Animal models of drug addiction: advantages and limitations

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Various animal models have been developed to investigate the neurobiological and behavioral mechanisms of drug addiction. The most popular of these animal models include the locomotor sensitization paradigm, the place conditioning procedure and the self-administration technique. With these techniques, it is possible to mimic in rodents the major aspects of human drug addiction. The self-administration procedure is the most widely used and show an excellent natural and predictive validity. In the self-administration protocol, experimental animals, usually rats or mice, are allowed to press a lever in order to gain access to a small dose of an addictive drug. The drug may be given to the animal through the oral, the intravenous or the intracranial route of administration, according to the purpose of the study. In recent years, the classical self-administration procedure has been adapted to study the specific neurobiological basis of drug relapse. In this now called drug reinstatement paradigm, when drug self-administration behaviors are well established, an extinction procedure starts, during which lever pressing is no longer reinforced by drug access. After a number of such extinction sessions, lever pressing gradually declines and eventually stops. Drug-seeking behaviors are therefore said to be extinguished. It is then possible to test various stimuli in order to investigate whether they reinstate drug-seeking behaviors and use such a reinstatement as an animal model of drug relapse. Three types of stimuli have been shown to reinstate drug-seeking behaviors: a small priming dose of drug, drug-associated cues and a stressful stimuli. The effects of these three relapse-triggering stimuli are mediated by different neurobiological mechanisms, leading to the expectation that they may be targeted by different pharmacotherapeutic and behavioral interventions. Despite the high value of the current animal models of drug addiction, there show several limitations. In particular, it is difficult to differentiate between self-controlled and compulsive drug use in animals. As only uncontrolled compulsive drug consumption characterizes drug addiction in humans, such a limitation might explain the high frequency of false positive results in animal experiments. Indeed, it is common that therapeutic interventions successfully developed in animals later proved to be disappointing in humans.