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The Effects of Electric Shock on Responding Maintained by Cocaine in Rhesus Monkeys

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BERGMAN, J. AND C. E. JOHANSON. *The effects of electric shock on responding maintained by cocaine in rhesus monkeys.* PHARMAC. BIOCHEM. BEHAV. 14(3) 423–426, 1981.—Under baseline conditions, responding was maintained by intravenous cocaine delivery (100 μg/kg/infusion) under a fixed ratio 10 schedule in three rhesus monkeys. During test sessions, the onset of each cocaine infusion was accompanied by a delivery of electric shock of pre-determined duration and intensity. At intermediate intensity levels, the electric shock delivery initially reduced cocaine maintained responding. Although test sessions were separated by at least three baseline sessions, adaptation to the punishing effect of shock occurred within five test sessions in each monkey. Adaptation did not occur at higher intensity levels which completely eliminated cocaine-maintained responding, even when this intensity was tested prior to intermediate intensity levels.

Electric shock Cocaine Lever pressing

PUNISHMENT is the reduction in the probability of a response which is followed by the immediate delivery of a stimulus [2]. A stimulus leading to such a reduction is termed a punishing stimulus [11]. Many studies have shown that the delivery of electric shock can serve as an effective punishing stimulus when responding is concurrently maintained by a number of events (e.g., food or water) under a variety of schedules [2,13]. For instance, when food-maintained responding under fixed-ratio schedules of delivery is also followed by electric shock delivery, the degree of response reduction is dependent upon several variables, including the intensity and duration of the electric shock stimulus [2,11]. Furthermore, attenuation of the suppressant effect of the shock delivered under fixed ratio schedules occurs gradually over consecutive sessions [1]. Such adaptation does not occur, however, when the intensity of the shock is severe enough to initially eliminate responding completely [2]. When electric shock is no longer delivered, studies have shown that responding temporarily increases above non-punished baseline rates of responding [2].

Although the effects of non-contingently administered drugs on punished responding maintained by events such as food have been extensively studied [4,6], few studies have been conducted on punishment of drug-maintained responding [5, 8, 16]. These studies are important since punishment is considered an effective technique for eliminating human drug abuse. In addition, a considerable literature indicates that responding maintained by the intravenous delivery of psychotropic drugs is functionally similar to responding maintained by events such as food and water [9,18]. Although these studies would predict that the effects of delivering a punishing stimulus on drug-maintained responding would be similar to its effects on responding maintained by other events, the nature of the response-maintaining event, i.e., the self-administered drug, may interact with the punishing stimulus to produce unique effects [3]. The possibility of a drug-behavior interaction receives some support from studies showing that drugs administered non-contingently will differentially modify the effects of punishment on responding maintained by other events [12]. Therefore, when the drug itself is the maintaining event, it may differentially modify the effects of punishment on the responding to which its delivery is consequent.

In one of the first studies of punishment of drug-maintained responding, Grove and Schuster [5] showed that responding maintained by intravenous cocaine delivery under a FR 1 schedule in rhesus monkeys decreased as a direct function of the intensity of electric shock which accompanied the onset of the drug infusion. In a study by Johanson [8] rhesus monkeys were given a choice between two doses of cocaine. When the doses were the same, the animals chose the non-shocked alternatives. However, as the dose of the shocked alternative was increased, this higher dose was preferred. Thus, although electric shock can suppress drug-maintained responding, its effectiveness can be modified by a variety of variables.

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The present study was designed to further assess the conditions under which electric shock can function as a punisher of responding maintained by drug delivery. In particular, rhesus monkeys self-administering cocaine under fixed-ratio schedules of drug delivery were exposed to a pre-determined electric shock stimulus delivered with the onset of each infusion. The shock intensity delivered was varied in a systematic manner in order to investigate adaptation to the punishing stimulus.

METHOD

Animals

The animals in this study were three experimentally naive adult rhesus monkeys, two males (5107 and 5026) and one female (6056), weighing between 4.6 and 5.8 kg. Each monkey was anesthetized with sodium pentobarbital (up to 30 mg/kg, IV) and surgically prepared with both an intravenous silicone catheter (0.08 cm internal diameter; 0.24 cm external diameter) and two intramuscularly placed electric shock electrodes. Each electrode, a concave, gold-plated brass disk, 3–5 mm in diameter, was secured by suture within a lumbar muscle 3–4 cm from the other electrode. The proximal end of the catheter was inserted into a major vein; the distal end was threaded subcutaneously and exited the body through an incision in the monkey's back. Similarly, the 28 ga. teflon-coated electrode lead wires were passed subcutaneously and exited the body through the same incision. Resistance values across these leads, recorded prior to each daily session, typically ranged from 3.0 to 7.0 kohms. Whenever resistance values increased during this study to a value of 20 kohms or more, new electrodes were placed in the contralateral side of the monkey's back and the original ones removed.

All monkeys had ad lib access to water and Purina monkey chow biscuits and received a daily liquid vitamin supplement. Occasionally antibiotics were administered intramuscularly to arrest a catheter tract infection.

Apparatus

Monkeys were individually housed throughout the entire experiment in wooden, front-opening, sound-attenuating chambers that served as both experimental cubicles and home cages. Each chamber was 68.6 cm wide, 72.6 cm high and 83.8 cm deep and was ventilated by a fan mounted on the front door. On the inside door of each cubicle were mounted two 10×10×15 cm steel boxes on either side of a removable food dish. Each box contained a response lever (LVE/BRS PRL 001/121-07, Beltsville, Maryland) and above each lever, four stimulus lights, two covered with red Dialco lens caps and two with green Dialco lens caps. Additionally, white and red houselights were mounted in a 20×20×30 cm Plexiglas-faced steel box bolted to the ceiling.

Each monkey was fitted with a stainless steel harness connected to a spring arm 46 cm in length and 1.3 cm in diameter (E & H Engineering, Chicago, Illinois). This arm attached, in turn, to the back wall of the cubicle, allowing relatively unrestricted movement for the monkey and safe passage for the catheter and electrode wires out the back of the cubicle. Outside the cubicle, the catheter lumen connected to a peristaltic infusion pump (7540×, Cole-Parmer Instrument Co., Chicago, Illinois) which delivered solutions at the rate of 6 ml/min. The electrode wires connected to a 50 kohm constant current shock generator (BRS/LVE SG-903, Beltsville, Maryland). This generator insured reliable delivery of a given shock intensity in the face of minor fluctuations in tissue resistance.

The experimental chambers were connected by cables to solid state equipment in an adjacent room which arranged the programming of stimulus events in the cubicles and recording of lever presses, infusions, and shock delivery on counters and a cumulative response recorder.

TABLE 1

NUMBER OF TEST SESSIONS AT EACH ELECTRIC SHOCK INTENSITY IN THE ORDER OF PRESENTATION

Monkey	Intensities	Sessions
5107	4 mA	6
	8	7
	4	4
5026	4 mA	6
	8	7
	12	7
6056	8 mA	12
	4	3

Procedure

Training sessions were initiated after a monkey was prepared with a catheter and electrodes. In the presence of the white houselight and green stimulus lights, a depression of the right lever occasioned a change of lights (white houselight and green stimulus lights to red houselight and red stimulus lights) and a programmed ten second infusion of a cocaine HCl solution (100 μg/kg). Responses on the left lever had no programmed consequences. Once lever pressing was established in each monkey (1–2 days), the fixed-ratio requirement (i.e., number of lever presses required) for cocaine delivery was gradually raised to ten (FR 10). At this point, daily three hour sessions were initiated. Stable rates of responding were achieved in each monkey within two weeks. The criterion for stability was defined as not more than a 10% deviation in the number of infusions during any one session from the mean number of daily infusions in a three session period. Such a three session period then served as control for a test session the following day.

Once stability was achieved, test sessions were begun. These differed from daily sessions in that the completion of each FR 10 occasioned the delivery of a 200 msec electric shock simultaneously with the onset of the cocaine delivery. No more than one test session was conducted per week.

During initial test sessions for monkeys 5107 and 5026, the shock intensity was 4 mA. Based on preliminary data, this intensity was expected to moderately reduce drug-maintained responding. In each monkey, this intensity was tested during six sessions. Rhesus 6056 was initially exposed to a shock intensity of 8 mA, intended to severely reduce cocaine-maintained responding. This intensity was repeated for 12 test sessions. When these initial exposures were completed, each animal was tested with the other electric shock intensity. In rhesus 5026 it was necessary to test a 12 mA intensity since 8 mA did not completely eliminate responding. Table 1 summarizes the order and duration of testing.

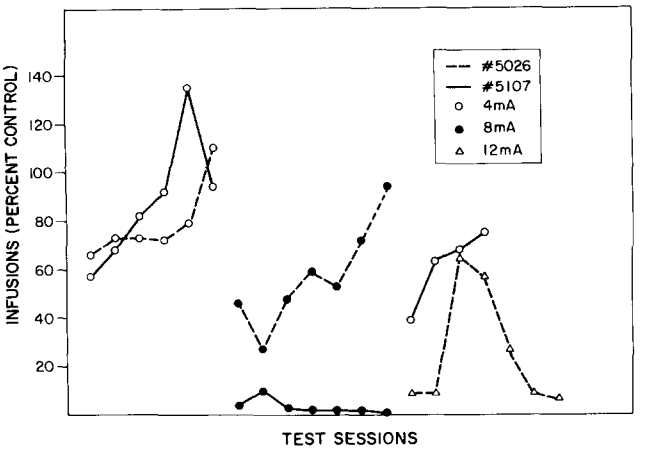

FIG. 1. Effects of electric shock on fixed-ratio responding maintained by 100 μg/kg injection of Cocaine HCl expressed as percent of number of infusions in control sessions. Points connected by solid lines represent data for rhesus 5107; those connected by dashed lines represent data for rhesus 5026. Unfilled circles show the effect of 4 mA shock delivery. Filled circles show the effects of 8 mA shock; triangles represent 12 mA intensity. The order of test sessions for each animal is sequential along the abscissa.

Drug Solutions

Cocaine HCl was dissolved in 0.9% physiological saline and delivered in a 1 ml volume per infusion. Doses refer to the salt. Cocaine HCl solutions were changed at least once a week.

RESULTS

Cocaine self-administration under the FR 10 schedule was established in all three monkeys. In agreement with previous reports [15], very stable daily intake occurred for each animal. Intake did not vary significantly over the course of the study for any monkey.

Figure 1 shows the effects of electric shock delivery on cocaine-maintained responding in monkeys 5107 and 5026 expressed as the percentage of the mean number of infusions per session over the three sessions immediately preceding the test session. Although the first exposure to 4 mA reduced responding for monkey 5107 to 57% of control, adaptation gradually developed and, by the sixth test session with 4 mA, the electric shock delivery no longer reduced cocaine-maintained responding. Although responding in the baseline session following the test session (not shown) was moderately reduced after the first test session with 4 mA, it was unaffected following subsequent test sessions with this intensity.

In sessions 7 to 13, the shock intensity tested in rhesus 5107 was increased to 8 mA. As Fig. 1 shows, 8 mA almost completely eliminated self-administration behavior, with no adaptation even after 6 additional test sessions. Responding on the following non-test session, although initially suppressed, gradually returned to control values. To determine whether exposure to the 8 mA shock intensity altered the effect of 4 mA, a series of test sessions at this lower intensity was repeated. Figure 1 shows that once again, there was an initial response suppression followed by a recovery of responding to 75% of control values. In additional manipulations with monkey 5107 (not shown), a series of 2–3 test sessions with 4 mA were alternated with 2–3 test sessions with 8 mA. Although 8 mA continued to eliminate responding, a trend toward baseline levels of responding was consistently seen with the lower intensity.

In monkey 5026, the initial series of 4 mA electric shock deliveries produced results similar to those for monkey 5107. Responding maintained by 100 μg/kg cocaine in the first 4 mA test session was reduced by 35% as shown in Fig. 1. By the sixth test session, adaptation to the punishing effect of 4 mA electric shock was complete. Responding in the baseline session following test sessions was affected similarly to that of monkey 5107, i.e., rapid adaptation after several sessions. Unlike for monkey 5107, 8 mA shock presentation reduced responding of rhesus 5026 by only 54% and by the seventh test session, responding had recovered to 94% of control values. The intensity of shock presented in the following six test sessions was increased to 12 mA in the attempt to completely eliminate responding. As shown in Fig. 1, although responding in each of the first two test sessions was virtually eliminated, cocaine-maintained responding in the third 12 mA session recovered to 65% of control values. By the seventh session at this intensity, however, responding was again severely reduced. When test sessions with 8 mA were repeated (not shown), adaptation, following an initial response decrement, again developed. When the 12 mA intensity was reintroduced in subsequent test sessions, only one ratio was completed during each of several test sessions.

To determine if initial exposure to a high intensity would affect adaptation to a lower intensity, 8 mA was presented in the first series of test sessions for monkey 6056. Eight mA completely eliminated cocaine-maintained responding in this monkey over the course of 12 test sessions. When 4 mA was subsequently presented, responding recovered and, in the third session, returned to 87% of control values. Although responding in baseline sessions following test sessions was eliminated following the first two sessions with the 8 mA intensity, it showed a 60% increase over control values after the third test session and was not suppressed or increased for the remainder of the 8 mA series of test sessions. Although responding was again eliminated in the baseline session following the initial 4 mA test session, this effect was transitory and responding recovered in subsequent sessions following 4 mA test sessions.

DISCUSSION

All three monkeys initiated and maintained responding under a fixed-ratio 10 schedule of 100 μg/kg intravenous cocaine delivery and patterns and rates of responding remained stable over considerable periods of time. The delivery of electric shock coincident with the onset of each cocaine infusion produced an initial reduction in responding. The degree of response reduction was greater when the intensity of the electric shock was 8 mA than when a 4 mA intensity was used. This agrees with previous studies where responding was maintained under fixed-ratio schedules of food presentation [2]. In the present study when the electric shock stimulus did not completely eliminate responding, a trend was seen toward adaptation to its suppressant effect. This occurred rapidly compared to previous reports [1].

It is unclear whether the nature of the maintaining event influenced this rapid adaptation. As with other psychomotor stimulant drugs, cocaine has not been shown to attenuate the effects of punishment on schedule-controlled behavior main-

tained by other events [17]. Previous research by Grove and Schuster [5], which also found intensity-dependent decreases in cocaine-maintained responding punished by electric shock, did not report adaptation to the effects of the shock stimulus. In that study, responding was maintained under a multiple FR 1; FR 1 schedule of cocaine delivery in which responses in only one component were shocked. It is quite possible that differences in schedule contingencies account for the lack of adaptation in that study. Behavioral contrast, for example, is commonly reported for the non-shocked components in other multiple schedule studies [10]. Grove and Schuster [5], however, reported only transitory increases in response rate for responding in non-shocked components.

The present data demonstrate that the development of adaptation is affected by the extent to which responding is reduced by the punishing stimulus. When responding was completely eliminated in monkey 5107 and 6056 by 8 mA shock stimuli, no recovery was seen. This is similar to results for food-maintained responding under fixed-ratio schedules of reinforcement punished by electric shock [2]. However, for monkey 5026, some adaptation was seen to 12 mA, a shock intensity under which responding was virtually eliminated by first exposure. Nonetheless, responding progressively decreased over the remaining sessions in the 12 mA series.

It is interesting that monkey 6056 did show considerable adaptation to the 4 mA shock in spite of having shown no recovery of responding when shocked with 8 mA before the 4 mA series of sessions. The order of intensity presentation had no apparent consequences. Further, although some evidence for behavioral contrast was seen, responding in the baseline session following test sessions showed adaptation to the initial punishing effects at all intensities. The adaptation seen in these animals is highlighted by the observation that, after the first few test sessions, each animal completed at least one fixed-ratio 10 at the beginning of each session, test or control. These findings suggest that drug-maintained responding by these animals rather than depending on the magnitude of just one stimulus—reinforcing or punishing—was a product of dose-dependent and intensity dependent interactions. Based on data such as those of Johanson [8] on the effects of electric shock on responding maintained by cocaine injections in a choice procedure in the rhesus monkey, it is conceivable that changing the magnitude of the drug stimulus would have led to differences in the effects of the shock intensities used in this report. Other investigators [11] have also suggested that in the design of a stimulus to effectively punish behavior maintained under fixed-ratio schedules of behavior, the magnitude of the reinforcing stimulus becomes a critical variable. Finally, the adaptation seen in this experiment may not develop when responding is maintained by drugs other than cocaine or under other schedules of reinforcement or punishment. Obviously, variables such as these need to be systematically investigated to further clarify the effects of punishment on drug-maintained responding.

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