

Research News

Psychological Trait Helps Identify Boys at Risk of Substance Use Disorder

A psychological trait called neurobehavioral disinhibition (ND), which consists of a measurable decrease in behavior control, modulation of emotion, and higher-level thought, may help identify boys at risk of habitual drug abuse after experimentation with an addictive substance, according to a study published in the December 2007 issue of *Psychology of Addictive Behaviors*. Investigators funded by NIDA evaluated 278 boys between the ages of 10 and 12 for the ND trait. The boys returned for a follow-up evaluation at age 16, and again at 19, when they were diagnosed with the presence or absence of substance use disorder (SUD) by a clinical committee. The investigators found that the ND trait score measured at ages 10 to 12 could significantly predict SUD at age 19, as well as a history of arrests, violent behavior, and concussive injury. Interestingly, neuroimaging of 21 of the boys showed that activation of the frontal cortex, a region of the brain thought to play a role in regulating higher-level cognitive behavior, correlated more strongly with the ND trait score than did activity in any other region of the brain. Although the study had several limitations—including that the boys were not randomly selected but instead chosen based on the presence or absence of SUD in their fathers, and that no girls were included in the cohort—the ND trait has “potential value as a screening tool...for detection of high-risk youths,” as well as value as a tool for future research, state the authors.

Mezzich AC, Tarter RE, Feske U, Kirisci L, McNamee RL, Day BS. Assessment of risk for substance use disorder consequent to consumption of illegal drugs: psychometric validation of the neurobehavior disinhibition trait. *Psychol Addict Behav*. 2007;21(4):508–515.

Fluoxetine Does Not Add to Benefit of Cognitive Behavior Therapy for Depression in Adolescents with Substance Abuse Disorder

Doctors are often reluctant to prescribe antidepressants for depression in adolescents with substance use disorders (SUD) due to the lack of research in this area. NIDA-funded investigators recently addressed this research gap with a 16-week controlled trial, in which 126 adolescents (ages 13–19) with major depression (MD) and SUD were randomly assigned to receive the antidepressant fluoxetine or placebo daily along with weekly cognitive behavioral therapy (CBT) for drug abuse. Participants were evaluated weekly for adverse side effects (including suicidal thoughts), symptoms of conduct disorder, and drug use (using urine tests); and monthly for changes in depression (on two measures) and self-reported drug use. There was a significant reduction in conduct problems and self-reported drug use in both groups, but investigators found no difference between groups. Adolescents receiving placebo with CBT actually had a greater proportion of weekly drug-free urine tests compared to those receiving fluoxetine with CBT. For treating depression, fluoxetine with CBT was more effective than placebo with CBT on one, but not both, outcome measures, although both groups demonstrated greater treatment response than previous fluoxetine controlled trials. The higher-than-expected improvement in depression in both groups may be an indication that the CBT received by all participants was an active ingredient in the treatment of depression, despite its primary focus on drug abuse. In the context of the individual CBT used in this study, co-occurring depression may improve or remit without antidepressant pharmacotherapy. However, in patients whose depression does not improve, the addition of fluoxetine may be a safe and effective option with careful monitoring of side effects, state the authors.

Riggs PD, Mikulich-Gilbertson SK, Davies RD, Lohman M, Klein C, Stover SK. A randomized controlled trial of fluoxetine and cognitive behavioral therapy in adolescents with major depression, behavior problems, and substance use disorders. *Arch Pediatr Adolesc Med.* 2007;161(11):1026–1034.

“Missing Piece” of Receptor Decreases Effects of Nicotine

Little things can have big effects. In the case of the receptors in the nervous system that bind nicotine and mediate its effects on the body, including heart rate and alertness, that little thing is a subunit—a piece of the receptor. A variety of different subunits can combine and form functional nicotine receptors in the body; however, different combinations of subunits can produce receptors that work quite differently. Studies in mice have shown that animals lacking the ability to produce a particular subunit called $\alpha 5$, due to a genetic mutation, are much less sensitive to the physical effects of nicotine, such as nicotine-induced seizures. In their study published in the October 2007 *Journal of Neurochemistry*, NIDA-funded researchers investigated whether the number of nicotinic receptors or their function changed depending on whether or not mice produced the $\alpha 5$ subunit. They found that mice lacking $\alpha 5$ had the same amount of nicotinic receptors as mice that had $\alpha 5$, but their receptors experienced a loss of function in certain brain regions suggesting that the $\alpha 5$ subunit is responsible for increasing nicotinic receptor function in these brain areas.

Brown RW, Collins AC, Lindstrom JM, Whiteaker P. Nicotinic alpha5 subunit deletion locally reduces high-affinity agonist activation without altering nicotinic receptor numbers. *J Neurochem.* 2007;103(1):204–215.

HCV Infection Associated with Increased Diabetes Risk in Older Persons With or At Risk of HIV Infection, Particularly Obese Individuals

Previous studies have shown a link between chronic hepatitis C (HCV) infection and an increased risk of type 2 diabetes, particularly among older, overweight individuals. However, these studies have not used sensitive screening tests or controlled for classic diabetes risk factors such as family history and sedentary lifestyle. Recently, a NIDA-funded research team conducted a study including these important variables to confirm the relationship between HCV, insulin resistance, and abnormal glucose tolerance, among older individuals with or at risk for HIV. The researchers interviewed a total of 446 individuals to collect sociodemographic characteristics and family and medical history, including the use of antiretroviral drugs. Study participants also underwent tests to determine HCV status, glucose tolerance, and insulin resistance. Participants who tested positive for HCV had higher fasting insulin levels and greater insulin resistance than those who tested negative; this was not affected by HIV status, use of highly active antiretroviral therapy (HAART), use of protease inhibitors, or demographic risk variables. However, despite the association between HCV and insulin resistance, HCV was only linked to abnormal glucose tolerance in individuals with an obese body mass index. Although the mechanisms underlying the association between HCV infection and insulin resistance are not well understood, these study findings highlight the problem of obesity among individuals with HIV and HCV, and the increased potential for type 2 diabetes mellitus in this population.

Howard AA, Lo Y, Floris-Moore M, Klein RS, Fleischer N, Schoenbaum EE. Hepatitis C virus infection is associated with insulin resistance among older adults with or at risk of HIV infection. *AIDS.* 2007;21(5):633–641.

Anxiety Sensitivity Impacts Smoking Cessation

People with anxiety disorders tend to smoke at higher rates than persons without such conditions. Similarly, an anxiety-related vulnerability called anxiety sensitivity (AS)—a sensitivity to and fear of anxiety-related physical sensations and emotions—has been linked to smoking behavior. In particular, smokers with AS have particular difficulty with smoking cessation; however, little is known about the psychological mechanisms underlying this correlation. Recently, NIDA-funded researchers, using a series of interviews and questionnaires, gathered data from 329 smokers to assess their psychiatric history, cigarette and alcohol consumption, and motivations for and barriers to quitting. As expected, AS was found to be related to smoking cessation: it increased both the level of motivation to quit and the perceived barriers to quitting. In general, respondents with AS wanted to quit smoking in order to maintain control over their lives and to respond to social influences on their smoking behavior. Surprisingly, smokers with AS were not as concerned about health reasons for quitting. Although smokers with AS were motivated to quit, they also perceived more barriers to quitting, experiencing

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the process of quitting as stressful and personally threatening. Therefore, further research “should help guide the future development of specialized intervention programs for smokers with anxiety vulnerabilities,” perhaps incorporating cognitive behavioral strategies to better prepare them for success in quitting, conclude the authors.

Zvolensky MJ, Vujanovic AA, Miller MO, Bernstein A, Yartz AR, Gregor KL, McLeish AC, Marshall EC, Gibson LE. Incremental validity of anxiety sensitivity in terms of motivation to quit, reasons for quitting, and barriers to quitting among community-recruited daily smokers. *Nicotine Tob Res.* 2007;9(9):965–975.

Adolescent Male Rats Self-Administer Nicotine More Than Their Adult Counterparts

Research has found that most tobacco use starts during adolescence, and that smokers who start as adolescents are more likely to be life-long smokers. A recent NIDA-supported research project evaluated differential nicotine effects in adolescent and adult male rats, and the persisting effects of early nicotine exposure on brain receptors. Adolescent and adult male rats were allowed to self-administer varying doses of nicotine over the course of four weeks. During the first two weeks, the adolescent rats self-administered at rates more than triple those of the adults. As the adolescent rats aged into adulthood, the rates of self-administration decreased to approach the rates of the adult rats. Nicotinic receptor binding was also compared to assess the relationship of altered nicotinic receptor binding to nicotine self-administration. In the midbrain, the adolescent group showed binding values almost 30 percent higher than those in the adult group, with smaller differences detected in the striatum, and none in the hippocampus.

The findings of this study are consistent with comparable studies that suggest adolescents are particularly vulnerable to nicotine reinforcement. Interestingly, previous work from the same lab showed that while adolescent female rats also showed greater nicotine self-administration compared to adults, that increase persisted into adulthood, in contrast to what was seen for males in the present study. This study and future research investigating the mechanisms underlying this vulnerability will hopefully provide greater insight into adolescent-onset tobacco addiction and its treatment.

Levin ED, Lawrence SS, Petro A, Horton K, Rezvani AH, Seidler FJ, Slotkin TA. Adolescent vs. adult-onset nicotine self-administration in male rats: duration of effect and differential nicotinic receptor correlates. *Neurotoxicol Teratol.* 2007;29(4):458–465.

Meetings of Interest

Blending Science and Treatment: The Impact of Evidence-Based Practices on Individuals, Families, and Communities

June 2–3, 2008, Cincinnati, Ohio

REGISTER EARLY!

Don't miss out on NIDA's state-of-the-art conference highlighting the science of addiction treatment, *Blending Science and Treatment: The Impact of Evidence-Based Practices on Individuals, Families, and Communities*. This conference will be convened on June 2–3, 2008, in Cincinnati, Ohio.

Join your colleagues and engage in stimulating discussions between treatment professionals and researchers covering the most current drug abuse and addiction findings and their application to clinical practice. The NIDA Blending Conference also provides a wonderful opportunity to learn more about the NIDA–SAMHSA Blending Team Products and how they may be utilized to improve addiction treatment so more people recover from addictive disorders.

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Featured speakers include NIDA Director Dr. Nora D. Volkow. A full agenda and speaker list is available at: <http://www.sei2003.com/nida/blendingcinci/topics.htm>

For registration, please visit: <https://www.sei2003.com/nida/blendingcinci/registration.asp>

NIDA To Present Addiction and Drug Abuse Information at the American Psychiatric Association Annual Meeting

NIDA will present special research-based activities at the American Psychiatric Association's 161st Annual Meeting, May 3–8 in Washington, DC.

Issues that will be addressed in NIDA–sponsored workshops include:

- Emerging trends in drug abuse
- Core deficits in substance abuse
- Cognitive dysfunction and
- Criminal justice populations and addiction.

For additional information, please visit:

<http://www.psych.org/MainMenu/EducationCareerDevelopment/Meetings/AnnualMeeting.aspx>

For more information about any item in this *NewsScan*:

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- **Reporters**, call **Dorie Hightower** at 301-443-6245.
- **Congressional staffers**, call **Geoffrey Laredo** at 301-594-6852.

The National Institute on Drug Abuse (NIDA) is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports most of the world's research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to ensure the rapid dissemination of research information and its implementation in policy and practice. Fact sheets on the health effects of drugs of abuse and other topics are available in English and Spanish. These fact sheets and further information on NIDA research and other activities can be found on the NIDA home page at www.drugabuse.gov.

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