Simultaneous cocaine and alcohol intravenous self-administration in young-adults rats

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Alcohol is widely consumed as a legal drug, whereas cocaine is the illicit psychostimulant most commonly used in western countries. The combined use of alcohol and cocaine is very prevalent and leads to further aggravation of health consequences compared to individual consumption. In addition, to extend the euphoria caused by cocaine, alcohol modulates the less desirable effects of cocaine and appears to be a trigger for compulsive cocaine consumption/craving behavior. The combined use of alcohol and cocaine leads to psychiatric problems, a higher risk of suicide, and an increased propensity for violent and antisocial behaviors. The presence of alcohol modulates the biotransformation of cocaine, leaving higher plasma levels of cocaine and modifying the phamacokinetic of cocaine derivatives. Additionally, a new molecule is produced: cocaethylene. This molecule increases motor activity and establishes instrumental behavior patterns. As assessed under the conditioning place preference paradigm cocaethylene's rewarding effects are stronger than those of cocaine or alcohol alone. This could explain why it is so common to find consumers of both substances. Exposure to alcohol or other drugs during the early stages of life affects the development of the central nervous system and it may predispose to a greater drug use. Based on the premise that drugs affect the early development and that these effects are different depending on the sex of the individual, we carried out a study of the effects of the simultaneous use of cocaine and alcohol on "young adult" male and female rats aged 55 ± 2 days. Intravenous administration allows a greater control of variables such as the abuse liability or motivational effects of the psychoactive substance, it also enables a better understanding of the behavioral and pharmacological factors affecting drug use. Although widely used for cocaine, ethanol self-administration has always been difficult to carry out in rats. A polyvinyl chloride catheter (0.064" internal diameter) was implanted in the right jugular vein. One day before initiating drug administration, the patency of the catheters was tested by the infusion of sodium thiopental (10 mg/kg). For 21 days and during 120-minute sessions, the drugs were made available to the rats in a fixed-1 ratio schedule. This regime was limited to a maximum of 15 effective responses. The rats that reached the 15 responses received: 15 mg / kg BW of cocaine and 2 g / kg BW of alcohol. Behavior was maintained for 21 days via intravenous delivery of a cocaine/alcohol cocktail and was assessed using a FR-1 schedule of reinforcement. All rats that received the cocktail displayed the maximum number of responses. We observed a more consistent rate of response in females than in males. These preliminary results suggest that the self-administration behavior can be feasibly studied in rats at the dose used.

KEYWORDS: Cocaine, alcohol, self-administration, rats.

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