

## Marijuana Abuse: Age of Initiation, Pleasure of Response Foreshadow Young Adult Outcomes

By Robin Eisner, NIDA NOTES Contributing Writer

A boy or girl who is smoking marijuana at 13 is likely to earn less money as a young adult than peers who aren't abusing the drug. An adolescent who smokes less marijuana than a friend but enjoys the experience more is likelier to be addicted to the drug at 21. These are findings from two recent studies that looked at adult outcomes associated with marijuana abuse in adolescence.

Dr. Phyllis L. Ellickson and colleagues at the RAND Corporation in Santa Monica, California, surveyed 5,800 adolescents from 30 schools in California and Oregon about their marijuana use between ages 13 and 23. A statistical analysis of the responses revealed four distinct patterns related to marijuana abuse:

- Approximately 45 percent did not smoke marijuana. The researchers called these youths *Abstainers*. Of those who did smoke marijuana:
- Some 5 percent were considered *Early High Users*—teens who smoked marijuana from once a week to monthly at age 13, decreased their abuse by age 18, and as young adults smoked 3 to 10 times a year.
- About 17 percent were *Stable Light Users*—teens who smoked infrequently at age 13 and never abused the drug more than 10 times a year, on average.
- *Occasional Light Users* made up 53 percent of the marijuana-abusing population. They were similar to Stable Light Users but started after age 13 and abused lower

Relationship Between Number of Positive Responses to Marijuana and Later Addiction	
Positive Responses	Marijuana-Addicted Subjects
0	5.2%
1	8.5%
2	13.3%
3	19.9%
4	28.7%
5	39.1%

Source: Fergusson, D.M.; Horwood, L.J.; Lynskey, M.T.; and Madden, P.A.F. (2003).

Researchers examined whether teens' positive responses to marijuana were related to later marijuana addiction. Positive responses noted by participants included "got really high," "felt happy," "felt relaxed," "did silly things," and "laughed a lot." Almost 40 percent of teens with five positive responses were addicted to marijuana between ages 16 and 21 compared with 5.2 percent of those who had no positive response.

amounts than Stable Light Users throughout the study period.

- *Steady Increases*, approximately 25 percent of the abusers, started after age 13 and increased their usage during the study period.

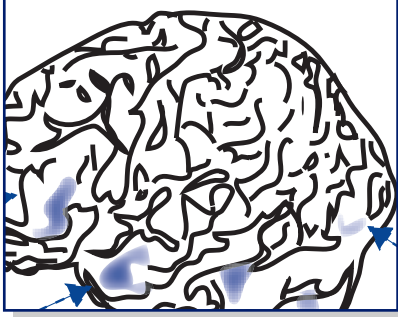
The researchers found that the Early High Users lagged behind all other groups in earnings and education when resurveyed at age 29. Their average yearly earnings were \$20,940, compared with about \$32,000 for the Occasional Light Users and Abstainers and \$28,140 for the Steady Increases. Both groups that initiated marijuana abuse by age 13 reported less schooling than Abstainers and those who first smoked after age 13: Early High Users and Stable Light Users did not usually go to college, while Steady Increases completed on average one year of college, Occasional Light Users almost two years of college, and Abstainers, almost three years of college.

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**View of brain from left side**



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# Confronting the Rise in Abuse of Prescription Drugs

By NIDA Director Nora D. Volkow, M.D.



The misuse and abuse of prescription medications is a growing public health concern. The National Survey on Drug Use and Health (NSDUH), conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA), estimates that in 2003, 6.3 million Americans aged 12 and older abused prescription drugs (that is, took medications not prescribed for them or took medications solely for pleasure or entertainment) in the month preceding the survey. Most abused pain relievers (4.7 million); others abused tranquilizers (1.8 million), stimulants (1.2 million), and sedatives (0.3 million).

The abuse of prescription medications has increased in all segments of the population, and in recent years the increase in abuse of prescription painkillers has been particularly sharp and worrisome. In 2002, the NIDA-supported Monitoring the Future survey initiated questions about the prescription pain medications oxycodone (OxyContin) and hydrocodone (Vicodin). In that year and in 2003, about 4 percent and 4.5 percent, respectively, of high school seniors reported nonmedical use of oxycodone in the 12 months preceding the survey. Roughly 10 percent of seniors reported nonmedical use of hydrocodone, making it the third most widely abused illicit substance (after marijuana and amphetamine) in this age group.

The abuse of prescription pain medications is increasing among adult Americans as well. Among young adults aged 18 to 25, the rate increased from 22.1 percent in 2002 to 23.7 percent in 2003, NSDUH data show. Abuse of oxycodone increased among all age groups from 2002 to 2003: by more than 10 percent among Americans aged 12 to 17, by nearly 40 percent among 18- to 25-year-olds, and by 60 percent for Americans aged 26 or older.

NIDA is responding to the increase in prescription drug abuse on several fronts. In September, a Consultant Workgroup meeting brought together researchers and physicians with expertise in pain management and the epidemiology, prevention, and treatment of opiate abuse. This panel developed an outline for a large-scale clinical study of treatment for prescription opiate abuse that will be designed and conducted by NIDA's Clinical Trials Network. NIDA research also is expanding our understanding of the risks posed by prescription medications in different populations—women, adolescents, racial and ethnic groups, health professionals, those with comorbid substance abuse and mental health disorders, and those with HIV/AIDS and other infectious diseases. One group that may be especially at risk is the elderly. Age-related changes may influence the way in which their bodies metabolize and respond to prescription drugs. Older adults are more likely to have undiagnosed psychiatric

and medical illness. They also are more likely to be taking several medications in complex drug regimens, increasing the risk of drug interactions or errors in dosing. Any of these circumstances may contribute to development of unwanted dependence or even addiction to prescribed medications.

Patients with chronic pain need medications; the potential for abuse should not deter physicians from prescribing appropriate medications in adequate dosages. To help primary care providers confidently select the most appropriate medication for the situation, NIDA is working to develop screening and diagnostic tools that primary care physicians can use to assess the potential for misuse, abuse, and dependence on prescription drugs in their patients.

## NIDA Updates Prescription Drug Abuse Program Announcement

**Program Announcement Number: PA-04-110**

**Expiration Date: January 3, 2008, unless reissued.**

In revising and reissuing this Program Announcement, NIDA encourages applications across a broad range of experimental approaches, including basic, clinical, epidemiological, prevention, and treatment studies. Full details of the PA, including contact information for questions concerning scientific, technical, or grant management issues, are available on the Web at: <http://grants.nih.gov/grants/guide/pa-files/PA-04-110.html>.

Developing new medications free of potential for abuse or diversion to illegal markets is another NIDA priority. We are evaluating potential new medications such as cannabinoids that relieve certain types of pain but have reduced risk for addiction and abuse (see "Novel Cannabinoid Appears Promising for Treatment of Chronic Pain," *NIDA NOTES*, Vol. 19, No.2, p.1).

We also are working to understand more fully the role of environmental and social factors in misuse or abuse of prescription medications. For example, how great a threat is posed by Internet sites offering controlled substances for sale? Do some health professionals contribute to abuse of prescription drugs through inappropriate prescribing? Do others provide inadequate treatment because they fear their patients will become addicted? If these risks are significant, what educational efforts will most effectively guide physicians in prescribing appropriate medications for patients who need them?

NIDA's expanded commitment will help ensure the availability of safe and effective treatment with lessened risk of dependence or addiction. **NN**

# Dopamine Enhancement Underlies a Toluene Behavioral Effect

By Carl Sherman, *NIDA NOTES* Contributing Writer

Overall drug abuse among teenagers has declined in the past several years, but inhalant abuse is on the rise. The National Survey on Drug Use and Health (NSDUH) for 2002 found that nearly 10 percent of youths aged 12 to 17 had misused inhalants to get high at least once in their lives. Nearly 2.6 million young people have put themselves at risk for toxic brain effects from glue, gasoline, and a wide variety of other household and workplace products. These fumes can strip the myelin insulation from nerve cells throughout the brain, sometimes inflicting severe brain damage.

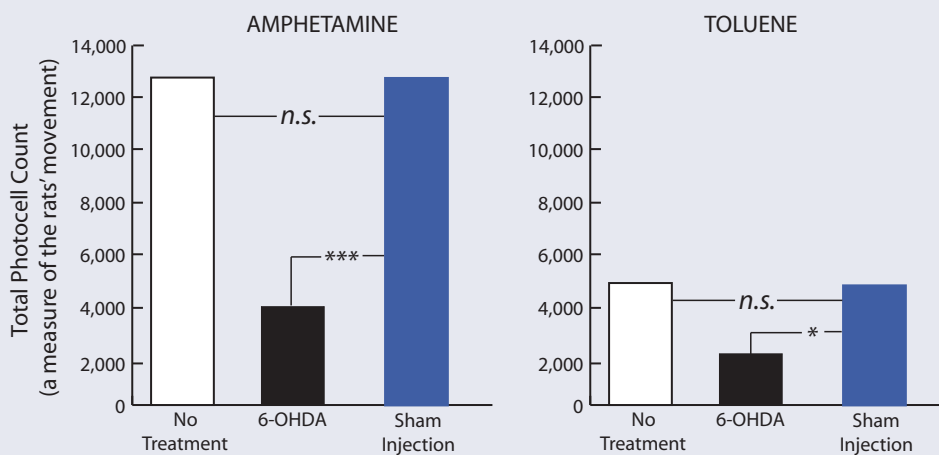
The drug effects that cause people to take such risks have been difficult to pin down, largely because of the variety of different inhalants and their multiple effects in many parts of the brain. Recently, however, Drs. Art Riegel and Edward French at the University of Arizona in Tucson shed light on how one much-abused inhalant—toluene, a solvent contained in gasoline, spray paint, and glue—may motivate abuse. The NIDA-funded team demonstrated that toluene causes one of its typical behavioral effects, locomotor stimulation—increased roaming—by enhancing dopamine activity in the brain's pleasure center, the nucleus accumbens (NAc). Other drugs that cause locomotor stimulation in this way also promote euphoria—a motivator for drug abuse—by the same mechanism.

To test whether toluene-induced locomotor stimula-

tion might be related to dopamine activity, the researchers compared the drug's effects in rats with intact dopamine neurotransmission and others treated to block dopamine from reaching the NAc. They injected the latter group of rats with 6-hydroxydopamine (6-OHDA), a neurotoxin that inactivates dopamine-releasing nerve terminals. To ensure that any effects they might observe in these rats truly would be due to dopamine reduction in the NAc, the researchers administered the injections directly into the NAc and also gave the rats desipramine. Without this latter precaution, 6-OHDA would also have shut down the terminals that release another important neurotransmitter, norepinephrine.

Fourteen days after the 6-OHDA treatment, the researchers began injecting the experimental animals with three different drugs—toluene, amphetamine, and scopolamine—at 2-day intervals. Three groups of rats were used: the rats treated with 6-OHDA; a second group, which had received sham treatment with an inert substance; and untreated rats. As hypothesized, the sham-procedure rats and untreated rats showed locomotor stimulation when given toluene, amphetamine, or scopolamine. But in those pretreated with 6-OHDA, the locomotor response to toluene declined by 55 percent, nearly as much as did the response to amphetamine (67 percent), which is known to work through the

## Neurotoxin Test Shows a Role for Dopamine in Both Toluene- and Amphetamine-Induced Behaviors



Statistical significance levels: \*\*\* 0.001, \* 0.05; n.s. indicates nonsignificant

*A dose of toluene increased locomotor stimulation in rats, just as a dose of amphetamine did. When the neurotoxin 6-OHDA, which inactivates dopaminergic neurons, was injected into the rats' nucleus accumbens, it attenuated locomotor stimulation in response to both substances, while a sham injection had no effect. These results suggest that the inhalant affects the brain much like a classic drug of abuse, through activity of the same neurotransmitter (dopamine) in the same part of the brain (nucleus accumbens).*

dopamine system. The response to scopolamine, which induces locomotor stimulation through neurotransmitters other than dopamine, was unchanged. Postmortem examination confirmed that the neurotoxin had reduced the amount of dopamine in the NAc of the rats' brains.

In a second experiment, rats were injected with LY379268, which activates glutamate receptors, abundant in the NAc, that inhibit the release of dopamine. Earlier experiments have

*“The findings put inhalants squarely in the same category as other drugs of abuse, suggesting that a similar mechanism of action is involved.”*

shown LY379268 to lessen the dopamine-dependent behavioral effects of PCP and amphetamine. Here too, when the rats were treated with LY379268, locomotor stimulation in response to toluene was significantly reduced.

The results of both experiments were consistent with the hypothesis that increased dopamine activity in the NAc is behind toluene's locomotor stimulation effect, Dr. Riegel says. “Using two very different approaches, we came up with the same end result. The findings put inhalants squarely in the same category as other drugs of abuse, suggesting that a similar mechanism of action is involved.”

That toluene-induced dopamine release in the NAc underlies locomotor stimulation suggests that it may cause addiction in very similar fashion to other drugs of abuse. “Locomotor stimulation is a good behavioral

marker for the abuse potential of a drug,” Dr. Riegel says. Previous animal studies have closely linked increased dopamine activity in the NAc and increased locomotion to the behavioral response of drug-seeking following exposure to cocaine, amphetamine, PCP (phencyclidine), and nicotine. Along with increased roaming activity, the rats press a lever to obtain those drugs and favor the side of the cage in which the drug has been provided to them. Inactivating the dopamine-releasing nerve terminals in the NAc with a toxic substance attenuates both behavioral responses to the drugs.

Toluene's similarity to other drugs of abuse may be characteristic of other abused inhalants as well.

“Toluene is the prototypical inhalant,” explains Dr. Riegel, now with NIDA's Division of Intramural Research. “Toluene is itself abused, and it shows up in a wide variety of inhaled substances. Given the choice among two dozen colors of spray paint, abusers prefer gold and silver, which have the highest concentrations of toluene.”

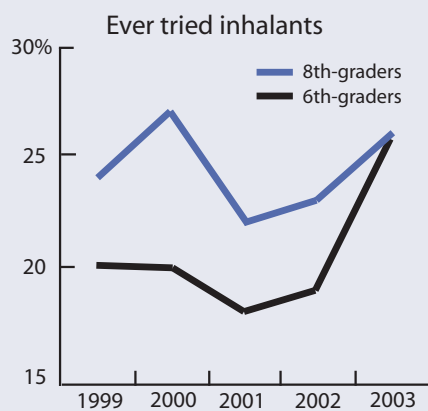
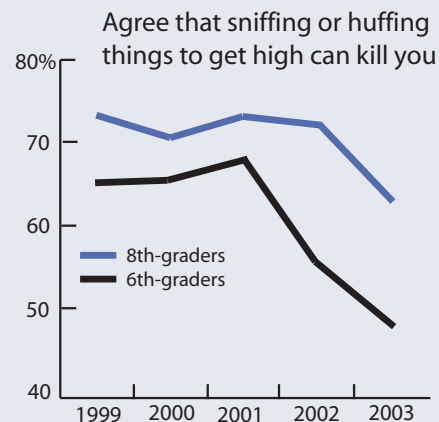
Dr. Riegel says that further research is indicated to clarify just what toluene does to neurons to increase dopamine release. A report on anatomical studies to elucidate such processes is currently in preparation.

On a practical level, the findings suggest that “we shouldn't be thinking of inhalants only in terms of their toxicity,” says Dr. Riegel. “Because they activate the same areas of the brain as other important drugs of abuse, there is a strong likelihood that they are highly addictive substances and that some of the same strategies that work for other addictions may effectively combat inhalant abuse as well.”

### Sources

- National Survey on Drug Use and Health. Inhalant use among youths: 2002 update. *The NSDUH Report*. March 18, 2004.

## Inhalant Abuse Rises, Awareness of Its Dangers Drops



Source: Partnership for Drug-Free America, 2004

*Awareness that inhalant use can kill has decreased significantly among sixth- and eighth-graders, which may translate into an increasing number of inhalant-related injuries and deaths. NIDA Director Dr. Nora D. Volkow says deafness, blindness, tremors, and permanent personality changes are just some of the brain-related problems caused by inhalant abuse. “These substances, when inhaled, can cause deaths by multiple mechanisms by triggering arrhythmia of the heart, which can lead to cardiac arrest, or through asphyxiation.”*

- Riegel, A.C.; Ali, S.F.; and French, E.D. Toluene-induced locomotor activity is blocked by 6-hydroxydopamine lesions of the nucleus accumbens and the mGluR2/3 agonist LY379268. *Neuropsychopharmacology* 28(8):1440-1447, 2003. **NN**

## Marijuana Abuse: Age of Initiation, Pleasure of Response Foreshadow Young Adult Outcomes

*continued from page 1*

“The bad news is that if you start marijuana use by age 13, even if you eventually decrease your usage, you are likely to have a lower income and lower level of schooling by age 29,” Dr. Ellickson says. “The good news is that 45 percent of the youths in our sample did not use marijuana between adolescence and emerging adulthood. We need to understand what helped those kids abstain over time.”

Dr. Ellickson says although her findings show an association between marijuana abuse and reduced income and educational performance, they do not prove that marijuana contributes causally to those outcomes, which result from multiple factors. The results also suggest that delaying initiation of marijuana abuse does not necessarily guarantee better outcomes, especially if the late starters escalate abuse. Youths who started after age 13, but steadily increased their marijuana use during and after high school, abused marijuana more than any other group as young adults, smoking 3 to 10 times during the past month on average. In young adulthood, the late starters who intensified their use of marijuana also abused other illegal drugs at rates similar to those of the early starters, with 32 percent admitting to past-year abuse of illegal drugs besides marijuana.

The patterns of abuse revealed by the study suggest that interventions against marijuana abuse may be important from primary school through to high school graduation, says Dr. Kathleen Etz, of NIDA’s Division of Epidemiology, Services and Prevention Research.

“At each stage, the goal will be to prevent children who are at risk from initiating use, and to persuade any who have already started to reduce or

## Marijuana Abstainers Enter Adulthood Ahead

### Outcomes of Five Marijuana User Groups at Age 29

	Early High Users n=37	Steady Increases n=336	Stable Light Users n=171	Occasional Light Users n=753	Abstainers n=1,229
Overall Health <sup>1</sup>	3.53 <sup>c</sup>	3.82 <sup>b</sup>	3.86 <sup>b</sup>	3.89 <sup>b</sup>	4.03 <sup>a</sup>
Mental Health <sup>1</sup>	3.64 <sup>ab</sup>	3.67 <sup>b</sup>	3.82 <sup>ab</sup>	3.72 <sup>b</sup>	3.84 <sup>a</sup>
Life Satisfaction <sup>1</sup>	3.88 <sup>b</sup>	3.99 <sup>b</sup>	4.03 <sup>b</sup>	4.10 <sup>b</sup>	4.27 <sup>a</sup>
Educational Attainment <sup>2</sup>	5.56 <sup>d</sup>	6.48 <sup>c</sup>	5.99 <sup>d</sup>	6.89 <sup>b</sup>	7.43 <sup>a</sup>
Yearly Earnings (\$ in thousands)	20.94 <sup>c</sup>	28.14 <sup>b</sup>	27.71 <sup>b</sup>	32.29 <sup>a</sup>	31.93 <sup>a</sup>
“Yes” to Past-Year Other Drug Use	27.4% <sup>c</sup>	31.9% <sup>c</sup>	30.3% <sup>c</sup>	18.3% <sup>b</sup>	8.5% <sup>a</sup>
Frequency of Past-Month Marijuana Use <sup>3</sup>	.90 <sup>c</sup>	2.17 <sup>a</sup>	1.32 <sup>d</sup>	.53 <sup>b</sup>	.14 <sup>a</sup>

*Source: Ellickson, P.L.; Martino, S.C.; and Collins, R.L. (2004).*

Note: Means/percentages are adjusted for sex, race/ethnicity, parental education, and nuclear family. A result marked by *a* represents a significantly more favorable outcome such that  $a > b > c > d > e$ . Same-letter superscripts in each row indicate no statistically significant differences between those entries.

<sup>1</sup>Averages based on a scale of 1 to 5, with 1 indicating poor and 5, excellent.

<sup>2</sup>Values ranged from 1 indicating 8th grade or less, to 11 indicating an advanced professional degree.

<sup>3</sup>Based on a five-category index: 0 indicates no use; 1, < 3 times; 2, 3-10 times; 3, 11 times; and 4, > 11 times and 6 or more days in the past month.

quit,” Dr. Etz says. “The counseling ideally would educate children about the potential problems of marijuana abuse and address the broad goal of self-awareness leading to healthy life choices.”

### Positive Initial Response Linked to Later Dependence

In the second study, led by Dr. David Fergusson of the Christchurch School of Medicine and Health Sciences in Christchurch, New Zealand, researchers found that positive emotional responses to initial marijuana use by adolescents predicted later addicted to the drug better than did the amount of marijuana smoked.

The researchers worked with data from the Christchurch Health and Development study, a 21-year longitudinal project that followed a group of children born in the city from birth through adolescence. Dr. Fergusson’s analysis included 1,011 of these youths.

When the study participants were 15 or 16, they answered a series of interview questions about their cannabis exposure in the preceding year. These included their frequency of abuse as well as feelings about their most recent experience: Did they get “really high,” feel happy, feel relaxed, do silly things, laugh a lot, feel ill or dizzy or frightened, or pass out?

In this first interview, 20 percent of those later included in Dr. Fergusson's study had abused marijuana. Study participants were interviewed again at ages 18 and 21. By then, approximately 9 percent reported signs of being addicted to marijuana; the prevalence among those who started before age 16 was 21.7 percent. Almost half (46.7 percent) of those who had reported five or more pleasurable responses to the drug in the first interview reported being addicted by age 21, compared with 3.9 percent of those reporting no positive responses.

The results indicate that the pleasure of early use, not how much marijuana is used, determines the likelihood of later addiction. "There are people smoking a lot of marijuana who aren't addicted to it," Dr. Fergusson explains. "Others are smoking less but are addicted or headed for addiction."

Dr. Fergusson says his findings parallel those of studies on cigarette

***"At each stage, the goal will be to prevent children who are at risk from initiating use."***

smoking and alcohol use among adolescents, which suggest that initial subjective response to a drug might be a behavioral marker for biological addiction-vulnerability. This growing body of research indicates that vulnerable individuals seem to experience enhanced sensitivity to a drug's positive effects, diminished sensitivity to its negative effects, or a combination of the two responses.

Dr. Wilson Compton, director of the Division of Epidemiology, Services and Prevention Research at the National Institute on Drug Abuse, says that research in animals has revealed genetic differences between those that prefer alcohol and those that do not. Similar research might identify the neurobiological factors underlying differences in the response to marijuana, perhaps eventually leading to risk-reduction treatments, says Dr. Compton.

### Sources

- Ellickson, P.L.; Martino, S.C.; and Collins, R.L. Marijuana use from adolescence to young adulthood: Multiple developmental trajectories and their associated outcomes. *Health Psychology* 23(3):299-307, 2004.
- Fergusson, D.M.; Horwood, L.J.; Lyndskey, M.T.; and Madden, P.A.F. Early reactions to cannabis predict later dependence. *Archives of General Psychiatry* 60(10):1033-1039, 2003. **NN**

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# Economists Offer Program for Costing Out Drug Abuse Treatment

By Marion Torchia, *NIDA NOTES* Contributing Writer

**N**IDA-supported economists are offering drug treatment program administrators a comprehensive program to estimate their costs. The Drug Abuse Treatment Cost Analysis Program (DATCAP) features materials and a method to capture and put dollar values on the full range of treatment resources. Along with analyzing their own economic operations, administrators eventually will be able to use a nationwide DATCAP database to compare their costs with those of similar programs, become more efficient, and achieve better treatment outcomes. Dr. Michael T. French of the University of Miami in Coral Gables, Florida, one of the system's designers, says that ultimately, the database should provide answers to the questions asked by cost-conscious public agencies and insurers: How much do today's drug treatment programs cost? What are the most cost-effective treatment approaches? Which programs return the greatest net benefits?

## DATCAP Features

Administrators can download DATCAP survey forms and user manuals free of charge from [www.DATCAP.com](http://www.DATCAP.com). DATCAP's developers note, however, that most programs will require the services of an economist trained in cost analysis and program evaluation to obtain the most useful results.

DATCAP captures both accounting costs (the costs usually entered on an institution's financial statements, such as outlays for labor and supplies) and economic costs (all the resources a treatment center uses to serve its patients). Economic costs include resources that are partially subsidized or made available at no charge, such as volunteer labor. DATCAP's inclusive cost perspective permits comparison of treatment programs that have very different financial structures.

Mean Patient Flow and Costs of Substance Abuse Treatment Programs					
<b>Outpatient Programs</b>					
<i>Information gathered between 1993 and 2002 from 53 outpatient programs.</i>					
Program Type (Number Surveyed)	Average Length of Stay, weeks (SD)	Average Daily Census (SD)	Total Annual Economic Cost (SD)	Weekly Economic Cost Per Client <sup>1</sup> (SD)	Economic Cost Per Treatment Episode <sup>2</sup> (SD)
Methodone clinics (11)	99 (53)	388 (186)	\$1,684,254 (\$674,444)	\$91 (\$33)	\$7,358 (\$3,849)
Standard outpatient (14)	17 (9)	212 (188)	\$1,080,690 (\$757,227)	\$121 (\$85)	\$1,944 (\$1,960)
Intensive outpatient (6)	7 (8)	13 (9)	\$328,007 (\$411,364)	\$462 (\$243)	\$4,445 (\$6,302)
Adolescent outpatient (13)	13 (6)	8 (2)	\$48,170 (\$50,518)	\$194 (\$91)	\$2,678 (\$2,787)
Drug court (9)	46 (20)	205 (184)	\$539,660 (\$136,713)	\$82 (\$43)	\$3,463 (\$2,187)
<b>Residential Programs</b>					
<i>Information gathered during the same period from 32 residential programs.</i>					
Program Type (Number Surveyed)	Average Length of Stay, weeks (SD)	Average Daily Census (SD)	Total Annual Economic Cost (SD)	Weekly Economic Cost Per Client <sup>1</sup> (SD)	Economic Cost Per Treatment Episode <sup>2</sup> (SD)
Adult residential (18)	13 (14)	34 (21)	\$1,104,189 (\$643,053)	\$700 (\$343)	\$9,426 (\$11,023)
Adolescent residential (1)	8	22	\$1,307,064	\$1,138	\$9,347
Therapeutic community (5)	33 (22)	152 (265)	\$3,330,137 (\$4,821,587)	\$587 (\$194)	\$18,802 (\$12,409)
In-prison therapeutic community (8)	28 (12)	265 (288)	\$1,083,017 (\$1,587,030)	\$55 (\$11)	\$1,534 (\$947)

Source: Roebuck, M.C.; French, M.T.; and McLellan, A.T. (2003).

Notes: All amounts, including dollar amounts, are means. All costs are reported in 2001 dollars.

<sup>1</sup> Total annual economic cost divided by the average daily census, divided by 52.14 weeks.

<sup>2</sup> Weekly economic cost per client multiplied by the average length of stay.

The program is adaptable to any treatment setting. By focusing on the cost of specific treatment methods rather than on entire programs, it can capture costs in settings that also offer other services. The same questionnaire

is provided for inpatient and outpatient services.

"Program DATCAP" gathers detailed information about a program's resources, revenues, and expenses, and about its clients and the services



they receive. “Brief DATCAP” is a less labor-intensive alternative to the full instrument. “Client DATCAP” surveys clients directly and assigns a dollar value to costs they incur as a result of getting treatment, such as travel and child care. Although the DATCAP project is still in its early stages, administrators who use it can identify costs they were unaware of and find opportunities to strengthen their operations.

## The Nationwide Database

Dr. French hopes that as program administrators around the country begin to use DATCAP to track their own costs, they will see the advantage of reporting their findings to a central repository. “Only when everyone’s costs are pooled will it be possible for a program to compare itself with other programs,” he says.

To encourage wider participation in the ongoing research on DATCAP, its creators have published some early survey results. Among these, they found that among 85 programs surveyed between 1993 and 2002, methadone maintenance programs had lower labor costs (55 percent of total costs compared with 68 percent for standard outpatient programs) and relatively higher costs for supplies and materials. Not surprisingly, standard outpatient programs were much less expensive than intensive programs: The 14 standard programs reported a mean weekly economic cost per client of \$121; for the intensive programs, the weekly cost was nearly four times that amount—or \$462 per client. However, the intensive programs generally offered a shorter course of treatment, so their mean total cost for a client’s treatment episode was only slightly more than twice the cost of the standard outpatient programs (\$4,445 versus \$1,944).

The new database has limitations, the authors caution. The programs were not selected randomly and are not geographically representative. Also, the costs of a small number of atypical programs sometimes skewed the results. Nevertheless, says Dr. French, the results of the 85 surveys constitute

a rich new source of information. “The database will get better as new programs are added, and eventually the cost estimates will be updated continually on the DATCAP Web site,” he says.

## Next Step: Link Cost to Outcome

Although program managers find it useful to compare their costs with those of their peers, policymakers are much more interested in the relationship between costs and the intended program outcomes. Cost-effectiveness analysis and cost-benefit analysis of drug abuse treatment have demonstrated encouraging results. One California study found that \$1 invested in substance abuse treatment saves taxpayers \$7 in future costs, including those related to crime and care for medical problems resulting from drug use. [“Evaluating Recovery Services: The California Drug and Alcohol Treatment Assessment (CALDATA),” California Department of Alcohol and Drug Programs, April 1994.]

In a recent study using DATCAP, Dr. Jody Sindelar and her colleagues at Yale University in New Haven, Connecticut, found that Philadelphia treatment programs that offered “enhanced care” produced better outcomes with regard to drug abuse compared with those that offered only standard care. However, standard care programs had better results with respect to other treatment outcomes.

Says Dr. Sindelar, “Looking at treatment programs with too narrow a focus may produce misleading results. Reduced drug use is certainly the most

direct outcome of treatment, but it is not necessarily the only one, or even the most important one to society. We need to find ways to give appropriate weight to all the outcomes we believe are important. But we believe that combining DATCAP and ASI [Addiction Severity Index] is a good first step.”

Dr. William S. Cartwright, an economist with NIDA’s Division of Epidemiology, Services and Prevention Research, believes DATCAP is the beginning of something important. “We know more about where the hidden costs are, and we are able to link costs to outcomes. I hope this information will enable us to make better use of scarce resources, toward our shared goal of reducing drug abuse and the problems it causes.”

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## Techniques of Economic Analysis of Drug Treatment

- **Cost-Effectiveness Analysis:** A technique for evaluation of clinical outcomes. It asks whether one treatment produces a better outcome at the same cost as another, comparable outcomes at less cost, or if an enhanced outcome is “worth” the additional cost.
- **Cost-Benefit Analysis:** Decisionmakers use cost-benefit analyses in determining how to allocate their budgets. The “cost” part of the analysis estimates the dollars necessary to achieve each alternative policy goal—for example, reducing drug abuse by 10% or raising school test scores by 10%. The “benefit” part estimates the dollar value of all the positive effects of success—for example, reduced medical costs because of fewer health problems associated with drug abuse, or a better educated, more skillful workforce attracting new industry to the area. All other concerns being equal, the goal that produces the most benefits for the lowest cost gets budget priority.

# Study Suggests Cognitive Deficits in MDMA-Only Drug Abusers

By Robin Eisner, NIDA NOTES Contributing Writer

A recent NIDA study has identified a potential association between heavy use of MDMA (Ecstasy) and persistent deficits in mental processing speed and problem-solving. The preliminary study, with a population carefully selected to demonstrate the effects of MDMA in the absence of other drug abuse, also indicated that a threshold amount of MDMA exposure may have to occur before measurable impairments develop.

Dr. John Halpern and colleagues at Harvard Medical School's McLean Hospital, in Belmont, Massachusetts, and the University of New Mexico, Albuquerque, recruited 23 MDMA-abusing and 16 non-MDMA-abusing rave culture participants, all of whom consumed marijuana and alcohol only rarely if at all. To find such a population, Dr. Halpern's team recruited their volunteers in the vicinity of Salt Lake City, an area culturally dominated by the Mormon church, which frowns on the use of alcohol and other substances. Study participants included Mormons but also atheist, Hindu, and Catholic youths who were influenced by growing up in a devout, conservative area.

Study participants took urine and breath tests to confirm that none had taken any intoxicating or illicit substances for at least 10 days. Dr. Halpern and his colleagues then administered a battery of neuropsychological assessments. The MDMA abusers performed less well than nonabusers on almost all of the tests, but the differences were not large enough to rule out the possibility they were simply due to chance. To probe for slower developing exposure-dependent effects, the researchers conducted an additional analysis, comparing MDMA abusers who had

taken between 60 and 450 lifetime doses with the moderate abusers and nonabusers.

The heavy abusers still did not exhibit any verbal handicap compared with the other groups when given tests that asked them to pair words for their meaning, name words beginning with the same letter, and read a shopping list and recall items on the list.

At the same time as it raises interesting questions about possible cognitive deficits in MDMA users, this study also illustrates the complexity of evaluating MDMA's effects in humans, notes Dr. Timothy Condon, Deputy Director of NIDA.

"The major strength of this study is its inclusion of a unique group of MDMA users who, unlike MDMA users in other studies to date, have had minimal or no exposure to other drugs. The researchers took great care to control for other possible variables to explain their results," says Dr. Steven Grant of NIDA's Division of Clinical Neuroscience, Development and Behavioral Therapies. Still, he adds, there are a number of uncontrollable factors: the volunteer sample may not be representative of MDMA users; the purity or actual MDMA content of drugs said to be Ecstasy is uncertain; differences in performance on any of the tests may be the result of still-unrecognized confounding factors; and the tasks that showed positive association with MDMA exposure have not been used in other studies and therefore need to be replicated.

## Stroop Test Assessed Mental Response In Heavy Abusers of MDMA



**Black**      **Blue**  
**Green**      **Orange**

*MDMA abusers were slower and made more errors on the Stroop, a test of attention and mental processing speed, than did moderate abusers and nonabusers. The test requires subjects to respond as quickly as possible with the color of ink in which each word is printed while suppressing the urge to read the word. In the above illustration, the correct answers are (first line, left to right) "blue" and then "black;" second line, "black" and then "blue."*

However, the heavy MDMA abusers did show deficits on two tests of mental processing: the Stroop Interference and the R-SAT.

The Stroop Interference test measures the subject's ability to efficiently isolate and process salient information in confusing contexts. In this test, the names of colors are printed in the "wrong" color ink—for example, the word "black" in blue ink. The administrator asks the subject to list, as fast as possible, the colors of the inks. The discrepancy between the meaning of the word and the color of the word can cause a momentary confusion that slows response time, and subjects frequently mistakenly read the word instead of naming the ink color. In the study, heavy MDMA users took longer to read the lists and made more errors than the moderate users.

The R-SAT test, which has been used to assess frontal lobe damage in severely impaired people, has never been used before to test substance abuse effects. The test measures a subject's ability to find the most efficient strategy to solve simple problems in a limited time. Subjects are given papers with tasks to do, such as

adding up numbers. The rules explain that some items have higher value than others and that pages that have a “frown face” should be skipped.

Heavy MDMA users completed on average two fewer items in the R-SAT test than did moderate users (between 22 and 50 lifetime uses), who performed on par with nonabusers. This is a large difference in terms of the

test, but the researchers cannot qualify it as mild, moderate, or severe because of the small size of the sample.

The R-SAT differentials between heavy MDMA abusers and moderate and nonabusers need to be validated by further studies before they can be regarded as established, says Dr. Halpern.

### Source

• Halpern, J.H., et al. Residual neuropsychological effects of illicit 3,4-methylenedioxymethamphetamine (MDMA) in individuals with minimal exposure to other drugs. *Drug and Alcohol Dependence* 75(2):135-147, 2004. **NN**

## MDMA May Reduce Gray Matter in Key Brain Regions

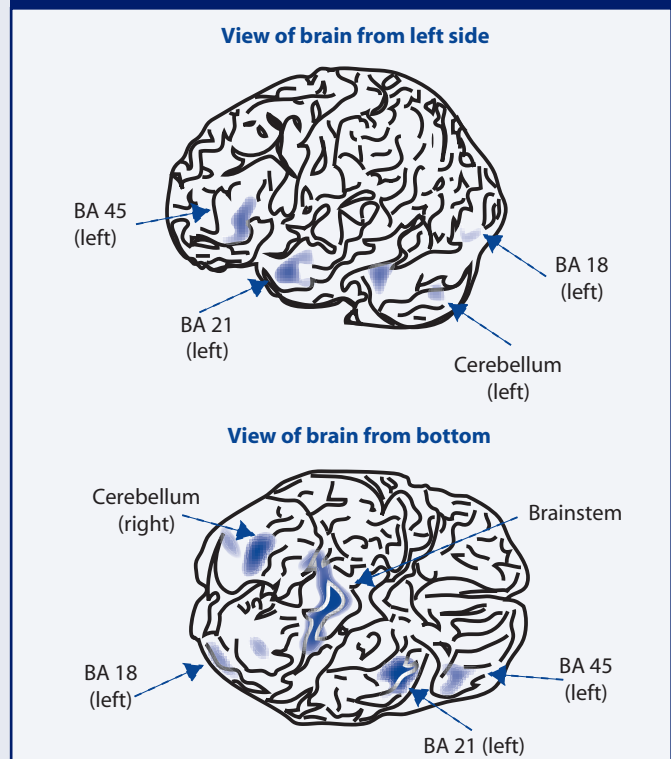
A small study using a new imaging technique revealed an association between MDMA (Ecstasy) abuse and lower gray matter density in key brain structures that affect language, movement, and vital functions such as breathing and heartbeat.

Drs. Ronald Cowan, Perry Renshaw, In Kyoon Lyoo, and colleagues at the McLean Hospital in Belmont, Massachusetts, set out to find evidence in people for an MDMA effect that some animal studies have pointed to: damage to nerve fibers that deliver the neurotransmitter serotonin to certain regions of the brain. Serotonin promotes the growth of neurons and glial cells, which together comprise the brain’s gray matter. The researchers hypothesized, accordingly, that if the suspected effect were true, MDMA-abusing individuals would come to have less abundant gray matter in the regions served by the damaged fibers compared with nonabusers of the drug. Such hypotheses have recently become testable with the development of a new imaging technique, voxel-based morphometry (VBM), which measures gray matter density.

The researchers examined 60 volunteers aged 18 to 35 at McLean Hospital in Belmont, Massachusetts. Thirty-one of the study participants had abused MDMA at least 5 times, while 29 had never taken it. Brain images of the MDMA abusers were taken at least 3 weeks after their last exposure to the club drug. The results bore out the researchers’ hypothesis: They showed smaller concentrations of gray matter in the MDMA abusers than in the controls. The reductions in density do not amount to “holes” in the brain, Dr. Cowan says, but are instead subtle but statistically significant differences seen in several brain regions. Some of the regions with less gray matter were parts of the neocortex that may be involved in word definition. Other implicated areas were the cerebellum, which controls movement, motor learning, and spatial sense, and the brainstem, which controls respiration and heart rhythms and integrates information between the peripheral nervous system and the spinal cord.

The study findings are consistent with the previously existing evidence that MDMA may damage serotonin fibers, but they do not prove it. Dr. Cowan cautions that his study

### New Brain Imaging Technique Detects Brain Density Differences in MDMA Abusers



Preliminary results from voxel-based morphometry suggest decreased density in some brain areas of people who abuse MDMA. Affected areas included the bilateral Brodmann area (BA) 18, the left BA 21 and left BA 45, and the bilateral cerebellum and midline brainstem.

had too few participants to fully rule out the possibility that the MDMA abusers had less gray matter before they took the drug.

### Source

• Cowan, R.L., et al. Reduced cortical gray matter density in human MDMA (ecstasy) users: A voxel-based morphometry study. *Drug and Alcohol Dependence* 72(3):225-235, 2003. **NN**

# NIDA-Sponsored Conference Highlights Intensive Research Focus on Lipids

By Patrick Zickler, NIDA NOTES Staff Writer

Within each human cell, molecules called lipids serve as an energy reserve and as structural components of cell membranes. These molecules also do much more, researchers are learning. Lipids help regulate energy metabolism and are involved in communication within and between cells. As messenger molecules, lipids are crucial for the regulation and control of numerous biological processes, including those influencing how drugs affect cell functions. Investigators have begun to focus increasing interest on these versatile molecules, and NIDA recently sponsored the first-ever international conference devoted to the emerging field of inquiry known as lipidomics—the systematic study of the structure and function of lipids.

Lipidomics is a further exploration of research avenues opened by previous NIDA-supported study, explained Dr. Timothy Condon, deputy director of NIDA, in welcoming researchers to the conference, “Targeted Lipidomics: Signaling Lipids and Drugs of Abuse,” held in Washington, D.C. “NIDA’s marijuana research helped bring into focus the variety of functions of just one group of lipids—the endogenous cannabinoids,” Dr. Condon said. “Marijuana-derived cannabinoids contribute to the effects that make marijuana the country’s number-one drug of abuse, but cannabinoids that occur naturally in the body play a role in obesity, pain, and immune responses to agents like HIV. Other lipids are crucial to the way in which drugs and pathogens behave in the body. So it is clear that describing the roles played by lipids and similar compounds will be one of the most important areas of NIDA research in the next decade. This conference will help us develop the agenda for that research,” Dr. Condon said.

The conference was organized by Dr. Rao Rapaka of NIDA’s Division of Basic Neurosciences and Behavioral Research. “We are learning that lipid interactions are crucial to drug effects, but our understanding of lipids is very superficial,” Dr. Rapaka said. “As a first step, lipidomics will bring to bear the same sort of comprehensive research that was used in genomics.” Genomics—the scientific effort that led to description of the instructions specified on each of the human body’s roughly 30,000 genes—was a scientific milestone, Dr. Rapaka says, but much

*“Lipidomics will bring to bear the same sort of comprehensive research that was used in genomics.”*

work remains to understand how those instructions play out in the functioning of the organism. The genes use combinations of nucleic acids to instruct organelles within each cell to synthesize proteins. The proteins, in turn, interact with other chemical compounds—including an estimated 1,000 different lipids, which include energy storage molecules like fatty acids, biologically active sterols such as testosterone and estrogen, and the amide anandamide, a cannabinoid that is active as a chemical messenger in the central nervous system and immune system. Lipids interact with other compounds in temporary or long-lived configurations that have multifarious biological properties and play a role in

various cellular activities. “We want to use this conference to develop ideas that will direct a systematic investigation into the structure and function of lipids and their behavior in these complex interactions,” Dr. Rapaka said.

At the Washington conference, Dr. Edward Dennis of the University of California-San Diego provided an overview of lipid researchers’ major investigative resource—a collaboration of more than 30 researchers at 18 universities known as the Lipid Metabolites and Pathways Strategy (MAPS) Consortium, funded by the National Institute of General Medical Sciences. “We plan to generate ‘road maps’ that will define how all the lipid components of a cell move through the complex lipidomic network, from biosynthesis to removal, including their important roles as secondary messengers,” he explained. Lipid MAPS is divided into focus areas that concentrate on major groupings of lipids, informatics, cell biology, lipid detection and quantitation, and lipid synthesis.

“NIDA’s leadership in this important field is invaluable,” Dr. Dennis noted. “Lipidomics research is much more than an exercise in basic cell science. The identification of endogenous cannabinoids clearly illustrates the relevance of lipid research to the field of drug abuse, and other discoveries will clarify the complex biochemical relationships between drugs and biological systems ranging from signaling within the central nervous system to immune response.”

In addition to the Washington, D.C., conference, NIDA has organized lipid symposia that were held as part of the annual meetings in June of the College on Problems of Drug Dependence in San Juan, Puerto Rico, and the International Cannabinoid Research Society in Paestum, Italy, Dr. Rapaka said. **NN**

# Eighth Annual PRISM Awards Honor Accurate Depiction of Drug, Alcohol Issues in Film, TV, Music

By Martha Pien, *NIDA NOTES* Contributing Writer

**A**ccurate depictions of drug and alcohol abuse in film, TV, and music were the focus as NIDA and The Robert Wood Johnson Foundation joined the Entertainment Industries Council (EIC) in presenting the eighth annual PRISM Awards at the Hollywood Palladium.

The awards honor the entertainment industry for serious treatment of destructive social issues. In a Capitol Hill Premiere of the awards, held for the fifth consecutive year, leaders of Congress and of national organizations addressing substance abuse celebrated the entertainment industry's achievements in tackling this difficult subject. The awards were broadcast nationally by the FX Network, a Fox Entertainment Group basic cable network reaching 79 million homes.

## Teens and Drugs on the Big Screen

Two films that focused on teen drug abuse received awards. *City of God*, winner of the Theatrical Feature Film PRISM Award, is set in the slums of Rio de Janeiro. It chronicles the harsh fate of young people trapped in a gang culture of drugs, poverty, crime, violence, and death. *City of God*, directed by Fernando Meirelles, is a Miramax Films production.

*Thirteen*—a graphic depiction of two girls' foray into an adolescence marked by alcohol, drugs, and sex—earned several awards, including a Theatrical Feature Film PRISM Commendation. The film captured award-winning performances by Evan Rachel Wood (PRISM Award for Performance in a Theatrical Feature Film) and Holly Hunter and Nikki Reed (PRISM Commendations). The film was directed by Catherine

Hardwicke and produced by Fox Searchlight Pictures and Working Title Films.

At the Capitol Hill Premiere, NIDA Director Dr. Nora D. Volkow said, "We view these nominations as vehicles to put familiar and authentic faces on drug and alcohol abuse and addiction." The public is well served by storylines that draw on knowledge developed through NIDA research to accurately convey the complexity of drug abuse issues, she added.

A new award category, the PRISM President's Award, recognizes an entertainment industry project that not only raises awareness of substance abuse but leaves behind a legacy. Receiving this new award was Songs of Hope and Recovery for Everyone (SHARE), a Nashville project featuring nearly 20 country musicians and supported by many others in the country music industry. Some of those contributing to the production of SHARE are in recovery, others have observed friends and loved ones suffer through substance abuse and work through recovery.

## Nomination Tallies

Film and television studios were invited to submit thematically appropriate works for consideration; the EIC then nominated five submissions for each award category. Leading the major studios and production companies in nominations was 20th Century Fox, with 11 nominations. Paramount



From left: NIDA Deputy Director Timothy Condon, NIDA Director Nora D. Volkow, and former NIDA Director Alan I. Leshner attended the PRISM Awards Capitol Hill Premiere.

had nine nominations; Universal, eight; Warner Bros., six; and David E. Kelley Productions and Steven Bochco Productions had three nominations each. Lions Gate, Carsey Werner Mandabach, Wolf Films, Greenblatt Janollari, John Wells Productions, Hallmark Entertainment, LMNO Productions, Acme Productions, and Tannenbaum Co. each received two nominations, and Miramax Films had one nomination.

In television, Lifetime earned 11 nominations, followed by ABC with nine; NBC, eight; CBS and E! Entertainment, six each; Discovery Channel, four; HBO, MTV, and Showtime, three each; UPN, two; and FOX, MSNBC, AMC, and ESPN with one nomination apiece.

"We're encouraged by the increase in the number of television programs and movies that have addressed substance abuse issues during 2003," says Brian Dyak, EIC president and CEO. Dyak noted that the PRISM nominations not only reflect some of the most important issues threatening society, but also the determination of the entertainment industry to act responsibly when dealing with these topics. **NN**

# Advisory Council Welcomes New Members

The National Advisory Council on Drug Abuse (NACDA) introduced six new members at its February meeting. Leaving the Council after fulfilling their terms were Dr. James Smith, Dr. David Rosenbloom, Dr. Steven Hayes, and Dr. A. Thomas McLellan.

The Council serves a crucial role in advising NIDA to identify, review, and support scientific research of the highest caliber. Its 18-person membership—12 experts in scientific fields and 6 knowledgeable members of the general public, as well as ex officio members who provide liaison with other Government entities—provides a valuable and unique source of consultation.

## New Council Members

**Jeanne Brooks-Gunn, Ph.D.**, is the Virginia and Leonard Marx Professor of Child Development and Education at Teachers College and the College of Physicians & Surgeons at Columbia University. She codirects the National Center for Children and Families and the Columbia University Institute of Child and Family Policy. Dr. Brooks-Gunn's specialty is policy-oriented research focusing on family and community influences on the development of children and youth. Dr. Brooks-Gunn also conducts research on transitional periods in childhood and adolescence, focusing on school, family, and biological transitions in childhood, adolescence, and adulthood.

**Bankole Johnson, M.D., Ph.D.**, is a William and Marguerite S. Wurzbach Distinguished Professor as well as the Deputy Chair for Research and Chief of the Division of Alcohol and Drug Addiction at The University of Texas Health Science Center at San Antonio. His primary area of research expertise is the psychopharmacology of addictive medications. A board-certified psychiatrist, Professor Johnson is the Principal Investigator on NIH-funded research studies using neuroimaging and molecular genetic techniques. His clinical expertise is in addiction, biological, and forensic psychiatry.

**Herbert D. Kleber, M.D.**, is Professor of Psychiatry and Director of the Division on Substance Abuse at the College of Physicians & Surgeons of Columbia University and the New York State Psychiatric Institute, a division he cofounded with his late wife, Dr. Marian Fischman, in 1992. In addition to serving on the editorial boards of several scientific journals, Dr. Kleber is a Fellow in several professional associations, including the College on Problems of Drug Dependence, the American Academy of Addiction Psychiatry, and the American College of Neuropsychopharmacology.

**Thomas E. Lucking, Ed.S.**, is a consultant who specializes in system design and organizational development for community-based behavioral care systems. In the past decade, he has worked with substance abuse systems in 27 States. Recently, Mr. Lucking helped facilitate the consolidation of State departments and provider organizations, enhancing the efficiency and capability of all parties in treating persons with multiple disorders. Before becoming a consultant, Mr. Lucking was director of a nonprofit organization that became the largest provider of substance abuse treatment in western Michigan.

**Patricia Isbell Ordorica, M.D.**, is the Associate Chief of Staff for Mental Health and Behavioral Sciences at the Central Florida Veterans Administration Healthcare System, where she leads an interdisciplinary clinical, training, and research enterprise committed to innovations in treatment and scientific discovery. She is also President of the National Association of VA Psychiatrists in Administration and Leadership and a nationally recognized expert in addictive disorders. In addition, Dr. Ordorica is a consultant to the Roskamp Institute, where her research interests include genomic and proteomic approaches in drug abuse research.

**Linda Porrino, Ph.D.**, is Professor, Department of Physiology and Pharmacology, at Wake Forest University

School of Medicine, where she conducts research on the long-term effects of chronic drug use in humans and animal models. She also serves as Director of the Neuroimaging Laboratory. Dr. Porrino's research interests include the use of brain imaging methods to visualize the effects of substances of abuse on structure and function in the central nervous system and to relate those effects to the behavioral changes that accompany the use of these substances. She is also interested in the use of brain imaging techniques to evaluate the functional consequences of lesions of dopaminergic systems and the evaluation of the effects of pharmacological and surgical replacement therapies in animal models of dopamine deficiency.

NN

## Advisory Council Meeting Schedule

NACDA meets three times a year—usually in February, May, and September—and always at NIDA's Rockville, Maryland, office. The first day is a closed session for Federal staff with a need to hear the Council's deliberations.

Day 2, a half-day session, is open to the public and addresses issues such as programs, policy, research dissemination, and training. Attendees also hear the Director's address, touching on scientific and administrative topics in the Director's Report; subcommittee reports; and staff and other speaker presentations. A portion of this session is set aside for public comment, fulfilling the purpose of this second meeting day: *to offer a forum for effective public involvement in shaping NIDA's research and related scientific activities.*

Agendas for both days of Council meetings are available online 4 weeks before each meeting at [www.drugabuse.gov/about/organization/NACDA/NACDAHome.html](http://www.drugabuse.gov/about/organization/NACDA/NACDAHome.html).

# NIDA's Latest *Research Report* Focuses on MDMA (Ecstasy) Abuse

The most recent issue of NIDA's *Research Report* Series highlights the current science on 3,4-methylenedioxymethamphetamine (MDMA, or "Ecstasy"). The series is part of NIDA's continuing effort to provide science-based information to the public. Each report focuses on a particular drug abuse topic of national interest. For the complete *Research Report* and for additional information on illicit drugs, please visit [www.drugabuse.gov](http://www.drugabuse.gov).

Because of its use by young adults at all-night dance parties, or "raves," MDMA is classified as a "club drug." In the past few years, however, MDMA abuse has spread to a wide range of other settings and demographic subgroups. Despite growing evidence of its potential harmful effects, MDMA still has a deceptive reputation as a "safe" drug among its abusers. The latest findings in the *Research Report* highlight dangers, effects, and addiction potential.

**Potential Dangers.** Because of its stimulant properties and the environment in which it is often taken, MDMA is associated with vigorous physical activity for extended periods. This can cause a dangerous increase in body temperature that can lead to cardiovascular failure. MDMA also can produce dehydration and increase heart rate, blood pressure, and heart wall stress. Other potential adverse health effects include nausea, chills, sweating, involuntary teeth clenching, muscle cramping, and blurred vision. MDMA overdose may be characterized by high blood pressure, faintness, panic attacks, and in severe cases, loss of consciousness and seizures.

**Behavioral Effects.** In the hours after taking the drug, MDMA significantly impairs memory and information processing. These deficits can interfere with performing skilled activities, such as driving a car. In the week following moderate exposure to the drug, many MDMA abusers report

feeling anxiety, restlessness, irritability, and sadness that in some individuals can be as severe as clinical depression. Regular MDMA abusers demonstrate elevated anxiety, impulsiveness, aggression, sleep disturbances, lack of appetite, and reduced interest in and pleasure from sex.

**Brain Effects.** By releasing large amounts of serotonin, MDMA significantly depletes the brain of this important neurotransmitter, contributing to the negative behavioral effects that abusers often experience for several days. A number of studies show that long-term heavy MDMA abusers suffer persistent cognitive deficits, including problems with memory.

**Possible Reproductive Effects.** The potential adverse effects of MDMA on the developing fetus are of great concern. Behavioral studies in animals have found significant adverse effects on tests of learning and memory from exposure to MDMA during a developmental period equivalent to the third trimester in humans. However, more research is needed to determine the effects of MDMA on the developing human nervous system.

**Potential for Addiction.** For some people, MDMA can be addictive. A survey of adolescents and young adults found that 43 percent of those who reported MDMA abuse met the accepted diagnostic criteria for dependence—that is, the individual continues to use the drug despite withdrawal effects, tolerance, and knowledge of harm. More than a third (34 percent) met the clinical criteria used to diagnose a need for drug abuse treatment. MDMA affects many of the same neurotransmitter systems in the brain that are targeted by other addictive drugs. Behavioral studies in animals corroborate MDMA's potential for abuse. Rats prefer places associated with the drug and learn to self-administer MDMA, behaviors associated with most addictive drugs.

## Source

- Substance Abuse and Mental Health Services Administration. Overview of findings from the 2002 National Survey on Drug Use and Health (Office of Applied Studies, NHSDA Series H-21 DHHS Publication No. SMA 03-3774). Rockville, MD. **NN**

## The Extent of MDMA Use

It is difficult to determine the exact scope of MDMA abuse. It often is used with other substances and does not appear in some traditional data sources. However, the following snapshot emerges:

- In 2002, more than 10 million Americans over age 12 reported having used MDMA at least once, up from 6.4 million in 2000.
- Past-year MDMA use among people over age 12 decreased from 3.2 million to 2.1 million between 2002 and 2003. In this period, the number of past-month users fell from 676,000 to 470,000.
- The initiation of MDMA use in the U.S. rose steadily from 1992 until 2000, when the number of new users reached 1.9 million. Following overall declines in hallucinogen use, the number of people initiating MDMA use fell from 1.8 million to 1.1 million between 2001 and 2002.
- MDMA use decreased among 8th-, 10th-, and 12th-graders in 2003, continuing a decline that began in 2002. Past-year use among 8th-graders decreased from 2.9 percent to 2.1 percent; from 4.9 percent to 3.0 percent among 10th-graders; and from 7.4 to 4.5 percent among 12th-graders.
- MDMA use extends across many demographic subgroups. Among 12th graders, for example, 6.4 percent of Whites, 5.3 percent of Hispanics, and 1.4 percent of African Americans reported using MDMA in the year prior to the survey.
- Mentions of MDMA in hospital emergency departments increased 94 percent from 1999 to 2001 (from 2,850 to 5,542).

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This publication was produced and printed by MasiMax Resources, Inc., under Contract No. N01DA-1-1107 from the National Institute on Drug Abuse.



**NIDA NOTES** covers drug abuse research in the areas of treatment and prevention, epidemiology, neuroscience, behavioral science, health services, and AIDS. The publication reports on research; identifies resources; and promotes communication among clinicians, researchers, administrators, policymakers, and the public. Readers are encouraged to identify subject areas they would like to see highlighted.

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**NIH Publication No. 05-3478  
Printed January 2005**

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