

Tobacco and Nicotine Research

An Update from the National Institute on Drug Abuse – August 2008

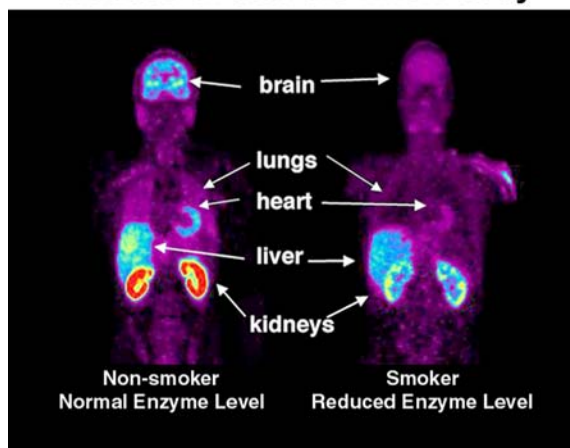
Tobacco use is the leading preventable cause of disease, disability, and death in the United States. Cigarette smoking results in more than 400,000 preventable deaths each year – about one in every five U.S. deaths. Despite the well-documented health costs of smoking, many smokers have great difficulty quitting, and many others are still becoming addicted – about 1200 per day in the U.S. Researchers are striving to understand the numerous effects of nicotine on the brain and body, determine why it is so addictive, and help smokers break its hold for good.

Basic Research on the Biological Effects of Nicotine and Tobacco

Research has shown that nicotine influences the same brain regions as other drugs of abuse, the so-called “reward system.” Like cocaine, heroin, and marijuana, nicotine increases levels of the neurotransmitter dopamine in the reward system, producing lasting changes in the cells of the brain. These changes can eventually lead to addiction. Current priorities at NIDA include:

- Understanding the structure and function of nicotinic receptors - the molecules on cells in the brain and spinal cord that bind and respond to nicotine.
- Exploiting new imaging technologies to visualize regions of the brain affected by nicotine, including those involved in rewarding effects, withdrawal, and craving. Imaging studies have already revealed that smoking alters the chemistry of cells throughout the body in unexpected ways (see figure).
- Understanding nicotine’s role in learning and memory, managing pain and stress, and other cognitive functions.
- Identifying the cellular and molecular mechanisms that underlie the transition from tobacco use to addiction.

Imaging studies show that smoking tobacco affects the whole body



PET scans reveal reduced enzyme activity in smokers' vital organs. Adapted from Fowler et. al., "Low monoamine oxidase B in peripheral organs in smokers." *PNAS*, 2003

Genes, Environment, and Addiction

Why do some smokers become addicted, while others don't? Studies indicate that as much as half of a smoker's risk of becoming addicted depends on his or her genes. Recent technical advances have enabled researchers to conduct large-scale studies of the complex genetic contribution to addiction. For example, a recent NIDA-supported study found that having a certain variant in the gene for a nicotinic receptor subunit more than doubled the risk for addiction among smokers, as well as increasing their vulnerability to lung cancer and peripheral arterial disease.

While genetic studies reveal exciting new directions for research, environmental risk factors are equally important. NIDA supports targeted research on factors correlated with tobacco use and addiction, including prenatal exposure to tobacco smoke; social environments; gender; ethnicity; age; comorbid conditions like depression and schizophrenia; and exposure to other drugs of abuse.

Teens and Smoking

According to NIDA's 2007 Monitoring the Future survey, 21.6 percent of 12th graders reported using cigarettes in the past month. Of those adolescents who try smoking, about one out of three will become regular smokers. Research shows that adolescents are especially vulnerable to nicotine addiction; the prefrontal cortex does not fully mature until the twenties, so the adolescent brain may be less able to override impulsive decisions or cravings for drugs. In addition, acetaldehyde, a compound found in tobacco smoke, may enhance nicotine's addictive effects, especially in adolescents. NIDA directs significant resources toward monitoring teen tobacco use, understanding the biology behind it, and developing prevention programs targeted at teens.

Prenatal Exposure, Persistent Effects

In addition to increasing risk for miscarriage, stillborn or premature infants, and low birth weight, maternal smoking predisposes children to a host of long-term behavioral problems, some of which only become apparent later in life. Children whose mothers smoke during pregnancy are also more likely to become dependent on tobacco if they start smoking. Understanding the persistent, deleterious effects of nicotine on the developing fetal brain is a priority for NIDA.

Treatment and Medication Development

70% of current adult smokers in the US would like to quit, but most have difficulty overcoming their addiction and managing withdrawal symptoms and cravings. NIDA is translating knowledge gained from basic research into more effective treatments and medications to help smokers quit.

- NIDA develops, evaluates, and implements behavioral interventions to help with treatment and relapse, including programs targeted to specific groups such as teens, incarcerated women, and people with PTSD, HIV, or schizophrenia. Researchers also study the best way to offer treatment services, from the impact of smoke-free policies to the implementation of quitlines. NIDA's Clinical Trials Network serves as a conduit to optimize the most promising new treatments and integrate them into practice faster.
- A nicotine vaccine is being tested in humans, with promising results. The vaccine stimulates the body to produce antibodies able to sequester nicotine in the bloodstream, preventing the drug from entering the brain and exerting its rewarding effects. The vaccine could be a powerful tool to prevent relapse in recovering individuals.
- NIDA is working with the pharmaceutical industry to develop and evaluate medications to treat tobacco addiction. For example, NIDA researchers are currently completing a multi-center trial evaluating a transdermal form of selegiline for smoking cessation.

NIDA's 2007 Monitoring the Future survey indicates that teen smoking has reached its lowest level since the survey began in 1975. This bodes well for the future, but too many teens continue to smoke – 22 percent of 8th graders report having tried cigarettes. New prevention strategies are urgently needed, as are treatments to help teens and adults who are already addicted. Through science, NIDA is meeting these challenges, and reducing the national health burden created by tobacco and nicotine addiction.

For further information please visit NIDA on the web at www.drugabuse.gov or contact:

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Boys whose mothers smoked while pregnant have a greater risk of behavioral problems

