

Research News

Hepatitis C Virus Can Be Transmitted by Drug Use Through the Nose

In most cases of hepatitis C virus (HCV), the virus is transmitted through contact with infected blood, usually through the sharing of needles and other drug injection instruments. However, for up to 20 percent of HCV infections, the method of transmission is unknown. Researchers have suggested that for some of these cases, HCV may be transmitted through the nose via the use of contaminated drug-sniffing implements. To test this hypothesis, investigators funded in part by NIDA tested mucus samples from 38 intranasal drug users with chronic, active HCV infection for the presence of blood and HCV. They also asked participants to snort air through a straw in a way that would mimic their normal drug-sniffing behavior to determine whether sniffing implements became contaminated. The straws were then tested for blood and HCV. The investigators found trace amounts of blood in 74 percent of mucus samples and on 8 percent of the straws used for sniffing. In addition, they detected HCV in 13 percent of mucus samples and on 5 percent of the straws. Only 8 percent of the samples contained both HCV and trace amounts of blood. Participants had a high rate of nasal inflammation and other nasal problems, including nosebleeds and damage to the inside of the nose from drug use, which may have contributed to the passage of blood and HCV from the nose. These results lend support to the hypothesis that HCV can be transmitted through shared use of contaminated sniffing implements, stated the authors.

Aaron S, McMahon JM, Milano D, Torres L, Clatts M, Tortu S, Mildvan D, Simm M. Intranasal transmission of hepatitis C virus: Virological and clinical evidence. *Clin Infect Dis.* 2008;47(7):931-934.

Smoking Cessation More Difficult for African-Americans, Hispanics

Racial and ethnic minorities in the United States bear a disproportionate share of the burden of tobacco-related diseases, including cancer and cardiovascular disease. While smoking cessation aids are widely used, their effectiveness in minority versus Caucasian populations has not been adequately examined. In a study funded in part by NIDA, researchers tested a smoking cessation regimen of bupropion, nicotine patches, and counseling in 126 African-American, 73 Hispanic, and 360 Caucasian smokers who smoked at least 10 cigarettes daily and had previously attempted to quit smoking at least once. Following treatment, 53 percent of participants successfully achieved 4 weeks of smoking abstinence. The proportion of participants who were successfully abstinent, however, varied between racial and ethnic groups: only 38 percent of African-Americans and 41 percent of Hispanics achieved 4 weeks of abstinence, compared with 60 percent of Caucasian smokers. Interestingly, different characteristics correlated with successful smoking cessation between racial and ethnic groups. For African-Americans, participants with a higher body mass index (BMI) and without another smoker at home had greater success quitting. Older Hispanics and Caucasians were more likely to quit successfully than younger participants in the same groups. In addition, Caucasian smokers who had greater confidence in their ability to quit smoking or had a lower BMI were more successful at abstaining. These characteristics could be potential targets for interventions, such as household restrictions against smoking inside the home or counseling about attitudes toward weight and weight gain.

Covey LS, Botello-Harbaum M, Glassman AH, Masmela J, LoDuca C, Salzman V, Fried J. Smokers' response to combination bupropion, nicotine patch, and counseling treatment by race/ethnicity. *Ethn Dis.* 2008;18(1):59-64.

Adolescent Mouse Brains More Sensitive to Oxycodone Than Adult Brains

Illicit drug use by young people has declined in recent years, with the exception of nonmedical use of some opioid painkillers, including OxyContin (oxycodone), which has remained at stubbornly high levels. It is not known whether the nonmedical use of opioids during adolescence increases the likelihood that an adolescent will abuse or become addicted to opioid drugs later in life. To better understand the differences in how the brains of adolescents and adults may react to oxycodone, NIDA-funded researchers taught 4-week-old (adolescent) and 10-week-old (adult) mice how to self-administer oxycodone. Later, animals were re-exposed to three different, increasing amounts of oxycodone through injections given by the researchers, and changes in their brain dopamine levels were observed. (Dopamine is a brain chemical that mediates the effects of drugs of abuse.) Overall, adolescent mice self-administered less oxycodone compared with adults. However, the adolescent brains seemed more sensitive to the drug—only adolescent brains experienced an increase in dopamine levels in response to the lowest level of oxycodone injected by the researchers. “These results suggest that oxycodone-induced rewarding effects differed between adolescent and adult mice. Further, they demonstrate a potential mechanism [increased sensitivity of adolescents to oxycodone]...that could lead to further self-administration,” explain the authors.

Zhang Y, Picetti R, Butelman ER, Schlussman SD, Ho A, Kreek MJ. Behavioral and neurochemical changes induced by oxycodone differ between adolescent and adult mice. *Neuropsychopharmacology*. 2008 Sep 10;[Epub ahead of print].

Brain Activity Prior to Drug Treatment May Predict Treatment Outcomes for Cocaine Addiction

Since no medications are currently approved by the Food and Drug Administration for the treatment of cocaine dependence, behavioral therapies remain a mainstay of treatment. However, there is currently no way to predict which patients are likely to respond best to certain behavioral therapies. In a study funded in part by NIDA, researchers used functional magnetic resonance imaging (fMRI) to determine if patterns of brain activity before treatment correlate with treatment success. The researchers recruited 20 people entering clinical trials for the treatment of cocaine dependence. Before beginning treatment, all participants performed a computer-based task while fMRI images of brain activity were recorded. Greater brain activity before treatment in a region called the right putamen correlated with a larger percentage of negative urine screens during and after treatment. Longer duration of self-reported abstinence from cocaine use during and after treatment was correlated with greater before-treatment activation in several parts of the brain, including the right putamen, the left ventromedial prefrontal cortex, and the left posterior cingulate cortex. Further, longer treatment retention was correlated with decreased activation of the left dorsolateral prefrontal cortex before treatment. Though larger studies are needed to confirm these results, these findings “hold promise to help target specific therapies for specific individuals and improve treatment outcomes,” conclude the authors.

Brewer JA, Worhunsky PD, Carroll KM, Rounsaville BJ, Potenza MN. Pretreatment brain activation during stroop task is associated with outcomes in cocaine-dependent patients. *Biol Psychiatry*. 2008;64(11):998–1004.

Family-Based Intervention Improves Children’s Early Problem Behavior

Behavior problems in early childhood are associated with increased risk of substance abuse in young adulthood. Interventions to reduce behavior problems during early developmental transition points, as early as 1 to 2 years of age, may help prevent continued development of behavior problems in adolescence, including substance use. Researchers funded by NIDA conducted a clinical trial testing an intervention called the Family Check-Up (FCU), which teaches parental support for positive behaviors. The researchers recruited 731 ethnically and geographically diverse families with one or more children at least 2 years of age who had been identified as being at risk of future behavior problems. Each family underwent a videotaped assessment in their home, which the researchers evaluated for parental involvement, support of positive behavior, engaged parent-child interaction time, and proactive parenting (the tendency to anticipate potential problems). After the initial assessment, participating families were randomly assigned to the FCU group or to a control group that received no further intervention. Families in the FCU group underwent two additional steps: an interview session and a feedback session. In the interview session, a counselor discussed the parents’ concerns about parenting, with a focus on family issues that were currently the most important to the children’s well-being. The feedback session explored the parents’ willingness to engage in more effective parenting practices, reinforced existing positive parenting skills, and identified further services available to the families. The researchers found that FCU participation significantly predicted improvements in parental positive behavior support for children from age 2 to 3, which, in turn, was predictive of fewer

future behavior problems in the children. Although the overall effect of the intervention was modest, it was most pronounced among children at the highest risk. The authors state that “these data support the hypothesis that a brief, adaptive, and tailored approach to supporting positive behavior support practices can prevent the growth of problem behavior in young children at a critical 2-year period in development.” The researchers plan to follow the children as they enter school, to observe whether the improvements in their behavior endure.

Dishion TJ, Shaw D, Connell A, Gardner F, Weaver C, Wilson M. The family check-up with high-risk indigent families: Preventing problem behavior by increasing parents’ positive behavior support in early childhood. *Child Dev.* 2008;79(5):1395–1414.

Social Contexts of College Drinking Explored

Heavy alcohol consumption is known to be a problem for college students in the United States. Understanding more about the social context of college students’ drinking patterns—where, when, why, and with whom they are drinking—may help with earlier identification of students at risk for alcohol problems and aid in the design of better interventions to prevent problem drinking. Researchers funded in part by NIDA performed a study examining six social contexts of drinking among college students: social facilitation, peer acceptance, emotional pain, family drinking, sex seeking, and motor vehicle use. The researchers screened 3,401 first-year college students and recruited 1,253 to participate in the study. Of those students, 728 were current drinkers, 108 (about 15 percent) met the diagnostic criteria for alcohol abuse, 121 (about 17 percent) met the criteria for alcohol dependence, and 168 were non–problem drinkers. The remaining 319 students met 1 or 2 of the criteria for dependence but none for abuse. Over half of the current drinkers reported that they had been a passenger in a car where the driver was under the influence of alcohol, and 50 percent had driven after drinking. “Both alcohol abusers and alcohol-dependent drinkers were more likely to drink in a motor vehicle context than were non–problem drinkers,” explained the authors. Overall, students reported drinking most frequently in the context of social facilitation. However, about 7 percent of the current drinkers were classified as being depressed and reported that they were more likely to drink to relieve emotional pain than to facilitate social interactions. The authors concluded that future research is needed “to determine the extent to which the social contexts of drinking can be manipulated to reduce adverse consequences of drinking among college students.”

Beck KH, Arria AM, Caldeira KM, Vincent KB, O’Grady KE, Wish ED. Social context of drinking and alcohol problems among college students. *Am J Health Behav.* 2008;32(4):420–430.

HealthWise Program Tested for Reduction of Substance Use and Risky Sexual Behavior in South African Schools

Use of drugs or alcohol is associated with increased risk for HIV transmission. This observation is especially of concern in countries that have a high rate of HIV infection. Researchers funded by NIDA evaluated a school-based program designed to reduce both substance use and risky sexual behavior in adolescents in South Africa, which has the highest number of HIV infections in the world. The HealthWise risk-behavior prevention program consists of 12 lessons in grade 8 and 6 booster lessons in grade 9, covering topics such as anxiety and anger management, decisionmaking, positive use of free time, and substance use and sexual risk. The program was tested in four schools in a low-income urban area; five additional schools were included in the study as control schools and thus did not teach the HealthWise program. HealthWise had positive impacts on alcohol and tobacco use—recent alcohol and cigarette use increased to a lesser extent for both boys and girls enrolled in the program than for their peers at the control schools. Although the program did not strongly influence the age of first sexual experience or alter the behavior of adolescents who were already sexually active, significantly more students in the HealthWise program reported that they had access to condoms. More students in the HealthWise schools than in the control schools were already sexually active, which could have influenced some of the results. The HealthWise program “may be helpful in reducing some risk behaviors among low-income adolescents in South Africa and perhaps elsewhere,” conclude the authors.

Smith EA, Palen LA, Caldwell LL, Flisher AJ, Graham JW, Mathews C, Wegner L, Vergnani T. Substance use and sexual risk prevention in Cape Town, South Africa: An evaluation of the HealthWise program. *Prev Sci.* 2008;9(4):311–321.

DNA Variation Influences Neural Response to Negative Stimuli

CREB1, a gene that has been shown to be important in how the brain processes the rewarding effects of drugs of abuse, is also thought to play a role in how the brain processes aversive (negative) stimuli. Studies have suggested that a type of variation in DNA called a single nucleotide polymorphism (SNP)—a small change in the sequence of DNA—near the *CREB1* gene may influence differences in this processing between individuals. To better understand how this genetic variation may affect brain activity, researchers funded in part by NIDA tested 28 volunteers for specific SNPs—termed TT, CT, and CC. The researchers also performed a type of brain scan called functional magnetic resonance imaging (fMRI) on the volunteers to measure brain activity while they were shown pictures of facial expressions reflecting different emotional states such as anger, fear, sadness, and happiness. In another test, the volunteers again viewed the same pictures but were given the ability to control how long they viewed them by pressing certain keys on a keyboard. FMRI scans showed that activity in a brain region called the insula—which helps process pleasant or unpleasant experiences—was changed by viewing the pictures. The level of insular activity, however, depended on which *CREB1* variation an individual possessed. For example, volunteers with the CT or CC SNP showed less activity in the insula when exposed to angry faces compared with volunteers with the TT SNP; in turn, these volunteers were more likely to perform key presses to avoid viewing the angry expression. In general, people with the TT SNP produced fewer key-press responses for any emotion, including anger. “These findings suggest a hypothesis of increased suppression of neural and behavioral responses to anger [in individuals] with the T allele,” explained the authors. Further research is needed to understand what function the SNP plays in relation to *CREB1* at the molecular level.

Perlis RH, Holt DJ, Smoller JW, Blood AJ, Lee S, Kim BW, Lee MJ, Sun M, Makris N, Kennedy DK, Rooney K, Dougherty DD, Hoge R, Rosenbaum JF, Fava M, Gusella J, Gasic GP, Breiter HC; Phenotype Genotype Project on Addiction and Mood Disorders. Association of a polymorphism near *CREB1* with differential aversion processing in the insula of healthy participants. *Arch Gen Psychiatry*. 2008;65(8):882–892.

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