

## Addictive Properties of Cocaine: Mode of Action

Although not fully understood as yet, a great deal of evidence suggests that the action of cocaine at central dopaminergic (and other adrenergic) neurons may provide the underlying cause of the craving for cocaine. The blocking of the re-uptake of dopamine and subsequent enhanced activity of this neurotransmitter at dopaminergic receptor sites located in the limbic system of the brain, may account for the euphoria associated with cocaine use. The repeated blocking of dopamine in chronic users may lead to a state of functional deficiency of dopamine in these individuals. By blocking re-uptake of the neurotransmitter, less is available in the presynaptic vesicles for use in normal neuronal regulation. In the case of dopamine, that may lead to depression in the user. What is especially insidious is that this depression might last for days or weeks after the last use of cocaine, forming the basis for craving (i.e. drug hunger), which ultimately will end up in bodily harm (Fig. 40).

It is this craving that is thought to be the cause of psychological dependence seen with cocaine use. Taking this one step further, the behavioral pattern known as *addiction* may be fostered by such craving. Thus, the biochemical (physical) cause can manifest itself in a psychological symptom (craving), and ultimately form the basis for a behavioral pattern known as *addiction*.

According to Jerome Jaffe in Goodman & Gilman's [15] the definition of "*addiction*" consists of various elements. Each element describes a behavioral pattern, devoid of any mention, of physical effects, tolerance, or underlying psychological etiology. It matters not why the individual has the condition and engages in this pattern of behavior, but what the essential elements of that behavior are.

- (a) One notices first: Compulsive use of a substance, possibly related to physical and/or psychological effects as noted above.
- (b) Second: Securing a supply of the substance (i.e. the hunt) the preoccupation with getting it at any cost, disregarding physical, financial, legal margins.
- (c) And finally: A high tendency to relapse after withdrawal of the substance.

It is believed that repetitive overactivation of the dopaminergic reward system within the deep brain structures (Fig. 41) is the cause for an addictive behavior pattern. If physical dependence was all there was to "addiction", withdrawal could cure the problem. Once there is no more drug in the system, no more "addiction" would result.

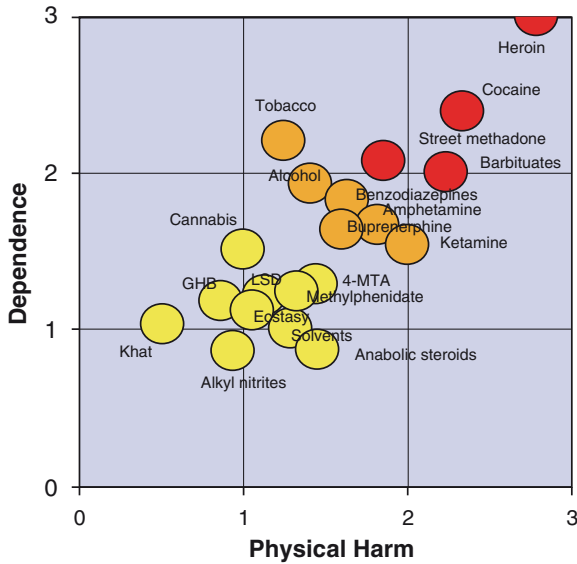


Fig. 40 A rational scale to assess the harm of drugs (Adapted from [14])

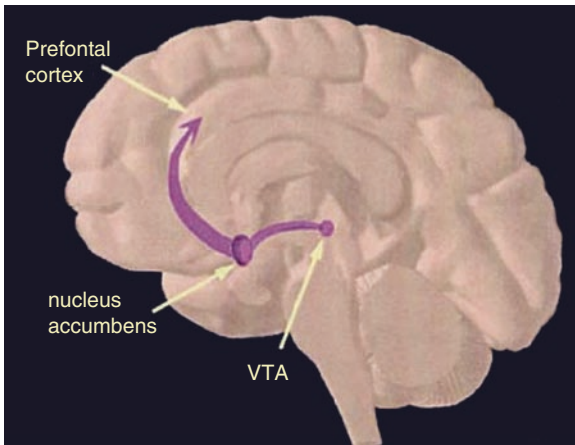


Fig. 41 The dopaminergic reward system in the deep brain structures (mesolimbic system) with the VTA (= ventral tegmental area), where mostly all addictive agents exert their action. It is here where cocaine directly activates the nucl. accumbens resulting in an increased release of dopamine with ensuing euphoria (Modified from [16, 17])

However, there is more to “addiction” than the mere presence of the drug itself. It is this fact more than any other that is persuasive for labelling cocaine as addictive. Presence of the drug on a chronic basis is not necessary. Therefore users who use only once a week, for example, may indeed fit the description of “**addiction**” if

they feel compelled to use, they are driven by craving the “drug hunger”, they are preoccupied with the “hunt” for the drug, taking economic, social and legal risks in the process, and continue to use it even after expressing a desire to stop resulting in a relapse. It is said that “addiction” occurs when the user doesn’t feel “normal” without.

**Addiction** “A behavioral pattern of drug use, characterized by compulsive use, the securing of its supply, and a high” tendency to relapse after “withdrawal”. Adapted from [18]

Contrary to addiction, the label *drug abuse* alone is insufficient to describe every use of illegal drugs, even cocaine. In order to get a perspective on what constitutes abuse one needs a clearer picture of what psychoactive substances can do to mankind. Although *physical dependence* to some is the same as “addiction” there are subtle differences. Being exposed to the concept of physical dependence through movies and television, where addicts go into withdrawal if they can’t get a “fix” (opioid users), the concept of physical dependence became synonymous with “addiction”. It is this simple mistake that has led many to dismiss cocaine as *non-addictive* or *non-dependence producing* substance. A quick review of many medical textbooks will confirm that there is a long-held belief that cocaine does not produce **physical dependence** because there isn’t a definitive withdrawal syndrome associated with it, nor is there tolerance to its effects. This erroneous belief was based on trying to compare the effects of cocaine to those of narcotics (i.e. opioids). As will be seen, when cocaine is looked at alone, it indeed has a unique withdrawal syndrome, and fits the definition of physical dependence set forth here. But physical dependence alone is not *addiction*.

**Physical Dependence** It is an altered physiological state produced by repeated administration of a drug, necessitating its continued administration to prevent the appearance of a withdrawal or abstinence syndrome.

## Psychological Dependence

It is here that things really get complex, as we are now dealing with concepts that are not as verifiable with objective tests such as blood tests, or X-rays. This is not to suggest that there isn’t a biochemical basis for the effects described here but that these symptoms are usually manifested in psychological or behavioral abnormalities that are a product of several forces, environmental, biological and social. The feelings

range in intensity, and can be mild or overwhelming in nature. It is essential to understand that the craving (“drug hunger”) is not necessarily related to any physical need. That is, the user does not have to be physically dependent in order to crave the substance. Acceptance of this fact will help in divorcing “addiction” from simplistic explanations such as mere physical need. When **physical dependence** is also a factor however, it can become a powerful secondary reinforcer of craving, so that now the user not only has hunger for the substance, but is also pushed into further use by the prospect of unpleasant side effects. A more complicated explanation is related to the positive vs. negative reinforcing effects. To summarize, it is necessary to separate the various forces that act upon a user and lead to the behavioral condition defined as psychological dependence.

**Psychological Dependence** Intensity may range from mild desire to strong compulsion.

Craving is not necessarily related to any physical need. However, when physical dependence becomes established after chronic use, it becomes a powerful secondary reinforcer of psychological dependence.

Cocaine is highly addictive – once a person has used cocaine the urge to use it again is almost irresistible, and in this respect it is one of the most insidious “recreational” drugs around. However, despite the feelings of overpowering a drug like ecstasy brings, cocaine never produces satisfaction. The user is left with an irresistible craving to experience the joy of cocaine over and over again, which leads to tolerance and an ever-increasing dose. Laboratory research has shown that given an option, animals prefer cocaine to food, water and even sex. If given free access to it, they continue to take the drug until they overdose and die. The same, unfortunately, is true for humans as well. For this reason cocaine is classified as an illegal substance in most countries of the world.