

If you're using drugs, scientists want to help you avoid addiction

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Abstinence is the best way to avoid drug addiction. But in many societies, drug use is the norm, not the exception, especially by youth. What keeps the majority of users from becoming addicted? How drugs are taken has something to do with it, according to pharmacology researchers at the University of Montreal. "Why do some drug users become addicts? The amount of drugs they take over time is one factor, but the speed with which the substance enters and exits the brain can be just as important," explained Professor Anne-Noël Samaha, who supervised the study into how pharmacokinetic factors govern addiction.

"Pharmacokinetics is about what happens to a <u>drug</u> once it is inside the body and <u>brain</u>," she said. "For example, when you smoke a joint, the level of cannabis in the brain increases and decreases much more quickly than when you eat a magic brownie. And this variation depends on how you are taking the drug". What emerges from this research is that in addition to the social context and the predispositions of the individual, the risk of becoming addicted is influenced both by how fast a drug gets to the brain and by whether the amount of drug in the brain fluctuates or remains constant during intoxication. In other words, people using drugs must be aware that specific ways of using and routes of administration influence their risk of addiction.

Samaha and study co-authors Florence Allain, Ellie-Anna Minogianis and David C. Roberts came to their conclusions by undertaking an analysis of the available literature on the subject. This included findings from Dr. Samaha and Dr. Roberts' laboratories. Firstly, they dissected



the results of clinical studies demonstrating that how a drug is taken can predict the risk of addiction. For example, a drug that can be addictive when smoked can in fact be therapeutic when it is swallowed (e.g. methadone) or administered by a skin patch (nicotine). They then looked at the findings of preclinical rodent trials measuring the effects of pharmacokinetic variables on the development of behaviours and changes in the brain linked to addiction. The studies show that how fast a drug reaches the brain and how often brain levels rise and fall are critical to the development of <u>drug addiction</u>.

When a person smokes or injects a drug intravenously, the amount of drug in the brain increases and decreases very quickly in comparison to when the drug is snorted or swallowed. Injection and smoking are the two means of administration most likely to lead to addiction. "Intravenous and smoked doses provoke a high and rapid peak of the concentration of the drug in the brain, followed by a rapid decline," Samaha explained. "We don't yet know how, but such spikes in brain levels of drug increase the desire to take more drug and to consume compulsively."

Various studies show that the maximum intoxication felt by intravenous cocaine users occurs within one to five minutes, compared to 15 to 20 minutes for those who snort it. This is because when a drug is snorted or even swallowed, this leads to a slower and smaller peak, which then declines progressively. "The brain is a sensing organ that responds to changes," Samaha said. "The faster the change, the stronger the brain responds, meaning that the more the levels of drugs in the brain increase and decrease abruptly, the more the brain modifies itself to adapt."

Some of these modifications make drugs more and more irresistible, leading to addiction. A great example is nicotine. "When you smoke a cigarette, the levels of nicotine increase and decrease very quickly in your brain. But when you use nicotine patches, the levels increase slowly



and remain stable. Smoking cigarettes can be addictive, using patches is not," Samaha explained.

Pharmacokinetic principles are already used to control certain addictions - continuous nicotine patches that help smokers quit are a case in point. Likewise, orally-taken methadone acts slower and can help a heroin addict get off the drug. These principles could one day guide the development of new treatments to reduce cocaine addiction, for which there is currently no approved medication.

In the meantime, Samaha and her colleagues believe that efforts must be invested to better prevent the development of addiction amongst users of both legal and illicit drugs. "In our society, drug use is the norm, not the exception," Samaha said. "Amongst recreational users, 15 to 30% will become addicted, depending on the type of drug they use. Drug pharmacokinetics contribute to this distinction. We are obviously not suggesting that people start using drugs, as virtually all forms of drug use can lead to addiction, but it is important to be aware that if you smoke or inject drugs you are exponentially increasing this risk."

More information: Allain, F., Minogianis, E.-A., Roberts, D. C. S., & Samaha, A.-N. (2015). How fast and how often: The pharmacokinetics of drug use are decisive in addiction. *Neuroscience & Biobehavioral Reviews*, 56, 166–179. DOI: 10.1016/j.neubiorev.2015.06.012

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