How much can we blame our genes for addictive behavior?



he Oscar-nominated actor Robert Downey Jr., star of countless films including *Chaplin*, the *Iron Man* series, *Tropic Thunder* and *Zodiac*, started making movies when he was just five years old. He's also famous for his descent into drug addiction, which he says started even earlier than age five.

Downey has told a number of interviewers that he believes he has an addictive personality, and that he may have passed that personality on to his son, Indio, who recently <u>pled guilty</u> to felony cocaine possession and entered a rehabilitation program. Meanwhile, Downey (the elder) has talked about how his own father introduced him to drugs.

Downey's stories beg critical questions about how humans handle drugs and addiction:

- Is addiction inherited, and genetic?
- Is addiction more a cultural and environmental phenomenon?
- Is there such a thing as an addictive personality?

Drug rehabilitation, medical and psychological treatments and even the criminal justice system depend heavily on the right answers to those questions.

According to the National Institute on Drug Abuse (one of the National Institutes of Health), illegal drug abuse costs the United States more than \$181 billion each year "in health care, productivity loss, crime, incarceration and drug enforcement." And these costs are based on an assumption that drug addiction, as NIDA puts it, "is a chronic, relapsing brain disease."

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But that doesn't

necessarily make it genetic. Nor does a pattern of heritability for, say, alcoholism, make that disorder entirely genetic. Researchers are looking at addiction as a complex interaction of genes, metabolism, environment and behavior. This has come a long way from the early 20^{th} century, when addiction was seen more as a morality problem, or even since the 1980s, when we witnessed the primitive eggs-on-a-frying pan "this is your brain on drugs" advertisements. Researchers have largely abandoned the search for an overarching "addictive personality," in which a person shows an archetypal vulnerability for any addiction, be it cigarettes, alcohol, heroin, or gambling.

Case for genes

Of all the people who try alcohol or illegal drugs, only 10 to 20 percent get addicted. No single gene has ever been isolated for people who get hooked on alcohol, drugs or other substances. But a number of studies show that genetics does play some significant role:

 Identical twin studies <u>have shown</u> a fairly strong concordance (sharing a behavior and genetic trait), but even these <u>show some variability</u>. For example, a Medical College of Virginia twin study on cocaine use showed a 54 concordance rate for identical twins versus 42 percent for fraternal twins, but for cocaine abuse showed a 47 percent concordance for identical twins and only eight percent for fraternal twins.

- Other studies showed some differences depending on type of substance. A Washington University, St. Louis, <u>review showed</u> that 33 to 71 percent of the variation in nicotine addiction was inherited, while 48 to 66 percent of variation in alcohol addiction was inherited, and 49 percent of variation in gambling addiction was inherited.
- A search for genes has uncovered a number of genetic clusters that affect behavior and mood, and could be connected with addiction. Genes on no fewer than eight chromosomes have been tagged for some role in chemical dependence.

Case for the environment

Also taking a step away from the early focus on moral fiber, behavioral scientists have been examining external factors that could lead to addiction:

- Twin studies, this time looking at identical twins who did not have the exact same upbringing, showed that the twin who had experienced childhood sexual abuse did show a strong tendency toward substance abuse, while the twin who did not have these experiences did not share this addiction.
- Some researchers have pointed to social structures as a key factor in addiction. <u>Monkey studies</u>
 have shown that those who were dominated by other monkeys are more likely to take cocaine than
 more socially powerful monkeys. Others have looked at poverty, and living on the fringes of society
 as something that prods addiction.
- Certain behavioral disorders, like anxiety or impulsive behavior, have been suspected of driving addiction. Feeling anxious can fuel the need to consume drugs that alleviate these feelings and other social fears, while teenagers may become addicted because they can't yet control their emotions effectively.

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Case for nature and nurture

- Many <u>alcohol abuse studies</u> have focused on the gene ALDH2, which controls the conversion of acetaldehyde, a rather toxic metabolite of alcohol. Some variants of ALDH2 don't convert acetaldehyde into acetate very well, particularly in Asian populations. While some studies show that people with this version of ALDH2 were far less likely to get addicted to alcohol, the heavy-drinking business culture that developed in Japan and other Asian nations in the 1980s and 1990s forced businessmen (mostly men) to drink anyway.
- While addicts may behave as if they have a disease state (compulsive drug seeking and use, despite harmful consequences), and addiction does change how certain neurotransmitters like dopamine are metabolized, they also can completely recover on their own, at rates up to 80 percent.

• Epigenetic changes, as we've written about in the <u>Genetic Literacy Project</u>, have been shown to also affect who becomes an addict and why. Excessive cocaine and alcohol use can determine how genes that protect against addiction are regulated, while increases in dopamine receptor numbers (and activity) can help prevent addiction.

Was Robert Downey Jr. right?

Recently, a NIDA director estimated that the genetic risk of addiction averages about 50 percent. So, Downey may have passed on a tendency for substance abuse to his son, but it may have just as much been the same way he was influenced by his father as it was through his own DNA.

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