



A General in the Drug War

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Nora Volkow:

An interview with the neuroscientist in charge of the National Institute on Drug Abuse, who also happens to be the great-granddaughter of Leon Trotsky.

From heroin and cocaine to sex and lies, Tetris and the ponies, the spectrum of human addictions is vast. But for Dr. Nora D. Volkow, the neuroscientist in charge of the National Institute on Drug Abuse, they all boil down to pretty much the same thing.

She must say it a dozen times a day: Addiction is all about the dopamine. The pleasure, pain and devilish problem of control are simply the detritus left by waves of this little molecule surging and retreating deep in the brain.

A driven worker with a colorful family history and a bad chocolate problem of her own, Dr. Volkow (pronounced VOHL-kuv), 55, has devoted her career to studying this chemical tide. And now, eight years into her tenure at the institute, the pace of addiction research is accelerating, propelled by a nationwide emergency that has sent her agency, with a \$1.09 billion budget, into crisis mode.

The toll from soaring [rates of prescription drug abuse](#), including both psychiatric medications and drugs for pain, has begun to dwarf that of the usual illegal culprits. Hospitalizations related to prescription drugs are up fivefold in the last decade, and overdose deaths up fourfold. More high school seniors report recreational use of tranquilizers or prescription narcotics, like [OxyContin](#) and Vicodin, than heroin and cocaine combined.

The numbers have alarmed drug policy experts, their foreboding heightened by the realization that the usual regulatory tools may be relatively unhelpful in this new crisis.

As Dr. Volkow said to a group of drug experts convened by the surgeon general last month to discuss the problem, “In the past, when we have addressed the issue of controlled substances, illicit or licit, we have been addressing drugs that we could remove from the earth and no one would suffer.”

But prescription drugs, she continued, have a double life: They are lifesaving yet every bit as dangerous as banned substances. “The challenges we face are much more complex,” Dr. Volkow said, “because we need to address the needs of patients in pain, while protecting those at risk for substance use disorders.”

In other words, these drugs must be somehow legal and illegal, encouraged yet discouraged, tightly regulated yet easily available.

The experts are looking to the institute for scientific tools that might help by loosening the tight bonds between pain relief and addiction in the brain.

And that, Dr. Volkow told her audience with a small smile, is all about the [dopamine](#).

She knows a little about dopamine firsthand: She is a dedicated runner and a helpless pawn in face of dark chocolate. Her most significant long-term addiction, though, has been to the science of scanning the brain with techniques that expose its workings like a map, a passion she has pursued like a guided missile since medical school.

That was in Mexico, where Europe’s 20th-century upheavals had tossed both her parents: Her mother fled Franco’s Spain, while her father, the son of [Leon Trotsky](#)’s elder daughter, joined his grandfather in exile as an orphaned teenager. Dr. Volkow and her three sisters grew up in the house in Mexico City where Trotsky was murdered in 1940, giving tours of the premises on weekends.

In medical school she read an article in Scientific American about one of the first American [positron emission tomography scanners](#), able to photograph not only the brain’s structures but also its invisible processes. She never looked back.

“It blew my mind,” she said. After a residency in psychiatry at New York University, chosen because it owned that PET scanner, she took a job in Houston, then transplanted her research to [Brookhaven National Labs](#) on Long Island, home of groundbreaking research into dopamine and PET scanning. She and her husband, Stephen Adler, a physicist with the National Cancer Institute, now live in Bethesda, Md.

Dr. Volkow’s research career, still based at Brookhaven, has been notable for its “brilliant science,” said Don C. Des Jarlais, an expert in drug addiction who directs the Baron Edmond de Rothschild Chemical Dependency Institute at Beth Israel Medical Center in New York. Dr. Des Jarlais cited her recent [widely reported study showing that cellphones alter brain metabolism](#) as a typical example of her unusually creative scientific thinking.

A Merging of Missions

Her days now veer from reviewing raw laboratory data with her research colleagues to leading the back-to-back meetings of a government functionary, but the two roles are joined by the mantra of her time at

the institute: Policy should be grounded in valid science. One recent decision in the upper echelons of the National Institutes of Health reflects a similar conclusion: The drug abuse institute and the National Institute on Alcohol Abuse and Alcoholism are on track to be merged into a joint institute on addiction still in the planning stages.

National Institutes of Health [watchers have already started a body count](#). “It will be a big loss that Nora Volkow, current N.I.D.A. director, cannot possibly be selected to head a new institute,” wrote one anonymous blogger on the Scientopia Web site. “This would be too much like N.I.D.A. ‘winning.’”

But Dr. Volkow says she is all for the merger, calling the current structure “an artificial division with many missed opportunities,” like having an institute for every particular variety of cancer. Addictions tend to move together, she said, sharing many triggers and a great deal of biology.

Again, it is all about the dopamine.

All addictive substances send dopamine levels surging in the small central zone of the brain called the nucleus accumbens, which is thought to be the main reward center. Amphetamines induce cells to release it directly; cocaine blocks its reuptake; alcohol and narcotics like morphine, heroin and many prescription pain relievers suppress nerve cells that inhibit its release.

Addicts and first-time users alike get the high that correlates with the dopamine wave. Only a minority of novices, however, will develop the compulsion to keep taking the drug at great personal cost, a behavior that defines addiction.

Researchers now postulate that [addiction requires two things](#). First is a genetic vulnerability, whose variables may include the quantity of dopamine receptors in the brain: Too few receptors and taking the drug is not particularly memorable, too many and it is actually unpleasant. Second, repeated assaults to the spectrum of circuits regulated by dopamine, involving motivation, expectation, memory and learning, among many others, appear to fundamentally alter the brain’s workings.

For instance, Dr. Volkow’s group showed several years ago that when cocaine addicts watched videos of people taking drugs, dopamine levels surged in the part of their brains associated with habit and learning, correlating with the intense drug cravings the subjects began to experience.

Her research and that of others has also shown that even after addicts are successfully detoxed and long clean, their dopamine circuits remain abnormally blunted. Substances that elevate dopamine levels in normal subjects had notably muted responses in ex-addicts.

This observation, experts say, may explain the intense difficulty addicts have staying clean, as the ordinary rewards of daily life may have little effect on the recovering brain. Only the drug of choice will send dopamine levels high enough for any kind of pleasure.

“Nora is as responsible as anyone,” Dr. Des Jarlais said, “for showing that addiction really does cause changes in brain function. Her work is a primary basis for considering it a disease, rather than poor choices or immoral behavior.”

Arming Doctors With Tools

Dr. Volkow has watched the microscopic events of addiction play out in fluorescent rainbow colors on brain scans for decades now. But those scans are used entirely for research, not for patient care. To the average doctor, she knows, the addict’s brain is impenetrable. All that is visible is irrational, illegal and sometimes threatening behavior. Surveys show most doctors prefer to keep their distance from addiction and addicted patients.

“My obsession is to engage the health care system in addiction,” Dr. Volkow said, to medicalize what is often considered mainly a criminal problem by arming doctors with their accustomed tools: effective treatments, even a vaccine.

“She’s been a champion of bringing addiction science into mainstream medicine,” said A. Thomas McLellan, director of the Penn Center for Substance Abuse Solutions at the University of Pennsylvania. Medicine is finally beginning to understand, Dr. McLellan said, that if you pay no attention to the behavioral factors leading to a chronic illness, be it diabetes or substance addiction, you can never catch up. “That’s been one of Nora’s big contributions.”

In a study published in 2000, Dr. McLellan pointed out that while the overall success rate for curing drug addiction with medications, therapy or both is not high (about half of treated individuals return to active substance use within a year), it is quite similar to overall successful treatment rates for other chronic medical conditions like asthma, diabetes and high blood pressure. Failure to take prescribed medications and backsliding to old bad habits is endemic, no matter what the condition.

The success of [treatment for addiction](#) is particularly dependent on the social milieu of the addicted individual, Dr. Volkow said. “So, for example, the best successes in treatment generally are physicians, for they are also the ones with the strongest support.”

But treating people with the prescription drug problems is particularly challenging, because, of course, for these particular drugs, physicians are the nation’s pushers.

The number of prescriptions written for potentially addictive pain medications has soared in the last decade, reaching more than 200 million in 2010, Dr. Volkow said. Surveys asking teenagers where they get pills find that relatively few buy from strangers. Many have their own prescriptions, often from dental work. Even more are given pills by friends and relatives, presumably out of other legitimate prescriptions.

Doctors may be flooding the country with narcotics, but most have never learned much about pain control. Dr. Volkow said that some data suggests that medical schools devote considerably less time to the subject than veterinary schools do. [The Obama administration addressed exactly this deficiency in April with a call for doctors to undergo special training before being allowed to prescribe some of the most addictive painkillers.](#)

“Students and residents have gotten the message that pain is undertreated,” said Dr. Mitchell H. Katz, an internist who directs the Los Angeles County Department of Health Services. “So they just prescribe higher and higher doses.” Meanwhile, he said, there is no evidence that treatment with opioids for more than four months actually helps chronic pain, or that higher doses work where lower ones fail. There is good evidence, however, that higher doses raise the risk of overdose and death.

“The dichotomy between good drugs prescribed by doctors and bad drugs sold on the street is just bad science,” Dr. Des Jarlais said. “N.I.D.A. is now having to address the fact that there are real problems with prescription drugs.”

The institute is starting a multipronged effort to teach and to learn more about pain control as it relates to addiction. The teaching part includes sponsoring performances of excerpts from Eugene O’Neill’s “Long Day’s Journey into Night” at medical conferences, in order to humanize for doctors the problem of addiction.

The learning part is continuing: New science for pain control may take some time to devise, Dr. Volkow said.

New Approaches

One promising way to lessen the addictive properties of pain relievers, she said, is to slow the speed with which they reach the brain: A dribble of dopamine is far less addictive than a surge. New formulations to deliver pain relief slowly should minimize older drugs’ addictive potential. Skin patches are one example of this effort (although they can still cause fatal overdoses) and research is under way into others.

Another technique is combining drugs to deter abuse. The drug suboxone, an alternative to methadone, is constructed with this intent. It combines a methadonelike drug for maintaining addicts on an even keel with another drug that counteracts overdoses and opiate-associated highs. If the suboxone is taken orally, as intended, the methadone effect predominates.

But all hard-core addicts know that if an oral drug is injected into the bloodstream, it will rush into the brain and create a far more dramatic high. If suboxone is injected, the second substance kicks in immediately and prevents the high.

Dr. Volkow's confidence in the eventual success of these measures is unshakable. Her headful of corkscrew blond curls and her lush Mexican accent may contradict the stereotype of subdued government scientist, but she remains firmly on message, like a seasoned bureaucrat.

Every once in a while, though, a deeper, slightly darker perspective on her unstinting efforts to save people from themselves peeks through. It was her great-grandfather, after all, who tacked a small caveat onto 20th-century history: "The end may justify the means, but the end in its turn needs to be justified."

Dr. Volkow generally forswears any interest in politics per se, but midway through a long day of meetings last month she sighed and acknowledged, "science and politics are intertwined." We think we have free will, she continued, but we are foiled at every turn. First our biology conspires against us with brains that are hard-wired to increase pleasure and decrease pain. Meanwhile, we are so gregarious that social systems — whether you call them peer pressure or politics — reliably dwarf us as individuals. "There is no way you can escape."

She said she was in the midst of reading "The Man who Loved Dogs," by the Cuban novelist Leonardo Padura. The book is a novelized treatment of Trotsky's assassination, not yet translated into English. Her father had validated its accuracy. Someday, she said, she wouldn't mind writing a novel herself, "a biological novel."

Just as historical fiction can illuminate a era, she said — its heroism and its bloody lunacy alike — so her book would use its characters to clarify exactly the same remarkable contradictions in the brain and its tangled circuits.

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