Available online at www.sciencedirect.com
SCIENCE DIRECT
Pharmacology, Biochemistry and Behavior 81 (2005) 459 – 465
PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR
www.elsevier.com/locate/pharmbiochembeh

The effects of alcohol preexposure on cocaine, alcohol and cocaine/alcohol place conditioning

Gregory D. Busse[a,*], Elizabeth T. Lawrence[b], Anthony L. Riley[b]

[a]Center for Drug and Alcohol Programs, Institute of Psychiatry, Medical University of South Carolina, 67 President St., PO Box 250861, Charleston, SC 29425, United States
[b]Psychopharmacology Laboratory, Department of Psychology, American University, Washington, DC 20016, United States

Received 29 October 2004; received in revised form 28 March 2005; accepted 6 April 2005
Available online 19 May 2005

Abstract

The present experiment examined the effects of alcohol preexposure on place conditioning with cocaine, alcohol or the cocaine/alcohol combination. Specifically, 91 male Sprague–Dawley rats were injected i.p. with 1.5 g/kg alcohol ($n=46$) or vehicle ($n=45$) every fourth day for 17 days prior to conditioning. On day 21, half of the animals from each preexposure condition were injected with 20 mg/kg cocaine, 1.5 g/kg alcohol or the cocaine/alcohol combination before being restricted for 30 min to a distinctive compartment of a place conditioning apparatus. The remaining subjects were injected with vehicle and restricted to the alternative side of the chamber. The following day, subjects previously given drug (or vehicle) were given vehicle (or drug) and placed in the alternative compartment of the chamber. Following four conditioning cycles, subjects were allowed 15-min access to the entire chamber. Both alcohol- and vehicle-preexposed animals conditioned with cocaine displayed a preference for the cocaine-paired compartment. Those conditioned with alcohol had an aversion to the alcohol-paired compartment. Consistent with our previous work, animals given the cocaine/alcohol combination displayed no compartment preference, indicating that concurrent alcohol affected the reinforcing effects of cocaine. Further, the attenuating effect of concurrent alcohol was unaffected by alcohol history. Under the present parameters, alcohol pretreatment has no effect on the rewarding (and possibly aversive) properties of cocaine alone or the cocaine/alcohol combination. Continued investigation of the conditions under which preexposure to alcohol might modulate the aversive/reinforcing properties of a cocaine/alcohol combination may be important for understanding vulnerability to the use and/or abuse of this drug combination.

Keywords: Alcohol; Aversion; Cocaine; Conditioned place preference; Polydrug; Rats; Reward

1. Introduction

Although cocaine and alcohol have been reported to interact within a variety of behavioral and physiological preparations (see Boyer and Petersen, 1990; Foltin and Fischman, 1989; Henning et al., 1994; Perez-Reyes and Jeffcoat, 1992), little is known how such interactions are affected by drug history (Grakalic and Riley, 2002a; Grathwohl et al., 2001; Hedaya and Pan, 1996; Peris et al., 1997). In one of the earlier assessments of the effects of alcohol history on the interaction of cocaine and alcohol, Peris et al. (1997) demonstrated that the disruptive effects of a cocaine/alcohol combination on rotarod performance were weakened in animals preexposed to alcohol. Specifically, rats pretreated with saline and given a cocaine/alcohol combination displayed a disruption in locomotor coordination (as evidenced on a rotorod test). Conversely, alcohol-pretreated rats exhibited little disruption when given the cocaine/alcohol combination. More recently, Grakalic and Riley (2002a) have extended these findings to the conditioned taste aversion (CTA) preparation. Specifically, they reported that, in drug-naïve animals, alcohol given concurrently with cocaine potentiated cocaine-induced taste aversions (see also Etkind et al., 1998). Conversely, concurrently

* Corresponding author. Tel.: +1 843 792 5809.
E-mail address: GregoryDBusse@aol.com (G.D. Busse).

0091-3057/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.pbb.2005.04.003

administered alcohol did not potentiate cocaine-induced aversions in animals that had been preexposed to alcohol (five exposures every fourth day prior to the initiation of taste aversion conditioning), suggesting that alcohol preexposure attenuated the subsequent interaction of the two drugs.

The fact that the effect of alcohol preexposure on the interaction between cocaine and alcohol was extended to a measure that examines the aversive properties of the cocaine/alcohol combination (i.e., the conditioned taste aversion preparation; see Riley and Freeman, 2004; see also www.CTAlearning.com) may be important for understanding its impact on the vulnerability to use and abuse this particular drug combination. Specifically, given that the acceptability of a drug (or drugs) appears to be a function of the balance between its rewarding and aversive effects (Cunningham and Henderson, 2000; Gaiardi et al., 1991; Gauvin et al., 2000; Grakalic and Riley, 2002a; Hunt and Amit, 1987; Riley and Simpson, 2001; White et al., 1977; Wise et al., 1976), any change in either of these properties with drug pretreatment may affect the subsequent acceptability of the drug (or drug combination). That preexposure to alcohol reduced the aversive effects of the alcohol/cocaine combination suggests that it may impact the subsequent use and abuse of this combination (see Grakalic and Riley, 2002a).

The present experiment extended the analysis of the effects of alcohol preexposure on the cocaine/alcohol combination. Specifically, the effects of preexposure to alcohol on the interaction of cocaine and alcohol in the conditioned place preference procedure were examined. The conditioned place preference procedure entails exposing an animal to one side of a two-chambered place preference apparatus after it has been injected with a drug (or drugs) and the other side of the apparatus following an injection of the drug's vehicle (see Mucha et al., 1982; Tzschentke, 1998). Following this conditioning period, animals are then placed in the apparatus and given unrestricted access to both compartments in a drug-free state. Such a procedure generally results in a relative preference for the drug-associated compartment if the drug (or drug combination) is reinforcing (for a bibliography, see Schechter and Calcagnetti, 1993, 1998). We have previously reported that, although cocaine readily produces a place preference for the drug-associated side, this preference is significantly attenuated when alcohol is given concurrent with cocaine (see Busse et al., 2004; Busse and Riley, 2002). That is, concurrently administered alcohol appears to attenuate the rewarding effects of cocaine within the CPP design. Given that alcohol preexposure affects the interaction of alcohol/cocaine within assessments of the aversive properties of drugs (Grakalic and Riley, 2002a), the present study examined the effects of this preexposure on alcohol's ability to attenuate cocaine's rewarding effects within the conditioned place preference design. Determining how these properties are affected by drug preexposure may be important to a more complete understanding of the behavioral vulnerability to drugs of abuse.

2. Methods

2.1. Subjects

Ninety-one drug-naïve, male Sprague–Dawley rats (Harlan Sprague Dawley Laboratories), weighing approximately 250 to 350 g at the start of the experiment, were housed in separate hanging wire cages in a room maintained on a 12 L:12 D light cycle (lights on at 0800 h) and at an ambient temperature of 23 °C. Food and water were available ad-libitum throughout the experiment. Animals were handled daily beginning 2 weeks prior to the start of the experiment in order to limit any effects of handling stress during conditioning and testing. Procedures recommended by the Guide for the Care and Use of Laboratory Animals (1996), the Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research (2003) and the Institutional Animal Care and Use Committee at American University were followed at all times.

2.2. Drugs

Cocaine hydrochloride (generously supplied by the National Institute on Drug Abuse) was dissolved in distilled water and was injected intraperitoneally (i.p.) in a concentration of 10 mg/ml (cocaine doses are expressed as the salt). Ethyl alcohol was prepared in a 15% solution with distilled water (v/v) and was also injected i.p. Vehicle injections were distilled water.

2.3. Apparatus

The place conditioning apparatus consisted of six identical shuttle-box chambers ($72.4 \times 30.5 \times 42.9$ cm). Each chamber had three compartments (i.e., two conditioning and one induction compartment) separated by two removable wooden barriers. One conditioning compartment ($30.5 \times 30.5 \times 41.9$ cm) was black in color and had a smooth Plexiglas floor. The other conditioning compartment ($30.5 \times 30.5 \times 41.9$ cm) was white in color and had a textured floor (cracked-ice polypropylene) with black stripes (2.54×30.5 cm) painted horizontally 3.85 cm apart. The induction compartment ($10.16 \times 30.5 \times 41.9$ cm) was gray in color and had a steel grated floor. Preliminary data from our laboratory using this apparatus indicated no systematic compartment bias.

2.4. Procedure

Following adaptation, animals were assigned to be injected i.p. with vehicle (V, $n=45$) or 1.5 g/kg alcohol (A, $n=46$) every fourth day for a total of five vehicle or