

Genetic variations put youth at higher risk for lifetime of tobacco addiction

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Common genetic variations affecting nicotine receptors in the nervous system can significantly increase the chance that European Americans who begin smoking by age 17 will struggle with lifelong nicotine addiction, according to researchers at the University of Utah and their colleagues at University of Wisconsin-Madison. The study, published in the July 11, 2008 issue of *PLoS Genetics*, highlights the importance of public health efforts to reduce the number of youth who begin smoking.

These common gene variations, called single nucleotide polymorphisms (SNPs), are changes in a single unit of DNA. Scientists call SNPs that are linked and inherited together a haplotype. The researchers found that one haplotype for the nicotine receptor put European American smokers at greater risk of heavy nicotine dependence as adults, but only if they began daily smoking before the age of 17. A second haplotype actually reduced the risk of adult heavy nicotine dependence for people who began smoking in their youth.

The researchers studied 2,827 long-term European American smokers, recruited in Utah and Wisconsin, and to the National Heart, Lung, and Blood Institute's Lung Health Study. They assessed the level of nicotine dependence for all smokers, and recorded the age they began daily smoking, the number of years they smoked, and the average number of cigarettes smoked per day. DNA samples were taken from all smokers, and the researchers recorded the occurrence of common SNPs, grouped into four haplotypes, which had been identified earlier in a subset of participants.

They found that people who began smoking before the age of 17 and possessed two copies of the high-risk haplotype had from a 1.6-fold to almost 5-fold increase in risk of heavy smoking as an adult. For people who began smoking at age 17 or older, presence of the high-risk haplotype did not significantly influence their risk of later addiction. The high-risk haplotype is common in the three study populations, and European American populations in general, ranging in frequency from 38 percent to 41 percent.

Although the authors caution that different haplotype frequencies would likely be observed in different ethnic populations, Robert Weiss, Ph.D., professor of human genetics at the University of Utah and lead author of the study explains, "We know that people who begin smoking at a young age are more likely to face severe nicotine dependence later in life. This finding suggests that genetic influences expressed during adolescence contribute to the risk of lifetime addiction severity produced from the early onset of tobacco use."

According to Dr. Nora Volkow, director of the National Institute on Drug Abuse (NIDA), "In recent years we've seen an explosion in the understanding of how small genetic variations can impact all aspects of health, including addiction. As we learn more about how both genes and environment play a role in smoking, we will be able to better tailor both prevention and cessation programs to individuals." The study was funded in part by NIDA and the National Heart, Lung, and Blood Institute (NHLBI), parts of the National Institutes of Health (NIH).

The NIDA-funded 2007 Monitoring the Future Study showed that 7.1% of 8th graders, 14.0% of 10th graders, and 21.6% of 12th graders had used cigarettes at least once in the month prior to being surveyed. Although cigarette use has declined slightly in youth in recent years, just over 3 million young people between the ages of 12 and 17, or 13 percent of those in the United States, still smoke cigarettes.

Source: University of Utah

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