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New Imaging Technology Confirms Earlier PET Scan Evidence: Methamphetamine Abuse Linked To Human Brain Damage

By Neil Swan
NIDA NOTES Contributing Writer

A new magnetic resonance imaging (MRI) technology that measures blood flow in the brain corroborates earlier positron emission tomography (PET) scan studies that showed evidence of brain abnormalities caused by methamphetamine abuse. Perfusion MRI, or pMRI, measures blood flow into key brain regions by producing images based on hundreds of electronic cross-sections showing brain structure and blood flow.

Dr. Linda Chang and colleagues at Brookhaven National Laboratory in Upton, New York, used pMRI scans to document blood-flow abnormalities in test subjects in brain regions that control response times and immediate, short-term memory. Their research correlated these abnormalities with response times during cognitive testing, where methamphetamine abusers consistently reacted more slowly on computerized tasks than did closely matched nonusers. The slower reaction times, evident in abusers even after months of abstinence, are seen as evidence of brain injury.

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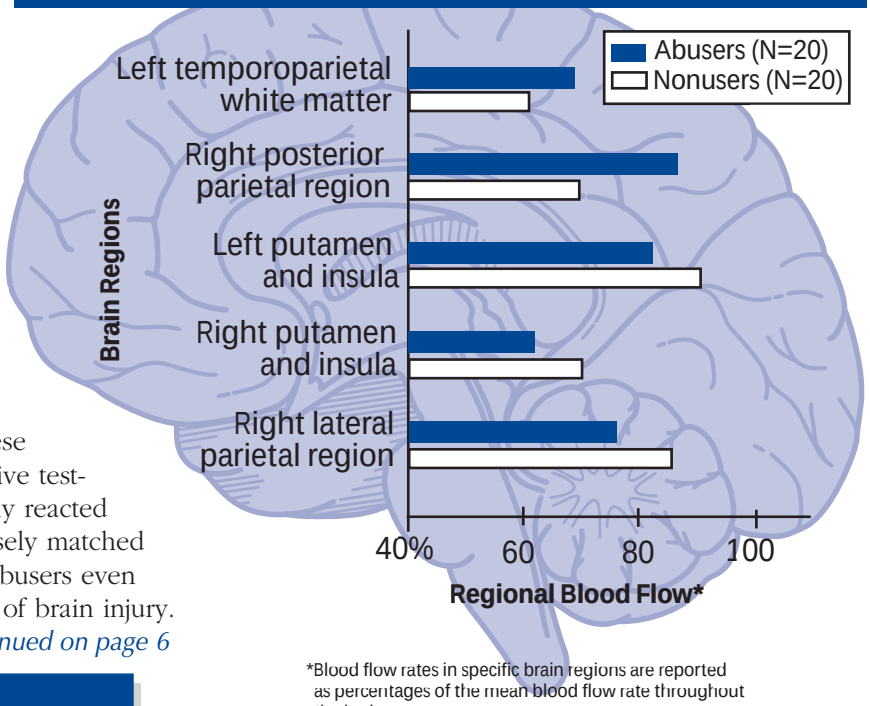
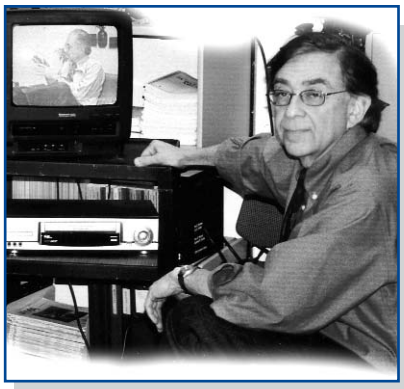
Brain Blood Flow Differs Between Meth Abusers And Nonusers, Suggests Damage



*Blood flow rates in specific brain regions are reported as percentages of the mean blood flow rate throughout the brain.

In methamphetamine abusers, brain scans reveal increased *blood flow in certain parts of the abusers' parietal regions (the left temporoparietal white matter and right posterior parietal area). Scans also show* decreased *blood flow in the frontal, other parietal, and basal ganglia regions (specifically, the left and right putamen and insular areas and the right lateral parietal area). Researchers believe that increased blood flow in parietal regions is evidence that glial cells—designed to protect or repair nerve cells in harm's way—are responding to drug-induced injury. They also theorize that decreased blood flow in other areas of the brain may indicate that nerve cells already have been damaged.*

What's Inside



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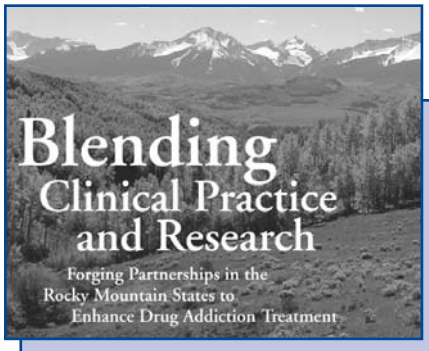

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Brain Imaging: Bringing Drug Abuse Into Focus

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

Imaging techniques are providing new views of brain structure and activity, allowing researchers to watch small brain structures in minute detail and observe changes over fractions of seconds after drugs enter the brain's tissues.

The brain images produced by positron emission tomography (PET) and magnetic resonance imaging (MRI) have broadened our understanding of drug addiction as a brain disease. Imaging techniques are providing new views of brain structure and activity, allowing researchers to watch small brain structures in minute detail and observe changes over fractions of seconds after drugs enter the brain's tissues.

Imaging technology also allows us to observe more indirect effects—how craving for drugs changes brain activity and the mechanisms by which inherited characteristics influence vulnerability to drug abuse or susceptibility to a drug's toxic or addictive properties. And with NIDA's continuing commitment to refinement of imaging techniques, our newfound scientific insight at the cellular level will merge with the broader focus that links the workings of an individual's brain to his or her behavior, emotion, reasoning, and decisionmaking.

PET imaging in drug abuse research relies on ligands—chemical compounds created in the laboratory that selectively attach to the same key sites (receptors) on brain cells as do drugs of abuse. Radioligands incorporate radioactive atoms that emit energy. PET "cameras" capture the energy these ligands emit when attached to target sites, and computers convert that energy to images that reveal the location and intensity of drug activity in the brain.

NIDA-sponsored research at Brookhaven National Laboratory in Upton, New York, led to the development of the first ligands designed to mimic cocaine in binding to one type of dopamine receptor, making it possible to trace the effect of cocaine on the brain's dopamine system. Other ligands allow researchers to study aspects of brain systems that involve other neurotransmitters, such as serotonin. At NIDA's Intramural Research Program (IRP), a multiyear effort has yielded a new ligand that binds to nicotine receptors. Researchers there have begun using this important new compound to study the activity of the brain's nicotine receptors in nonsmokers as well as smokers.

A broader selection of ligands that mimic more drugs and are specific to more aspects of neurotransmitter systems will allow researchers greater access to unexplored areas of the molecular realm where drugs act on the brain. For example, there are five types of dopamine receptors and more than a dozen receptors specific to nicotine, each with subtly different properties and functions. New ligands will improve our ability to use imaging techniques to observe and understand the activity of nicotine and other drugs in the brain and—just as important—potential medications to counter their effects.

To speed the development of new ligands, NIDA and the National Institute of Mental Health (NIMH) have encouraged researchers to

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Brain Imaging: Bringing Drug Abuse Into Focus

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participate in National Cooperative Drug Discovery Groups. NIDA already has made awards to more than a dozen grantees, who are beginning work on this important research.

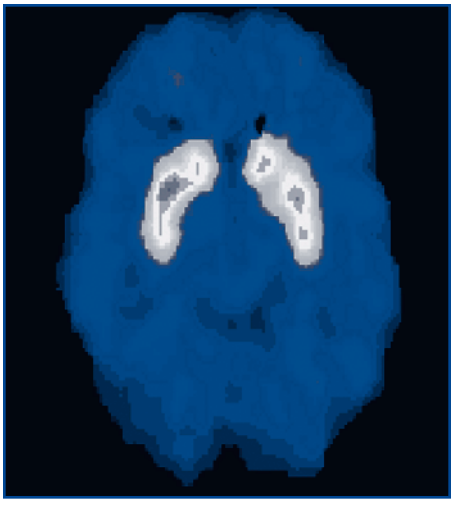
Our new initiatives will lead to a better understanding of the impact of drugs on the development and functioning of the human brain.

Unlike PET, MRI does not rely on radioactive compounds to monitor a drug's activity in the brain. Because MRI does not expose study participants to the risks associated with radiation, researchers can conduct long-term studies, in repeated sessions lasting several hours, on the same person. At Brookhaven National Laboratory, NIDA-supported scientists using MRI have found evidence that methamphetamine abusers suffer abnormal blood flow in brain regions that control response times and short-term memory as long as 8 months after last using the drug (see "New Imaging Technology Confirms Earlier PET Scan Evidence: Methamphetamine Abuse Linked to Human Brain Damage," p. 1). At IRP, investigators are now using a newly installed functional MRI (fMRI) system that makes possible more comprehensive observation of drugs' effects on the functioning brain (see "New Technology Expands the Scope of NIDA's Intramural Brain Imaging Program," p. 14).

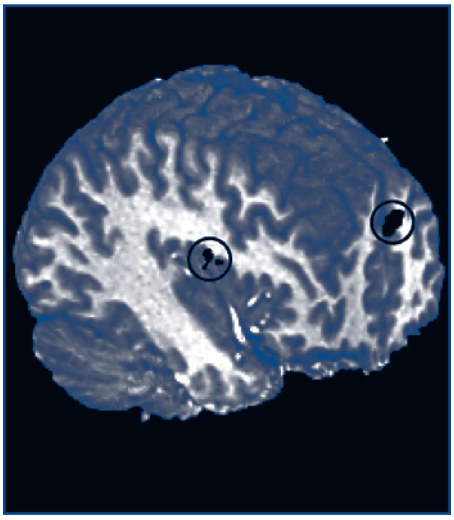
In fMRI studies, investigators can watch drug-exposed and unexposed brains function during tasks involving reasoning and memory and compare brain activity with how well participants perform on the tasks. Scientists also can use fMRI to observe how the brain works in response to treatments that address the weaknesses revealed in tests of function and performance, thereby speeding development and evaluation of both pharmacological and behavioral treatments.

In February, NIDA opened another area of brain imaging research when it announced a request for research projects to enhance understanding of the consequences of drug exposure, abuse, and addiction on the developing human brain—from prenatal exposure to the transition to adulthood. This research program (Neuroimaging the Effects of Drugs of Abuse on the Development of the Human Nervous System, RFA DA-04-002) will use a variety of imaging techniques—including PET, MRI, conventional optical imaging, and electroencephalography.

By comparing brain maturation processes in people who have and have not been exposed to drugs, this program will help us more clearly define how the timing and amount of drug exposure can disrupt brain development. NIDA's investment in brain imaging research is beginning to yield a more comprehensive picture of the disease of addiction. Our new initiatives will lead to a better understanding of the impact of drugs on the development and functioning of the human brain. And our continued investment in finding better chemical tools, techniques, and technology will provide increased understanding of drug abuse and, ultimately, a brighter outlook for drug abuse prevention and treatment. NN



This PET image is formed from energy emitted by a radioactively labeled ligand that selectively attaches to dopamine D_2 receptors on brain cells. PET studies can be used to evaluate and compare the distribution and density of receptor or transporter sites in drug abusers and nonusers.



Functional magnetic resonance imaging shows activation of brain sites (circled) in cocaine addicts as they watch a film that induces cocaine craving.

Network Therapy Expands Treatment Capabilities Of Small Practice Providers

By Patrick Zickler
NIDA NOTES Staff Writer

NIDA-supported researchers have found that clinicians without access to the resources of a comprehensive substance abuse program can treat cocaine abuse with "network therapy," a treatment approach that combines individual therapy and the involvement of patients' friends or family members. The patient completion rate—a key measure of the likelihood that patients will remain drug free—is comparable to that of other outpatient treatment approaches, the researchers say.

Network therapy was developed through NIDA's Behavioral Therapies Development Program by Dr. Marc Galanter and his colleagues at the New York University School of Medicine in New York City. The treatment combines cognitive-behavioral therapy, which enables patients to identify and develop strategies to avoid or cope with circumstances that lead to their drug use, with network sessions that include the patient and one or more "network members"—family members or peers who are not substance abusers.

"Network therapy expands the practitioner's capability to treat cocaine abuse by enlisting family and peer support to provide the reinforcement necessary for the patient's success," says Dr. Galanter. "Physicians in small practices do not have the benefits offered by a large clinical environment, such as social workers, multidisciplinary psychiatric staff, or the opportunity to schedule nightly group meetings. This approach helps overcome those limitations."

Dr. Marc Galanter, of New York University School of Medicine, reviews a training tape to be shown to clinicians learning network therapy. Developed through NIDA's Behavioral Therapies Development Program, network therapy combines individual cognitive-behavioral therapy with sessions that include the patient and members of his or her network—family members or peers.

The researchers trained 28 psychiatry residents to provide network therapy. Training involved classroom seminars and video presentations based on a 122-page manual. The residents then treated 47 patients who had applied for cocaine abuse treatment and had no other substance abuse or psychiatric disorder.

The patients (mean age 35 years, 85 percent male, 62 percent white) paid $20 per session over a 24-week sequence of twice-weekly individual therapy sessions. Network sessions were held weekly for the first month and monthly thereafter. Twelve patients dropped out of the program after the first week. Of the 35 who remained beyond the first week, nearly half (17) completed the full 24-week course of treatment, a completion rate comparable to those in other outpatient treatment programs.

Treatment success for each participant was based on two measures: the proportion of drug-free weekly urine tests and the participant's drug-free status for the last three tests. Overall, 73 percent of tests throughout treatment were drug free; 20 participants (43 percent of the entire group) were drug free the last 3 weeks of treatment. Success was most likely among patients who involved network members and remained in treatment longest.

"The network sessions involved training network members to provide

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New Imaging Technology Confirms Earlier PET Scan Evidence: Methamphetamine Abuse Linked to Human Brain Damage

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In earlier research, Dr. Chang, together with Dr. Nora Volkow and others at Brookhaven, used PET scans to measure brain metabolism, or glucose consumption levels. Scientists know that the more active brain areas use more glucose, which is fuel for cells, and that this indicates higher localized metabolism. The NIDA-supported PET studies revealed that methamphetamine abusers showed regional increases and decreases in glucose metabolism that were consistent with mounting evidence that methamphetamine abuse injures brain cells.

Explaining the significance of her latest study, Dr. Chang said, "We used pMRI to show that methamphetamine abuse is related to changes in blood flow in the same critical regions of the human brain in which PET scans have shown increases in glucose usage in methamphetamine abusers. Finding similar patterns of drug-related changes or abnormalities in the brain using two different scanning technologies makes the evidence of methamphetamine-induced damage to brain cells more credible."

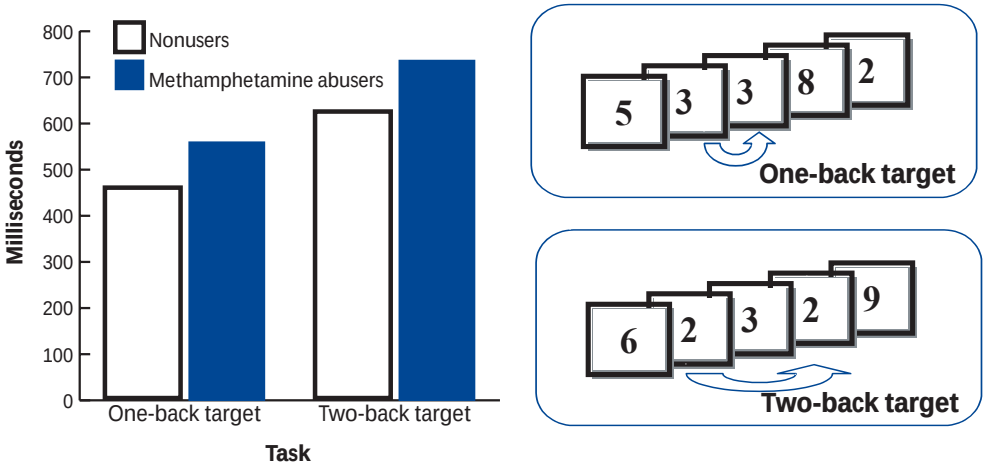
In the pMRI study, increased brain blood flow was detected in the parietal regions of methamphetamine abusers' brains. These regions are involved in receiving and processing information from the sensory receptors in the skin, muscles, and joints and in the integration of auditory, visual, and somatic information. Dr. Chang's study also found that methamphetamine users had decreased blood flow in other areas of the brain's parietal regions and in the frontal and basal ganglia regions. These regions are involved in controlling response speed and attention span and in coordinating motor functions and psychomotor speed.

Dr. Chang theorizes that *increased* blood flow in parietal regions indicates an increase in activity by glial cells, or supporting cells, rather than neurons, or nerve cells, since glia have a higher metabolic rate than neurons. Glia are a cell type that gears up to try to shield and repair nerve cells that are damaged or exposed to toxins, such as drugs. Animal experiments have demonstrated similar glial responses to repair drug-induced injury. On the other hand, Dr. Chang reports, *decreased* blood flow observed in the parietal and other brain regions might indicate that nerve cells there are already damaged beyond glial cells' power to repair them.

Forty subjects participated in Dr. Chang's study—20 abstinent methamphetamine abusers and 20 nonusers. Each control group member was selected to match one of the methamphetamine abusers by age and gender, an unusually precise matching. Those in the abusers' group had abused an average of 2.8 g or more of methamphetamine a day, an average of 6.5 days a week, for approximately 8 years, but had been abstinent for an average of 8 months.

The researchers administered standard neuropsychological tests, on which the methamphetamine

Methamphetamine Abusers Have Slower Reaction Times on Computerized Cognition Tests



Computer-task sequential reaction time tests require subjects to press a key when they see a number appear twice in a row (one-back target) or when a number repeats after one intervening number (two-back target). On the one-back test, methamphetamine abusers' average response time was 21.5 percent slower than that of the nonusers; on the two-back test, their average response time was 18 percent slower.

abusers performed within normal ranges, and a battery of more sensitive computerized tests designed to detect subtle or early signs of cognitive decline. The battery, called the CalCAP, assesses a range of cognitive functions, including brief, sustained, and divided attention; immediate memory; rapid visual scanning; discrimination between various forms or shapes; and language skills.

Three of the CalCAP tests showed the most dramatic results. In the simple reaction time test, subjects are asked to press a keyboard key as soon as they see anything appear on the computer screen. Average reaction time for the methamphetamine users was 21 percent slower than that of the nonusers, as measured in milliseconds.

The single-digit recognition test involves immediate memory and requires subjects to press a key when they see a specific letter, but only when the letter appears immediately after another specific letter ("X" only after "A"). Methamphetamine abusers' average response time was 30 percent slower than that of the nonusers.

The sequential reaction time tests also involves immediate memory. Numbers are flashed one at a time on the computer screen and the participant is asked to press a key whenever the currently flashing number matches the one just before (one-back target) or when the current number matches the one two flashes before (two-back target). On the one-back test, methamphetamine abusers' average response time was 21.5 percent slower than that of the nonusers; on the two-back test, their response time was 18 percent slower.

Altogether, the nine CalCAP tests revealed consistently slower response times for methamphetamine abusers, particularly on tasks that required working memory, the immediate storage of information, and mental concentration. Dr. Chang interprets these results as evidence of subclinical Parkinsonism—brain damage that is not yet noticeable in routine activities but which in more severe form could produce the symptoms associated with Parkinson's disease, a chronic neurological condition marked by physical slowness, tremors, unstable posture, and a peculiar gait.

Altogether, the nine CalCAP tests revealed consistently slower response times for methamphetamine abusers, particularly on tasks that required working memory, the immediate storage of information, and mental concentration.

"The computer response tasks measure response times very precisely, in ways not noticeable in everyday activities but consistent with subclinical Parkinsonism," says Dr. Chang. "This possibility is further supported by numerous studies with animals that have indicated that methamphetamine may injure the brain's dopamine system, which is involved with working, or immediate, memory."

"The important advance here is not that we have confirmed earlier PET scan evidence of brain injury in methamphetamine abusers, but that we have done so with a new imaging technology that is simpler and relatively inexpensive to administer," comments Dr. Chang. PET scans involve injection of radioactive materials into the blood of test subjects, a procedure that can be extremely sensitive in detecting small quantities of specific molecules in the brain, but that is expensive, technically difficult, and more invasive to test subjects.

"Because of the need to limit excess radiation exposure, PET scans can be repeated on a subject only once or twice in a given year, but these pMRI scanning procedures can be performed relatively often on the same person, even daily if required," she says. "If blood-flow scans continue to prove viable for viewing and measuring evidence of drug-induced brain damage, they could hold potential for development as clinical tools to measure the effectiveness, over time, of a variety of pharmacological and behavioral therapies for drug addiction.

"These MRI techniques might also prove valuable in studying the long-term brain damage attributed to drug use and whether the damage can be reversed," concludes Dr. Chang.

Sources

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Alternative Cigarettes May Deliver More Nicotine Than Conventional Cigarettes

By Susan Farrer
NIDA NOTES Contributing Writer

Clove cigarettes, bidis, and additive-free cigarettes deliver at least as much nicotine as conventional cigarettes, suggests recent research conducted by NIDA Intramural Research Program (IRP) investigators in Baltimore. Smokers who choose these cigarettes are as likely to become addicted to nicotine as are other smokers and are exposing themselves to the increased risk of cancers, respiratory disease, and heart disease associated with smoking.

Dr. Wallace Pickworth and his IRP colleagues conducted two studies comparing the effects of smoking clove cigarettes, bidis, and additive-free cigarettes with the effects of smoking conventional filtered cigarettes as part of an ongoing IRP program that examines nicotine delivery of alternative cigarettes. Their findings refute some consumers' belief that alternative tobacco products—sold on the Internet and at health food stores, ethnic groceries, and drug paraphernalia shops—are safer than conventional cigarettes.

Bidi makers rolling tobacco into tendu leaves, a wrapping that has less porosity than that of conventional cigarettes and that lacks the filter ventilation holes seen in filtered brands. Despite having less nicotine, bidis deliver as much—or more—nicotine as conventional cigarettes.

Effects of Smoking Clove Cigarettes

In the clove cigarette study, the IRP investigators analyzed the physical composition of a particular clove cigarette brand and conventional cigarettes and measured the nicotine, tar, and carbon monoxide (CO) delivery of the clove cigarette. They also conducted a small-sample clinical study comparing the nicotine delivery and physiologic and subjective effects of smoking clove cigarettes and conventional cigarettes.

In the nonclinical portion of the study, the investigators removed, weighed, and chemically analyzed the contents of 10 clove cigarettes and 10 each of 4 popular conventional cigarette brands. To measure how much nicotine, tar, and CO the clove cigarette delivered, they used machine-smoking methods based on those developed by the Federal Trade Commission. Analysis showed that the clove cigarette contained less nicotine and tobacco, but the smoking-machine analysis revealed that the clove product delivered more nicotine, tar, and CO than did the conventional cigarettes. The researchers attribute the clove cigarette's higher delivery of toxins to the lower porosity of its paper wrapper and its lack of filter ventilation holes, which are found on most ordinary cigarettes and dilute the smoke inhaled with each puff.

In the clinical part of the study, 10 volunteers (7 men and 3 women) were asked to smoke a clove cigarette and a filtered conventional cigarette of their usual brand. The volunteers, whose mean age was 30.3 years, smoked an average of 21.3 cigarettes a day and had been smoking for an average of 13.4 years. Four of the volunteers had previously smoked clove cigarettes and all had smoked bidis in the past.

After the volunteers smoked the clove or conventional cigarette, the researchers measured their plasma nicotine levels, exhaled CO levels, blood pressure, and heart rates. They also recorded the time and number of puffs taken to smoke each cigarette, and the volunteers rated their satisfaction with smoking each cigarette and its sensory effects.

The researchers found comparable increases in the volunteers' plasma nicotine levels, exhaled CO levels, heart rates, and systolic blood pressure after smoking the clove and conventional cigarettes. However, the volunteers took longer and more frequent puffs of the clove cigarette than of their own cigarette brands (mean of 549 seconds and 15.1 puffs for the clove cigarette versus 314 seconds and 9.4 puffs for their own brands). This change in smoking behavior increases the amount of nicotine extracted from each cigarette, making it possible for smokers to achieve comparable blood concentrations of nicotine, even though clove cigarettes contain less of the drug per cigarette than do conventional brands.

Effects of Smoking Bidis and Additive-Free Cigarettes

In a related study, Dr. Pickworth and his colleagues compared the clinical effects of smoking bidis, additive-free cigarettes, and conventional cigarettes. As in the clove cigarette study, this research involved 10 volunteers (9 men and 1 woman), all of whom had a history of smoking bidis. However, the volunteers' average age was younger (24.5 years) and they smoked more per day (25 cigarettes) than participants in the clove cigarette study, although they had smoked for fewer years (8.7 years).

In each of four separate sessions, each volunteer smoked a single cigarette: an unfiltered, additive-free cigarette; a strawberry-flavored bidi; an unflavored bidi; and one of the subject's usual, filtered cigarettes. The researchers made the same analytical and physiological measurements and gathered the same behavioral information as they did in the clove cigarette study.

The analysis showed that 2 minutes after smoking, plasma nicotine levels increased the most for participants who had smoked the additive-free brand, followed by levels for smokers of the strawberry bidi, the unflavored bidi, and the conventional cigarette. The volunteers' average heart rate also increased significantly for all of the cigarettes, with the greatest difference (8.5 beats per minute) seen after smoking the additive-free brand and the least difference (2.5 beats per minute) after smoking their own brand. The volunteers spent more time smoking the additive-free cigarette and unflavored bidi (mean of 453 seconds, and 354 seconds, respectively) than the strawberry bidi or their own brands (322 seconds and 297 seconds, respectively). They also took more puffs to smoke any of the bidis and additive-free cigarettes

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Alternative Cigarettes and Young Smokers

Clove cigarettes, made in Indonesia and exported worldwide, are composed of 60 to 80 percent tobacco and 20 to 40 percent ground clove buds. They are usually machine rolled, are available with or without filters, and usually are sold in brightly colored packages. Clove cigarettes are sometimes referred to as "trainer cigarettes" and may serve as "gateway" products that introduce young people to smoking. The Monitoring the Future (MTF) survey, conducted by the University of Michigan's Institute for Social Research and funded by NIDA, tracks 8th-, 10th-, and 12th-graders' drug use, including use of tobacco products. In 2002, prevalence of clove cigarette smoking in the past year was 2.6 percent for 8th-graders, 4.9 percent for 10th-graders, and 8.4 percent for 12th-graders.

Bidis are small, brown, hand-rolled cigarettes that are made primarily in India and other South Asian countries. They are available in many flavors, such as chocolate, raspberry, and strawberry, making them appealing to adolescent smokers. The 2002 MTF survey reported that 2.7 percent of 8th-graders had smoked bidis in the past year; figures for 10th- and 12th-graders were 3.1 percent and 5.9 percent, respectively. In some geographic areas, rates are even higher. For example, a 1999 study by the Massachusetts Tobacco Control Program found that 16 percent of students in grades 7 through 12 in one large metropolitan area had smoked bidis in the 30 days prior to the study.

Additive-free cigarettes are made with whole-leaf tobacco and contain no chemical additives, preservatives, or reconstituted tobacco. IRP researchers report that many adolescents—and adults— believe that additive-free cigarettes are less harmful or less addictive than ordinary cigarettes, although scientific evidence contradicts that belief.

Network Therapy Expands Treatment Capabilities of Small Practice Providers

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a supportive environment for abstinence to help patients adhere to behavioral strategies, such as avoiding situations that might trigger drug use," Dr. Galanter explains. "Interestingly, it was the number of network sessions—not the number of individual sessions—that most closely correlated with a good outcome. This suggests the central role of involvement with network members in shaping outcome."

Dr. Dorynne Czechowicz of NIDA's Division of Treatment Research and Development says that the involvement of young doctors in the delivery of network therapy represents a significant additional accomplishment of this research. "The recent approval of buprenorphine for office-based treatment of opiate addiction represents a first step in the movement of drug abuse treatment out of specialized facilities and into the more routine world of health care," she says. "Training young doctors to deliver therapy is a crucial step in getting general practitioners involved in drug abuse treatment, and treatments such as network therapy can help accelerate that movement."

Dr. Galanter is now conducting a study of the effectiveness of network therapy in combination with the administration of buprenorphine in treating heroin addiction. "There is a need for training in psychosocial approaches to drug abuse treatment that are applicable to a practitioner's office, both as a stand-alone option and in combination with pharmacotherapy." Dr. Galanter says. "Our findings in the use of network therapy in treating cocaine addiction are promising. Results so far suggest that network therapy may also be a valuable, easily delivered approach to support buprenorphine treatment in an office setting."

Source

• Galanter, M.D.; Dermatis, H.; Keller, D.; and Trujillo, M. Network therapy for cocaine abuse: Use of family and peer supports. *American Journal on Addictions* 11(2):161-166, 2002. NN

Alternative Cigarettes May Deliver More Nicotine Than Conventional Cigarettes

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(approximately 14 puffs each) than to smoke their own brand (10 puffs).

Like clove cigarettes, the additive-free cigarette and bidis delivered more nicotine than did conventional cigarettes. Although both the flavored and unflavored bidis are smaller and contain less tobacco than conventional cigarettes, the bidis raised plasma nicotine to levels equal to or greater than the volunteers' own brands. The researchers theorize that like the thicker clove cigarette wrappers, the bidis' nonporous wrappers limit air dilution.

Not Safe Products

The NIDA scientists conclude that clove cigarettes, bidis, and additive-free cigarettes are not safe products and may be as harmful as conventional cigarettes. "Even though the bidis and the clove cigarettes have less nicotine in the cigarette rod—in the case of the bidis about one-third and in the case of the clove cigarettes about one-half or less—people are still able to extract about the same or even more nicotine than they would from a conventional cigarette," says Dr. Pickworth. "When individuals smoke these novel cigarettes, they adjust their cigarette smoking behavior to achieve plasma levels of nicotine comparable to those attained by smoking their own brands of cigarette. By that standard, they are at least equally dependence-producing. As a consequence, smokers will increase their smoking as dependence increases, exposing themselves to ever-greater smoking-related health risks."

Sources

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Relationships Matter: Impact of Parental, Peer Factors on Teen, Young Adult Substance Abuse

By Arnold Mann
NIDA NOTES Contributing Writer

The influence of family and peers on adolescent substance abuse has been well documented in the scientific literature. Generally, positive family influences, such as family bonding and consistent rules, appear to reduce the risk of tobacco, marijuana, and other drug abuse among teens, while negative family influences tend to increase risk. The same is true of positive and negative peer factors. Little research, however, has been conducted to see how parental and peer factors interact to influence adolescent's initiation to and young adults' use of drugs.

Two new NIDA-funded studies—one looking at initiation of substance use, the other at continued substance abuse—show that some aspects of family and peer influences remain potent from early initiation into young adulthood and across socioeconomic, ethnic, and gender lines. Both studies yielded surprises and implications for intervention. For example, the first study found that although family and peer factors had similar effects on males and females, family monitoring and rules had a stronger protective effect for males than females. The second study found that for either gender, peer influence was not mediated by the quality of the relationship, except for female peer influence on young adult marijuana use.

Impact of Family on Teen's Initiation to Drugs

University of Washington researchers recruited 808 5th-graders from 18 Seattle elementary schools in high-crime areas and followed them from ages 12 to 21 to see how peer, family, and sociodemographic factors interacted to influence drug initiation.

As part of an ongoing NIDA study directed by Dr. J. David Hawkins, data from this group were gathered annually through age 16 and again at 18 and 21. The sample included a high proportion of low-income families, "but not all children came from homes in high-risk neighborhoods," says Dr. Karl Hill, one of the study's

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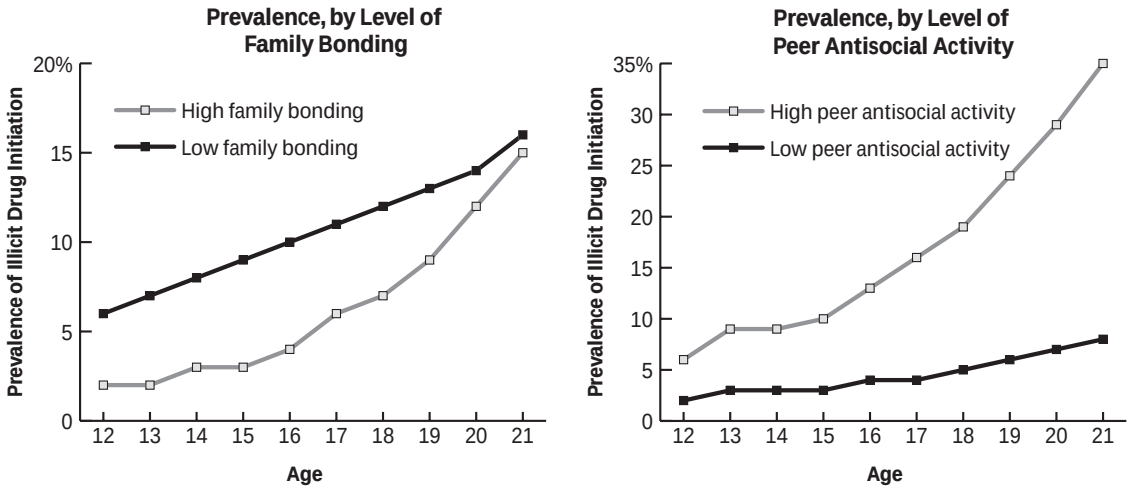
Family Bonding and Peer Antisocial Activity Impact Drug Initiation Among Adolescents



Source: Guo, J., et al., Journal of the Academy of Child and Adolescent Psychiatry, 2002.

Low levels of family bonding and high levels of peer antisocial activity were consistently associated with higher prevalence of illicit drug initiation among youths ages 12 to 21 compared with prevalence seen when high levels of family bonding and low levels of peer antisocial activity were present. By age 21, however, a high level of family bonding had far less impact than in earlier years on adolescent drug initiation.

Relationships Matter: Impact of Parental, Peer Factors on Teen, Young Adult Substance Abuse

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authors. Of concern were the extent of bonding to family, family involvement (time spent interacting with parents), family conflict resolution and parenting practices (monitoring, rules, and consistent discipline), peers' prosocial and antisocial activities, and measures of use for tobacco, marijuana, cocaine, amphetamines, tranquilizers, sedatives, and psychedelics.

Initiation of tobacco and illicit drug use for the entire study group was 4.6 percent by age 12, 8.4 percent by age 13, 12.6 percent by age 18, and 40.5 percent by age 21. By age 21, 45.4 percent of male participants had initiated illicit drug use, as had 35.5 percent of females. Native Americans had the highest rate of initiation, at 55.9 percent, compared to 53.6 percent of European Americans, 33.3 percent of African Americans, and 14.6 percent of Asian Americans.

All of the measured family factors were influential, with the terms *low level* referring to families in the lowest 10 percent for a specific factor and *high level* referring to those in the highest 10 percent. Higher levels of family monitoring and rules were associated with a "significantly" lower risk of illicit drug initiation, according to Dr. Hill. For example, youths with low levels of family monitoring and rules at age 18 were twice as likely (14 percent versus 7 percent) to initiate illicit drugs as those with high family monitoring. The same was true for a higher level of moderate and consistent family discipline—youths with low consistent family discipline were over twice as likely (15 percent versus 6 percent) at age 18 to initiate illicit drugs as those with high consistent family discipline.

Family bonding was particularly influential before the age of 18—youths with low family bonding at age 15 were three times more likely (9 percent versus 3 percent) to initiate illicit drugs than those with high family bonding. Higher levels of family conflict were associated with a higher risk of initiation. For example, youths with high family conflict at age 18 were over twice as likely (15 percent versus 6 percent) to initiate illicit drugs as those with low family conflict. High levels of peer antisocial activity, especially after age 15, found youths at age 18 nearly four times as likely (19 percent versus 5 percent) to initiate illicit drugs as those with low antisocial peer influence (in the bottom 10 percent).

Family monitoring and rules seemed to reduce the risk of initiation primarily by affecting the child's choice of peer groups. "Some family factors operate through peers and some are independent of peer groups," Dr. Hill explains. "Kids with low bonding to parents are more likely to get involved with narcotics and stimulants, even if they don't hang out with bad peers. So you end up with this set of independent risks with high family conflict, low bonding, and bad peer involvement. All these things stack the deck toward initiation of serious drug use.

"In general, family and peer factors had similar effects on boys and girls," Dr. Hill observes. "Only family monitoring and rules had a stronger protective effect for males than for females." Family monitoring and bonding were more predictive for European Americans than for African Americans. Otherwise, says Dr. Hill, "family and peer factors affecting illicit drug initiation were similar across gender and ethnic groups."

The message is clear: Family factors matter. "The impact of only one factor—family bonding—begins to decline after age 18," Dr. Hill says. Peer factors also matter. Having antisocial peers, especially after age 15, increases the risk of drug initiation. "Both sets of influences contribute," he says, "even after controlling for sociodemographic background and prior alcohol, tobacco, and marijuana initiation."

In terms of intervention, "family and peer factors should be important targets for preventive efforts," Dr. Hill says. The effort should start early and continue into the twenties, emphasizing family bonding early and family monitoring, rules, and reduction of conflict throughout. "Programs that address these family and peer factors should work relatively well across gender and ethnic groups," he concludes.

Influence of Peers on Young Adults' Substance Abuse

Another NIDA-funded study took a slightly different path, looking at peer influence on young adults. As part of a long-range study led by Dr. Hyman Hops of the Oregon Research Institute in Eugene, Oregon, the researchers gathered data from 294 participants ages 19 to 25. Each participant brought one same-sex and one opposite-sex peer into the study; those who were married brought their marital partner as their opposite-sex peer. Data gathered annually for 3 years included the quality of these relationships, the extent of any substance abuse, and the problems associated with drug use.

At the beginning of the study, 30 percent of the 294 participants had smoked cigarettes, 29 percent had smoked marijuana in the previous month, 10 percent had used other illicit drugs, and 41 percent reported problems associated with drug use in the previous 12 months. Thirty-nine percent had not used any drugs in the period specified. Men who smoked marijuana did so, on average, more often than female marijuana smokers did—an average of 5.5 times per month versus women's average of 2.7 times a month. "Other differences between genders were not significant," says Dr. Judy Andrews, lead author of the Oregon team. "Correlations between various substances were moderate."

Use of drugs by male peers positively influenced subsequent use by both men and women. "I expected females, in general, to be more influenced by males than by females," Dr. Andrews says, "and we found that to be true only in cases where the user reported problems associated with drug use. For example, friends of both genders also influenced both males' and females' subsequent cigarette smoking."

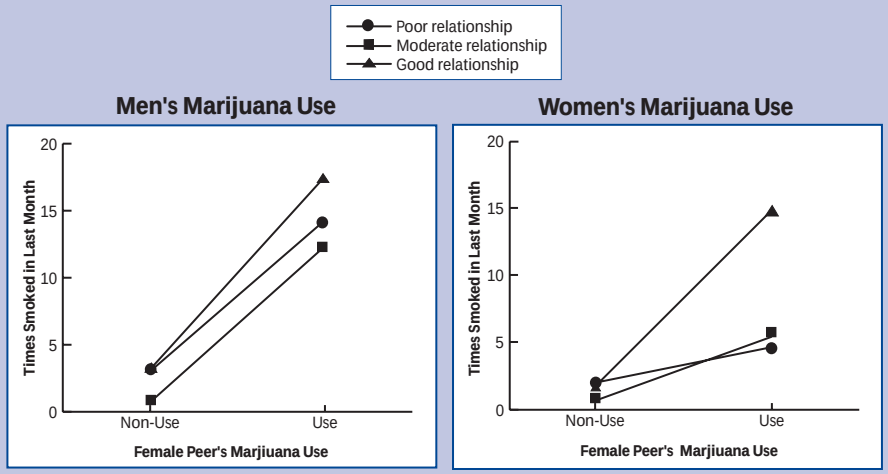
Another surprise emerged in the effect of good versus bad peer relationships. In general, the quality of the relationship with the friend did not matter when it came to substance use. "We expected that peer influence would be mediated by the quality of that relationship," explains Dr. Andrews. "If you don't like somebody, why would you emulate him or her? But we found this effect only with marijuana use when the peer was female. Good female friends influenced the marijuana use of both males and females. But if the good friend was male, he did not influence the marijuana use of either his male or female friend."

Again, the overall message is clear: Young adults are influenced by their friends. "It's an important finding," observes Dr. Andrews. "Interventions with substance-abusing young adults should not only be with individuals, but with their peers as well."

"We are continuing to see family and peer effects into early adulthood," says Dr. Kathleen Etz of NIDA's Division of Epidemiology, Services and Prevention Research. "People assume that families become less important as kids move out of the house, and this does not appear to be the case.

"Many of our interventions target adolescents and very few target young adults. Given that in the Oregon Research Institute study marijuana use was initiated after high school, it's clear that we have to look more carefully at interventions for young adulthood."

Quality of Female Peer Relationship Impacts Young Adult Marijuana Use



Source: *Andrews, J.A., et al.,* Health Psychology, *2002.*

Each participant brought one same-sex and one opposite-sex peer into this study; participants who were married brought their spouse as their opposite-sex peer. The quality of the relationship with a female peer was a factor in young adults' marijuana use; with young adults' use of other substances, however, the quality of the peer relationship was not a factor.

Sources

• Andrews, J.A.; Tildesley, E.; Hops, H.; and Li, F. The influence of peers on young adult substance use. *Health Psychology* 21(4):349-357, 2002.

• Guo, J.; Hill, K.G.; et al. A developmental analysis of sociodemographic, family, and peer effects on adolescent illicit drug initiation. *Journal of the Academy of Child and Adolescent Psychiatry* 41(7):838-845, 2002.

NN

New Technology Expands the Scope of NIDA's Intramural Brain Imaging Program

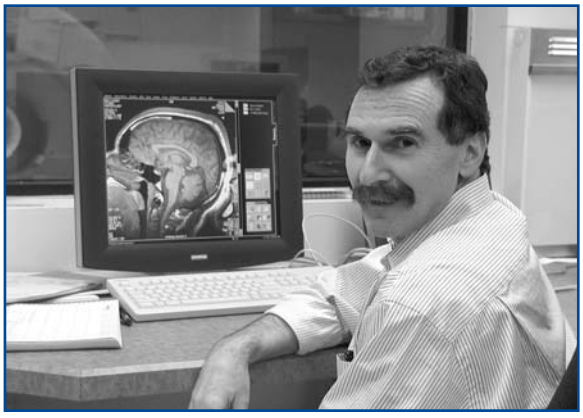
In February, Dr. Elliot Stein, chief of the Neuroimaging Research Branch at NIDA's Intramural Research Program (IRP), and other IRP scientists began using a new magnetic resonance imaging system to evaluate the functional effects of drugs. Dr. Stein explains the unique research opportunities this technology offers IRP.

"Using functional magnetic resonance imaging [fMRI], IRP researchers will be able to make observations that are not possible in any other type of study," he says. "The technique doesn't require use of radioactive compounds as PET imaging does, and it doesn't use radiation to create an image as conventional x-ray or CT does.

"We can use fMRI to actually watch the brain at work and see what regions are active while participants perform cognitive tasks or are presented images or other environmental cues related to drug abuse," continues Dr. Stein. "This provides quantitative measurements of functional activity for different areas of the brain—not just paper-and-pencil scores or ratings on a 1-to-10 scale—to help us understand a drug's effect on reasoning, anticipation, or reward. Does the brain work differently, in some fundamental way, when a person is using drugs? When she or he is abstinent or going through withdrawal?"

Moreover, fMRI studies are not limited to investigating the effects of drugs. They can also be used to evaluate treatment, notes Dr. Stein. "If we understand the effect of a drug on how a patient learns, remembers, or pays attention, we can try to develop behavioral treatments that focus on those functions.

"By watching the brain perform the same tasks before and after treatment, we literally can see if there is a functional effect of the treatment and use that information to determine if it is more likely than other treatments to help the patient. Using fMRI to guide development of treatments and evaluate their impact will make it possible to tailor a behavioral treatment to how a patient's brain actually works." NN



Dr. Elliot Stein, chief of the Neuroimaging Research Branch, within NIDA's Intramural Research Program, says functional magnetic resonance imaging makes it possible to see the impact of drugs on the brain at work.

Heads Up Poster Winner Selected

NIDA and Scholastic Classroom Magazines unveiled the Grand Prize artwork from the national *Heads Up: Real News About Drugs and Your Body* poster contest on May 16 at Scholastic Headquarters in New York City. The contest was part of the ongoing *Heads Up* science-based drug education campaign, for which NIDA and Scholastic partnered.

Eighth-grader Ania Lisa Etienne, from Brooklyn, New York, created the winning poster. Selected from nearly 1,100 entries, Ania's poster features a distressed teenager looking into a shattered mirror, a symbol of the bad luck that results from drug abuse, Ania explains. Her winning artwork and slogan, "You Can't Sniff Away Your Sorrows," will form the basis of a poster to be included in the *Heads Up* program during the 2003-2004 school year.

Gender and Ethnic Patterns in Drug Use Among High School Seniors

Although rates of marijuana, alcohol, and tobacco use by 12th-grade boys and girls declined over the 25-year period ending in 2000, the "gender gap" in use of these drugs remained largely unchanged. According to data compiled by the annual Monitoring the Future (MTF) survey, senior girls were 77 percent as likely as boys (compared with 78 percent in 1976) to have reported using marijuana in the past month. Girls in the 12th-grade class of 2000 were 64 percent as likely (up from 54 percent in 1976) to have had five or more drinks in a row during the past 2 weeks, and girls and boys were equally likely to be daily smokers.

Ethnic differences in drug use—for boys as well as girls—are much wider than are gender differences. A recently published review of MTF data reveals that these ethnic differences are significant and have persisted since MTF began collecting drug use data in 1976. Key substance use patterns among ethnic groups and gender differences within those groups are presented below.

Substance Use Among High School Seniors, 1976-2000*

	12th-Grade Females					12th-Grade Males				
	'76-'80	81-'85	'86-'90	'91-'95	'96-'00	'76-'80	'81-'85	'86-'90	'91-'95	'96-'00
Daily Cigarette Smoking										
White	28.8	23.6	22.6	22.2	27.2	24.4	18.6	19.2	22.3	26.3
Black	20.8	12.2	5.8	3.4	5.1	21.9	10.8	7.7	6.5	10.9
Mexican American	15.6	13.2	8.4	9.3	11.0	19.1	13.2	11.8	12.6	15.1
Puerto Rican/**	18.0	15.0	12.4	15.2	17.9	18.7	13.7	12.4	22.5	23.4
Other Latin American				10.8	9.8				8.9	15.3
Asian American	13.3	10.2	8.0	8.6	10.1	14.5	11.5	10.8	12.9	14.3
Native American	49.8	39.8	30.5	34.2	34.2	38.7	30.8	25.7	32.4	24.7
Heavy Alcohol Use Within Past 2 Weeks										
White	32.1	34.1	30.8	24.6	28.0	53.4	52.9	46.8	39.7	42.4
Black	12.1	11.1	8.6	7.6	8.3	27.5	24.8	22.9	19.9	18.0
Mexican American	25.0	26.8	21.4	19.6	23.4	52.0	48.3	44.1	38.8	40.6
Puerto Rican/**	21.9	18.5	13.0	16.2	18.0	36.6	34.6	30.3	34.2	27.0
Other Latin American				15.5	19.4				26.7	32.6
Asian American	14.7	11.4	9.0	8.2	11.1	28.4	22.4	19.4	15.2	18.9
Native American	40.9	38.3	30.8	26.9	32.5	62.8	57.6	46.8	46.2	41.5
Marijuana Use Within Past 30 Days										
White	30.8	24.6	17.9	15.0	20.8	40.4	31.6	22.5	19.7	26.0
Black	22.1	20.1	7.2	6.8	12.7	36.6	29.2	14.6	15.9	26.6
Mexican American	25.9	21.2	11.7	10.5	18.7	39.8	36.9	19.5	19.9	29.3
Puerto Rican/**	19.5	14.4	8.7	10.8	20.7	34.7	22.7	17.2	26.4	26.7
Other Latin American				11.0	12.9				13.7	19.6
Asian American	18.3	13.8	5.2	5.1	9.1	31.2	13.0	9.8	9.0	16.0
Native American	44.7	30.3	19.7	21.5	32.0	50.9	36.1	26.6	25.5	27.2

*Percentage prevalence shown as the mean for each 5-year span.

**Beginning in 1990, the data distinguish between Puerto Rican and Other Latin American.

Smoking

Daily smoking declined among all ethnic groups between 1976 and 1990, then leveled off before beginning to increase modestly between 1996 and 2000. Among ethnic groups, Native Americans were most likely to smoke and African Americans least likely. Within ethnic groups, African-American girls were less likely than boys to be daily smokers.

Alcohol

Girls were less likely than boys to report heavy alcohol use (five or more drinks in a row within the past 2 weeks), and the prevalence for girls and boys over the 25-year period ending in 2000 generally decreased. Among ethnic groups, Native Americans were most likely to report heavy drinking; Asian-American and African-American 12th-graders reported the lowest prevalence. No significant gender differences in alcohol use emerged within ethnic groups.

Marijuana

Overall, 12th-grade boys in all ethnic groups were somewhat more likely than girls to have used marijuana within the past 30 days. Prevalence rates for girls and boys declined between 1976 and 1990, held steady until 1995, and increased between 1996 and 2000. Among ethnic groups, Native Americans were most likely and Asian Americans least likely to have used marijuana within the past month.

Source

• Wallace, J.M., et al. Gender and ethnic differences in smoking, drinking and illicit drug use among American 8th, 10th and 12th grade students, 1976-2000. *Addiction* 98(2):225-234, 2003. NN

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