Physiology & Behavior 138 (2015) 150–153

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Brief communication

Cocaine induces state-dependent learning of sexual conditioning in male Japanese quail

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HIGHLIGHTS

- State-dependent learning effects of cocaine in a sexual conditioning paradigm.
- State dependent effects may alter sexual motivation.
- State dependent effects of cocaine may contribute to risky sex.

ARTICLE INFO

Article history:
Received 25 March 2014
Received in revised form 1 October 2014
Accepted 22 October 2014
Available online 4 November 2014

Keywords:
Cocaine
Pavlovian conditioning
State-dependent learning
State-dependent memory
Sexual behavior
Japanese quail

ABSTRACT

State dependent learning effects have been widely studied in a variety of drugs of abuse. However, they have yet to be studied in relation to sexual motivation. The current study investigated state-dependent learning effects of cocaine in male Japanese quail (*Coturnix japonica*) using a sexual conditioning paradigm. Cocaine-induced state-dependent learning effects were investigated using a 2 × 2 factorial design with training state as one factor and test state as the other factor. During a 14-day training phase, male quail were injected once daily with 10 mg/kg cocaine or saline and then placed in a test chamber after 15 min. In the test chamber, sexual conditioning trials consisted of presentation of a light conditioned stimulus (CS) followed by sexual reinforcement. During the state dependent test, half of the birds received a shift in drug state from training to testing (Coc → Sal or Sal → Coc) while the other half remained in the same drug state (Coc → Coc or Sal → Sal). Results showed that male quail that were trained and tested in the same state (Coc → Coc or Sal → Sal) showed greater sexual conditioning than male quail that were trained and tested in different states (Sal → Coc) except when cocaine was administered chronically prior to the test (Coc → Sal). For the latter condition, sexual conditioning persisted from cocaine training to the saline test. The findings suggest that state dependent effects may alter sexual motivation and that repeated exposure to cocaine during sexual activity may increase sexual motivation which, in turn, may lead to high risk sexual activities. An alternative explanation for the findings is also discussed.

1. Introduction

State-dependent learning occurs when learned information is better recalled when an organism is in the same state of consciousness as when the memory was formed [1]. In a classic experiment by Goodwin and colleagues [2], male volunteers were asked to perform various memory tasks while under the influence of alcohol or while sober. The following day, they were retested under similar or opposite conditions. The results indicated that subjects who learned the material while intoxicated had difficulty recalling the task in a sober state. Conversely, subjects who were tested and retested under the influence performed as well as subjects who were tested and retested under sober conditions [2]. Thus, in accordance with state-dependent learning, memories appear to be best recalled in the same physiological state in which they were encoded.

State-dependent learning has been observed for several addictive drugs including ethanol [2–5], pentobarbital [2], morphine [6–9] methylphenidate [10], and amphetamine [11]. Romieu and colleagues [12] used a modified passive avoidance task and found that relatively low doses (0.1 and 0.3 mg/kg) of cocaine induced state-dependent learning in mice. Low doses were used because they did not affect acquisition or consolidation of the memory. In addition, it was found that the cocaine-induced state-dependent effect could be altered by GABA and opioid receptor modulation [12].

Several studies have shown that repeated pre-exposure to addictive drugs may facilitate sex seeking behavior [13–16]. Levens and Akins [17] conducted an experiment to determine whether repeated preexposure to cocaine would increase sexual conditioning in male Japanese quail. Chronic cocaine administration (10 mg/kg, once a day for 6 days) resulted in increased locomotor activity compared to saline.

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http://dx.doi.org/10.1016/j.physbeh.2014.10.020
0031-9384/

After a 10 day withdrawal period, male quail received sexual conditioning trials that consisted of the presentation of an arbitrary conditioned stimulus (CS) followed by sexual reinforcement. Males that received repeated administration of cocaine demonstrated more conditioned approach behavior to the CS compared to males that received repeated administration of saline. The findings and others like it (e.g., [14,15]) suggest that cocaine and similar psychostimulants may facilitate sexual conditioning and thereby contribute to a drug-facilitated increase in sexual activity.

The current research used a well-studied Pavlovian sexual conditioning paradigm to test for state-dependent effects of cocaine in male Japanese quail. In the Pavlovian sexual conditioning paradigm, male quail are presented with a light CS and this is followed by a mating opportunity with a receptive female quail [18]. Males learn that the CS predicts a mating opportunity and as such, they approach and remain near the CS. This sexually conditioned approach behavior is viewed as an index of sexual motivation. As described above, pre-exposure to chronic cocaine has been shown to enhance this sexually conditioned approach behavior [17,19]. In addition, Troisi & Akins [20] found that cocaine functioned as an interoceptive discriminative cue that predicted an association between a CS and a mating opportunity. Thus, cocaine may not only facilitate sexual conditioning but it may also function as a discriminative cue or occasion setter.

The purpose of the current experiment was to test state-dependent effects of cocaine using a 2 × 2 factorial design with training state (drug or no drug) as one factor and test state (drug or no drug) as the other factor (see [21,22] and [23] for reviews). Two groups will have a shift in drug state from training to testing while two groups will remain in the same state during training and testing. A state-dependent account would predict that sexually conditioned approach behavior would be attenuated in groups that receive a shift in drug state relative to those that do not receive a shift [21–23].

2. Materials and methods

2.1. Animals

Thirty one (n = 31) experimentally and sexually naïve male quail, approximately 6 months old, served in the experiment. An equal number of female quail were used as copulation partners. Eggs were supplied by Northwest Gamebirds (Kennewick, WA) and quail chicks were hatched and then raised in mixed-sex groups until approximately 28 days of age. At 28 days of age, male quail were housed individually and female quail were group housed in wire mesh cages (supplied by GQF Manufacturing, Savannah, GA). Female quail were housed individually when selected for the experiment. Subjects were raised in long-daylight (16L:8D) conditions to maintain reproductive readiness [23] with food and water available ad libitum. All subjects were drug naïve prior to the experiment.

Male quail were selected as subjects on the basis of a pretest for copulation. A female quail was placed in the home cage of each male for 5 min. Only males that successfully copulated within 5 min were used in the experiment. Male quail are not likely to copulate with a female bird if they have not done so within 5 min [24].

Female quail were assigned to male quail on a rotation basis across acquisition trials so that male quail were never paired with the same female quail more than once. All of the experimental procedures were approved by the Institutional Animal Care and Use Committee and were conducted under the guidelines of the Division of Laboratory Animal Research at the University of Kentucky.

2.2. Apparatus

Six large Plexiglas test chambers (91.4 cm wide × 61.0 cm deep × 30.5 cm tall) were used during the training phase. The side walls of the chambers were covered with white paper and the floors of the chambers were covered with white corrugated paper. A smaller Plexiglas side cage (30.5 cm wide × 61.0 cm deep × 27.9 cm tall) was attached to one end of each test chamber and was used to house a female bird during training. A door connecting the test chamber and the side cage allowed male quail to access the female's side cage. The door was covered with white paper so that males and females could not see each other unless the door was opened. A 25 W red light (15.25 cm above the floor) was used as the conditioned stimulus (CS). The CS zone was marked on the corrugated floor (36.6 cm × 36.6 cm) in front of the female's test cage door.

2.3. Drugs

Cocaine hydrochloride (National Institute on Drug Abuse, Bethesda, MD) was dissolved in physiological saline (0.9% NaCl) at a dose of 10 mg/kg and injected intraperitoneally (i.p.). Drug was injected 15 min prior to testing.

2.4. Procedure

2.4.1. Training

The training phase consisted of fourteen trials, one per day, with each subject receiving the same treatment throughout training. During each training trial, male quail were injected with 10 mg/kg of cocaine (n = 16) or saline (n = 15) intraperitoneally (i.p.). Males were then placed back in their home cage for 15 min. After the 15 min, they were transported to the test room and placed in the test chamber. Quail received a 30 s pre-CS period, after which the CS light was illuminated for 30 s and was then turned off. Subsequently, the door to the female's side cage was raised and males were allowed to enter the side cage for a copulatory opportunity with a female quail for 5 min. The amount of time (s) that male quail spent in the CS zone during the CS light presentation was recorded. Approach behavior (time in CS zone) was defined as both feet crossing into the CS zone.

2.4.2. Withdrawal period

The training phase was followed by a 10-day withdrawal period. During this phase, quail remained in their home cage and did not receive drug or saline.

2.4.3. State-dependent test

Following a 10-day withdrawal period, quail were given a state-dependent test. During the test, half of the male quail that received repeated cocaine administration during the training phase were injected with saline and half of the males that received repeated administration of saline during training were injected with cocaine. The other half of the male quail that received repeated cocaine administration during the training phase were injected with cocaine and the other half of the males that received repeated administration of saline during training were injected with saline. Therefore, half of the birds received a shift in drug state from training to testing (Coc → Sal or Sal → Coc) while the other half remained in the same drug state from training and testing (Coc → Coc or Sal → Sal). The state-dependent test consisted of one test and was conducted on a single day.

2.4.4. Data analyses

Training data were analyzed with a two-way (training state × trials) repeated measures analysis of variance (ANOVA). Data for the state-dependent test were analyzed with a between-subjects ANOVA (training state × test state). Pair-wise comparisons were conducted with Fisher's LSD test where appropriate. For all analyses, 0.05 was chosen as the significance level.