Ms. Study) were interviewed to determine whether they experienced hot flashes and/or vaginal dryness and to what they attributed these symptoms. Of 278 women, 70% were perimenopausal; 54% were HIV-infected; and 52% had used crack, cocaine, heroin, and/or methadone within the past 5 years. Hot flashes were reported by 189 women and vaginal dryness was reported by 101 women. Overall, 69.8% attributed hot flashes to menopause and 28.7% attributed vaginal dryness to menopause. In bivariate analyses, age 45 years and older was associated with attributing hot flashes and vaginal dryness to menopause, and postmenopausal status and at least 12 years of education were associated with attributing vaginal dryness to menopause, but HIV status was not associated with attribution to menopause. In multivariate analysis, significant interactions between age and menopause status were found for both attribution of hot flashes ( $P = 0.019$ ) and vaginal dryness ( $P = 0.029$ ). Among perimenopausal women, older age was independently associated with attribution to menopause for hot flashes (adjusted odds ratio = 1.2, 95% CI: 1.1-1.4,  $P = 0.001$ ) and vaginal dryness (adjusted odds ratio = 1.3, 95% CI: 1.1-1.6,  $P = 0.011$ ). None of the tested factors were independently associated with attribution to menopause among postmenopausal women. The authors conclude that tailored health education

programs may be beneficial in increasing the knowledge about menopause among HIV-infected and drug-using women, particularly those who are perimenopausal. Johnson, T.M., Cohen, H.W., Howard, A.A., Santoro, N., Floris-Moore, M., Arnsten, J.H., Hartel, D.M., and Schoenbaum, E.E. Attribution of Menopause Symptoms in Human Immunodeficiency Virus-Infected or At-risk Drug-Using Women. *Menopause*, 15(3), pp. 551-557, 2008.

#### Biochemical and Virologic Parameters in Patients Co-Infected with Hepatitis C and HIV versus Patients with Hepatitis C Mono-Infection

Previous studies of patients with hepatitis C virus (HCV) infection looking at the effect of human immunodeficiency virus (HIV) co-infection on biochemical parameters and HCV RNA level have shown conflicting results. Accurate characterization of the effect of HIV is important for evaluation and treatment of HCV in co-infected persons. The authors studied 315 HCV mono-infected and 75 HCV-HIV co-infected subjects to determine the effect of HIV on biochemical parameters and HCV RNA and to determine the predictors of elevated serum alanine aminotransferase (ALT) levels and HCV RNA levels. Results showed that the co-infected subjects were more likely to be African-American (55% vs 26%,  $P < 0.0005$ ), have used injection drugs (68% vs 60%,  $P = 0.02$ ), have detectable HCV RNA (84% vs 70.5%,  $P = 0.018$ ), have HCV RNA levels  $>6 \log_{10}$  IU/mL (60% vs 38%,  $P = 0.001$ ), and have lower mean serum ALT levels (50.4 IU/mL vs 73.7 IU/mL,  $P = 0.006$ ). In multivariable analyses, the following factors predicted an ALT level  $>50$  IU/mL:  $\log_{10}$  HCV RNA (OR, 1.15; 95% CI, 1.00 to 1.32); HIV co-infection (OR, 0.48; 95% CI, 0.25 to 0.89); and having ever been treated for HCV (OR, 1.92; 95% CI, 1.16 to 3.18). The only significant predictor of HCV RNA level  $>6 \log_{10}$  IU/mL was HIV co-infection (OR, 2.75; 95% CI, 1.46 to 5.15). Significant predictors of having a detectable HCV RNA level were female sex (OR, 3.81; 95% CI, 1.18 to 12.25); HIV co-infection (2.45; 95% CI, 1.14 to 5.26); and ever being treated for HCV (OR, 1.96; 95% CI, 1.10 to 3.48). The authors conclude that HCV-HIV co-infected persons have higher HCV RNA levels but lower serum ALT levels than HCV mono-infected patients. Criteria for performing liver biopsy and treating HCV infection in co-infected patients may need to be revisited. Butt, A.A., Tsevat, J., Ahmad, J., Shakil, A.O., Mrus, J.M. Biochemical and Virologic Parameters in Patients Co-infected with Hepatitis C and HIV Versus Patients with Hepatitis C Mono-infection. *Am. J. Med. Sci.* 333(5), pp. 271-275, 2007.

#### The Insulin-like Growth Factor Axis and Risk of Liver Disease in Hepatitis C Virus/HIV-Co-Infected Women

Insulin-like growth factor (IGF) I stimulates the proliferation of hepatic stellate cells (HSC), the primary source of extracellular matrix accumulation in liver fibrosis. In contrast, insulin-like growth factor binding protein (IGFBP) 3, the most abundant IGFBP in circulation, negatively modulates HSC mitogenesis. To investigate the role of the IGF axis in hepatitis C virus (HCV)-related liver disease among high-risk patients, the authors prospectively evaluated HCV-viremic/HIV-positive women. This study comprised a cohort investigation in which total IGF-I and IGFBP-3 were measured in baseline serum specimens obtained from 472 HCV-viremic/HIV-positive subjects enrolled in the Women's Interagency HIV Study, a large multi-institutional cohort. The aspartate aminotransferase to platelet ratio index (APRI), a marker of liver fibrosis, was assessed annually. Normal APRI levels ( $< 1.0$ ) at baseline were detected in 374 of the 472 HCV-viremic/HIV-positive subjects tested, of whom 302 had complete liver function test data and were studied. IGF-I was positively associated [adjusted odds ratio comparing the highest and lowest quartiles (AOR<sub>q4-q1</sub>), 5.83; 95% confidence interval (CI) 1.17-29.1;  $P_{\text{trend}} = 0.03$ ], and IGFBP-3 was inversely associated (AOR<sub>q4-q1</sub>, 0.13; 95% CI 0.02-0.76;  $P_{\text{trend}} = 0.04$ ), with subsequent (incident) detection of an elevated APRI level ( $> 1.5$ ), after adjustment for the CD4 T-cell count, alcohol consumption, and other risk factors. The authors conclude that high IGF-I may be associated with increased risk and high IGFBP-3 with reduced risk of liver disease among HCV-viremic/HIV-positive women. Strickler, H.D., Howard, A.A., Peters, M., Fazzari, M., Yu, H., Augenbraun, M., French, A.L.,

Young, M., Gange, S., Anastos, K., and Kovacs, A. The Insulin-like Growth Factor Axis and Risk of Liver Disease in Hepatitis C virus/HIV-co-infected Women. *AIDS*, 22(4), pp. 527-531, 2008.

#### Immune Status at Presentation to Care Did not Improve among Antiretroviral-Naive Persons from 1990 to 2006

Human immunodeficiency virus (HIV) prevention initiatives to improve access to HIV services have increased over time. Despite this, >250,000 cases of HIV infection in the US are undiagnosed, and many infected persons do not present for care until their HIV infection is advanced. Late presentation may increase the risk of HIV transmission and make HIV infection more difficult to treat effectively. With more effective HIV therapy, it has been the hope that patients might present earlier in their disease course. To assess immune status and time of HIV diagnosis in patients who newly presented for care, researchers analyzed data for the period 1990-2006 from patients who were antiretroviral naive at presentation to the Johns Hopkins HIV Clinic in Baltimore, Maryland. They compared CD4 (+) cell count and time from HIV diagnosis at presentation by demographic characteristics at enrollment. The median presenting CD4(+) cell count decreased from 371 cells/mm<sup>3</sup> during 1990-1994 to 276 cells/mm<sup>3</sup> during 2003-2006 (P<.01) overall and decreased within individual demographic groups. There was also a decrease in the median time from HIV diagnosis to presentation for care (271 days in 1990-1994 to 196 days in 2003-2006; P<.01). Multivariate analysis revealed that, in addition to CD4(+) cell count at presentation, male sex was associated with lower CD4(+) cell counts (-93 cells/mm<sup>3</sup>), as was black race (-71 cells/mm<sup>3</sup>) and older age (-20 cells/mm<sup>3</sup> per 10 years). These findings show that there has been a decrease in time from diagnosis of HIV infection to presentation for care, coupled with an increase in the severity of immunodeficiency at time of presentation, over the past 16 years in Maryland. The findings highlight the urgent need to develop effective strategies for providing earlier HIV testing and referral into care. Keruly, J., and Moore, R. Immune Status at Presentation to Care Did not Improve among Antiretroviral-Naive Persons from 1990 to 2006. *Clin.Infect. Dis.*, 45(10), pp. 1369-1374, 2007.

#### Herpes Simplex Virus-2 and HIV among Noninjecting Drug Users in New York City

This study sought to examine the relationship between herpes simplex virus 2 (HSV-2) seroprevalence and HIV seroprevalence among noninjecting heroin and cocaine users in New York City. Four hundred sixty-two noninjecting cocaine and heroin users were recruited from a drug detoxification program in New York City. Smoking crack cocaine, intranasal use of heroin, and intranasal use of cocaine were the most common types of drug use. A structured interview was administered and a serum sample was collected for HIV and HSV testing. HIV prevalence was 19% (95% CI 15%-22%) and HSV-2 seroprevalence was 60% (95% CI 55%-64%). The adjusted risk ratio for the association between HSV-2 and HIV was 1.9 (95% CI 1.21%-2.98%). The relationship between HSV-2 and HIV was particularly strong among females, among whom 86% were HSV-2 seropositive, 23% were HIV seropositive, and all HIV seropositives were also HSV-2 seropositive. The findings suggest that HSV-2 is an important factor in sexual transmission of HIV among noninjecting cocaine and heroin users in New York City, especially among females. The estimated population attributable risk for HIV infection attributable to HSV-2 infection in this sample was 38%, underscoring the importance of programs to manage HSV-2 infection as part of comprehensive HIV prevention for noninjecting drug users. Des Jarlais, D., Hagan, H., Arasteh, K., McKnight, C., Perlman, D., and Friedman, S. Herpes Simplex Virus-2 and HIV among Non Injecting Drug Users in New York City. *Sex Transm. Dis.*, 34(11), pp. 923-927, 2007.

#### Factors Associated with the Prevalence and Incidence of Trichomonas Vaginalis Infection among African American Women in New York City Who Use Drugs

Trichomoniasis vaginalis, the most prevalent nonviral sexually transmitted infection, is associated with negative reproductive outcomes and increased HIV transmission and may be overrepresented among African Americans. A total of 135 African American women who used drugs were screened for



*Trichomonas vaginalis* on  $\geq 2$  occasions between March 2003 and August 2005. Women were administered a structured questionnaire in a community-based research center, underwent serological testing for HIV and HSV-2, and were screened for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Fifty-one women (38%) screened positive for *T. vaginalis* at baseline. Twenty-nine (31%) of 95 women with negative results of baseline tests became infected, for an incidence of 35.1 cases per 100 person-years at risk (95% confidence interval [CI], 23.5-49.0). Prevalent infection was associated with drug use in the past 30 days, and incident infection was associated with sexual behavior in the past 30 days, namely having  $>1$  male sex partner. Women who reported having  $>1$  partner were 4 times as likely as women with fewer partners to acquire *T. vaginalis* (hazard ratio, 4.3; 95% CI, 2.0-9.4). These findings suggest that *T. vaginalis* may be endemic in this community of African American women. A control strategy that includes *T. vaginalis* screening in nonclinical settings and rapid point-of-care testing could contribute to the disruption of transmission of this pathogen. Miller, M., Liao, Y., Gomez, A. M., Gaydes, C., and D'Mellow, D. Factors Associated with the Prevalence and Incidence of *Trichomonas Vaginalis* Infection Among African American Women in New York City Who Use Drugs. *J. Infect. Dis.*, 197(4), pp. 503-509, 2008.

### Risk Factors for Methadone outside Treatment Programs: Implications for HIV Treatment among Injection Drug Users

Diversion of methadone outside treatment programs occurs, yet reasons for use of "street methadone" are characterized poorly. Self-medication for withdrawal symptoms is one plausible hypothesis. Among HIV-infected drug users, some antiretroviral medications can reduce potency of methadone, yet any association between such effects and the use of supplemental methadone sources remains undetermined. This study sought to estimate the frequency and risk factors for use of street methadone. Injection drug users (IDUs) recruited through extensive community outreach in 1988-89 and 1994 were followed semi-annually with questionnaires about health history, use of licit and illicit drugs including methadone and HIV-related assays. Analyses were performed using generalized estimating equation logistic regression. Of 2811 IDUs enrolled and eligible for analysis, 493 people reported use of street methadone over 12,316 person-years of follow-up (4.0/100 person-years). In multivariate analyses, street methadone use was more common among women, whites, those 40-59 years old, those who reported withdrawal symptoms, past methadone program attendance (6-12 months before visit), recent heroin injection with or without cocaine (but not cocaine alone), smoking or sniffing heroin and reported trading sex. Street methadone was not associated with HIV infection or treatment. The results suggest that older IDUs still using heroin may be using street methadone to treat signs of withdrawal. The absence of a higher rate of street methadone use in HIV seropositive IDUs reveals that antiretroviral/methadone interactions are not a primary determinant of use outside of treatment settings. Vlahov, D., O'Driscoll, P., Mehta, S., Ompad, D., Gern, R., Galai, N., and Kirk, G. Risk Factors for Methadone outside Treatment Programs: Implications for HIV Treatment among Injection Drug Users. *Addiction*, 102(5), pp. 771-777, 2007.

### A Ten-Year Analysis of the Incidence and Risk Factors for Acute Pancreatitis Requiring Hospitalization in an Urban HIV Clinical Cohort

To assess the incidence of and risk factors for acute pancreatitis in HIV-infected patients in the contemporary highly active antiretroviral therapy (HAART) era, researchers evaluated all cases of acute pancreatitis requiring hospitalization between 1996 and 2006 in a cohort receiving care from Johns Hopkins Hospital's HIV clinic. A nested, case-control analysis was employed for initial episodes of acute pancreatitis, and conditional logistic regression was used to assess risk factors. Of 5970 patients followed for 23,460 person-years (PYs), there were 85 episodes of acute pancreatitis (incidence: 3.6 events/1000 PYs). The incidence of pancreatitis from 1996 to 2000 was 2.6 events/1000 PYs; the incidence from 2001 to 2006 was 5.1 events/1000 PYs ( $p = 0.0014$ , comparing rates in two time periods). In multivariate regression, factors associated with pancreatitis included female gender (adjusted odds ratio [AOR] 2.96 [1.69, 5.19];  $p < 0.001$ ); stavudine [an antiretroviral therapy] use (AOR 2.19 [1.16, 4.15];  $p = 0.016$ );

aerosolized pentamidine use (OR 6.27; [1.42, 27.63];  $p = 0.015$ ); and a CD4 count  $<50$  cells/mm<sup>3</sup> (AOR 10.47 [3.33, 32.90];  $p < 0.001$ ). Race/ethnicity, primary HIV risk factor, HIV-1 RNA, and newer HAART regimens were not associated with an increased risk of pancreatitis after adjustment for the above factors. Pancreatitis remains a significant cause of morbidity in the HIV population in the HAART era. Acute pancreatitis is associated with female gender, severe immunosuppression, and stavudine and aerosolized pentamidine usage. Of note, newer antiretrovirals were not associated with an increased risk of pancreatitis. Riedel, D., Gebo, K., Moore, R., and Lucas, G. A Ten-Year Analysis of the Incidence and Risk Factors for Acute Pancreatitis Requiring Hospitalization in an Urban HIV Clinical Cohort. *AIDS Patient Care STDS*, 22(2), pp. 113-121, 2008.

## **SERVICES RESEARCH**

### Primary Medical Care Reduces HIV Risk Behaviors in Adults with Addictions

Human immunodeficiency virus (HIV) risk behaviors are prevalent in persons with addictions. This study assessed whether exposure to primary medical care is associated with decreases in HIV risk behaviors. This was a prospective 2-year cohort study of 298 adults with addictions. Outcomes evaluated were sex and drug-related HIV risk behaviors, measured by the Risk Assessment Battery. The predictor variables were the cumulative number of primary care visits (0, 1,  $>$  or = 2). Associations were tested using regression models for correlated data. It was found that in women, receipt of primary care was associated with less sex risk behavior (mean decrease 2.1,  $p <$  or = 0.1). Among women and men,  $>$  or = 2 primary care visits was associated with lower odds of any drug risk behavior (OR = 0.37,  $p = 0.03$ ). From this study it is shown that exposure to primary care can impact HIV risk behavior favorably among adults with addictions. Takizawa, C., Cheng, D., Samet, J., Winter, M., Larson, M., and Saitz, R. Primary Medical Care and Reductions in HIV Risk Behaviors in Adults with Addictions. *J. Addict. Dis.*, 26(3), pp. 17-25, 2007.

### Unprotected Sex among Ukrainian Addicts Forecasts Escalated HIV Infection Rates

From June 2004 through November 2006, outreach workers recruited 1557 Ukrainian IDUs, including 526 from Kiev, 494 from Odessa, and 537 from Makeevka/Donesk. Participants were administered a standardized computer-assisted interview assessing HIV-related drug and sex risk behaviors, self-efficacy for practicing safe sex, and HIV knowledge. Overall, 80% of the participants were sexually active in the 30-day period before their interview. They also engaged in high-risk sex behavior with 53% reporting anal or vaginal sex without a condom, 27% having sex with more than 1 partner, 41% having an IDU sex partner, and 37% having an HIV-positive sex partner or a partner whose HIV status they did not know. Overall, serology found significantly more women (40%) compared to men (32%) were HIV-positive. Men were twice as likely to have multiple sex partners ( $X^2 = 33.42$ ,  $df=1$ ;  $p < .001$ ). The extremely high HIV prevalence rate in Ukraine and in this cohort, combined with their recent high-risk sex behaviors, forecasts not only a continuance of the AIDS epidemic in the region but an escalation. Booth, R., Lehman, W., Brewster, J., Sinitsyna, L., and Dvoryak, S. Gender Differences in Sex Risk Behaviors among Ukraine Injection Drug Users. *J. Acquir. Immune Defic. Syndr.*, 46(1), pp. 112-117, 2007.

### Long-term Drug Abstinence Is Related to Psychiatric Trajectory

This study examines psychiatric trajectories of individuals entering chemical dependency treatment in a private, managed care health plan, and estimates relationships among those trajectories, individual characteristics, and abstinence (in the 30 days prior to follow-up) from drugs over 9 years. The original sample consisted of 1,204 adult men and women who met criteria for alcohol or other drug dependence or abuse and were admitted to treatment between April 1994 and April 1996. Interview data were collected at 6 mo., and 1, 5, 7, and 9 years after intake. This study is based on the 934 clients who had at least one follow-up interview within in 1 year and another between years 1 and 9. Psychiatric outcomes were

measured using the ASI Psychiatric Composite scale. Other variables included age, gender, race/ethnicity, income, education, marital status, employment status, all seven ASI composite scores, and dependence and abuse measures based on the Diagnostic Interview Schedule for Psychoactive Substance Dependence. Four discrete trajectory groups of clients with homogenous longitudinal traits based on their patterns of psychiatric status over time were identified: consistent low-severity, deteriorating, improving, and consistent high-severity. Results, reported as odds ratios (OR), indicate that compared to clients in low severity groups, those in the deteriorating (OR = 0.61, 95% CI: 0.42 – 0.87), improving (OR = 0.61, 95% CI = 0.40-0.93) and high-severity (OR = 0.43, 95% CI: 0.29-0.66) all had lower levels of abstinence at follow-up. A higher ASI Drug Composite score was also negatively associated with attaining abstinence at follow-up. Variables associated with higher follow-up abstinence rates included higher index treatment length of stay, higher ASI Medical Composite score, being female, being married at follow-up, and being employed at follow-up. Age demonstrated a non-linear effect, with those aged 30-39 years and 50 to 59 years experiencing better outcomes than those aged 40-49 years in comparison to those younger than 30 years of age. These results suggest that careful attention be paid to client's psychiatric status during treatment assessment, treatment, and aftercare. Chi, F.W., and Weisner, C.M. Nine-Year Psychiatric Trajectories and Substance Use Outcomes. *Eval. Rev.*, 32(1), pp. 39-58, 2008.

### Substance Abuse Treatment Provider Views of “Culture”: Implications for Behavioral Health Care in Rural Settings

Mandates for culturally competent substance abuse and mental health services call for behavioral health providers to recognize and engage cultural issues. These efforts to incorporate culture typically focus on client culture, but provider views of culture can also influence the provision of services. Analysis of 42 semi-structured interviews with behavioral health providers suggests that culture is considered by many to be an obstacle to help seeking and treatment of substance-abusing youth. Although some providers do not highlight cultural issues, others conceptualize culture in terms of (a) generalized Hispanic cultural attributes, (b) male-dominant gender roles, and (c) the culture of poverty. Quintero, G.A., and Lillioth, E. Substance Abuse Treatment Provider Views of “Culture”: Implications for Behavioral Health Care in Rural Settings. *Qual. Health Res.*, 17(9), pp. 1256-1267, 2007.

### Exposure to Secondhand Smoke At Home and in Public Places in Syria: A Developing Country's Perspective

This study employs sensitive methods to address the issue of exposure to secondhand smoke among children and women in an understudied developing country setting (Syria). The study combines data collected by the Syrian Center for Tobacco Studies as part of two international studies conducted in 2006: by Johns Hopkins and the Roswell Park Cancer Institute. The authors employed objective measures (hair nicotine, and ambient household nicotine assessed by passive monitors) to assess children's and mother's exposure to secondhand smoke at home, and used the TSI SidePak personal aerosol monitor to sample respirable suspended particles less than 2.5 micron diameter (PM(2.5)) in the air in public places (40 restaurants/cafés in Aleppo). Mean level of hair nicotine was 11.8 ng/mg among children (n = 54), and was higher if the mother was a smoker (19.4 +/- 23.6 ng/mg) than nonsmoker (5.2 +/- 6.9 ng/mg) (p < .05). Children's hair nicotine level was strongly correlated with ambient household nicotine and number of cigarettes smoked daily in the house (r = .54 and r = .50, respectively, p < .001), and also was related to having a father who smoked in the children's presence. In public places, average PM(2.5) in the monitored 40 hospitality venues was 464 microg/m(3) and correlated with smoker density measured as cigarettes-waterpipes/100 m(3) (r = .31, p = 0.049). Thus, children in Syria are exposed to high levels of secondhand smoke at home, in which mothers smoking plays a major role. Also, levels of respirable hazardous particles are high in public hospitality venues, putting customers and workers at serious health risks. Maziak, W., Ali, R., Fouad, M., Rastam, S., Wipfl, H., Travers, M., Ward, K., and Eissenberg, T. Exposure to Secondhand Smoke at Home and in Public Places in Syria: A Developing Country's Perspective. *Inhal. Toxicol.*, 20(1), pp. 17-24, 2008.

### A Ten-Year Analysis of the Incidence and Risk Factors for Acute Pancreatitis Requiring Hospitalization in an Urban HIV Clinical Cohort

To assess the incidence of and risk factors for acute pancreatitis in HIV-infected patients in the contemporary highly active antiretroviral therapy (HAART) era, the researchers evaluated all cases of acute pancreatitis requiring hospitalization between 1996 and 2006 in patients followed at Johns Hopkins Hospital's HIV clinic. A nested, case-control analysis was employed for initial episodes of acute pancreatitis, and conditional logistic regression was used to assess risk factors. Of 5,970 patients followed for 23,460 person-years (PYs), there were 85 episodes of acute pancreatitis (incidence: 3.6 events/1000 PYs). The incidence of pancreatitis from 1996 to 2000 was 2.6 events/1000 PYs; the incidence from 2001 to 2006 was 5.1 events/1000 PYs ( $p = 0.0014$ , comparing rates in two time periods). In multivariate regression, factors associated with pancreatitis included female gender (adjusted odds ratio [AOR] 2.96 [1.69, 5.19];  $p < 0.001$ ); stavudine use (AOR 2.19 [1.16, 4.15];  $p = 0.016$ ); aerosolized pentamidine use (OR 6.27; 1.42, 27.63];  $p = 0.015$ ); and CD4 count less than 50 cells/mm<sup>3</sup> (AOR 10.47 [3.33, 32.90];  $p < 0.001$ ). Race/ethnicity, HIV risk factor, HIV-1 RNA, and newer non-nucleoside reverse transcriptase inhibitors (NNRTI) - and protease inhibitor (PI)-based HAART regimens were not associated with an increased risk of pancreatitis after adjustment for the above factors. Pancreatitis remains a significant cause of morbidity in the HIV population in the HAART era. Acute pancreatitis is associated with female gender, severe immunosuppression, and stavudine and aerosolized pentamidine usage. Newer anti-retrovirals, articularlyatazanavir, lopinivir/ritonavir, tenofovir, abacavir, and efavirenz, were not associated with an increased risk of pancreatitis. Riedel, D.J., Gebo, K.A., Moore, R.D., and Lucas, G.M. A Ten-Year Analysis of the Incidence and Risk Factors for Acute Pancreatitis Requiring Hospitalization in an Urban HIV Clinical Cohort. *AIDS Patient Care STDS*, 22(2), pp. 113-121, 2008.

### Uncovering Patterns of HIV Risk through Multiple Housing Measures

Understanding the relationships between housing and HIV has been limited by reliance on a single housing indicator based on current living arrangements (e.g., stable, unstable, or homeless). This paper examines the cross-sectional and longitudinal relationships between five housing indicators (objective housing stability, subjective housing stability, supportive housing, number of residences in the last 6 months, and housing services needs) and four HIV risk behaviors (hard drug use, needle sharing, sex exchange, and unprotected intercourse) among women at-risk for HIV and with recent criminal justice system involvement ( $n = 493$ ). In cross-sectional analyses, each risk behavior was associated with multiple indicators of poor housing, and the patterns of association varied by risk behavior. In the longitudinal analyses, changes in risk behavior were associated with changes in housing status since the previous assessment. These indicators reflect different aspects of housing and are uniquely associated with different risk behaviors. The relationships between housing and HIV risk are complex, and both constructs must be recognized as multidimensional. Weir, B.W., Bard, R.S., O'Brien, K., Casciato, C.J., and Stark, M.J. Uncovering Patterns of HIV Risk through Multiple Housing Measures. *AIDS Behav.*, 11, pp. S31-S44, 2007.

### Decline in Availability of Tailored Outpatient Care for Women from 1995 to 2005

Tailoring substance abuse treatment to women often leads to better outcomes. This investigation sought to depict recent changes in outpatient substance abuse treatment (OSAT) tailoring to women. Data were from 2 waves of a national OSAT unit survey ( $N = 618$  in 1995,  $N = 566$  in 2005). Multiple logistic regressions with generalized estimating equations test associations between unit and contextual attributes and tailoring to women. Two measures of tailoring to women declined significantly between 1995 and 2005: availability of single sex therapy (from 66% to 44% of units) and percent of staff trained to work with women (from 42% to 32% of units). No aspect of tailoring to women became more common. Methadone treatment (O.R. = 2.3;  $p < .001$ ), and private for-profit status (O.R. = .23 to .49;  $p < .01$ ) and government managed care financing (O.R. = 3.64;  $p < .001$ ) were associated with higher odds of tailoring to women. Campbell, C.,

Wells, R., Alexander, J., Jiang, L., Nahra, T., and Lemak, C. Tailoring of Outpatient Substance Abuse Treatment To Women, 1995-2005. *Med. Care*, 45(8), pp. 775-780, 2007.

#### Comparison of Demographic and Clinical Characteristics between Opioid-dependent Individuals Admitted to a Community-based Treatment Setting and Those Enrolled in a Research-based Treatment Setting

Despite the significant developments in pharmacotherapy and behavioral treatments for addiction, the dissemination of new treatment methods into the community has been slow. It has been pointed out that treatments developed in research settings may be impractical in community treatment settings, which might help explain the transition lag. Screening and recruitment of participants for research studies might partially explain this, as there is evidence that substance-abusing individuals who participate in clinical research are different on a number of measures from treatment seekers. However, no study has directly compared treatment seekers with research participants drawn from similar populations using prospective methods. This study compared the demographic characteristics, drug use and psychosocial problem severity levels, and personality traits of opioid-dependent individuals seeking help in a community setting (n = 502) with those of opioid-dependent individuals in a primarily research-based drug abuse treatment setting (n = 459); both settings offered a similar set of treatment services (opioid agonist medication and counseling). Although the overall findings revealed numerous similarities between the groups, differences were also observed. Most notably, there were significantly fewer women in the research sample than in the community-based treatment sample. Other differences included a modest but statistically significant increase in psychosocial problem severity levels in the community-based treatment sample and higher drug use problem severity levels in the research sample. Interestingly, many of these differences were strongest in women as compared with men. Carroll, C.P., Kidorf, M., Strain, E.C., and Brooner, R.K. Comparison of Demographic and Clinical Characteristics Between Opioid-dependent Individuals Admitted to a Community-based Treatment Setting and Those Enrolled in a Research-based Treatment Setting. *J. Subst. Abuse Treat.*, 33 pp. 355-361, 2007.

### **CLINICAL TRIALS NETWORK RESEARCH**

#### Addressing Ethnic Disparities in Drug Abuse Treatment in the Clinical Trials Network

Ethnic minorities have significantly higher rates of unmet needs for treatment of substance use disorders and are often underrepresented in clinical trials and treatment research. The National Drug Abuse Treatment Clinical Trials Network (CTN) was established in 1999 to conduct research in a wide variety of community based treatment programs across the United States. Through its size and scope, the CTN provides a unique opportunity to address a variety of underserved populations, and in particular to evaluate access to and effectiveness of treatments for ethnic minorities. The CTN has continually sought to reduce barriers to all its studies and has attended carefully to recruitment and retention of women and ethnic minority groups. This article describes a symposium from the June 2006 CPDD annual meeting that included four presentations on ongoing CTN activities and strategies used to address the issues of ethnic disparities. Kathleen Carroll described a protocol developed specifically to address retention in treatment among Spanish-speaking substance users. Ray Daw described the special issues raised in clinical research among American Indian communities, including those encountered by a CTN protocol that was adapted on site so it could be implemented among American Indian communities. Kathryn Magruder summarized results of a secondary analysis of CTN data, evaluating rates of retention among ethnic minorities. And Lawrence Brown described a secondary analysis of a CTN survey study on national practices regarding the availability of specialized treatment for sexually transmitted diseases in drug abuse treatment, focusing specifically on services for ethnic minorities. Carroll, K.M., Rosa, C., Brown, Jr., L.S., Daw, R., Magruder, K.M., Beatty, L. Addressing Ethnic Disparities in Drug Abuse Treatment in the Clinical Trials Network. *Drug Alcohol Depend.*, 90(1), pp. 101-106, 2007.

### Improving the Transition from Residential to Outpatient Addiction Treatment: Gender Differences in Response to Supportive Telephone Calls

Substance use relapse rates are often high in the first months after discharge from inpatient substance abuse treatment, and patient adherence to aftercare plans is often low. Four residential addiction treatment centers participated in a feasibility study designed to estimate the efficacy of a post-discharge telephone intervention intended to encourage compliance with aftercare. A total of 282 participants (100 women, 182 men) with substance use disorders were included in this secondary analysis. The findings revealed that women were more likely than men to attend aftercare. This "gender effect" persisted after adjustment for a number of potential mediators. Carter, R.E., Haynes, L.F., Back, S.E., Herrin, A.E., Brady, K.T., Leimberger, J.D., Sonne, S.C., Hubbard, R.L., and Liepman, M.R. Improving the Transition from Residential to Outpatient Addiction Treatment: Gender Differences in Response to Supportive Telephone Calls. *Am. J. Drug Alcohol Abuse*, 34(1), pp. 47-59, 2008.

### No Smoking Allowed: Integrating Smoking Cessation with Treatment

Substance abuse counselors, programs, and treatment systems are considering how to address smoking and nicotine dependence in the populations they serve. This article reports on the results from a survey within the National Drug Abuse Treatment Clinical Trials Network (CTN) that assessed whether the surveyed treatment agency provided smoking cessation treatment as part of their regular services. The survey also assessed the attitudes of staff regarding the feasibility of offering smoking cessation treatment. Analyses explored those factors associated with whether or not smoking cessation services were provided, and factors that predict staff attitudes toward smoking cessation treatment in these drug treatment strategies. Overall, the study found that smoking cessation treatment was more likely to be available in units that offered other ancillary services, including detoxification. Additionally, clinics that provide smoking cessation care were more likely to have a staff with a supportive attitude toward such services. This was especially true in clinics with a high number of pregnant women, but the proportion of youth admissions was neither a predictor for staff attitudes nor for the provision of smoking cessation services. Overall, this study presents some challenges to the treatment field to focus on evidence-based services regarding smoking cessation treatment, and raises some ethical issues as well. Fuller, B.E., and Guydish, J. No Smoking Allowed: Integrating Smoking Cessation with Treatment. *Counselor*, 9(1), pp. 22-27, 2008.

## **INTERNATIONAL RESEARCH**

### **PUBLICATIONS BY FORMER NIDA INVEST DRUG ABUSE RESEARCH FELLOWS**

#### Cross-National Prevalence and Risk Factors for Suicidal Ideation, Plans and Attempts

INVEST Fellow: Guilherme Borges (Mexico, 1997-1998)

Suicide is a leading cause of death worldwide; however, the prevalence and risk factors for the immediate precursors to suicide - suicidal ideation, plans and attempts - are not well known, especially in low- and middle-income countries. The aim of this study was to report on the prevalence and risk factors for suicidal behaviors across 17 countries. A total of 84,850 adults were interviewed regarding suicidal behaviors and socio-demographic and psychiatric risk factors. Results showed that the cross-national lifetime prevalence of suicidal ideation, plans, and attempts is 9.2% (s.e.=0.1), 3.1% (s.e.=0.1), and 2.7% (s.e.=0.1). Across all countries, 60% of transitions from ideation to plan and attempt occur within the first year after ideation onset. Consistent cross-national risk factors included being female, younger, less educated, unmarried and having a mental disorder. Interestingly, the strongest diagnostic risk factors were mood disorders in high-income countries but impulse control disorders in low- and middle-income countries. The authors conclude that there is cross-national variability in the prevalence of suicidal behaviors, but strong consistency in the characteristics and risk factors for these behaviors. These findings have significant implications for the prediction and prevention of suicidal behaviors. Nock, M.K., Borges, G., Bromet, E.J., Alonso, J.,

Angermeyer, M., Beautrais, A., Bruffaerts, R., Chiu, W.T., de Girolamo, G., Gluzman, S., de Graaf, R., Gureje, O., Haro, J.M., Huang, Y., Karam, E., Kessler, R.C., Lepine, J.P., Levinson, D., Medina-Mora, M.E., Ono, Y., Posada-Villa, J., and Williams, D. Br. J. Psychiatry.192, pp. 98-105, 2008.

#### Suicide Ideation, Plan, and Attempt in the Mexican Adolescent Mental Health Survey

INVEST Fellow: Guilherme Borges (Mexico, 1997-1998)

No representative data among adolescents in Mexico exist on the prevalence and risk factors for suicide ideation, plan, and attempt despite a recent increase in suicide deaths. Data are presented from the Mexican Adolescent Mental Health Survey, a representative household survey of 3,005 adolescents ages 12 to 17 in metropolitan Mexico City who were gathered in 2005, regarding lifetime prevalence and age-of-onset distributions of suicide ideation, plan, and attempt and demographic and psychiatric disorders risk factors. Lifetime ideation was reported by 11.5% of respondents, whereas 3.9% reported a lifetime plan and 3.1% a lifetime suicide attempt. Onset of suicidality started around age 10 and at age 15 showed the highest hazards. Suicide ideators were more likely to report a plan and attempt within the first year of onset of ideation. Suicidality was more likely to occur among females. The presence of one or more mental disorders was strongly related to suicide ideation, plan, and attempt. Among ideators only dysthymia was consistently related to a plan and attempt. The authors conclude that intervention efforts should focus on assessment and target adolescents with mental disorders, particularly mood disorders, to be effective in prevention. Borges, G., Benjet, C., Medina-Mora, M.E., Orozco, R., and Nock, M. J. Am. Acad. Child Adolesc. Psychiatry, 47(1), pp. 41-52, 2008.

### **PUBLICATIONS BY FORMER NIDA HUBERT H. HUMPHREY DRUG ABUSE RESEARCH FELLOWS**

#### Hypotension Caused by Therapeutic Doses of Venlafaxine: Case Report and Proposed Pathophysiological Mechanisms

HHH Fellow: Arthur Guerra de Andrade (Brazil, 1991-1992)

Although venlafaxine is usually associated with modest increases in blood pressure and not so often clinical hypertension, there are a few reported cases of hypotension related to overdoses of this specific antidepressant. The case study of a young female patient with a history of Major Depressive Disorder who initiated treatment with venlafaxine 75 mg/day and developed hypotension when the dosage was titrated up to 225 mg/day is described. The patient did not present comorbid diseases nor use other medication. A temporal association and a dose-dependent relationship between the hypotension and the use of venlafaxine is shown. To the best of the knowledge of the authors, this is the first case report that specifically associates regular doses of venlafaxine with the presence of hypotension. A pathophysiological mechanism is proposed, involving the participation of presynaptic alpha2-adrenergic receptors and the presence of a possible genetic polymorphism of cytochrome P4502D6, which is associated with lower drug metabolism, to explain the relationship between venlafaxine in regular dosage and development of hypotension. Alexandrino-Silva, C., Mauá, F.H., De Andrade, A.G., and De Toledo Ferraz Alves, T.C. Hypotension caused by therapeutic doses of venlafaxine: case report and proposed pathophysiological mechanisms. J. Psychopharmacol, 22(2), pp. 214-6, Epub 2008 Jan 21.

#### Drugs and Fatal Traffic Accidents in the Czech Republic

HHH Fellow: Tomas Zabransky (Czech Republic, 2003-2004)

The aim of the study was to determine the prevalence of psychotropic drug use in active participants in traffic accidents who died during the accident or shortly after it due to injuries resulting from the accident. A special mortality register containing data of all forensic autopsies was analyzed. The studied sample consisted of persons who died during traffic accidents and were active participants in those ones (pedestrians, cyclists, or drivers), and were toxicologically tested during the forensic examination. The

sample consisted of 1,213 cases, 1,039 (85.7%) males and 174 (14.3%) females who died in 2003-2005. Ethanol was found in 34.7% of cases, however a significant declining trend over the years was noted. The proportion of positive detections for any psychotropic drug other than alcohol was 7.2%; benzodiazepines were found most frequently (3.6%), followed by cannabis (2.2%), and stimulants (1.7% of the sample). Positive findings of ethanol were significantly more common among males, whereas positive benzodiazepine tests were more frequent in females. Positive cases were significantly younger than negative ones for ethanol, volatile substances, stimulants, and cannabis; in cases of positive medicaments tests, the positive cases were significantly older than the negatives. Mravcik, V., Vorel, F., and Zabransky, T. Cent. Eur. J. Public Health, 15(4), pp. 158-162, 2007.

### Schizophrenia Modifying the Expression of Gender Identity Disorder

HHH Fellow: Arthur Guerra de Andrade (Brazil, 1991-1992)

According to the Brazilian Federal Medical Association, transsexualism is recognized as a gender identity disorder if a long-term diagnostic therapeutic process has demonstrated that the transposition of gender roles is irreversible, and if only hormonal and surgical procedures are appropriate to relieve the stress associated with the gender identity. Although such treatment will only be initiated with caution and after a long phase of intense diagnostic screening, the differentiation between pure identity disorders and transsexual feelings secondary to an ongoing psychopathologic process, such as schizophrenia, can be arduous for many health professionals. The aim of this article was to report a case of a female patient with schizophrenia and transsexualism and the risks of a potential diagnostic confusion. A 19-year-old black woman, with an 8-year history of undifferentiated schizophrenia and intense gender dysphoria, was referred for sex reassignment surgery evaluation in the Ambulatory for the Treatment of Sexual Disorders of the ABC Medical School. After a more adequate antipsychotic treatment, her masculine behavior has persisted, but her desire to change her own genital organs has decreased. A better acceptance of the multiplicity of possible genders should neither contribute to inadequate interpretations of the signs and symptoms of our patients nor facilitate dangerous clinical or surgical recommendations. Baltieri, D.A., and De Andrade, A.G. Schizophrenia Modifying the Expression of Gender Identity Disorder. J. Sex Med., December 7, 2007, Epub ahead of print.

## **INTRAMURAL RESEARCH**

### **CHEMISTRY AND DRUG METABOLISM, CPTRB**

#### Validation and Application of a Novel Method for the Determination of Buprenorphine, Norbuprenorphine and Their Glucuronide Conjugates in Human Meconium

A novel liquid chromatography tandem mass spectrometry (LCMSMS) method for buprenorphine, norbuprenorphine, and glucuronidated conjugates' quantification in meconium was developed and fully validated. Maternal self-report, the most common mechanism for identifying drug-exposed neonates is less reliable than biological monitoring of maternal and infant specimens. Meconium, the highly complex neonatal fecal material, is easy and non-invasive to collect and has higher sensitivity and specificity than urine to detect *in utero* drug exposure. Controlled administration of illicit drugs during pregnancy is unethical and unsafe, and administration of licit medications is recommended only as needed. Buprenorphine administration to pregnant opiate addicts to reduce illicit drug use and craving provides an important opportunity to study disposition of this drug in the maternal-fetal dyad. It is unknown whether buprenorphine dose is correlated to buprenorphine and/or metabolite concentrations in meconium, and if meconium concentrations predict neonatal outcomes. This research has not been possible due to the lack of a validated, quantitative chromatographic method for measuring buprenorphine in this neonatal matrix. This method will enable the question of whether drug doses predict meconium drug concentrations, and whether drug concentrations correlate with onset, magnitude and duration of neonatal abstinence syndrome and other outcomes. These findings could improve clinical care in this vulnerable population.



Development of this new biomarker assay for buprenorphine and metabolites in meconium is a critical step for conducting this research. This sensitive and specific method will monitor *in utero* buprenorphine exposure and determine if correlations exist between buprenorphine exposure and neonatal outcomes. Kacinko, S.L., Shakleya, D.M. and Huestis, M.A. Validation and application of a method for the determination of buprenorphine, norbuprenorphine, and their glucuronide conjugates in human meconium. *Analytical Chemistry*, 80, pp. 246-252, 2008.

#### MDMA, HMMA, MDA, and HMA Plasma Pharmacokinetics in Humans Following Controlled MDMA Administration

An extended pharmacokinetic analysis of MDMA or Ecstasy and three metabolites, HMMA, MDA and HMA, characterizing  $C_{max}$ ,  $T_{max}$ ,  $AUC_{\infty}$ , detection windows,  $t_{1/2}$ ,  $V_d/F$ ,  $CL/F$ , and metabolite ratios for up to 143 h after oral MDMA dosing in young adults was performed. The aim of the study was to document whether non-linearity in MDMA pharmacokinetics occurred at recreational doses, and to characterize MDMA pharmacokinetics in African-Americans and women for the first time. Seventeen female and male participants received placebo, low (1.0 mg/kg), and high (1.6 mg/kg) oral MDMA doses in a double blind, randomized, balanced, within-subject design. Study strengths included metabolite measurements, concentrations after low and high doses, frequent and extended plasma sampling, and residence of participants on a closed research unit with 24-h monitoring to prevent self-administration of MDMA or other drugs. A fully validated 2D-GC/MS method simultaneously quantified MDMA and metabolites. Mean  $\pm$  SD maximum plasma concentrations ( $C_{max}$ ) were  $162.9 \pm 39.8$  and  $171.9 \pm 79.5$  ng/mL for MDMA and HMMA, respectively, after low and  $291.8 \pm 76.5$  and  $173.5 \pm 66.3$  ng/mL after high MDMA doses, demonstrating non-linear MDMA pharmacokinetics. Mean MDMA volume of distribution was constant for low and high doses; clearance was significantly higher after the low dose. MDMA primarily affects the serotonergic system, acting as an indirect monoaminergic agonist; however, the mechanism(s) by which MDMA causes toxicity are not fully understood. Non-linearity in MDMA dose-concentration relationships and wide variability between subjects at typical recreational doses could contribute to observed MDMA toxicity. Preliminary data on gender differences in drug elimination also were noted. Kolbrich, E.A., Goodwin, R.S., Gorelick, D.A., Hayes, R.J., Stein, E.A., and Huestis, M.A. Presentation, 2008. American Academy of Forensic Sciences (AAFS) Annual Meeting, Washington, DC, February 18-22, 2008.

### **NICOTINE PSYCHOPHARMACOLOGY UNIT, TREATMENT SECTION CLINICAL PHARMACOLOGY AND THERAPEUTICS RESEARCH BRANCH**

#### Nicotine Enhances Mood and Cognition in Smokers

The discovery of the role of nicotinic receptors in attention and memory has led to the testing of nicotinic analogs as cognitive enhancing agents in patient populations. Empirical information about nicotine's ability to enhance elements of attention and memory in normal individuals might guide development of therapeutic uses of nicotine in cognitively-impaired populations. The purpose of this study was to determine the effect of nicotine on continuous attention, working memory, and computational processing in tobacco-deprived and nondeprived smokers. A total of 28 smokers (14 men, 14 women) participated in a double-blind, placebo-controlled, within-subject study, in which they were overnight (12 h) tobacco deprived at one session and smoked *ad libitum* before the other session. At each session, participants received 0, 1, and 2 mg nicotine via nasal spray in random order at 90-min intervals. Before and after each dose, a battery of cognitive, subjective, and physiological measures was administered, and blood samples were taken for plasma nicotine concentration. Overnight tobacco deprivation resulted in impaired functioning on all cognitive tests and increased self-reports of tobacco craving and negative mood; nicotine normalized these deficits. In the nondeprived condition, nicotine enhanced performance on the Continuous Performance Test and Arithmetic Test in a dose-related manner, but had no effect on working memory. In general, women were more sensitive than men to the subjective effects of nicotine. These results provide an unequivocal determination that nicotine enhanced attentional and computational abilities in nondeprived

smokers and suggest these cognitive domains as substrates for novel therapeutic indications. Myers, C.S., Taylor, R.C., Moolchan, E.T., and Heishman, S.J. Dose-related Enhancement of Mood and Cognition in Smokers Administered Nicotine Nasal Spray. *Neuropsychopharmacology*, 33, pp. 588-598, 2008.

# DIRECTOR'S REPORT TO COUNCIL

September 2008

## BASIC BEHAVIORAL RESEARCH

### Menstrual Cycle Modulates Striatal Dopamine in Drug-Naive Cynomolgus Monkeys

Several studies have reported that the subjective effects of abused stimulants in women vary with the menstrual cycle. Given the role of the brain dopamine system in abused drugs, these menstrual cycle effects may be mediated by interactions between gonadal hormones and dopamine. Drs. Paul Czoty and Michael Nader and colleagues at Wake Forest University School of Medicine conducted the first non-human primate study to examine whether basal measures of DA D2 receptor availability vary with the menstrual cycle phase. They tested seven drug-naïve, individually-housed female cynomolgus monkeys using the D2-like receptor ligand [<sup>18</sup>F]fluorocleobopride (FCP). Menstrual cycle phase was determined by serum progesterone levels on the day of the PET scan. In both the caudate nucleus and the putamen, D2 receptor availability was found to be lower during the follicular phase than in the luteal phase. Previous studies examining menstrual cycle effects on D2 receptor availability in female human subjects have reported mixed results, including effects consistent with the present results, opposite the present results, and a report of no effects. Drs. Czoty, Nader and colleagues note that there are several potential explanations for these discrepancies, including their use of monkeys with no drug history of any kind (other than veterinary care with ketamine) and their use of a state-of-the-art primate microPET camera with high resolution. Whether the lower D2 receptor availability observed in the follicular phase this study reflects lower D2 receptor densities or higher levels of extracellular dopamine in the follicular phase is unclear; however, the authors note that rodent studies have shown that estrogen, which is higher in the follicular phase than luteal, has been shown to increase dopamine release. Several studies have shown that D2 receptor availability is inversely related to vulnerability to the abuse-related effects of cocaine. The present data, therefore, suggest that such effects in females would be greater in the follicular phase, which is an outcome that has been observed in several studies examining the subjective effects of stimulants in humans. Also, NIDA grantee Dr. Nancy Mello of the Harvard Medical School reported in 2007 that a low dose of cocaine produced a considerably greater progressive ratio breakpoint during the follicular phase than in the luteal phase in cynomolgus monkeys (Mello, N.K., Knudson, I.M., and Mendelson, J.H.. Sex and Menstrual Cycle Effects on Progressive Ratio Measures of Cocaine Self-Administration in Cynomolgus Monkeys. *Neuropsychopharmacology*, 32, pp. 1956-1966, 2007). Although only females were studied in the present study, data from a prior published study by these researchers examining D2 receptor availability in individually-housed male monkeys permitted an examination of sex differences. Results from that study indicated that D2 receptor availability in both the caudate nucleus and the putamen was lower than seen in females in either the luteal or follicular phase. This research highlights the need for models of the neurobiology of addiction to incorporate sex differences and the interactions of gonadal hormones and neurotransmitter systems underlying addiction. Czoty, P.W., Riddick, N.V., Gage, H.D., Sandridge, M., Nader, S.H., Garg, S., Bounds, M., Garg, P.K., and Nader, M.A. Effect of Menstrual Cycle Phase on Dopamine D2 Receptor Availability in Female Cynomolgus Monkeys. *Neuropsychopharmacology*. 2008, Feb 6. [E-pub ahead of print].

## **BEHAVIORAL AND BRAIN DEVELOPMENT RESEARCH**

### Fatty Acid Ethyl Esters in Meconium are Associated with Poorer Neurodevelopmental Outcomes to Two Years of Age

The aim of this study was to examine the relationship between fatty acid ethyl esters (FAEE) in meconium and neurodevelopment in infants at 6.5 months, 1 year, and 2 years of age who were exposed to alcohol in utero. The current study reports on a secondary analysis of the data collected in a prospective longitudinal study of high risk mothers and their infants. Meconium was collected from 219 newborns shortly after birth and neurodevelopment was assessed with the Bayley Scales of Infant Development (2nd edition) which included the Mental and Psychomotor scales. Increasing concentrations of FAEE were significantly correlated with poorer mental and psychomotor development at all follow-up visits even after controlling for a number of prenatal and maternal factors. The results of this study showed that elevated FAEE in meconium may be a marker in identifying newborn infants who may be at risk for mental and psychomotor delays from alcohol exposure in utero, but do not show the typical characteristic facies of FAS. Early intervention is critical in these children and the results of this study are important in that the meconium analysis described by these authors may be a reliable means of identifying these at-risk children at birth. Peterson, J., Kirchner, H., Xue, W., Minnes, S., Singer, L., and Bearer, C. Fatty Acid Ethyl Esters in Meconium are Associated with Poorer Neurodevelopmental Outcomes to Two Years of Age. *Journal of Pediatrics*, 152(6), pp. 788-792, June, 2008.

### Meaningful Differences in Maternal Smoking Behavior during Pregnancy: Implications for Infant Behavioral Vulnerability

Dr. Laurie Wakschlag and her colleagues used the 9-month-old sweep of the Millennium Cohort Study, a cohort of over 18,000 infants born in 2000-2, to examine the effects of smoking during pregnancy on problem behavior in offspring. Prior research has shown that the prenatal exposure to maternal smoking is associated with problem behavior in infants, but it is not clear whether these effects are associated with maternal characteristics that distinguish persistent smoking from quitting or whether they are due to teratological effects. In this study, mothers were classified as pregnancy non-smokers, quitters and light or heavy smokers. The Carey Infant Temperament Scale was used to assess temperamental positive mood, receptivity to novelty and regularity. Mothers who smoked heavily during pregnancy had infants with the lowest scores of easy temperament and low positive mood. In contrast, mothers who quit smoking during their pregnancy had infants with the highest scores of easy temperament. There also appeared to be a protective effect of quitting during pregnancy in that these mothers' infants had a decreased risk of distress to novelty and irregularity in comparison to those mothers who had never smoked. The results of this study suggest that offspring behavior associated with pregnancy smoking is complex and multi-determined. Future research is needed to elucidate the differences in maternal personality characteristics between quitters and persistent smokers and how these differences help to predict early vulnerabilities and offspring behavioral patterns over time. Pickett, K., Wood, C., Adamson, J., DeSouza, L., and Wakschlag, L. Meaningful Differences in Maternal Smoking Behavior during Pregnancy: Implications for Infant Behavioral Vulnerability. *Journal of Epidemiology and Community Health*, 62(4), pp. 318-324, 2008.

### Children's Cognitive-Behavioral Functioning at Age 6 and 7: Prenatal Drug Exposure and Caregiving Environment

This study examined the relationship of prenatal drug exposure (PDE) and caregiving environment to cognitive, academic, and behavioral performance. Participants included 111 with PDE that were part of a longitudinal randomized controlled trial of a home-based intervention among drug-using women and their infants. A total of 62 non-drug exposed children were recruited from the same community to serve as controls. At ages 6 and 7, children were administered the Stanford-Binet Intelligence Scales, Fourth

Edition, the Wide Range Achievement Test and the Child Behavior Checklist. Numerous theoretically and empirically derived confounders that examined perinatal and environmental factors were included in the multivariate analyses. The results indicated that after adjustment for the confounding variables, there were no significant exposure-group differences on measures of cognitive, academic or behavior problems. Females had higher scores on overall IQ, higher reading achievement scores and fewer caregiver-reported attention and aggression problems. This gender difference was evident regardless of PDE status. The children who participated in this study were from low income families and scores obtained were well below normative expectations. Future studies examining the effects of prenatal exposure to drugs need to be aware of the influence that poverty has on cognitive and behavioral development of children so that attributions to PDE are accurate. Nair, P., Black, M., Ackerman, J., Schuler, M., and Keane, V. Children's Cognitive-Behavioral Functioning at Age 6 and 7: Prenatal Drug Exposure and Caregiving Environment. *Ambulatory Pediatrics*, 8(3), pp. 154-162, 2008.

#### Prenatal Cocaine Exposure: Drug and Environmental Effects at 9 Years

Dr. Sonia Minnes and her colleagues investigated the effects of prenatal cocaine exposure (CE) in a large sample of children with a high follow-up rate, controlling for a number of confounding variables such as polydrug exposure, blood lead levels, iron-deficiency anemia (IDA), quality of caregiving environment and foster/adoptive care. Three hundred and seventy one children in a longitudinal, prospective study from birth were assessed for IQ and school achievement at 9 years of age (192 cocaine exposure; 179 non-cocaine exposure). No effects were seen in school achievement measures. Poorer perceptual reasoning IQ was seen in CE children; the degree of impairment was linearly related to a cocaine metabolite. Effects were mediated by smaller birth head circumference, indicating a relationship with fetal brain growth. Positive effects of the home environment and negative effects of alcohol, lead, and marijuana exposure were additive. The most pervasive negative effects were associated with lead exposure, underscoring the need for stronger public health efforts. Lower lead levels and better home environments were seen in those CE children who were placed in foster/adoptive care. This study shows the importance of documenting environmental factors in behavioral teratology studies. Singer, L., Nelson, S., Short, E., Min, M., Lewis, B., Russ, S., and Minnes, S. Prenatal Cocaine Exposure: Drug and Environmental Effects at 9 years. *Journal of Pediatrics*, 153(1), pp. 105-111, 2008.

#### The Development of Corpus Callosum Microstructure and Associations with Bimanual Task Performance in Healthy Adolescents

Studies utilizing conventional magnetic resonance imaging studies have provided important information regarding the development of the corpus callosum (CC). This study used diffusion tensor imaging to examine the relationship of fine motor skills with white matter microstructural development of the CC in healthy children, adolescents, and young adults (ages 9 - 24 years). Fractional anisotropy (FA), which is a measure of white matter's structural organization, was the primary DTI variable. An alternating finger tapping test was used to assess interhemispheric transfer and motor speed. Relationships between behavioral performance on the tapping task and white matter microstructure, age, and gender were examined. Younger subjects performed the unilateral and bimanual finger tapping task significantly slower. Improved motor performance was correlated with increased white matter integrity in the splenium. The splenium of the CC is believed to be primarily involved in the transmission of interhemispheric signals from the posterior cortical regions. Gender differences were also noted in that males outperformed females. Decreases in alternating finger tapping time and increases in FA likely reflect increased myelination in the CC and more efficient neuronal signal transmission. The data from this study suggest that white matter integrity continues to develop until 18 years of age, which is consistent with findings from conventional MRI studies that show similar age related changes in splenium white matter volume. This study has expanded the utility of diffusion tensor imaging by using this method to demonstrate relationships between fine motor skills and underlying white matter microstructure in childhood and adolescence. Muetzel, R., Collins, P., Mueller, B., Schissel, A., Lim, K., and Luciana, M. The

Development of Corpus Callosum Microstructure and Associations with Bimanual Task Performance in Healthy Adolescents. *Neuroimage*, 39(4), pp. 1918-1925, 2008.

## **CLINICAL NEUROSCIENCE RESEARCH**

### Individual Differences in Nicotine Dependence, Withdrawal Symptoms, and Sex Predict Brain Responses to Smoking Cues

McClernon and colleagues at Duke University used fMRI to study the influence of individual difference factors and withdrawal symptoms on brain cue reactivity. Multiple regression analysis was used to evaluate relations between individual difference factors and withdrawal symptoms and event-related fMRI responses to visual smoking cues in a sample of 30 smokers. Predictors were self-report nicotine dependence (Fagerström test of nicotine dependence, FTND), prescan withdrawal symptoms (craving and negative affect), and sex. The unique variance of each predictor was examined after controlling for each of the others. Positive associations were observed between FTND and reactivity to cues in right anterior cingulate and orbitofrontal cortex (OFC) whereas negative associations were observed between prescan craving and reactivity in ventral striatum. Higher negative affect or being male was associated with greater reactivity in left hippocampus and left OFC. Women exhibited greater cue reactivity than men in regions including the cuneus and left superior temporal gyrus. Individual difference factors and withdrawal symptoms were uniquely associated with brain reactivity to smoking cues in regions subserving reward, affect, attention, motivation, and memory. These findings provide further evidence that reactivity to conditioned drug cues is multiply determined and suggest that smoking cessation treatments designed to reduce cue reactivity focus on each of these variables. McClernon, F.J., Kozink, R.V., and Rose, J.E. Individual Differences in Nicotine Dependence, Withdrawal Symptoms, and Sex Predict Transient fMRI-BOLD Responses to Smoking Cues. *Neuropsychopharmacology*, 33(9), pp. 2148-2157, 2008.

## **EPIDEMIOLOGY AND ETIOLOGY RESEARCH**

### Developmental Trajectories of Young Adult Poly-Substance Use

Despite the prominence of comorbidity among substances and the recent attention focused on trajectory-based approaches to characterizing developmental change, little research in the substance use field has simultaneously considered both course and comorbidity. Using nationally representative panel data from the Monitoring the Future Project (MTF; n = 32,087; 56% female; 82% Caucasian), authors identified developmental courses of heavy drinking, smoking, and marijuana use using 4 waves of data spanning ages 18 to 26 in a multi-cohort young adult sample. Comorbidity was examined by cross-classifying group membership in substance use trajectories. Finally, the extent to which risk factors (sex, race, alcohol expectancies, delinquency, sensation seeking, depressive affect, religiosity, academic achievement, and parent education) accounted for combinations of comorbidity that occurred at a rate greater than chance was examined. For each substance, authors identified 4 courses of substance use that were largely consistent with those found in the literature (chronic high use, late-onset use, developmentally limited use, and low-use), with a fifth moderate smoking group. Heavy drinking, smoking, and marijuana use were each highly associated, and distinct patterns of comorbidity were evident, with greatest agreement along the diagonal. All risk factors explained comorbidity to some degree, with delinquency, sensation seeking, alcohol expectancies, and religion in particular predicting combinations of comorbidity that were characterized by early onset and chronic high use. Cross-substance trajectory concordance was high, with parallel changes in substance use over emerging adulthood. This suggests similar developmental timing of use, perhaps due to the experience of developmental transitions that have a common influence on use of different substances. Prediction of combinations of comorbidity characterized by early onset and persistently high use suggests that to some extent, individuals use multiple substances because of a common vulnerability to each, rather than directional relations among substances (e.g., cross-tolerance,

cueing). Jackson, K., Sher, K., and Schulenberg, J., Conjoint Developmental Trajectories of Young Adult Substance use. *Alcohol Clin. Exp. Res.*, 32(5), pp. 723-737, 2008.

### Long-term Trends in Adolescent and Young Adult Smoking in the US

The authors sought to describe long-term adolescent and young adult smoking trends and patterns by analyzing adolescent data from Monitoring the Future, 1976 to 2005, and young adult (aged 18-24 years, roughly 16,000 students per year) data from the National Health Interview Survey, 1974 to 2005 (n~1800-5600), overall and in subpopulations to identify trends in current cigarette smoking prevalence. Five metapatterns emerged (1) a large increase and subsequent decrease in overall smoking over the past 15 years, (2) a steep decline in smoking among Blacks through the early 1990s, (3) a gender gap reversal among older adolescents and young adults who smoked over the past 15 years, (4) similar trends in smoking for most subgroups since the early 1990s, and (5) a large decline in smoking among young adults with less than a high school education. Long-term patterns for adolescent and young adult cigarette smoking were decidedly nonlinear, and the authors found evidence of a cohort effect among young adults. Continued strong efforts and a long-term societal commitment to tobacco use prevention are needed, given these unprecedented declines in smoking among most subpopulations since the mid- to late 1990s. Nelson, D., Mowery, P., Asman, K., Pederson, L., O'Malley, P., Malarcher, A., Maibach, E., and Pechacek, T. Long-Term Trends in Adolescent and Young Adult Smoking in the United States: Metapatterns and Implications. *Am. J. Public Health*, 98(5), pp. 905-915, 2008.

### Individual, Social, and Environmental Influences Associated with HIV Infection among Injection Drug Users in Tijuana, Mexico

Researchers examined correlates of HIV infection among injection drug users (IDUs) in Tijuana, Mexico, a city bordering the United States, which is situated on major migration and drug trafficking routes. IDUs aged  $\geq 18$  years were recruited using respondent-driven sampling. Participants underwent antibody testing for HIV and syphilis and structured interviews. Weighted logistic regression identified correlates of HIV infection. Of 1056 IDUs, the median age was 37 years, 86% were male, and 76% were migrants. HIV prevalence was higher in female participants than in male participants (8% vs. 3%;  $P = 0.01$ ). Most IDUs testing HIV-positive were previously unaware of their serostatus (93%). IDUs reported injecting with a median of 2 people in the prior 6 months and had been arrested for having injection stigmata (ie, 'track-marks') a median of 3 times. Factors independently associated with HIV infection were being female, syphilis titers consistent with active infection, larger numbers of recent injection partners, living in Tijuana for a shorter duration, and being arrested for having track-marks. These findings reveal the range of individual, social, and environmental factors that are independently associated with HIV infection among IDUs in Tijuana. They point to the need to intervene not solely on individual risk behaviors but on social processes that drive these behaviors, including problematic policing practices. Strathdee, S., Lozada, R., Pollini, R., Brouwer, K., Mantsios, A., Abramovitz, D., Rhodes, T., Latkin, C., Loza, O., Alvelais, J., Magis-Rodriguez, C., and Patterson, T. Individual, Social, and Environmental Influences Associated with HIV Infection among Injection Drug Users in Tijuana, Mexico. *J Acquir Immune Defic Syndr*, 47(3), pp. 369-376, 2008.

### Predicting Hospitalization among HIV-Infected Antiretroviral Naïve Patients Starting HAART: Determining Clinical Markers and Exploring Social Pathways

In the era of highly active antiretroviral therapy (HAART), hospitalization as a measure of morbidity has become of increasing interest. The objectives of this study were to determine clinical predictors of hospitalization among HIV-infected persons initiating HAART and to explore the impact of gender and drug use on hospitalization. The analysis was based on a cohort of HIV-positive individuals initiating HAART between 1996 and 2001. Information on hospitalizations was obtained through data linkage with the BC Ministry of Health. Cox-proportional hazard models were used to assess variables associated with

time to hospitalization. A total of 1,605 people were eligible and 672 (42%) were hospitalized for one or more days. The final multivariate model indicated that there was an increased risk of hospitalization among those with high baseline HIV RNA (HR for > 100,000 copies/mL: 1.26; 95%CI: 1.16-1.59) or low CD4 cell counts (HR [95% CI] compared to > or = 200 cells/mm<sup>3</sup>: 1.62 [1.28-2.06] and 1.29 [1.07-1.56] for < 50 and 50-199 cells/mm<sup>3</sup>, respectively). Other factors, including adherence, previous hospitalization, gender and injection drug use remained predictive of hospitalization. These findings highlight the importance of closely monitoring patients starting therapy with low CD4 cell counts in order to mediate or prevent outcomes requiring hospitalization. Fielden, S., Rusch, M., Levy, A., Yip, B., Wood, E., Harrigan, R., Goldstone, I., Guillemi, S., Montaner, J., and Hogg, R. Predicting Hospitalization among HIV-Infected Antiretroviral Naïve Patients Starting HAART: Determining Clinical Markers and Exploring Social Pathways. *AIDS Care*, 20(3), pp. 297-303, 2008.

### Patterns of Opioid Analgesic Dependence Symptoms

This study examined symptoms of dependence related to the extramedical use of opioid analgesic medications. The 2002-2003 public data-files of the National Survey on Drug Use and Health were used to identify 7810 extramedical opioid analgesic users in the past-year. Latent Class Analysis was used to empirically define classes of past-year extramedical opioid analgesic users based on observed clustering of DSM-IV defined clinical dependence features; multinomial logistic regression was used to describe differences across these groups. The best-fitting four-class model identified classes that differed quantitatively and qualitatively, with 2% of the users in Class 4 (most severe) and 84% in Class 1 (least severe). Classes 2 and 3 had parallel symptom profiles, but those in Class 3 reported additional problems. Adolescents (12-17 year olds) were at higher odds of being in Class 3 versus older age groups; females were two times as likely to be in Classes 2 and 4, and those with mental health problems were at higher odds of belonging to the more severe classes. Differences by type of past year opioid users were also detected. This study sheds light on the classification and distribution of extramedical opioid analgesic dependence symptoms in the US general population and identifies significant subgroups. Ghandour, L., Martins, S., and Chilcoat, H. Understanding the Patterns and Distribution of Opioid Analgesic Dependence Symptoms Using a Latent Empirical Approach. *Int. J. Methods Psychiatr. Res.*, 17(2), pp. 89-103, 2008.

### Substance Use among Asian Americans and Pacific Islanders Sexual Minority Adolescents: Findings from the National Longitudinal Study of Adolescent Health

Researchers assessed the prevalence, incidence, and correlates of substance use among Asian American individuals transitioning from adolescence to young adulthood. Data were obtained from the National Longitudinal Study of Adolescent Health, Wave II (1996) and Wave III (2001). Information on substance use was abstracted from a nationally representative sample of 1108 Asian Americans and Pacific Islanders (APIs) from both Waves. Weighted prevalence, incidence, and patterns of smoking, binge drinking, marijuana use, and other drug use were analyzed by sexual orientation and gender. Multiple logistic regression analyses were conducted to investigate the unique contribution of being a sexual minority in relation to four types of substance use by gender. A link between sexual orientation and substance use behaviors among APIs did not emerge until young adulthood. Significant increases in the incidence and prevalence of all four types of substance use (tobacco, binge drinking, marijuana, and other drugs) were found among sexual minority APIs. Specifically being an API sexual minority young woman, compared with being a heterosexual young woman, a heterosexual young man, or a sexual minority young man, was significantly associated with substance use after controlling for demographic characteristics, problem behaviors, and substance use during adolescence. The highest prevalence of substance use was found among API sexual minority women. These findings bring new light to the importance of sexual orientation in the design of substance abuse programs. Hahm, H., Wong, F., Huang, Z., Ozonoff, A., and Lee, J. Substance Use among Asian Americans and Pacific Islanders Sexual Minority Adolescents: Findings from the National Longitudinal Study of Adolescent Health. *J. Adolesc. Health*, 42(3), pp. 275-283, 2008.



### The Role of Gender and Family on Long-Term Patterns of Drug Use among an Urban African-American Cohort

The current study uses longitudinal data from a community cohort of African-American inner-city males and females followed from first grade through mid-adulthood (n=1242 at baseline). It identifies the substance use patterns through mid-adulthood, including lifetime prevalence, age of onset and termination, and sequencing of substance classes, as well as the risk of initiation of substance use changes over the life course using survival analysis. It also investigates whether early family structure and process play a role in drug use initiation throughout the life course, and whether the relationship between family factors and drug initiation differs by gender. Overall, among the general trends of use, the authors find a considerable amount of abstinence with over 40% of the participants never using illegal drugs by mid-adulthood, over 70% never using cocaine, and over 90% never using heroin. With respect to onset, the authors find a long-term influence of early family factors on substance use, particularly for females. Family discipline in childhood and family cohesion and parental rule setting during adolescence seem to be key factors in predicting later substance use for females. The implications of these findings for future research and policy are discussed. Doherty, E., Green, K., Reisinger, H., and Ensminger, M. Long-Term Patterns of Drug Use among an Urban African-American Cohort: the Role of Gender and Family. *J. Urban Health*, 85(2), pp. 250-267, 2008.

### Factors Related to Correctional Facility Incarceration among Active Injection Drug Users in Baltimore

The authors investigated the moderating effect of impulse control on the association between drug use and incarceration among active injection drug users (IDU). The study sample consisted of 282 IDUs aged 15-50 years from the Baltimore metropolitan region who reported injection drug use within the past 6 months and indicated that heroin or speedball was their drug of choice. Impulse control was measured using commission error standardized scores from the Test of Variables of Attention (TOVA). Incarceration was obtained using self-reported lifetime history of incarceration in correctional facilities. Findings indicated that impulse control moderated the association between years of injection drug use and incarceration in correctional facilities adjusting for ethnicity, gender, estimated pre-morbid intelligence, and age of first injection use. Specifically, among individuals who were intact in impulse control, four or more years of injection drug use was associated with incarceration (AOR=4.97, 95% CI: 2.02-12.23). This finding was not observed among individuals with impaired impulse control (AOR=0.57, 95% CI: 0.10-3.23). Furthermore, impulse control moderated the association between regular cocaine use and incarceration. Among individuals who had a history of cocaine use, individuals with low impulse control but not impaired were more likely to have reported time in a correctional facility (AOR=6.28, 95% CI: 1.68-23.60). There was no association among individuals with impaired or intact impulse control. Results highlight the importance of considering cognitive measures of impulse control in addressing negative outcomes associated with drug use. Severtson, S., and Latimer, W. Factors Related to Correctional Facility Incarceration among Active Injection Drug Users in Baltimore, MD. *Drug Alcohol Depend.*, 94(1-3), pp. 73-81, 2008.

### The MAOA Promoter Polymorphism, Disruptive Behavior Disorders, and Early Onset Substance Use Disorder: Gene-Environment Interaction

Conduct, oppositional defiant, and attention deficit hyperactivity disorders, reflecting early antisociality and behavior dysregulation, are predictive of substance use disorders. Liabilities to these disorders share genetic and environmental variance. Parenting characteristics have been shown to influence development of antisociality, moderated by variation at the MAOA gene, which has also been associated with the risk for substance use disorders. To extend these findings, the authors tested the relationships between the MAOA promoter polymorphism (variable number tandem repeat), indices of child's perception of paternal and maternal parenting, and disruptive behavior disorders and substance use disorders. A sample of 148 European-American males was assessed prospectively at ages from 10-12 to 18-19 years and genotyped for

the monoamine oxidase A variable number tandem repeat. The Diagnostic and Statistical Manual of mental disorders-III-R diagnoses were obtained using standard methodology. Parenting was assessed using a scale summarizing the child's evaluation of the parenting style (parent's behavior toward him, parental emotional distance and involvement). Correlation, logistic regression, and Cox proportional hazard regression analysis were used to determine the relationships between the variables. The strength of association between parenting index and conduct and attention deficit hyperactivity disorders depended on the MAOA genotype. Unlike earlier findings, the parenting-risk relationships were observed in the 'high' rather than 'low-activity' genotypes. The strength and direction of relationships depended on the parental sex. The MAOA polymorphism's association with the risk for substance use disorders was detected when parenting was controlled for. The results are consistent with the contribution of the MAOA gene, parenting style, and their interactions to variation in the risk for early onset behavior disorders and liability to substance use disorders. Vanyukov, M., Maher, B., Devlin, B., Kirillova, G., Kirisci, L., Yu, L., and Ferrell, R. The MAOA Promoter Polymorphism, Disruptive Behavior Disorders, and Early Onset Substance Use Disorder: Gene-Environment Interaction. *Psychiatr. Genet.*, 17(6), pp. 323-332, 2007.

#### Reciprocal Influence of Parent Discipline and Child's Behavior on Risk for Substance Use Disorder

This study aimed at determining the association of father's and mother's (parental) substance use disorder (SUD) and discipline styles and son's neurobehavioral disinhibition (ND) with son's SUD from childhood (age 10-12) to young adulthood (age 19). It was hypothesized that (1) parental discipline styles and son's ND mediate the association between parental SUD and son's SUD, (2) son's ND mediates the association between parental discipline styles and son's SUD, and (3) parental discipline styles mediate the association between ND and SUD in the son. Two-hundred-sixty-three families including a 10-12 year-old son and both parents participated in the study. The authors found that mother's discipline styles predicted father's discipline styles, son's ND predicted mother's instilling guilt positively and father's punishment negatively, son's ND mediated the association between father's SUD and punishment and son's SUD, and mother's SUD predicted son's ND and SUD. The reciprocal prediction between son's ND and father's punishment and prediction of father's punishment by mother's punishment point to the need for family-based interventions that take into account the quality of specific dyadic interactions pertaining to discipline behaviors that amplify the risk for SUD in male children. Mezzich, A., Tarter, R., Kirisci, L., Feske, U., Day, B., and Gao, Z. Reciprocal Influence of Parent Discipline and Child's Behavior on Risk for Substance Use Disorder: a Nine-Year Prospective Study. *Am. J. Drug Alcohol Abuse*, 33(6), pp. 851-867, 2007.

#### Sex Work and HIV Status among Transgender Women: Systematic Review and Meta-Analysis

Transgender women are a key risk group for HIV, and epidemiologic studies have attributed high rates of HIV infection to behaviors associated with sex work in this population. This systematic review compared HIV prevalence among transgender female sex workers (TFSWs) with prevalence among transgender women who do not engage in sex work, male sex workers, and biologically female sex workers. The researchers conducted systematic searches of six electronic databases. They extracted data, appraised methodologic quality, assessed heterogeneity, and organized meta-analyses by comparison groups. They identified 25 studies among 6405 participants recruited from 14 countries. The overall crude HIV prevalence was 27.3% in TFSWs, 14.7% in transgender women not engaging in sex work, 15.1% in male sex workers, and 4.5% in female sex workers. Meta-analysis indicated that TFSWs experienced significantly higher risk for HIV infection in comparison to all other groups, and particularly in comparison to female sex workers. Significant heterogeneity was found among the included studies, along with methodologic limitations and imprecise definitions of sex work and gender. This study suggests that TFSWs could benefit from targeted HIV prevention interventions, HIV testing, and interventions to help reduce the risk of contracting or transmitting HIV. Operario, D., Soma, T., and Underhill, K. Sex Work and HIV Status among Transgender Women: Systematic Review and Meta-Analysis. *J. Acquir. Imm. Defic. Syndr.*, 48(1), pp. 97-103, 2008.

### Defining Risk Heterogeneity for Internalizing Symptoms among Children of Alcoholic Parents

Adopting a developmental epidemiology perspective, the current study examines sources of risk heterogeneity for internalizing symptomatology among children of alcoholic parents (COAs). Parent-based factors, including comorbid diagnoses and the number of alcoholic parents in the family, as well as child-based factors, namely child gender, formed the indicators of heterogeneity. Following a novel approach to cross-study methods, the authors present a three-stage analysis involving measurement development using item response theory, examination of study effects on latent trajectories over time using latent curve modeling, and prediction of these latent trajectories testing our theoretically derived hypotheses in two longitudinal investigations across both mother- and self-reported symptomatology. Data used were the Michigan Longitudinal Study (596 children from 338 families) and the Adolescent/Adult Family Development Project (454 adolescents and their families). Authors replicated previous findings that parent alcoholism has a unique effect on child internalizing symptoms, above and beyond those of both parent depression and antisocial personality disorder. However, they also found important subgroup differences, explaining heterogeneity within COAs risk profile in terms of the number of alcoholic parents in the family, comorbid diagnoses for the alcoholic parent and, for self-reported symptoms, child gender. Such factors serve to refine the definition of risk among COAs, suggesting a more severely impaired target group for preventive interventions, identifying the significance of familial alcoholism in individual differences underlying internalizing symptoms over time, and further specifying the distal risk matrix for an internalizing pathway to alcohol involvement. Hussong, A., Flora, D., Curran, P., Chassin, L., and Zucker, R. Defining Risk Heterogeneity for Internalizing Symptoms among Children of Alcoholic Parents. *Dev. Psychopathol.*, 20(1), pp. 165-193, 2008.

### Disaggregating the Distal, Proximal, and Time-Varying Effects of Parent Alcoholism on Children's Internalizing Symptoms

The authors tested whether children show greater internalizing symptoms when their parents are actively abusing alcohol by combining observations over ages 2 through 17 from two longitudinal studies of children of alcoholic parents and matched controls recruited from the community. This integrative analysis included data from the Michigan Longitudinal Study (n=596 children from 338 families) and the Adolescent/Adult Family Development Project (454 adolescents and their parents). Using a mixed modeling approach, investigators tested whether children showed elevated mother- and child-reported internalizing symptoms (a) at the same time that parents showed alcohol-related consequences (time-varying effects), (b) if parents showed greater alcohol-related consequences during the study period (proximal effects), and (c) if parents had a lifetime diagnosis of alcoholism that predated the study period (distal effects). No support for time-varying effects was found; proximal effects of mothers' alcohol-related consequences on child-reported internalizing symptoms were found and distal effects of mother and father alcoholism predicted greater internalizing symptoms among children of alcoholic parents. Hussong, A., Cai, L., Curran, P., Flora, D., Chassin, L., and Zucker, R. Disaggregating the Distal, Proximal, and Time-Varying Effects of Parent Alcoholism on Children's Internalizing Symptoms. *J. Abnorm. Child Psychol.*, 36(3), pp. 335-346, 2008.

### The Relationship among Cardiovascular Risk Factors, Diet Patterns, Alcohol Consumption, and Ethnicity among Women Aged 50 Years and Older

This study used cluster analysis to examine diet patterns and the association between diet patterns and the presence of major cardiovascular disease (CVD) risk factors among women over 50 years of age. Data from the cross-sectional National Health and Nutrition Examination Survey (NHANES) 2001-2002 were used. Women 50 years and older were included (n=1,313), and the following major CVD risk factors were examined: being overweight or obese (body mass index >24.9), having elevated systolic blood pressure (>120 mm Hg), and having low levels of high-density lipoprotein cholesterol (<50 mg/dL [ $<1.30$  mmol/L]). Dietary patterns were derived by cluster analysis using data from a 24-hour dietary recall. Odds

Ratios (ORs) and 95% confidence intervals (CIs) were calculated using logistic regression to determine the probability of having a risk factor according to diet pattern while accounting for race/ethnicity, physical activity, age, and smoking. Cluster analysis generated six nonoverlapping diet patterns labeled: Pasta and Yellow Vegetables; Sweets; Beef, Starches, Fruits, and Milk; Frozen Meals, Burritos, and Pizza; Meat Dishes; and Soft Drinks and Poultry. The majority of the women were grouped in the Sweets diet pattern. Factors associated with adequate levels of high-density lipoprotein cholesterol included being non-Hispanic African American (OR 0.59, 95% CI 0.44 to 0.81;  $P < 0.0001$ ), alcohol consumption (OR 0.76, 95% CI 0.69 to 0.84;  $P < 0.0001$ ), and being assigned to the Sweets diet pattern (OR 0.27, 95% CI 0.14 to 0.50;  $P < 0.0001$ ) or Meat dishes diet pattern (OR 0.94, 95% CI 0.54 to 1.65;  $P < 0.0075$ ). The Sweets pattern was also associated with having normal systolic blood pressure levels (OR 0.51, 95% CI 0.34 to 0.76;  $P < 0.0001$ ). Individuals grouped in the Beef, Starches, and Milk diet pattern were more likely to have an adequate body mass index (OR 0.42, 95% CI 0.23 to 0.77;  $P < 0.0032$ ). Significant associations between dietary patterns and major CVD risk factors were observed. Food and nutrition professionals can use this information to assess unhealthful food choices observed in the dietary patterns to guide nutrition recommendations and help reduce the incidence of CVD risk factors. Future research should aim to evaluate dietary intake via complementary methods (ie, dietary patterns and nutrient assessment) to better understand diet-disease relationships. López, E., Rice, C., Weddle, D., and Rahill, G. The Relationship among Cardiovascular Risk Factors, Diet Patterns, Alcohol Consumption, and Ethnicity among Women Aged 50 Years and Older. *J. Am. Diet. Assoc.*, 108(2), pp. 248-256, 2008.

#### Substance Use in Marital Dyads: Premarital Assortment and Change over Time

The purpose of this study was to examine change in substance use with marriage, premarriage similarity in substance use between spouses, and the role of spouse use in predicting changes in use with marriage. Nationally representative samples of high school seniors were followed longitudinally through age 35. The sample consisted of 2,169 adults from eight senior-year cohorts (1977-1984) from the Monitoring the Future study who completed a questionnaire at least once before their first marriage and at 2-year intervals at four consecutive points in time after marriage. Results indicate significant reductions in use with marriage for cigarette smoking, heavy drinking, and marijuana use. Both men and women reported reductions in all three substances following marriage. Changes in women's use followed a linear pattern. Although men's decreases in cigarette smoking and heavy drinking were initially rapid and then decelerated, their decrease in marijuana use accelerated over time. Declines in use for both genders were associated with getting married to individuals who also decreased their use. Those with higher premarriage levels of substance use experienced greater reductions in use. A significant association between respondent and spouse premarital use suggests assortative mating takes place for all three substances. This study affirms and further qualifies the presence of a marriage effect on substance use using multiwave and multicohort national data. Results suggest that the effects of marriage on smoking, heavy drinking, and marijuana use are related to one's own initial levels of use and the direction of change in the spouse's use. These findings have important implications for life span theoretical advances as well as interventions aimed at the marital dyad. Merline, A., Schulenberg, J., O'Malley, P., Bachman, J., and Johnston, L. Substance Use in Marital Dyads: Premarital Assortment and Change over Time. *J. Stud. Alcohol Drugs*, 69(3), pp. 352-361, 2008.

#### Movie Smoking Exposure and Smoking Onset: A Longitudinal Study of Mediation Processes in a Representative Sample of U.S. Adolescents

The authors tested 2 mechanisms for the relation of movie smoking exposure with onset of cigarette smoking in adolescence. Longitudinal data with 8-month follow-up were obtained from a representative sample of 6,522 U.S. adolescents, ages 10-14 years. Structural modeling analysis based on initial nonsmokers, which controlled for 10 covariates associated with movie exposure, showed that viewing more smoking in movies was related to increases in positive expectancies about smoking and increases in affiliation with smoking peers, and these variables were both related to smoking onset. A direct effect of

movie exposure on smoking onset was also noted. Mediation findings were replicated across cross-sectional and longitudinal analyses. Tests for gender differences indicated that girls showed larger effects of movie exposure for some variables. Wills, T., Sargent, J., Stoolmiller, M., Gibbons, F., and Gerrard, M. Movie Smoking Exposure and Smoking Onset: A Longitudinal Study of Mediation Processes in a Representative Sample of U.S. Adolescents. *Psychol. Addict. Behav.*, 22(2), pp. 269-277, 2008.

### The Drinking Culture of Alcohol Use

Binge drinking is a substantial health problem. Community norms about drinking may influence individual drinking problems. This study examined the relation between aspects of the neighborhood drinking culture and individual alcohol use by using data from the New York Social Environment Study conducted in 2005. The sample consisted of 4,000 New York City residents greater than 18 year of age. Methods to address social stratification and social selection, both of which are challenges to interpreting neighborhood research were applied. In adjusted models, permissive neighborhood drinking norms were associated with moderate drinking (odds ratio (OR) = 1.28, 95% confidence interval (CI): 1.05, 1.55) but not binge drinking; however, social network and individual drinking norms accounted for this association. By contrast, permissive neighborhood drunkenness norms were associated with more moderate drinking (OR = 1.20, 95% CI: 1.03, 1.39) and binge drinking (OR = 1.92, 95% CI: 1.44, 2.56); the binge drinking association remained after adjustment for social network and individual drunkenness norms (OR = 1.58, 95% CI: 1.20, 2.08). Drunkenness norms were more strongly associated with binge drinking for women than for men ( $p(\text{interaction}) = 0.006$ ). Propensity distributions and adjustment for drinking history suggested that social stratification and social selection, respectively, were not plausible explanations for the observed results. Results suggest that further epidemiologic studies investigating the social and structural factors that shape harmful drinking may inform efforts targeting the problematic aspects of alcohol consumption. Ahern, J., Galea, S., Hubbard, A., Midanik, L., and Syme, S. Culture of Drinking and Individual Problems with Alcohol Use. *Am. J. Epidemiol.*, 167(9), pp. 1041-1049, 2008.

## **PREVENTION RESEARCH**

### Universal Childhood Prevention Effects Developmental Course of Antisocial Personality Disorder and Violent and Criminal Behavior

Antisocial personality disorder (ASPD), violent and criminal behavior, and drug abuse disorders often share the common antecedent of early aggressive, disruptive behavior. In the 1985-1986 school year teachers implemented the Good Behavior Game (GBG), a classroom behavior management strategy targeting aggressive, disruptive behavior and socializing children to the student role. From first through seventh grade the developmental trajectories of 2311 students from 19 Baltimore City Public Schools were examined. GBG impact on these trajectories and ASPD and violent and criminal behavior by age 19-21 is reported. In five urban, poor to lower middle class predominately African-American areas, three to four schools were matched and within each set randomly assigned to one of three conditions: (1) GBG, (2) a reading achievement program, or (3) the standard program. Classrooms and teachers were randomly assigned to intervention or control. Measures at 19-21 included self reports and juvenile court and adult incarceration records. GBG impact was assessed via General Growth Mixture Modeling based on repeated measures of aggressive, disruptive behavior. Three trajectories of aggressive, disruptive behavior were identified. By young adulthood, GBG significantly reduced the rates of ASPD and violent and criminal behavior among males in the persistent high aggressive, disruptive trajectory. A replication was implemented with the following cohort of first-grade children using the same teachers, but with diminished mentoring and monitoring. Beneficial impact was found among persistent high males through seventh grade. By young adulthood GBG effects on ASPD and violent and criminal behavior were non-significant, but generally in the hypothesized direction. This study demonstrated strongest effects on high risk males, suggesting the need to understand the shared and non-shared developmental processes within and across genders. Petras, H., Kellam, S.G., Brown, C.H., Muthén, B., Ialongo, N., and Poduska, J. Developmental

Epidemiological Courses Leading to Antisocial Personality Disorder and Violent and Criminal Behavior: Effects by Young Adulthood of a Universal Preventive Intervention in First- and Second-Grade Classrooms. *Drug Alcohol Depend.*, 95S1 pp. S45-S59, 2008.

A Randomized Evaluation of Multidimensional Treatment Foster Care: Effects on School Attendance and Homework Completion in Juvenile Justice Girls

Despite growing evidence that child welfare youth are at increased risk for juvenile delinquency, little is known about gender-specific processes and effective treatment programs for girls. Multidimensional Treatment Foster Care (MTFC), an empirically validated intervention for child welfare and juvenile justice populations, has demonstrated efficacy in reducing arrest rates in delinquent boys and girls. In this study, the efficacy of MTFC on school attendance and homework completion was examined in juvenile justice girls who were referred to out-of-home care (N = 81). Results from this randomized intervention trial suggest that MTFC was more effective than group care in increasing girls' school attendance and homework completion while in treatment and at 12 months post baseline. In addition, the previously reported effect of MTFC on reducing girls' days in locked settings was mediated by homework completion while girls were enrolled in the intervention setting. Implications for policy and practice are described. Leve, L.D., and Chamberlain, P. A Randomized Evaluation of Multidimensional Treatment Foster Care: Effects on School Attendance and Homework Completion in Juvenile Justice Girls. *Res. Soc. Work Pract.*, 17(6), pp. 657-663, 2007.

A New Statistical Procedure to Examine Behavioral Transitions

The set of statistical methods available to researchers is continually being expanded, allowing for questions about change over time to be addressed in new, informative ways. Indeed, new developments in methods to model change over time create the possibility for new research questions to be posed. Latent transition analysis, a longitudinal extension of latent class analysis, is a method that can be used to model development in discrete latent variables, for example, stage processes, over 2 or more times. The current article illustrates this approach using a new SAS procedure, PROC LTA, to model change over time in adolescent and young adult dating and sexual risk behavior. Gender differences are examined, and substance use behaviors are included as predictors of initial status in dating and sexual risk behavior and transitions over time. Lanza, S., and Collins, L. A New SAS Procedure for Latent Transition Analysis: Transitions in Dating and Sexual Risk Behavior. *Dev. Psychol.*, 44(2), pp. 446-456, 2008.

Substance Abuse is Associated with HCV Viremia and HCV Transmission Potential

Co-infection with hepatitis C virus (HCV) is common among HIV-infected women. To further the understanding of risk factors for HCV viremia and the predictors of HCV viral load among women, sociodemographic, immunologic, and virologic factors associated with presence and level of HCV viremia were investigated among 1049 HCV-seropositive women, 882 of whom were HIV-infected and 167 HIV-uninfected at their entry into the Women's Interagency HIV Study. Plasma HCV RNA was detected in 852 (81%) of these 1049 women (range: 1.2-7.8 log<sub>10</sub>copies/ml). HCV-viremic women were more likely to have an HIV RNA level >100,000 copies/ml (p = 0.0004), to have reported smoking (p = 0.01), or to be Black (p = 0.005). They were less likely to have current or resolved hepatitis B infection. HCV RNA levels were higher in women who were >35 years old, or HIV-infected. Current smoking and history of drug use (crack/freebase cocaine, marijuana, amphetamines, or heroin) were each associated with both presence and level of viremia. Substance abuse counseling aimed at eliminating ongoing use of illicit drugs and tobacco may reduce clinical progression, improve response to treatment, and decrease HCV transmission by lowering levels of HCV viremia in women. Operskalski, E., Mack, W., Strickler, H., French, A., Augenbraun, M., Tien, P., Villacres, M., Spencer, L., Degiacomo, M., and Kovacs, A. Factors Associated With Hepatitis C Viremia in a Large Cohort of HIV-Infected and -Uninfected Women. *J. Clin. Virol.*, 41(4), pp. 255-263, 2008.

## The Use of Harmful Legal Products among Pre-adolescent Alaskan Students

This study examined pre-adolescent use of harmful but legally obtainable products (HLPs) “in order to get high” in 4 communities in northwest and southeast Alaska. These products include inhalants, over-the-counter medications, prescription medications taken without a doctor's prescription and common household products. A student survey was administered to the 447 students whose parents consented and who agreed to participate. The lifetime overall use of HLPs among fifth, sixth and seventh grade students in 4 Alaskan communities was 17.4%. The lifetime use of inhalants (6.8%) and prescription medications taken without a doctor's prescription (8.0%) appear to be comparable to use rates from other studies. The use of over-the-counter medications (5.7%) appears to be slightly higher than in other U.S. surveys. The use of common household products was 6.1%. No significant differences in the lifetime or 30-day use were found correlated to region, gender, and ethnicity or student grade. There was a strong association between 30-day or lifetime use of some HLPs and the (30-day or lifetime) use of alcohol, cigarettes and smokeless tobacco. The use of harmful everyday legal products by fifth, sixth and seventh graders in Alaska appears to be similar to data collected in other parts of the country. The possibility that there may be a link between the use of available legal substances and alcohol, tobacco and marijuana deserves additional attention. Saylor, B., Fair, M., Deike-Sims, S., Johnson, K., Ogilvie, K., and Collins, D. The Use of Harmful Legal Products among Pre-Adolescent Alaskan Students. *Int. J. Circumpolar Health*, 66(5), pp. 425-436, 2007.

## HIV Disclosure among Adults Living with HIV

Research on disclosure among heterosexual adult person(s) living with HIV (PLH) was reviewed, omitting disclosure of parental HIV to children. Disclosure has been studied within five additional relational contexts: with partners, family members, friends, healthcare professionals and in work settings. Disclosure is higher among women than men, among Latino and white compared to African-American families, and among younger compared to older HIV-positive adults. Most PLH disclose to their sexual partners and family members, yet there is a significant minority who do not disclose. Similarly, rates of disclosure to employers range from 27-68%, suggesting broad variability in perceived consequences of employment disclosures. Of concern, 40% of PLH do not consistently disclose to their healthcare professionals. Rather than examine HIV disclosures in the context of relationships, it is possible to understand disclosures around personal identity. Disclosure decisions are often made to tell everyone (making HIV status a central attribute of one's identity), no one (requiring strategies for securing social support while remaining anonymous) or some people (requiring strategic decisions based on context). Given that disclosure decisions are central to personal identity, future data on disclosure and interventions designed to increase disclosure or comfort with disclosure must focus on communication strategies adopted by PLH to present a coherent identity. Arnold, E.M., Arnold, E.M.E.R., Flannery, D., and Rotheram-Borus, M.J. HIV Disclosure among Adults Living with HIV. *AIDS Care*, 20(1), pp. 80-92, 2008.

## **RESEARCH ON BEHAVIORAL & COMBINED TREATMENTS FOR DRUG ABUSE**

### Menstrual Phase Effects on Smoking Relapse

The research on smoking cessation suggests that women have a more difficult time quitting than do men, although the reasons for this are not well understood. Some studies have found that smoking behavior fluctuates with the menstrual phase cycle, where smoking and craving is higher in the luteal than the follicular phase, making it more difficult to quit during that phase. To test this, Dr. Allen and colleagues from the University of Minnesota conducted a study to examine if menstrual phase affects relapse in 202 women who were attempting to quit smoking. The women were assigned to quit smoking in either the follicular (F) or luteal (L) menstrual phase and were followed for up to 26 weeks. They measured how many days before relapse and relapse phase to determine if those who begin a quit attempt during the F phase were more successful than those who begin during the L phase. The mean number of days to relapse

after a period of continuous abstinence for the F group was 13.9 versus 21.5 days for the L group. Relapse from prolonged abstinence for the F group was 20.6 versus 39.2 days for the L group. At 14 days, 84% of the F group had relapsed compared with 65% of the L group. At 30 days, 86% of the F group relapsed, compared with 66% of the L group. These results suggest that women attempting to quit smoking in the F phase had less favorable outcomes than those attempting to quit in the L phase. This could relate to ovarian hormones, which may play a role in smoking cessation for women. Allen, S.S., Bade, T., Center, B., Finstad, D., and Hatsukami, D. Menstrual Phase Effects on Smoking Relapse. *Addiction*, 103(5), pp. 809-821, 2008.

#### Effects of Voucher-Based Incentives on Abstinence from Cigarette Smoking and Fetal Growth among Pregnant Women

Drs. Heil and Higgins and colleagues from the University of Vermont examined whether vouchers that are given contingent upon smoking abstinence during pregnancy are an effective way to decrease maternal smoking and improve fetal growth. A total of 82 smokers entering prenatal care were randomly assigned to either contingent or non-contingent voucher conditions. Vouchers exchangeable for retail items were available during pregnancy and for 12 weeks postpartum. In the contingent condition, vouchers were earned for biochemically verified smoking abstinence; in the non-contingent condition, vouchers were earned independent of smoking status. Smoking outcomes were evaluated using urine-toxicology testing and self-report. Fetal growth outcomes were evaluated using serial ultrasound examinations performed during the third trimester. Contingent vouchers significantly increased abstinence at the end-of-pregnancy (41% versus 10%) and at the 12-week postpartum point (24% versus 3%). There was significantly greater fetal growth with the contingent condition in terms of estimated weight, femur length and abdominal circumference. These results provide further evidence that abstinent-contingent vouchers can substantially decrease maternal smoking during pregnancy, and provide new evidence of positive effects on fetal health. Heil, S., Higgins, S., Bernstein, I., Solomon, L., Rogers, R., Thomas, C., Badger, and G. Lynch, M. Effects of Voucher-Based Incentives on Abstinence from Cigarette Smoking and Fetal Growth among Pregnant Women. *Addiction*, 103(6), pp. 1009-1018, 2008.

#### Exercise as an Adjunct to Nicotine Gum in Treating Tobacco Dependence among Women

The acute effects of exercise on reducing withdrawal from and craving for cigarettes has suggested that exercise may be a useful adjunct for smoking cessation treatment. Dr. Kinnunen and colleagues from Harvard conducted the first randomized controlled trial assessing the efficacy of an exercise intervention as an adjunct to nicotine gum therapy. They compared the exercise intervention with both an equal contact control and a standard care control condition. Sedentary female smokers (N = 182) aged 18-55 years were provided with nicotine gum treatment along with brief behavioral counseling and were randomized into one of these three behavioral adjunct conditions. At the end of treatment and at 1-year follow-up, there were clear trends showing that both the exercise and equal contact control conditions had higher rates of abstinence than the standard care control, although the effect was not statistically significant. However, the equal contact condition had a significantly lower likelihood of relapse after 1 week compared with the standard care condition and there was a near significant trend in which exercise offered an advantage over standard care as well. While these findings suggest a slightly improved likelihood of abstinence with exercise compared with standard care, exercise did not differ from equal contact control in its efficacy. Potential explanations for these equivalent levels of efficacy and implications for the findings are discussed. Kinnunen, T., Leeman, R., Korhonen, T., Quiles, Z., Terwal, D., Garvey, A., and Hartley, H. Exercise as an Adjunct to Nicotine Gum in Treating Tobacco Dependence among Women. *Nicotine Tob. Res.*, 10(4), pp. 689-703, 2008.



### The Impact of Managed Care on Drug-Dependent Pregnant Women and their Children

Using archival data, this study examined the effects of managed care (MC) on a population of drug-dependent women and their children in a multidisciplinary, comprehensive care substance user treatment facility in pre- (1995, n=132) and post (2000, n=108)–managed care conditions. The two groups had similar birth parameters, but the MC group had more fetal and infant deaths, decreased immunization rates, and greater incidence of social services intervention. While these data are correlational and need to be interpreted with caution, they suggest that the shift from fee-for-service to managed care (MC) has resulted in poorer outcomes for drug-exposed children under MC. Jansson, L.M., Svikis, D.S., Velez, M., Fitzgerald, E., and Jones, H.E. The Impact of Managed Care on Drug-Dependent Pregnant and Postpartum Women and their Children. *Subst. Use Misuse*, 42(6), pp. 961-974, 2007.

### Higher Relapse Rate for Drug-Dependent Pregnant Women with Mood Disorders

The purpose of this study was to examine the potential treatment impact of co-occurring Axis I disorders in a sample of opiate-dependent pregnant women receiving methadone treatment. Participants were categorized into three groups according to their primary current SCID diagnosis: (1) absence of any current mood/anxiety disorder (ND, n = 29), (2) primary mood disorder (MD, n = 39), and (3) primary anxiety disorder (AD, n = 38). Demographically, the groups were similar. The MD group was significantly more likely to be positive for drugs while in treatment compared with both the ND and AD groups. The MD and AD groups had more psychosocial impairment and higher incidence of suicidal ideation compared with the ND group. Interestingly, the AD group spent more days in treatment compared with the ND or MD group. The authors conclude that the poor treatment outcomes in the MD group suggest the need for treatment that specifically targets the mood disorder in addition to the substance use disorder. While enhanced treatment resources for all substance-abusing pregnant patients with co-occurring disorders would be ideal, it may be possible to achieve improvement in treatment outcomes by recognizing the particular needs of different substance-abusing subpopulations and by tailoring treatments both at the programmatic and individual level to specifically address those needs. Fitzsimons, H.E., Tuten, M., Vaidya, V., and Jones, H.E. Mood Disorders Affect Drug Treatment Success of Drug-Dependent Pregnant Women. *J. Subst. Abuse Treat.*, 32(1), pp. 19-25, 2007.

## **RESEARCH ON PHARMACOTHERAPIES FOR DRUG ABUSE**

### Rural Opioid-using Pregnant Women Appear to Have Some Characteristics Associated With Better Treatment Outcomes

Historically, research on opioid use during pregnancy has occurred in urban settings and it is unclear how urban and rural populations compare. This study examined socio-demographic and other variables in opioid-using pregnant women seeking treatment and screened for participation in a multi-site randomized controlled trial. Women screened in rural Burlington, Vermont (n=54), were compared to those screened in urban Baltimore, Maryland (n=305). Rural opioid-using pregnant women appear to have some characteristics associated with better treatment outcomes (e.g., less severe drug use, greater employment). However, they may face additional barriers in accessing treatment (e.g., greater distance from treatment clinic). Heil, S.H., Sigmon, S.C., Jones, H.E., and Wagner, M. Comparison of Characteristics of Opioid-using Pregnant Women in Rural and Urban Settings. *Am. J. Drug Alcohol Abuse*, 34(4), pp. 463-471, 2008.

### Predictors of Cardiovascular Response to Methamphetamine Administration in Methamphetamine-dependent Individuals May Help in the Prevention and Treatment of Cardiovascular Events in a Population at High Risk

The goal of this study was to determine predictors of cardiovascular response to methamphetamine administered in the laboratory. Heart rate (HR) and blood pressure (BP) were measured at baseline and at several time points following the administration of methamphetamine or saline placebo. One-way ANOVA was used to determine the differences between female and male subjects in their cardiovascular response. In male subjects, linear regression and one-way ANOVA were used to determine the influence of potential predictors on cardiovascular response, including age, weight, drug use indicators, concurrent use of other substances, route of administration, and race. Methamphetamine administration provoked significant increases in HR and BP, as compared to placebo. Female gender was associated with larger peak change in diastolic BP following administration. Baseline HR and BP were found to be strong predictors of cardiovascular response to methamphetamine administration in male subjects. Lifetime use and recent use of methamphetamine and nicotine did not predict cardiovascular response to methamphetamine. Recent alcohol use was associated with increased peak change in diastolic BP. Also, current use of cannabis was negatively correlated with peak HR change. Male cannabis users show lower peak change in HR as compared to non-cannabis users. As compared to methamphetamine smokers, intravenous users demonstrated higher peak change in diastolic BP following drug administration. Race did not have a significant effect on cardiovascular response. Taken together, these findings may help in the prevention and treatment of cardiovascular events in a population at high risk of premature morbidity and mortality. Fleury, G., DeLaGarza, R., Mahoney, J.J., Evans, S.E., and Newton, T.F. Predictors of Cardiovascular Response to Methamphetamine Administration in Methamphetamine-dependent Individuals. *Am. J. Addict.* Mar-Apr; 17(2) pp. 103-110, 2008.

### Sex and Opioid Maintenance Dose Influence Response to Naloxone in Opioid-dependent Humans

Pooled self-report and physiological data from 32 male and 15 female methadone or LAAM maintained volunteers were retrospectively analyzed for individual differences in response to naloxone (0.15 mg/70 kg, IM) and placebo at 20 and 40 minutes post-injection. Males and females were each divided by the median split methadone maintenance dose (MMD, in mg/kg body weight) into high and low MMD groups and MMD was used as a factor in the analysis, along with sex, drug, and time post-drug. Females in the low, but not high, MMD group showed naloxone-induced increases in ratings on the Antagonist and Mixed-Action subscales of the Adjective Rating Scale, and the LSD sub-scale of the Addiction Research Center Inventory at 20 minutes post-injection. Males in the high MMD group showed significant naloxone-induced increases in scores of these measures at both post-injection time points. In addition, low MMD subjects showed more short-lived naloxone-induced increases on Visual Analogue Scale Bad and Any drug effects ratings than high MMD subjects. These results suggest that those on a lower MMD, especially women, experience a more intense, but short-lived, response to naloxone, whereas those on a higher MMD experience a more modest, but long lasting effect. Chopra, M.P., Feldman, Z., Mancino, M.J., and Oliveto, A. Sex and Opioid Maintenance Dose Influence Response to Naloxone in Opioid-dependent Humans. *Pharm. Biochem. Behav.*, 2008 Jun 7 (E-pub ahead of print).

### Changes in Mood, Cognitive Performance and Appetite in the Late Luteal and Follicular Phases of the Menstrual Cycle in Women With and Without PMDD (Premenstrual Dysphoric Disorder)

Although it's been reported that women with premenstrual dysphoric disorder (PMDD) have increased negative mood, appetite (food cravings and food intake), alcohol intake and cognitive deficits premenstrually, few studies have examined these changes concurrently within the same group of women or compared to women without PMDD. Thus, to date, there is not a clear understanding of the full range of PMDD symptoms. The present study concurrently assessed mood and performance tasks in 29 normally cycling women (14 women who met DSM-IV criteria for PMDD and 15 women without PMDD). Women

had a total of ten sessions: two practice sessions, 4 sessions during the follicular phase and 4 sessions during the late luteal phase of the menstrual cycle. Each session, participants completed mood and food-related questionnaires, a motor coordination task, performed various cognitive tasks and ate lunch. There was a significant increase in dysphoric mood during the luteal phase in women with PMDD compared to their follicular phase and compared to Control women. Further, during the luteal phase, women with PMDD showed impaired performance on the Immediate and Delayed Word Recall Task, the Immediate and Delayed Digit Recall Task and the Digit Symbol Substitution Test compared to Control women. Women with PMDD, but not Control women, also showed increased desire for food items high in fat during the luteal phase compared to the follicular phase and correspondingly, women with PMDD consumed more calories during the luteal phase (mostly derived from fat) compared to the follicular phase. In summary, women with PMDD experience dysphoric mood, a greater desire and actual intake of certain foods and show impaired cognitive performance during the luteal phase. An altered serotonergic system in women with PMDD may be the underlying mechanism for the observed symptoms; correspondingly, treatment with specific serotonin reuptake inhibitors (SSRIs) remains the preferred treatment at this time. Reed, S.C., Levin, F.R., and Evans, S.M. Changes in Mood, Cognitive Performance and Appetite in the Late Luteal and Follicular Phases of the Menstrual Cycle in Women With and Without PMDD (Premenstrual Dysphoric Disorder). *Horm. Behav.*, 54, pp. 185-193, 2008.

## **RESEARCH ON MEDICAL CONSEQUENCES OF DRUG ABUSE & CO-OCCURRING INFECTIONS (HIV/AIDS, HCV)**

### **HIV/AIDS**

#### C-reactive Protein: A Poor Marker of Cardiovascular Disease Risk in HIV+ Populations with a High Prevalence of Elevated Serum Transaminases

Blood lipids and high-sensitivity C-reactive protein (hsCRP) are used to assess cardiovascular disease (CVD) risk. The authors evaluated in a cross-sectional design the relationship of hsCRP to markers of liver function (aspartate and alanine transaminases [AST and ALT, respectively]), CVD risk factors and HIV-disease progression markers in 226 HIV-1 sero-positive drug users. hsCRP showed a significant inverse relationship with ALT and high-density lipoprotein, independent of age, gender, viral load, CD4 cell-count and antiretroviral (ARV) use, and was not significantly associated with HIV-disease progression markers. Serum markers of liver damage, AST and ALT, were associated with lower hsCRP, total cholesterol, low-density lipoproteins and triglycerides. Elevated liver enzymes ( $>$  or  $=40$  IU/L) were predictive of hsCRP levels that are considered a low risk for CVD. In conclusion, hsCRP may not be a reliable marker of CVD risk in populations with HIV at-risk for elevated liver enzymes due to high hepatitis B virus/hepatitis C virus prevalence and ARV use. Baum, M.K., Rafie, C., Sales, S., Lai, S., Duan, R., Jayaweera, D.T., Page, J.B., Campa, A. *Int. J. STD AIDS*. 19(6), pp. 410-413, 2008.

#### A Pilot Survey of Attitudes and Knowledge about Opioid Substitution Therapy for HIV-Infected Prisoners

A majority of inmates in the state of Connecticut Department of Corrections use opioids or are opioid dependent before incarceration. None of the state's prisons offer opioid substitution therapy other than for detoxification or maintenance therapy for women during pregnancy. On release to the community, most prisoners relapse to drug use and this has been associated with higher recidivism rates, and less adherence to antiretroviral medications for HIV-infected persons. Nationally and internationally, methadone (METH) and buprenorphine (BUP) have been found to decrease relapse to drug use, decrease recidivism rates, improve adherence to antiretroviral medications, decrease HIV-risk taking behaviors, and improve mortality. However, the general knowledge about opioid substitution therapy among correctional facility staff has been reported as substandard. This pilot study compiled results of answers to anonymous surveys from 27 individuals who work directly with inmates in a patient-care capacity for the Connecticut Department of Corrections (CT DOC) and CT DOC case-management referral program (Project TLC) in

the year 2006. The surveys included questions regarding current attitudes and knowledge about opioid substitution therapy for prisoners. A minority of respondents refer released prisoners with a history of opioid dependency to METH or BUP treatment. The majority of correctional workers and case-management referral workers did not have knowledge about BUP or METH's ability to improve health and decrease HIV risk taking behaviors. This study found that more education of individuals treating and caring for HIV-infected opioid dependent prisoners is needed. Springer, S.A., and Bruce, R.D. *J. Opioid Manag.* 4(2), pp. 81-86, 2008.

## **NON-INFECTION DRUG ABUSE MEDICAL CONSEQUENCES**

### Trends in Methamphetamine Use in Young Injection Drug Users in San Francisco from 1998 to 2004: the UFO Study

Secondary analysis of cross-sectional baseline data collected for a longitudinal study of young IDU from 1998 to 2004 were examined to describe temporal trends in methamphetamine use among young injection drug users (IDU) in San Francisco. Median age was 22 years [interquartile range (IQR) 20-25], 30.3% were women and median duration of injecting was 4.4 years (IQR 2-7). Prevalence of methamphetamine use was high, with 50.1% reporting recent injection, but overall there were no temporal increases in reported 'ever' injected use. Recent methamphetamine injection (past 30 days) increased significantly, and peaked at 60% in 2003. MSM-IDU had higher methamphetamine injection ever (92.3%) and recently (59.5%) compared to heterosexual male (non-MSM) IDU (81.6% and 47.3%, respectively) and to female IDU (78.4% and 46.1%, respectively). Findings disclosed that despite reports of ubiquitous increases in methamphetamine use, there were no significant increases in 6 years in ever injecting methamphetamine overall among young IDU. Further, the methamphetamine 'epidemic' appeared to have been under way among young IDU earlier than in other populations. Inglez-Dias, A., Hahn, J.A., Lum, P.J., Evans, J., Davidson, P., and Page-Shafer, K. *Drug Alcohol Rev.* 27(3), pp. 286-291, 2008.

## **SERVICES RESEARCH**

### Smoking Trends May Underly Increasing Education Level Differences in Health Status Relying on Data from the Multiple Cause of Death File and the National Longitudinal Mortality Study

This study examines educational disparities in mortality and life expectancy among non-Hispanic blacks and whites in the 1980s and 1990s. Age-standardized death rates per 100,000 Americans were estimated by education, race, sex and cause between 1990 and 2000. Differences in life expectancies between those with a high school diploma and those with some college education were significant. In 2000, a 25 year old with a high-school diploma could expect to live less than 50 years, until age 75, while a 25 year old with some college could expect to live 7 years longer. This gap had increased by about 30 percent over the study time period. Lung cancer and COPD, two diseases attributable largely to tobacco use, accounted for 21 percent of this widening gap overall, and 25 percent of the gap for less-educated white women over the age of 45, who have shown more modest declines in smoking rates. The gaps are increasing because, for most groups, longevity for more highly-educated individuals is increasing while that for less-educated groups is remaining the same. Meara, E., Richards, S., and Cutler, D. *The Gap Gets Bigger: Changes In Mortality and Life Expectancy By Education, 1981-2000.* *Health Aff (Millwood)*, 27(2), pp. 350-360, 2008.

### Special Gender-Specific Addiction Treatment Programs Had Superior Outcomes to Mixed-Gender Programs

This quasi-experimental, retrospective study reports on the continuity of care for women with children who were admitted to long-term residential substance abuse treatment. Women were admitted to seven agencies offering specialized, women's only treatment (SP, n = 747) or to nine agencies that provided standard

mixed-gender treatment (ST, n = 823). Client and treatment data were gathered from administrative sources. Multivariate analyses revealed that SP clients who completed treatment with longer stays were most likely to continue care. Women in SP programs (37%) were more likely than those in ST programs (14%) to continue care. The findings show that specialized treatment for women promotes continuing care and demonstrate the importance of treatment completion. Orwin, R., Claus, R., Kissin, W., Krupski, A., Campbell, K., and Stark, K. Does Gender-Specific Substance Abuse Treatment for Women Promote Continuity of Care? *J. Subst. Abuse Treat.*, 32, pp. 27-39, 2007.

#### HIV Risk Behaviors among Rural Stimulant Users: Variation by Gender and Race/Ethnicity

The researchers examined data from a community sample of rural stimulant users (n = 691) in three diverse states to identify gender and racial/ethnic differences in HIV risk behaviors. Bivariate and logistic regression analyses were conducted with six risk behaviors as dependent variables: injecting drugs, trading sex to obtain money or drugs, trading money or drugs to obtain sex, inconsistent condom use, multiple sex partners, and using drugs with sex. Controlling for state, income, age, heavy drinking, and type of stimulant used, men had lower odds than women for trading sex to obtain money or drugs (adjusted odds ratio [AOR] = 0.4, confidence interval [CI] = 0.28-0.59; p < .0001), greater odds than women for trading money or drugs to obtain sex (AOR = 44.4, CI = 20.30-97.09; p < .0001), greater odds than women of injecting drugs (adjusted odds ratio (AOR) = 1.6, CI = 1.11-2.42; p = .01), and lower odds than women of using condoms inconsistently (AOR = 0.6, CI = 0.35-0.92; p = .02); African Americans had lower odds than Whites of injecting drugs (AOR = .08, CI = 0.04-0.16; p < .0001), greater odds than Whites for trading sex to obtain money or drugs (AOR = 1.7, CI = 1.01-2.85; p = .04) and for trading money or drugs to obtain sex (AOR = 2.9, CI = 1.53-5.59; p = .001), and greater odds than Whites of using drugs with sex (AOR = 3.9, CI = 1.47-10.09; p = .006). These findings indicate HIV prevention efforts should be tailored to address gender and racial/ethnic differences in risk behaviors among rural stimulant users. Wright, P., Stewart, K., Fischer, E., Carlson, R., Falck, R., Wang, J., Leukefeld, C., and Booth, B. HIV Risk Behaviors among Rural Stimulant Users: Variation by Gender and Race/Ethnicity. *AIDS Educ. Prev.*, 19(2), pp. 137-150, 2007.

#### Nurse Case-Managed Intervention for Latent Tuberculosis among the Homeless

The efficacy of a nurse case-managed intervention was evaluated in subsamples of participants with one of the following characteristics: female gender, African American ethnicity, recruited from a homeless shelter, a history of military service, lifetime injection drug use, daily alcohol and drug use, poor physical health, and a history of poor mental health. The purpose of the study was to determine whether a validated nurse case managed intervention with incentives and tracking would improve adherence to latent tuberculosis infection treatment in subsamples of homeless persons with characteristics previously identified in the literature as predictive of non-adherence. A prospective 2-group site-randomized design was conducted with 520 homeless adults residing in 12 homeless shelters and residential recovery sites in the Skid Row region of Los Angeles from 1998 to 2003. Results revealed that daily drug users, participants with a history of injection drug use, daily alcohol users, and persons who were not of African American race or ethnicity had particularly poor completion rates, even in the nurse case-managed intervention program (48%, 55%, 54%, and 50%, respectively). However, the intervention achieved a 91% completion rate for homeless shelter residents and significantly improved latent tuberculosis infection treatment adherence in 9 of 12 subgroups tested (odds ratios = 2.51-10.41), including daily alcohol and drug users, when potential confounders were controlled using logistic regression analysis. It is concluded that nurse case management with incentives appears to be a good foundation for increasing adherence to 6-month isoniazid treatment in a variety of homeless subgroups and, in particular, for sheltered homeless populations. However, additional social-structural and environmental strategies are needed to address those at greatest risk of non-adherence. Nyamathi, A., Nahid, P., Berg, J., Burrage, J., Christiani, A., Aqtash, S., Morisky, D., and Leake, B. Efficacy of Nurse Case-Managed Intervention for Latent Tuberculosis among Homeless Subsamples. *Nurs. Res.*, 57(1), pp. 33-39, 2008.

### Intensive Case Management Is Associated with Improved Outcomes For Women With Substance Use Disorders

The aim of this study is to identify factors that predict, mediate or moderate the effects of intensive case management (ICM) on longer-term drug abstinence outcomes in women on welfare. In a parent study women were assigned randomly to usual care (UC) or intensive case management (ICM). Treatment was provided for 12 weeks and follow-up continued for 15 months after study intake. A set of hypothesized mediators was assessed at month 3 and a rigorous four-step mediational model was tested using outcomes in months 4-15. Participants were 302 drug-dependent women applying and eligible for federal welfare and not currently in drug abuse treatment. The ICM intervention provided intensive treatment engagement including voucher incentives for treatment attendance and case management services; UC provided primarily referral to community treatment programs. Substance use outcomes were assessed using the time-line follow-back interview and confirmed using biological and collateral measures. The authors report that participants in ICM had more case manager contacts, better treatment engagement and more self-help attendance than did those in UC. Each of these variables predicted, and was shown to be a mediator of outcome, but case management contact was an especially robust mediator. Further, ICM effects were strongest for those who attended treatment least. Contrary to prediction, greater psychopathology and environmental stressors did not predict worse outcomes. Findings suggest that case management is an active intervention that may both facilitate and substitute for formal drug abuse treatment. Morgenstern, J., Blanchard, K., Kahler, C., Barbosa, K., McCrady, B., and McVeigh, K. Testing Mechanisms of Action for Intensive Case Management. *Addiction*, 103(3), pp. 469-477, 2008.

### Alcohol, Cannabis, and Methamphetamine Use and Other Risk Behaviors among Black and Colored South African Women

There is a pressing need for brief behavioral interventions to address the intersection of high HIV prevalence, increasing substance use, and high-risk sex practices among South African women. The primary aim of this pilot, randomized trial was to examine whether an adapted evidence-based intervention would be equally, more, or less effective at reducing HIV risk behaviors when delivered using an individual or group format. The secondary aim was to examine differences between Black and Colored South African women across pre- and post-intervention measures of alcohol and illicit drug use and sex risk behaviors. The Cape Town Women's Health Co-Op was adapted from an evidence-based intervention known as the Women's Co-Op. Study participants included Black (n=60) and Colored (n=52) women living in the township communities of Cape Town, South Africa, who reported using illicit drugs and alcohol. Colored women reported greater methamphetamine use (13 days in the past 30 days) and Black women reported mostly cannabis use (27 days in the past 30 days). Although both groups reported having unprotected sex under the influence of alcohol and/or other drugs, Black women reported greater condom use and having one partner; Colored women reported having more than one sex partner. One-month post-intervention assessments indicated significant reductions in substance use and sex risk behaviors. After controlling for baseline measures, there were no significant differences between the two intervention conditions. Significant differences in risk behaviors were observed between Black and Colored South African women. However, both ethnic groups were responsive to the adapted intervention and no differences were found by intervention assignment. These findings support the assertion that group interventions may be more cost-effective in reaching at-risk women in resource-scarce environments. Larger studies are needed to show efficacy and effectiveness of woman-focused group prevention interventions. Wechsberg, W., Luseno, W., Karg, R., Young, S., Rodman, N., Myers, B., and Parry, C. Alcohol, Cannabis, and Methamphetamine Use and Other Risk Behaviors among Black and Colored South African Women: A Small Randomized Trial in the Western Cape. *Int. J. Drug Policy*, 19(2), pp. 130-139, 2008.

## Factors Associated with Dual Disorder Adolescent's Utilization of Mental Health Services

This study examined the rates and correlates of self-reported receipt for mental health services among 1,190 adolescents, aged 12-19, who were admitted to community-based substance abuse outpatient clinics and had a co-occurring mental health problem. Utilization of mental health service was ascertained 3 months post-intake. About one third (35%) of adolescents with a co-occurring mental health problem identified at intake received mental health service in the 3 months after treatment entry. After holding other correlates constant, history of mental health treatment, suicidal behavior, family history of mental disorder and insurance coverage at intake were associated with mental health service utilization at the 3-month follow up. Predictors of service utilization varied by gender and racial/ethnic status. The authors discuss implications for integrated substance use and mental health services. They recommend, for example, that substance abuse treatment programs provide a prompt and adequate mental health assessment for adolescents to design a treatment plan based on individual needs. In addition, youth with substance use and mental disorders have various and complex treatment needs, but may need additional insight and motivational counseling to address them. The authors also state that special attention and case management (e.g., linkage, advocacy) may be necessary for uninsured groups as they may be the least likely to obtain services without special assistance. Chan, Y., Godley, M., Godley, S., and Dennis, M. Utilization of Mental Health Services Among Adolescents in Community-Based Substance Abuse Outpatient Clinics. *J. Behav. Health Serv. Res.*, 2007 Dec 21. E-pub ahead of print, (Special Issue), pp. 1-17, 2007.

## **CTN-RELATED RESEARCH**

### Adverse Events in an Integrated Trauma-focused Intervention for Women in Community Substance Abuse Treatment

A substantial number of women who enter substance abuse treatment have a history of trauma and meet criteria for posttraumatic stress disorder (PTSD). Fear regarding the extent to which PTSD treatment can evoke negative consequences remains a research question. This study explored adverse events related to the implementation of an integrated treatment for women with trauma and substance use disorder (Seeking Safety) compared with a nontrauma-focused intervention (Women's Health Education). Three hundred fifty-three women enrolled in community substance abuse treatment were randomized to 1 of the 2 study groups and monitored weekly for adverse events. There were no differences between the two intervention groups in the number of women reporting study-related adverse events (28 [9.6%] for the Seeking Safety group and 21[7.2%] for the Women's Health Education group). Implementing PTSD treatment in substance abuse treatment programs appears to be safe, with minimal impact on intervention-related adverse psychiatric and substance abuse symptoms. More research is needed on the efficacy of such interventions to improve outcomes of PTSD and substance use. Killeen, T., Hien, D., Campbell, A., Brown, C., Hansen, C., Jiang, H., Kristman—Valente, A., Neuenfeldt, C., Rocz-de la Luz, N., Sampson, R., Suarez-Morales, L., Wells, E., Brigham, G., and Nunes, E. Adverse Events in an Integrated Trauma-focused Intervention for Women in Community Substance Abuse Treatment. *J. Subst. Abuse Treat.* 2008 Feb 20. [E-pub ahead of print].

### NIDA CTN Membership is Diverse, But Due to the Need For Large Samples, Over Represents Larger Facilities

Programs participating in the National Drug Abuse Treatment Clinical Trials Network (CTN) completed Organizational Surveys (n=106 of 112; 95% response rate) and Treatment Unit Surveys (n=348 of 384; 91% response rate) to describe the levels of care, ancillary services, patient demographics, patient drug use and co-occurring conditions. Analyses describe the corporations participating in the CTN and provide an exploratory assessment of variation in treatment philosophies. A diversity of treatment centers participates in the CTN; not for profit organizations with a primary mission of treating alcohol and drug disorders dominate. Compared to National Survey of Substance Abuse Treatment Services (N-SSATS), programs

located in medical settings are over-represented and centers that are mental health clinics are under-represented. Outpatient, methadone, long-term residential and inpatient treatment units differed on patients served and services provided. Larger programs with higher counselor caseloads in residential settings reported more social model characteristics. Programs with higher social model scores were more likely to offer self-help meetings, vocational services and specialized services for women. Conversely, programs with accreditation had less social model influence. The CTN is an ambitious effort to engage community-based treatment organizations into research and more fully integrate research and practice. McCarty, D., Fuller, B., Kaskutas, L., Wendt, W., Nunes, E., Miller, M., Forman, R., Magruder, K., Arfken, C., Copersino, M., Floyd, A., Sindelar, J., and Edmundson, E. Treatment Programs in the National Drug Abuse Treatment Clinical Trials Network. *Drug Alcohol Depend.*, 92(1-3), pp. 200-207, 2008.