

underpinnings of addiction will be modified, and a reduction in the prevalence of addiction may occur. One issue with this suggestion is the time frame over which this might happen. Although operations on both the genetic expression and the cultural environment itself may massively speed up the change in phenotype – that is, addictive behaviour – it may still be a very slow process. Mathematical modelling may help in verifying the validity of this hypothesis.

Why do we take drugs? From the drug-reinforcement theory to a novel concept of drug instrumentalization

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Abstract: The drug-reinforcement theory explains why humans get engaged in drug taking behavior. This theory posits that drugs of abuse serve as biological rewards by activating the reinforcement system. Although from a psychological and neurobiological perspective this theory is extremely helpful, it does not tell us about the drug-taking motives and motivation of an individual. The definition of drug instrumentalization goals will improve our understanding of individual drug-taking profiles.

Can one imagine how Yemenis would feel without having a daily khat chewing (80% of Yemenis chew khat containing the alkaloid called cathinone, an amphetamine-like stimulant)? Can one imagine how a Dutch person would feel without having her caffeine in the morning (90% of the Dutch drink coffee)? Can one imagine how a French person would feel without having a glass of wine along with his meal? I could go on with numerous examples of accepted drug-taking behaviors, most of them deeply, culturally embedded into our societies. Pondering these examples, one might easily realize the more philosophical question: Why do we take drugs? Roy Wise and other neuroscientists have formulated the drug reinforcement theory (Wise & Rompre 1989). This theory posits that all drugs of abuse activate the brain reinforcement system and thereby act as biological rewards. This drug-induced reinforcement process increases the rate or probability of further drug-taking behavior. The drug-reinforcement theory is extremely helpful for understanding the biological substrates of a drug-taking behavior in general (Sanchis-Segura & Spanagel 2006), but does not explain why person A likes to drink coffee in the morning and several glasses of beer when coming home from work, whereas person B might smoke a cigarette after each meal but not consume any other drug.

Müller & Schumann (M&S) have attempted to construct a new psychological/neurobiological framework – namely, drug instrumentalization – to provide an answer for individual non-addictive psychoactive drug use. Drug instrumentalization is a learned behavior designed to change the mental state and thereby improve the current quality of life by taking a psychoactive drug. M&S define an extensive list of drug instrumentalization goals, such as improved social interaction, the feeling of well-being, and many others. The definition and validation of drug instrumentalization goals will help to understand individual drug-taking profiles, which may change over the life course of an individual. However, at least three important drug instrumentalization goals are missing in M&S's target article:

1. **Positive taste perception:** Sometimes a self-reflection is very helpful. For example, without disclosing my lifetime drug-taking profile in full detail, at present I have a big cup of tea in the morning, drink different alcoholic beverages regularly in the evenings, and smoke a cigarette from time to time. Why do I consume these three different drugs on a regular basis? The

first reason that comes to my mind is that I enjoy the taste. Although there are no systematic population-based studies on whether positive taste perception can be considered as a drug instrumentalization goal, there are millions of coffee/tea shops around the world, millions of wine-tasting sessions, and cigarette advertisements have historically focused on the pleasing taste of tobacco. Positive taste perception as an instrumentalization goal may be limited to alcoholic beverages, coffee/tea, and tobacco, but these are the primary semi-luxury consumables on which money is spent. Positive taste perception may also play a role in betel nut and Khat drug chewing and to a certain extent even cannabis smoking.

2. **Adaptation to peer pressure:** Very commonly, we consume drugs as a result of peer pressure. Especially during adolescence, peer pressure is an intense motivator and might even be the most important driving force behind taking drugs at a younger age (Borsari & Carey 2001; Faggiano et al. 2008). Only by taking the drug does one adapt to this peer pressure and become rewarded as being a member of a particular group.

3. **Cultural and religious rituals:** Cultural and religious traditions can be considered drug instrumentalization goals. Many indigenous populations still consume drugs only in ritual settings; for example, Voodoo is a religion that originates in Haiti and involves a zombie creation ritual where a number of psychoactive compounds, such as tetrodotoxin, are ingested and lead to the mental and physical experience of a death-like state (Davis et al. 1983). However, Western societies also have several cultural rituals, such as champagne drinking on New Year's Eve. The purposes of these cultural and religious rituals can be diverse, but most of them are used to intensify spiritual beliefs or group affiliations.

It will be critical for the drug instrumentalization theory to provide a full list of goals that have to be integrated into a questionnaire for future validation in different ethnicities. I am really looking forward to a well-developed and validated questionnaire that will allow M&S to rigorously test their fascinating new theory!

Despite my great enthusiasm for this well-conceived novel theory that, in fact, does provide a new framework on non-addictive psychoactive drug use, I have to note one important point of criticism. M&S mention the use of methamphetamine to enhance daily performance as a drug instrumentalization goal (Lende et al. 2007). From my perspective, this is not a true instrumentalization goal as acute methamphetamine use carries immediate drawbacks and causes harm to the individual and its environment. In this context, it is important to recall a recent case of Tik (methamphetamine) use in Cape Town, South Africa, where a mother killed her own son because she could not endure his methamphetamine-induced personality changes (Maroldt 2011). By no means is there a beneficial effect of methamphetamine on overall functioning, as stated in the paper by Lende et al. (2007), to which M&S refer. Methamphetamine or crack smoking is too dangerous and too addictive, and the boundaries between a controlled drug-taking behavior and a highly compulsive one can vanish within hours.

But is it evolution. . . ?

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Abstract: We applaud Müller & Schumann (M&S) for bringing needed attention to the problem of motivation for common non-addictive drug

use, as opposed to the usual focus on exotic drugs and addiction. Unfortunately, their target article has many underdeveloped and sometimes contradictory ideas. Here, we will focus on three key issues.

First, it is unclear that Müller & Schumann's (M&S's) model of drug instrumentalization is necessarily an evolutionary argument. In their rationale for drug use as an adaptation, M&S state that "non-addictive psychoactive drug instrumentalization helps to solve an adaptational problem, employing species-general learning mechanisms that dynamically adapt the search for and consumption of plants and plant compounds" (sect. 4.1, para. 4). However, a domain-general cognitive model, which is what M&S are invoking here, does not require an evolutionary argument for a specific suite of behaviors like drug use – such a mechanism can putatively "solve" contextual problems based on trial-and-error learning. Note that similar arguments supported by empirical data have been made for functional situational exploitation of psychoactive drugs, without invoking adaptationist theory (e.g., Sahakian & Morein-Zamir 2007).

Other aspects of M&S's adaptationist hypothesis strike us as implausible. Psychoactive drugs have their effects because they alter neural signaling, often by mimicking neurotransmitters such as acetylcholine or dopamine, or by interfering with their metabolism or reuptake. Consider two evolutionary scenarios: (1) the evolution of a complex neurobiological mechanism to manipulate the central nervous system via untargeted systemic administration of environmental neurotoxins, which then accurately evaluates the social consequences of the resulting behavioral consequences, as M&S propose; or (2) the evolution of pathways to directly modulate endogenous neurotransmitter signaling systems in the CNS in response to social cues in the environment. We find (2) more plausible because it provides the same benefits as (1) but avoids its manifold costs.

To be clear, we believe that there might be adaptations to manipulate one's own CNS with plant neurotoxins, but only in circumstances, such as mental illness or nutritional deficiency, in which the brain would be unable to adequately modulate endogenous neurotransmitter signaling (Sullivan & Hagen 2002). We and others have also argued that plant neurotoxins could provide non-cognitive benefits, such as combating rapidly co-evolving pathogens (Hagen et al. 2009; Sorensen-Forbey et al. 2009; Sullivan et al. 2008).

Second, M&S have proposed a range of *new* or novel adaptive behaviors associated with drug use without considering how they might negatively affect *existing* cognitive mechanisms. For example, M&S propose that people may use drugs for "improved social interaction" (sect. 4.2.1). Primates are characteristically "social" and can be assumed to have cognitive adaptations to facilitate sociality and attention. One must assume that natural selection has "shaped" those adaptations to perform well on average. Any drug that affects the nervous system is also going to interfere with the existing primate mechanisms for sociality. How do we, or M&S, know that this interfering with the primate nervous system is going to improve or impair the existing mechanisms for sociality? M&S seem to have given this little thought, and their account is somewhat naïve in that no reference is made to the possibility of drugs causing impairment in social cognition. After all, there is overwhelming evidence that drugs such as alcohol interfere with other cognitive mechanisms, such as those involved with motor control.

M&S reiterate this theme in their proposal that drug use increases sensory curiosity and expands perceptual horizon. Given that all mammals have evolved senses, perception, and attention to survive and reproduce in their various environments, how is interfering with these existing mechanisms an adaptation? M&S do not address the possibility of impairing existing sensory adaptations. Again, their accounts seem somewhat hopeful at best.

Third, we disagree with M&S's characterization of our notion of "the paradox of drug reward." Our idea is that there is a conflict between the evolutionary biological view that plant toxins evolved to *deter* animal herbivores, and current proximate

neurobiological models that argue that commonly used drugs (which are also plant toxins or their close chemical analogs) are *rewarding* in animal nervous systems. M&S propose that the "paradox of drug reward" may be resolved at the dose-response level: In a low- to medium-dose range, the drug effect is not toxic in the sense of being an immediate threat to life. In the range of medium to low doses, therefore, a role for drugs in functional adaptation can reasonably be considered" (sect. 2, para. 2). We do not disagree with the latter part of M&S's statement, at least, but we are unclear what it has to do with the paradox. M&S seem to be saying that the "goal" of the toxin-bearing plant is to kill the herbivore, whereas functional benefits may occur at the sub-lethal dosage. Here M&S appear to have made the Spencerian "survival of the fittest" error with the presumption that evolution requires lethal selection. In reality, chemical defenses in plants are more likely to interfere with herbivore feeding and reproduction, not to kill them, and the dosage that will achieve this is different for insects and mammal herbivores in their respective ecological niches. The possible range of chemical defense dosages from wild plants indeed allows the possibility of functional benefits for invertebrates and vertebrates, as we have previously argued and outlined in great detail in the papers that M&S cite.

Finally, M&S include a section on the implications of their model for drug policy (sect. 7). In our view, M&S's ideas need development, and it is premature to make policy recommendations.

Flaws of drug instrumentalization

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Abstract: The adaptive use of drugs, or "drug instrumentalization," is presented as a reality that the scientific literature has largely ignored. In this commentary, we demonstrate why this concept has limited value from the standpoint of nosology, why it should not be viewed as "adaptive," and why it has dangerous implications for policy and public health efforts.

In their target article, Müller and Schumann (M&S) propose a "new neurobiological framework" for non-addictive drug use whereby people use psychoactive drugs to better perform specific behaviors that are relevant for their own "fitness." This concept, referred to as *drug instrumentalization*, is viewed as adaptive; and M&S present it as a reality that the scientific literature and policy makers have largely ignored because of their fears of promoting addiction. The vast majority of M&S's article is composed of a review of the literature of already well-documented facts. Unfortunately, M&S accord very little effort in: (1) defending the validity of this concept as a stable difference between "adaptive" drug users and those who develop addiction; and (2) demonstrating the benefits of promoting "successful" drug instrumentalization among potential or actual drug users. It is these two points alone that constitute the novel contributions of this target article. We contest both points based on the arguments presented below.

Drug instrumentalization: An unrecognized and "adaptive" class of drug users? Drug instrumentalization is a state phenomenon that refers to *momentary reasons* for using a drug. It is not indicative of the problems that the individual may or may not have relative to drug use and therefore cannot be used to separate "adaptive" from "non-adaptive" substance users. For example, even an individual with severe alcohol dependence may have a