Pharmacology, Biochemistry and Behavior 93 (2009) 460–464

Contents lists available at ScienceDirect

Pharmacology, Biochemistry and Behavior

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

Cocaine and automaintained responding in pigeons: Rate-reducing effects and tolerance thereto with different durations of food delivery

Amy Durgin [a], Lindsay K. Porter [a], Kelly P. Bradley [a], Sean Laraway [b], Alan Poling [a,*]

[a] Department of Psychology, Western Michigan University, Kalamazoo, MI 49008, United States
[b] Department of Psychology, San José State University, San José, CA 95192-0120, United States

ARTICLE INFO

Article history:
Received 17 February 2009
Received in revised form 11 June 2009
Accepted 13 June 2009
Available online 21 June 2009

Keywords:
Autoshaping
Automaintenance
Behavioral momentum
Tolerance
Cocaine
Pigeons

ABSTRACT

Pigeons were exposed to an automaintenance procedure in which 6-s key illuminations in one color (red or white) were immediately followed by 3-s food deliveries and key illuminations in the other color were followed by 9-s food deliveries. Both conditions engendered consistent responding. With both durations of food delivery, acute and chronic cocaine administrations (1.0–17.8 mg/kg) produced dose-dependent decreases in mean percent trials (key illuminations) with a response and mean total response per session. Tolerance developed to the disruptive effects of cocaine on both response measures. Food duration did not significantly affect either response measure or significantly interact with cocaine dose or drug regimen. The orderliness of the present findings, like those of a related study examining whether probability of food delivery modulated the effects of cocaine on automaintained responding [Porritt, M., Arnold, M., Poling, A., Cocaine and automaintained responding in pigeons: rate-reducing effects and tolerance thereto with different CS–US pairing probabilities. Pharmacol Biochem Behav 2007; 87:405–411.], suggests that the automaintenance procedure is a useful assay for examining tolerance to drug effects on classically-conditioned responding. Unlike the results of that study, however, the present findings are inconsistent with a behavioral momentum analysis of drug effects on such responding.

1. Introduction

The concept of behavioral momentum, developed by Nevin (1974, 1988, 1992), proposes (a) that resistance to change is a better measure of the "strength" of responding than response rate and (b) that frequency of reinforcement is the primary determinant of resistance to change. Nevin proposed that behavioral momentum, defined as a particular response's resistance to change, is primarily a function of how frequently a reinforcer, such as food, is delivered in the context of the antecedent stimulus exercising control over the response in question. He also proposed that magnitude of reinforcement directly affects resistance to change (Nevin, 1974). Although the behavioral momentum metaphor has been used primarily to conceptualize schedule-controlled operant behavior (e.g., responding under variable-ratio or variable-interval schedules of food delivery, see Nevin, 2002; Nevin and Grace, 2000), it also could be applied to automaintained responding (Porritt et al., 2007).

Automaintained responding is responding that persists across sessions under an autoshaping procedure. Brown and Jenkins (1968) first described the autoshaping procedure and noted that it involved "the standard arrangement for classical conditioning" (p. 7), in which pairings were arranged between a conditional stimulus (CS), key illumination, and an unconditional stimulus (US), food delivery. As Brown and Jenkins noted, although the experimenter arranges only stimulus–stimulus relations under the autoshaping (or automaintainence) procedure, because food delivery quickly follows any peck that occurs during a trial (key illumination), it is probable that pecks are affected by response-independent (i.e., "adventitious" or "superstitious") operant reinforcement, in addition to classical conditioning mechanisms. The relative contribution of classical conditioning and operant conditioning learning processes to autoshaped (and automaintained) responding has been long debated (e.g., Schwartz and Gamzu, 1977) but never entirely resolved. Indeed, it may be impossible to do so experimentally. Be that as it may, such procedures have proven valuable for delineating drug effects on the acquisition and retention of information (see review by Sparber, 2001).

Research on drug effects on automaintained performance has primarily focused on acute actions of drugs. To our knowledge, only one study (Porritt et al., 2007) has used automaintainance procedures to study tolerance or to examine whether drug effects on such responding are consistent with a behavioral momentum analysis. Porritt et al. investigated the effects of acute and chronic administrations of cocaine (1.0–17.8 mg/kg) on the automaintained responding of pigeons under conditions in which 6-s red, green, and white key illuminations were followed by food with a probability of 0.25, 0.5, and 1.0, respectively. Substantial responding occurred at all probabilities. Acute and chronic cocaine administration reduced percent trials with a response and total responses per session in dose-dependent fashion, with tolerance observed when acute and

* Corresponding author. Tel.: +1 269 387 4483; fax: +1 269 387 4550.
E-mail address: alan.poling@wmich.edu (A. Poling).

0091-3057/$ – see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.pbb.2009.06.008

chronic dose–response curves were compared. In general, the disruptive effects of cocaine were larger when the probability of food delivery was 0.25 or 0.5 than when it was 1.0. Porritt et al. suggested that these results are consistent with a behavioral momentum analysis of drug effects. That is, behavior was stronger (more resistant to drug-induced disruption) when the rate of reinforcement was higher, although response rates tended to be lower.

According to a behavioral momentum analysis, if rate of reinforcement is held constant, then magnitude of reinforcement should directly affect resistance to change, with larger magnitudes leading to greater response strength (Nevin, 1974). Research on classical conditioning supports this analysis with respect to resistance to extinction (Savastano and Miller, 2004). Little is known, however, regarding the effects of reinforcer magnitude on resistance to other perturbations, such as drugs, under classical conditioning paradigms, and the extension of the behavioral momentum metaphor to Pavlovian conditional responses, such as automaintained responding, deserves further attention (Grace and Nevin, 2004). Moreover, given the importance of behavioral factors in the occurrence of tolerance (Branch, 1993), further examination of such factors is of interest. Therefore, the present study determined the extent to which reinforcer magnitude (duration of food delivery) influenced the resistance of automaintained responding in pigeons to disruption by cocaine under acute and chronic conditions.

2. Method

2.1. Subjects

Five experimentally-naïve adult female pigeons, obtained from Palmetto Pigeon Plant (Sumter, SC), served as subjects. They were individually housed with unlimited access to water and grit in a temperature-controlled colony room (20–22 °C), maintained under a 12-hr light/12-hr dark schedule. Throughout the experiment, access to food was restricted to maintain each bird at approximately 80% of its free-feeding weight. This study was approved by the Institutional Animal Care and Use Committee and conducted in accordance with the *Guide for the Care and Use of Laboratory Animals* promulgated by the National Research Council (1996).

2.2. Apparatus

Four commercially available test chambers (MED Associates, St. Albans, VT) housed in sound attenuating shells were used. The front wall of each chamber contained three response keys, symmetrically located 24 cm above the floor, and a horizontally centered opening through which mixed grain could be reached when the food hopper was raised. Each response key could be illuminated in red, white, or green. A white bulb centered at the top of the back wall provided ambient chamber illumination and an exhaust fan provided continuous ventilation and masking noise. A personal computer equipped with MED PC® software was used to collect data and to arrange experimental events.

2.3. Behavioral procedure

The behavioral procedure was a discrete-trials procedure similar to that used by Porritt et al. (2007). In the present study, 6-s key illuminations were immediately followed by either 3- or 9-s access to food, regardless of the bird's behavior. Half of the key illuminations, selected at random with the provision that each color appeared equally often each session, were red. The other key illuminations were white. The key that was illuminated on a given trial (left, center, and right) also was selected at random, with the provision that each key was lighted equally often each session. For three birds, red key illuminations were always followed by 3-s food deliveries and white key illuminations were always followed by 9-s food deliveries. For the other two birds, red key illuminations were always followed by 9-s food deliveries and white key illuminations were always followed by 3-s food deliveries. Trials were separated by a variable inter-trial interval (ITI) with a mean length of 45 s and a range of 15 to 120 s. All keys were darkened during the ITI. Daily sessions comprised 24 trials and were conducted at about the same time each day (during the light portion of the light/dark cycle), seven days a week.

2.4. Pharmacological procedure

The automaintenance procedure was in effect for 25 sessions prior to pharmacological testing. By the end of this period, all birds regularly pecked during red and white key illuminations, and the percentage of trials with one or more responses (percent trials with a response) showed no obvious trend across 5 consecutive sessions. The same is true of the total number of responses per session.

Acute drug testing involved the administration of 1.0, 3.2, 5.6, and 10 mg/kg of cocaine to each bird. No higher dose was given because 10 mg/kg greatly reduced responding. Each bird received every dose twice, in an irregular order. Cocaine was given every third day; the session immediately preceding drug testing was a vehicle-control (0 mg/kg) session and the day preceding vehicle injection was a baseline session with no injection given. Throughout the study, cocaine hydrochloride (Sigma, St. Louis) was dissolved in isotonic saline solution and injected into the breast muscles at a volume of 1 ml/kg 5 min before behavioral testing. Vehicle (isotonic saline solution) was administered in comparable fashion.

During chronic administration, each bird received a daily dose of 5.6 mg/kg cocaine 5 min before the onset of behavioral testing. After 20 consecutive sessions of exposure to this dose, percent trials with a response and total responses per session showed no obvious trend across 5 consecutive sessions and post-chronic testing began. During chronic testing, doses of 0 (vehicle), 1.0, 3.2, 10, and 17.8 mg/kg, as well as the usual chronic dose of 5.6 mg/kg, were evaluated. Each bird received every dose other than 5.6 mg/kg twice, in an irregular sequence. Tests of doses other than 5.6 mg/kg were separated by 2 consecutive sessions during which 5.6 mg/kg was administered. When 0, 1.0, or 3.2 mg/kg doses were administered prior to the session, sufficient cocaine to equal the 5.6 mg/kg daily dose was administered immediately after behavioral testing.

2.5. Dependent variables and data analysis

We measured two dependent variables: (a) percent of trials with a response, and (b) total number of responses across all trials. For data analyses, data points for each bird are the means of the two administrations. We used three-factor repeated-measures analysis of variance (RM ANOVA) to analyze these data. Because pigeons did not receive 17.8 mg/kg in the acute phase, the RM ANOVA results exclude this dose. The RM ANOVA included the following within-subject factors: regimen (acute vs. chronic), duration of food delivery (3- vs. 9-s), and dose of cocaine (1.0, 3.2, 5.6, and 10.0 mg/kg). All data were transformed to percent vehicle control prior to testing. When significant interactions were present, simple effect tests were conducted using paired-samples *t* tests, with the Bonferroni correction applied to adjust the Type I error rate. These tests were only conducted when the graphed means did not overlap.

To characterize the development of tolerance, ED_{50} values and associated 95% confidence intervals (95% CIs) were computed for the acute and chronic data (cf., Tallarida, 2000, pp. 26–31). All doses were transformed to $\log_{10}$ (dose) for these calculations. The ED_{50} values for $\log_{10}$ (dose) were obtained by fitting regression lines to data points between 80% and 20% (or nearest values) of vehicle-control values on the descending limb of the dose–response curve. All tests were conducted with familywise $\alpha = .05$. The data for both dependent