

# Addiction: From genes to drugs

November 6 2013, by Sathya Achia Abraham

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She is a daughter, sister, wife and friend. She had a relatively normal childhood. Her teenage years yielded experimentation – alcohol with her pals, marijuana once or twice.

There were several defining and stressful episodes during those teenage years that cut her deep. Those events stayed with her, buried beneath the surface, never quite in the past.

Then, as she moved through her 30s, life began to spiral in directions she could not control. There was chronic residual pain following a surgery, family stress and job demands. She soon was drinking alcohol at the high end of normal.

She kept a bottle nearby – at home, even at work. She took a swig wherever and whenever she could. She started to neglect professional obligations.

She thought she was hiding it, but people started to talk – her family, her friends, her coworkers. Relationships with loved ones began to unravel fast.

The problems at work went from bad to worse. She was about to lose her job and life as she knew it.

However, unlike many others, she recognized how far she had fallen, and she sought help. She got better.

Not everyone does.

Addiction is a painful reality that affects 23.6 million Americans every day. It's a disease not only of individuals, but of families and communities.

"Addiction medicine is a very broad area," said Joel Silverman, M.D., chair of the Department of Psychiatry in the Virginia Commonwealth University School of Medicine. "The costs are huge."

These costs are not just to the addicts, but to their families and communities. Fifty percent of motor vehicle deaths involve substance use, Silverman said. Family violence usually has alcohol or drugs at its root. Not to mention the effect on the economy of an addict's days lost

from work – alcoholism alone costs the United States approximately 500 million lost workdays per year, according to the National Institutes of Health (NIH).

"Think about all the health care implications," Silverman said. "Alcohol affects the brain, heart, liver, kills countless people every year. And alcohol is just one of the substances people get addicted to."

Cocaine, heroin and crack may be the first drugs that come to mind when you think of [addiction](#)—images of addicts from shows such as "Breaking Bad" and movies such as "Requiem for a Dream" or "Trainspotting" —but less narcotic substances also cause social problems.

Tobacco, food, sex, pathological gambling and pornography all can be addictive. When people get into pathologic gambling, Silverman said, they tend to lose yearly about as much money as they earn. Obesity is clearly a major public health problem in the United States too, he added, much of it caused by [food addiction](#). Nicotine addiction can cause bronchitis in children whose parents smoke and put them at higher risk of asthma, cancer and heart disease.

There are scientists around the world working to find the root of all this suffering in order to heal it – several of those leading experts are right here at VCU – seeking answers. What are the roots of addiction – biological, psychological and social – and how might doctors recognize these risk factors to prevent addiction and treat people after they are hooked?

Researchers at VCU are exploring the origins of addiction, from genes to brains to behaviors. The goal: to develop new drugs and therapies, to move the science from lab to clinic.

In 2010, VCU received a \$20 million NIH grant – at the time, the largest federal award in its history – to become part of a nationwide consortium of research institutions working to turn laboratory discoveries into treatments for patients. VCU was the only academic health center in Virginia to receive one, and one of only 55 such centers around the country. A portion of that grant will be used to expand research in the field of addiction medicine at VCU.

## **The scope of the problem**

Alcoholism causes about 80,000 deaths per year in the U.S., the Center for Disease Control reported in 2012. Tobacco use is responsible for five million deaths worldwide each year, according to the National Institute on Drug Abuse (NIDA). Secondhand smoke – inhaled regularly by children whose parents' smoke, for example – increases a person's risk of lung cancer and heart disease by 25 to 30 percent and 20 to 30 percent respectively, the Surgeon General reported in 2006. Injected drugs such as heroin, cocaine and methamphetamine are involved in four out of 10 AIDS deaths in the U.S., according to the NIDA website. And the United Nations reported this year that drug abuse kills 200,000 people worldwide per year – roughly the population of Richmond.

Imagine drugs wiping out an entire city, every year.

Addiction is broader than illegal drugs. But the root of all these compulsions, from food-binging to porn-watching to smoking, drinking or shooting up heroin—may be the same.

"The biological mechanisms of addiction to different substances probably have loads of similarities," Silverman said.

When we become hooked on something, anything, our brains seem to be tricked in the same way: Addiction is one brain disease with many

flavors.

Similarly, addiction "vulnerability" genes may overlap with those predisposing a person to other mental illnesses, such as depression, attention-deficit disorder or anxiety. The underlying biology and genetics behind disorders that psychiatrists now call by separate names may actually be the same.

There may be some differences, too—genes that make a person particularly vulnerable to depressants, such as alcohol, or to stimulants, such as cocaine, for example. These biological signatures of addiction risk—genes and brain differences—are what scientists at VCU are searching for in their research today.

## **Addicts: Victims of disease**

Addiction is a medical illness. Like cancer, diabetes or schizophrenia, it is caused by genes exposed to experience.

There is no one gene for "alcoholism" or "[cocaine addiction](#)," but certain sequences of DNA make a brain more vulnerable to a drug's effects. Just as a particular sequence of nucleic acids codes for proteins producing "altered" lungs that are more prone to cancer when exposed to smoke, DNA may produce an "altered" brain more affected by nicotine, which predisposes a smoker to get hooked. But if you don't come in contact with cigarettes—if your family or community has religious or legal prohibitions on them, for example—then you won't become addicted: Genetic risks are curbed by experience.

Genes also can influence mental illness in multiple ways. As Kenneth S. Kendler, M.D., professor of psychiatry, and human and molecular genetics in the VCU School of Medicine, explained in a 2010 lecture, genes may impact the brain directly —programming proteins that cause

the brain to be abnormally shaped, to have unusual neurochemistry or a deviant number of neurons. This is what we usually mean by a "genetic" trait – innate biology.

But genes also may affect behavior, producing a personality that would be more likely to put itself at risk.

"Humans shape their own environments," as Kendler put it. If a person is introverted, he may be more likely to isolate himself, and to become depressed, or if he is risk-taking, he may put himself in a stressful life situation that could trigger a bipolar or schizophrenic breakdown. If a person is rebellious, thrill seeking or extroverted, he may be more likely to bring himself in contact with addictive drugs and to become an addict.

So the question of nature versus nurture in addiction and other mental illnesses is complex: Biology drives experience, and experience in turn shapes the brain.

Addictions are brain illnesses. Like other mental illnesses—schizophrenia, depression, anxiety and bipolar disorder, for example—addiction is a biopsychosocial disorder. But since addicts' antisocial behavior often alienates others, they are more stigmatized than victims of other illnesses.

Fighting this social stigma is another goal of VCU's addiction psychiatry research. As we understand the biologic roots of addiction, addicts may be treated more as medical patients, like diabetics or schizophrenics, and [new drugs](#) or talk-therapies may be found to correct the biologic imbalances that put them at risk.

## **VCU's range: Genes to brains to behavior**

Addiction psychiatry research at VCU covers the whole story, from

genes to brains to behavior.

Geneticists at the Virginia Institute for Psychiatric and Behavioral Genetics (VIPBG) at VCU, search for the genes that make people vulnerable to alcohol and addictive drugs—and what stages in life these genes are most influential.

Twin studies help scientists at the VIPBG find which aspects of addiction are innate, and which arise from experience.

Psychologists at VCU are finding out more about the environments that trigger addiction: How much does divorce, friends or neglectful parenting put a child at risk for addiction?

And brain-imaging research is giving a view into the brains of addicts: How is an addict's brain different, in terms of anatomy and function, from that of a person who avoids addiction? And how do different drugs damage the brain? Seeing this, scientists may design new therapies to prevent or counteract brain damage caused by addiction.

Finally, at the molecular level, gene sequencing of animals from flies to mice and even worms, allows scientists to confirm "susceptibility genes" identified in human addicts.

All this work is going on now at VCU—and the program is about to expand even more.

Provided by Virginia Commonwealth University

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