

Drug addiction as drive satisfaction ("antidrive") dysfunction

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Abstract. Drug addiction is a complex brain disorder, characterized by the loss of control over drug seeking and drug taking behavior, and by the risk of relapse, even after a prolonged period of abstinence. This disorder may have its source in a disturbed balance of drive-related behaviors, which control appetitive reactions aimed at seeking contact with an addictive substance. The act of consumption becomes more and more attractive, and the behavior takes on compulsive character. We suppose that drug addiction may involve a change in the mechanism of satisfaction of drives and states of satiation as well. To understand how the motivational processes are changed with the development of dependence, one must consider the mechanism of drive satisfaction and satiation states that occur in relation to the consumatory reflex. When a given drive is satisfied a state of fulfilment occurs. This state may be a result of a so-called "antidrive" mechanism (Konorski 1967). While a drive activity is characterized by general activation and tension, the drive satisfaction state ("antidrive") is characterized by relaxation and relief. When a particular drive is satisfied, the operation of other drives become possible. Therefore, we postulate that dysfunction of drive satisfaction leads to the sustained activation related to the current drug-related drive, which blocks the operation of other drives. In effect, uncontrolled compulsive appetitive behavior is released, and the operation of other drives is restrained, thus forcing the organism to focus on drug-related drive. The reason for an "antidrive" dysfunction may be related to adaptive changes which develop during a contact with an addictive substance.

Key words: dependence, addiction, drives, drive satisfaction, "antidrives", hypothesis

BRIEF DESCRIPTION OF ADDICTION

Drug dependence (addiction) is a poorly understood chronic brain disorder characterized by the loss of behavioural control and relapses of drug-seeking and drug-taking behavior, even after very long periods of abstinence. The essential features of addiction are compulsive behaviors focused on drug-seeking and drug-intake. Drug craving is related to excessive incentive salience of the drug. This process results in a subjective experience of "wanting" which leads to compulsive drug seeking (Holden 2001, Robinson and Berridge 2000, 2001, Koob and LeMoal 2001).

It remains unknown why drug abuse is voluntary at first and subsequently becomes involuntary. The rewarding action of drugs can explain why a given substance is used, but not why the substance is abused, and why addiction develops. Thus, a major goal of drug abuse research is to answer the question: what mechanisms are responsible for conversion from drug use to drug dependence? If rewarding properties of drugs *per se* are not sufficient for their addictive liability other mechanisms including disorders of motivation, emotion and learning could be involved. We suppose that among a variety of factors that contribute to drug addiction, mechanisms of drive satisfaction and satiation play an important role. According to our concept, drug dependence is linked to a dysfunction of the state of drive fulfilment and satisfaction, i.e., malfunction of a hypothetical "antidrive".

DRIVES AND "ANTIDRIVES"

Preparatory activities of the organism occur when the stimulus producing the consumatory unconditioned reflex (e.g., food reflex, copulatory reflex) is not present and must be provided. Most of these activities are more or less innate and rigid patterns of behavior called instincts, which are then modelled according to the individual organism's experience (Tinbergen 1955).

Drives are complex nervous processes controlling the basic preparatory activities (both conditioned and unconditioned) in order to allow the organism to accomplish the consumatory reflexes or guard it from the influence of harmful stimuli. The subjective experiences corresponding to drives are called emotions (Konorski 1967).

According to present concepts, addiction is characterized by an intensive appetite to take the drug to the

exclusion of many natural sources of reinforcement (American Psychiatric Association 1994). To understand how the motivational processes are changed with the development of addiction, one must consider the state of drive satisfaction and satiation that occurs in relation to the appetitive behavior and consumatory reflex. While the drive activity is characterized by general activation, arousal, and tension, the counterpart of drive, the state of drive satisfaction (called also "antidrive" by J. Konorski) is characterized by demobilization, relaxation and relief (Konorski 1967). This state corresponds to Thorndike's "satisfying state of affairs" (Konorski 1967). Therefore, the drives and "antidrives" represent two sides of the motivational mechanism of animal behavior. Notably, when a particular drive is not satisfied, it tends to suppress other drives and activities. On the other hand, if the given drive is fulfilled, and the "antidrive" comes into operation, it may facilitate the function of other drives, if the appropriate stimuli eliciting them are present (Konorski 1967) (Fig. 1).

It is commonly believed that drives are controlled mostly (but probably not exclusively) by the "emotive system", situated in brain areas such as the limbic system and hypothalamus (Konorski 1967).

Thus, the motivational and affective aspects of an organism's activity involves two opposite states: drives and "antidrives". It is possible, that although the general pattern of all drives is similar, they are quantitatively different. It is uncertain whether particular "antidrives" (e.g. sexual satiation, hunger satiation, sleep satiation etc.) are represented by one common "antidrive" pool or whether they are separate (Konorski 1967). Some arguments favour the concept of separate "antidrives", each attached to the corresponding drive. For example, Olds (1958) has shown that the satisfaction produced by stimulation of particular brain areas was not anonymous, but rather connected with particular drives. The question also arises whether a given drive system has only one "antidrive" counterpart (Konorski 1967).

Summing up, the motivational and affective aspects of an organism's activity involve two states: drives and "antidrives" which represent two sides of the organism's behavior. The former compels the organism to act for the sake of its preservation, whereas the latter allows the organism to become calm or to be concerned with consumatory activity. Thus it is possible that these states play the critical role in regulating and modelling an organism's adaptive behavior.

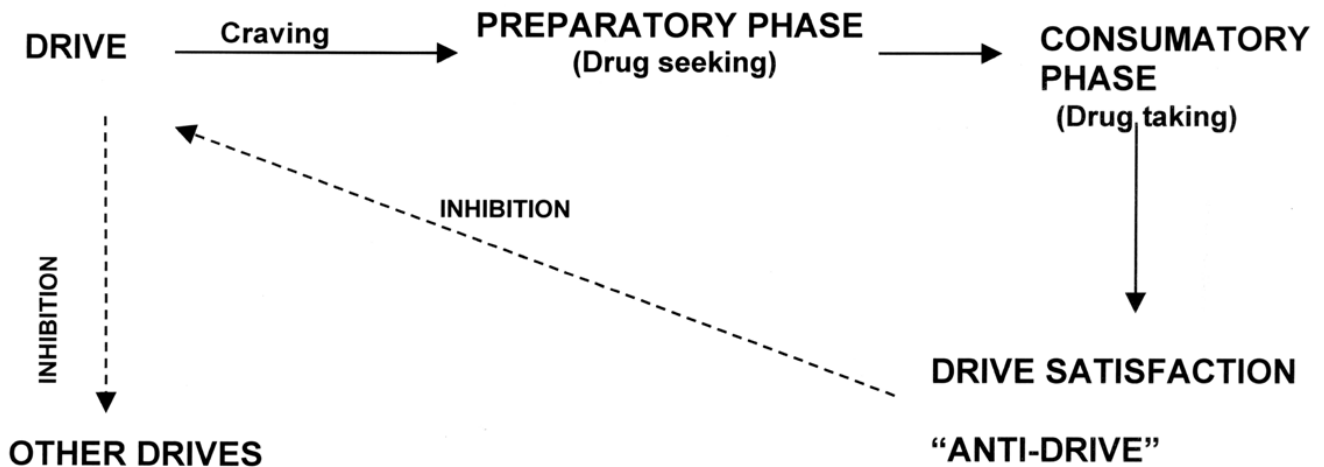


Fig.1. Diagram depicting relations between drive and drive satisfaction ("antidrive")

DOES DISRUPTION OF DRIVE SATISFACTION ("ANTIDRIVE") RESULT IN THE LOSS OF CONTROL OVER DRUG TAKING, AND DEVELOPMENT OF ADDICTION?

We propose a model of motivational changes that occur during the development of dependence. This concept referred to by us as the "antidrive deficiency model of addiction" points to a malfunction of the mechanism of drive satiation i.e., the "antidrive". The deficiency of the "antidrive" leads to at least two pathological states. First, the appetitive activity (drug seeking and taking) persists and is continued. Second, the operation of other drives is restrained, thus forcing the addict to concen-

trate on a drug-related drive. This results in compulsive drug-seeking and drug-taking activities i.e., the state of loss of control over behavior (Fig. 2).

Of particular interest to the present notion is a study conducted many years ago by Spragg (1940). In that study chimpanzees received daily injections of morphine. After becoming morphine-dependent, the animals were then trained to choose between a white box that hid a syringe filled with their daily dose of opiate and a black box that hid a banana. When deprived of morphine, the chimpanzees chose the white "morphine" box, but when pre-treated with their daily opiate dose the animals chose to open the black "banana" box. This result is open to several possible explanations. One hypothetical one in our opinion, is that satiation of the

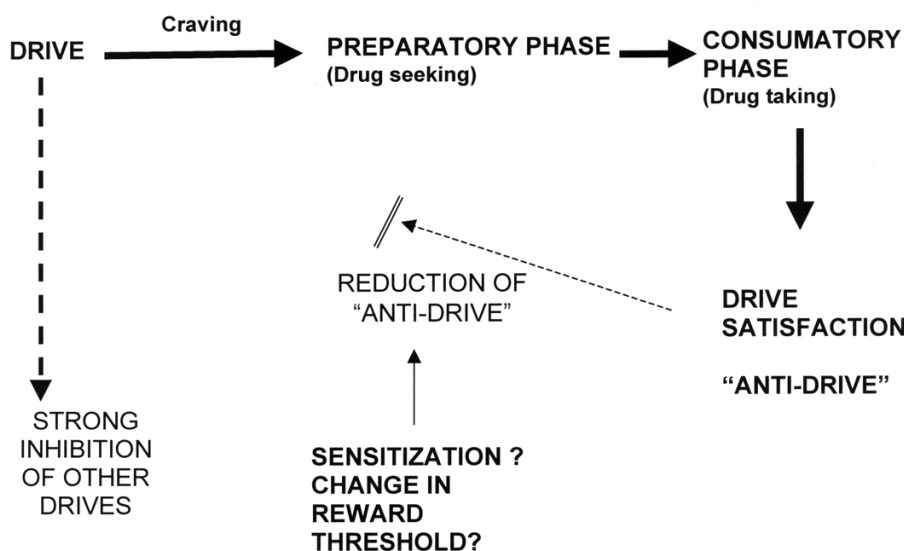


Fig. 2. Diagram illustrating the hypothetical mechanism of "antidrive" deficiency as a focal point for loss of control over appetitive (drug-seeking) behavior. Malfunction of "antidrive" and a breakdown of mechanism that suppresses the drug-related drive leads to compulsive drug seeking and use.

drive associated with morphine permitted the operation of the food- associated drive.

We also have another example showing the interactions between different drives, and the presumed role of drive satisfaction in animal's behavior. This example comes from a study on male rats' sexual behavior using an apparatus in which the goal compartment containing the receptive estrous female is connected with a runway by an one-way door (Beck 1997). In this apparatus, the males spontaneously opened the one-way door after the end of a mount bout, and passed to the start compartment of the runway, and a new run started. Our recent study (Beck et al. 2001) has shown that the dopamine D-1 receptor agonist SKF 38393 significantly prolonged the time spent by the male in the goal compartment. Assuming that postcopulatory departure reflects reduction of sexual drive after the act of copulation, the delayed departure might indicate that animals treated with the D-1 agonist were not fully satisfied. Theoretically, one may suppose that the rewarding properties of the D-1 agonist (Ranaldi and Beninger 1994, Beninger and Rolfe 1995) influences the rewarding value of sexual reward (elevates the reward threshold), thus affecting the mechanism of drive satisfaction.

MECHANISMS ASSUMED RESPONSIBLE FOR THE "ANTIDRIVE" DYSFUNCTION

The question arise: what mechanisms are responsible for the "antidrive" malfunction? As drive satisfaction represents processes associated with demobilization, relaxation and tranquillity, all the adaptive processes that provoke activation and mobilization would weaken "antidrive" mechanisms. In this respect psychomotor sensitisation and sensitization of "incentive salience", according to the incentive sensitization model of addiction, (Robinson and Berridge 1993, 2000, 2001) is worthy of particular notice. Numerous studies show that addictive drugs induce neural sensitization not only to the psychomotor stimulant effects, but also for the incentive motivational effects of drugs (Schenck and Partridge 1997, Robinson and Berridge 2001). There is evidence that behavioural sensitization is associated with neuroadaptations in groups of neurons belonging to the dopaminergic mesolimbic system (Robinson and Becker 1986, Kalivas et al. 1993, Robinson and Berridge 2001, White and Kalivas 1998, Wolf 1998). The major feature of the incentive sensitization theory is that with repeated

drug use drugs acquire greater and greater incentive value (i.e., drugs become compulsively "wanted") even if these drugs are "liked" less and less. In other words, addiction is characterized by increasing dissociation between the incentive value of drugs and their pleasurable effects. Considering this process from another perspective, we hypothesise, that sensitization of incentives weakens the mechanism of drive satisfaction and therefore, disturbs the normal functioning of drive-drive satisfaction ("antidrive") balance. It is also possible that a primarily deficient "antidrive" mechanism is unable to oppose excessive appetitive behavior (Fig. 3).

Another postulated mechanism that results in excessive control over behavior by addictive substances is abnormal dopamine-dependent associative learning (Di Chiara 1999). Furthermore, the negative affective states, according to opponent process theory (Solomon and Corbit 1974), also become "sensitized" and increase with chronic drug intake (Koob et al. 1997). These states may contribute to altered reward thresholds and drive satiety mechanisms. Thus, one may suppose that both counteradaptive processes and drug-induced sensitization may impair drive satisfaction ("antidrive") mechanisms.

Another important but not exclusive factor contributing to drive satisfaction is impulse control. There appears to be a relationship between impulsivity, motivational states and impairment of self-control mechanisms (Ciccocioppo 1999). Notably, a high co-morbidity has been reported between ethanol and drug abuse and disorders, characterized by increased impulsivity (e.g. bulimia nervosa and obsessive-compulsive disorder). Repeated drug exposure has been suggested to induce a state of deficient inhibitory control, that may contribute to the compulsive drug-seeking and drug-taking (Olausson et al. 1999). In concert with this notion, it is well known that drug addicts using psychostimulants display decision-making deficits (Rogers et al. 1999) and have decreased inhibitory control when assessed using neuropsychological tests (Allen et al. 1998, Bickel et al. 1999).

We believe that co-morbidity between drug addiction and mood disorders is also the case for our hypothesis. Notably, the characteristic clinical feature of depression is an inability to satisfy different drives and needs. According to DSM IV (American Psychiatric Association 1994), depression is characterized by "markedly diminished interest or pleasure in all, or almost all, activities most of the day". There is evidence showing an associa-

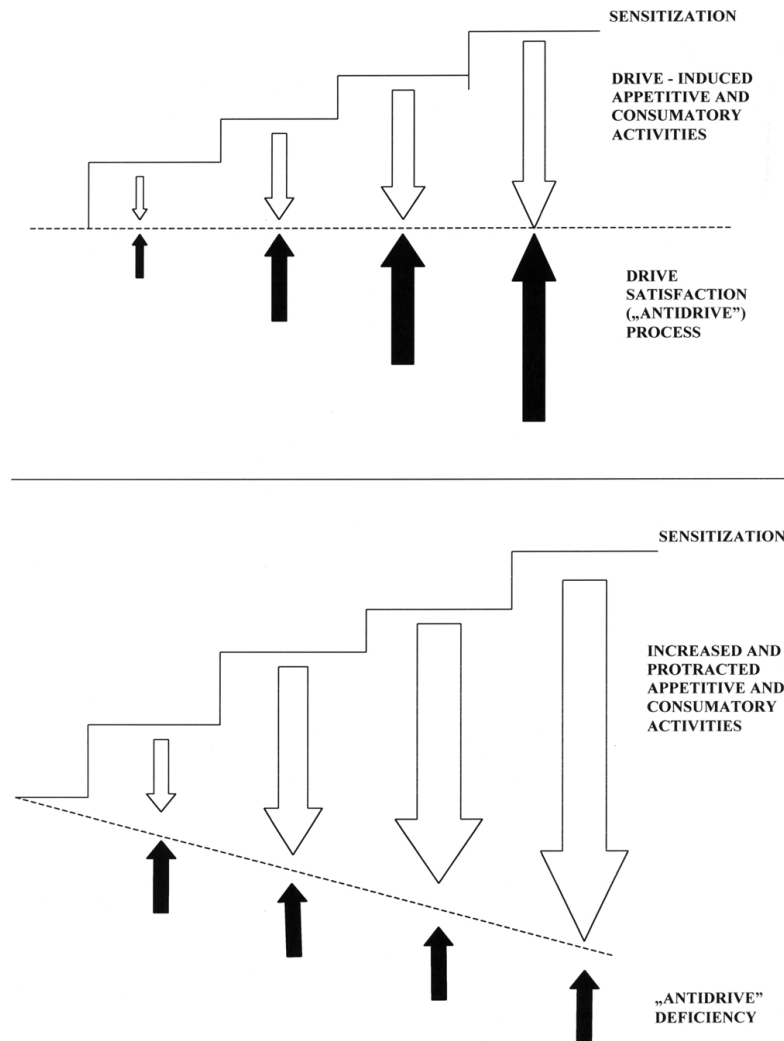


Fig. 3. The hypothetical role of sensitization of incentives in maintaining the balance between drive and drive satisfaction ("antidrive") mechanisms. (Top) In normal conditions (e.g. controlled appetitive behavior) sensitized appetitive processes that increase in amplitude are balanced with the efficient "antidrive" mechanism. (Bottom) Transition to an addiction: increased drug-related drive remains unopposed by deficient "antidrive" mechanism.

tion of depression and drug dependence. For example, the rates of depression among drug or ethanol abusers and the rates of drug abuse among patients suffering from depression are higher than expected from the individual rates of these disorders (Schuckit et al. 1997, Markou et al. 1998). Further, it has been reported that among drug users, antidepressant drugs appear to improve depression as well as drug abuse.

A very interesting integrative view of addiction as a disorder of homeostatic processes has recently been developed by Koob and LeMoal (1997, 2001). According to their formulation an allostatic state is defined as the process that maintains stability outside of the normal homeostatic frames. They postulate on that allostatic state is produced by neuroadaptations to the reward set point. As a consequence, the reward system in addicts must work harder and harder to stay in the same place (Koob and LeMoal 2001). Considering this disturbance

from the perspective of the drive satisfaction and "antidrive" mechanism, we suppose that an inability to appease an appetitive drug-related drive renders the neuronal substrates, that mediate drug reward unable to maintain homeostatic stability.

NEURAL SUBSTRATES OF "ANTIDRIVE" DYSFUNCTION

It remains unknown what neurotransmitter mechanisms have access to the mechanisms of drive satisfaction, and what neurotransmitter processes underlie the malfunction of the "antidrive". We suppose that the mechanism of "antidrive" lies within the defined motivational system in the brain. It is possible that the states of drive satisfaction (i.e. physiological "antipodes" of drives) are produced not merely by reduction of the excitability of drive centers, but also by activating other cen-

ters reciprocally related to the drive centers, and exerting upon them an inhibitory influence (Konorski 1967). As the drives are characterized in principle by general motor and emotional mobilization, we have good reason to assume that the drive satisfaction ("antidrive") mechanism is mediated through inhibitory neurotransmitters such as GABA, opioid peptides and so on.

FINAL REMARKS

In the recent years, despite the uncertainties and pitfalls, drug dependence research is going beyond the earlier conceptual framework (Holden 2001). Our proposed conceptualization is an attempt to define the neuroadaptations and disturbances produced by chronic drug use within the framework of drive satisfaction ("antidrive") - related mechanisms. We suppose that at least some of behavioural abnormalities occurring in addicts are related to drive satisfaction deficiency. The detailed mechanisms by which addictive drugs impair drive satisfaction is unknown. Several possibilities should be taken into consideration. Notably, drugs can stimulate brain reward system with a strength that exceeds any natural stimulus (Hyman and Malenka 2001). This excessive stimulation of reward system in addiction may impair the "antidrive" system. Other drug-related effects such as incentive sensitization of opponent processes may also contribute to "antidrive" deficiency. At present, we cannot determine whether the abnormalities of the "antidrive" mechanism may exist prior to drug use or may have been induced by drug use.

We are aware of the difficulty in providing more direct evidence for the existence of a connection between "antidrive" deficiency and addiction. Obviously, future research will eventually provide tests of the "antidrive" deficiency hypothesis.

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