Topics in Brief
National Institute on Drug Abuse

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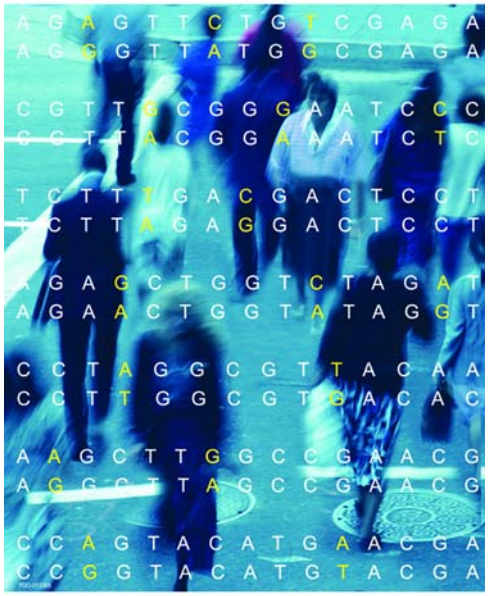
Genetics of Addiction
A Research Update from the National Institute on Drug Abuse — April 2008

Genetics: the blueprint of health and disease

Why do some people become addicted, while others do not? Studies of identical twins indicate that as much as half of an individual's risk of becoming addicted to nicotine, alcohol, or other drugs depends on his or her genes. Pinning down the biological basis for this risk is an important avenue of research for scientists trying to solve the problem of drug abuse.

Genes – functional units that make up our DNA – provide the information that directs our bodies' basic cellular activities. Research on the human genome has shown that the DNA sequences of any two individuals are 99.9% identical. However, that 0.1% variation is profoundly important, contributing to visible differences, like height and hair color, and to invisible differences, such as increased risks for, or protection from, heart attack, stroke, diabetes, and addiction.

Some diseases, like sickle cell anemia or cystic fibrosis, are caused by an error in a single gene. Medical research has been strikingly successful at unraveling the mechanisms of these single-gene disorders. However, most diseases, including addiction, are more complicated: variations in many different genes contribute to an individual's overall level of risk or resistance.



The International HapMap Project has identified 3.1 million single nucleotide polymorphisms (SNPs). In some cases, these tiny differences in DNA sequence may increase susceptibility to, or confer resistance against, disease. (US Department of Energy Genome Programs, http://genomics.energy.gov)

Linking genes to health: genome-wide association studies

Recent advances in DNA analysis are enabling researchers to untangle complex genetic interactions by examining a person's entire genome at once. These genome-wide association studies (GWAS) identify subtle variations in DNA sequence called single-nucleotide polymorphisms (SNPs) – places where individuals differ in just a single letter of the genetic code. If a SNP appears more often in individuals with a disease than those without, it is presumed to be located in or near a gene that influences susceptibility to that disease.

GWAS are extremely powerful because they are unbiased and comprehensive: they can implicate a known gene in a disorder, and they can identify genes which may have been overlooked or previously unknown. Building on GWAS results, scientists gather additional evidence from affected families, animal models, and biochemical experiments to verify and understand the link between a gene and risk for a disease.

Research Advance:
Genetic variation may increase risk of nicotine addiction and lung cancer

A NIDA-supported genome-wide association study recently found that a variant in the gene for a nicotinic receptor subunit doubled the risk for nicotine addiction among smokers (Saccone et al., 2007). A study in Iceland verified this association, finding that this region is also linked to vulnerability to lung cancer and peripheral arterial disease (Thorgeirsson et al., 2008). This is the first evidence of a genetic variation influencing both the likelihood of nicotine addiction and an individual's risk for the severe health consequences of tobacco use.

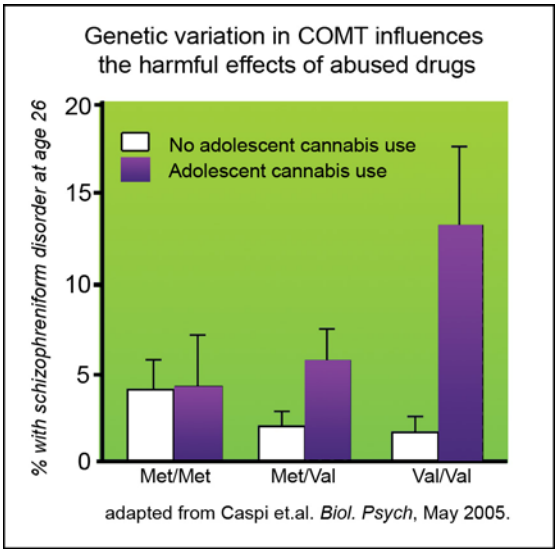
What role does the environment play in a disease like addiction?

That old saying “nature or nurture” might be better phrased “nature *and* nurture,” because research shows that individual health is the result of dynamic interactions between genes and environmental conditions. For example, susceptibility to high blood pressure is influenced by both genetics and lifestyle, including diet, stress, and exercise. Environmental influences, such as exposure to drugs or stress, can alter both gene expression and gene function. In some cases, these effects may persist throughout a person’s life. Research suggests that genes can also influence how a person responds to his or her environment, placing some individuals at higher risk than others.

Research Advance

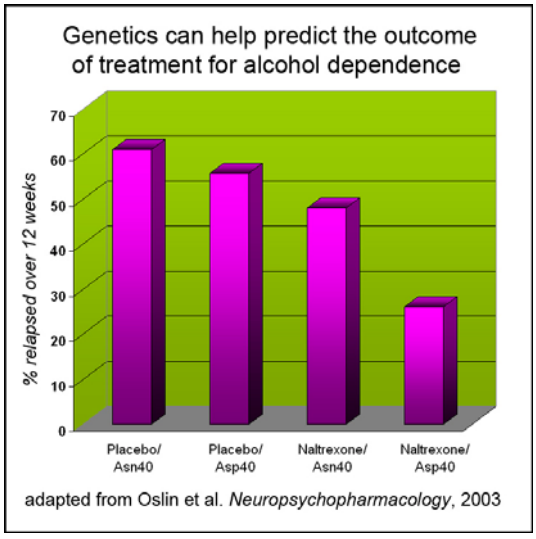
A recent study highlights the complex interactions between genetics, drug exposure, and age of use in the risk of developing a mental disorder.

The COMT gene produces an enzyme that regulates dopamine, a brain chemical involved in schizophrenia. COMT comes in two forms: “Met” and “Val.” Individuals with one or two copies of the “Val” variant have a higher risk of developing symptoms of psychosis and schizophrenic-type disorders if they used cannabis during adolescence.



The promise of personalized medicine

The emerging science of pharmacogenomics promises to harness the power of genomic information to improve treatments for addiction. Clinicians often find substantial variability in how individual patients respond to treatment. Part of that variability is due to genetics. Genes influence the numbers and types of receptors in our brains, how quickly our bodies metabolize drugs, and how well we respond to different medications.



Armed with an understanding of genetics, health providers will be better equipped to match patients with the most suitable treatments, adjust medication dosages, and avoid or minimize adverse reactions.

Research Advance

A NIDA-sponsored study of alcohol dependent patients treated with naltrexone found that patients with a specific variant in an opioid receptor gene, Asp40, had a **significantly lower rate of relapse** (26.1%) than patients with the Asn40 variant (47.9%).

In the future, identifying which mu-opioid receptor gene variant a patient possesses may help predict the most effective choice of medication for alcohol addiction.

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

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