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Effects of Phencyclidine on Aggressive Behavior in Squirrel Monkeys

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EMLEY, G. S. AND R. R. HUTCHINSON. *Effects of phencyclidine on aggressive behavior in squirrel monkeys.* PHARMACOL BIOCHEM BEHAV **18**(2) 163–166, 1983.—Effects of phencyclidine (PCP) on shock-induced and spontaneous aggression in the squirrel monkey were determined. The delivery of response-independent, fixed-time (4', S-S interval) electric shock to the tail of a restrained squirrel monkey generated post-shock, hose-bite attack responses and pre-shock lever press non-attack responses. In a separate procedure shock was not delivered and spontaneous aggression responses were measured. A PCP dose response function (0.01–1.0 mg/kg SC) was determined for each procedure. In the shock-induced aggression procedure initial increases in attack were observed but upon a second determination of the dose effect curve this effect decreased and an increase in non-attack was noted. PCP produced increases in non-attack responding at high dosages in the spontaneous aggression procedure.

Phencyclidine Aggression Fixed-time shock Hose bites Lever press Squirrel monkey

PHENCYCLIDINE, an anesthetic introduced in the 1950's, was discovered to produce bizarre psychomotor disturbances and violence in humans upon emergence from the anesthesia [11]. The drug has been used recreationally and because of the unpredictable outbursts of violence and aggression produced in users, such practice has become a topic of public concern [9,15]. Laboratory research on the effects of PCP on aggression has been limited.

Effects of PCP on isolation-induced aggression in mice and muricide in rats have been reported [12]. The low dose (1.0 mg/kg) blocked aggression after 14 days of isolation but only slightly inhibited aggression after 28 days of isolation. The high dose (5.0 mg/kg) increased aggression; although, this effect was smaller at the longer isolation period. No significant effects were reported on muricide; although, at the 5.0 mg/kg dose there was a tendency toward decreased mouse killing. Effects of phencyclidine on resident mice in the resident-intruder aggression procedure have also been reported [1]. The low dose (1.0 mg/kg) increased attack bites. The high dose (3.0 mg/kg) produced no change in attack bites. The results of these studies are inconsistent and procedural differences make comparisons difficult.

PCP has been studied on shock-elicited fighting in paired rats and shock-elicited target-biting and panel pressing in individual rats [15]. Results demonstrate a dose-dependent (0.5–2.0 mg/kg) decrease in paired fighting, a dose-dependent (0.25–2.0 mg/kg) decrease in target biting and a dose-dependent increase in panel pressing in individual rats.

Phenyclcidine has been observed to produce species-specific effects of excitation of gross motor behavior in rodents but calming in primates [4]. Therefore caution must be used in generalizing to other species.

The present experiment studied effects of PCP on aggression in the squirrel monkey. The response-independent, fixed-time presentation of tail shock generates post-shock hose biting and pre-shock lever pressing. These two responses, temporally and topographically distinct, have been shown to measure aggression and discriminative pre-noxious stimulus activation related to escape/avoidance processes [7]. The functional relations between environmental conditions and aggression in this paradigm have been preliminarily demonstrated to be the same functional processes responsible for human aggression [7,8]. Phencyclidine was tested on the shock-elicited aggression procedure and on a spontaneous aggression procedure in which electric shock was not delivered. A dose response function was determined for four squirrel monkey subjects in each procedure.

METHOD

Subjects

Subjects were eight male, adult squirrel monkeys (*Saimiri sciureus*) weighing 750–1100 g. Subjects were housed individually in a large temperature and illumination controlled colony, had free access to fluids, and were fed ad lib fruit and Wayne monkey diet.

Apparatus

A primate restraint chiar (Plas Labs, Lansing, MI) equipped with brass tail electrodes [6], a response lever, and a latex rubber bite hose, calibrated to record only bites, mounted on the front panel was used. The restraint chair was enclosed in a sound attenuating, ventilated chamber.

Procedure

During each 64 minute experimental session, 15 electric tail shocks (200 msec 400 V AC) were delivered under a four minute, fixed-time, response-independent schedule. The shocks were delivered through the brass tail electrodes resting on the shaved and cleansed distal portion of the tail. Four of the subjects were run in a "no shock" condition in which

shock was not delivered. Hose bites and lever responses were recorded on cumulative recorders and counters located in an adjacent room.

Drug Administration

All injections were given subcutaneously in a constant volume of 0.5 cc 30 minutes prior to the experimental session. Phencyclidine (PCP) was administered in a mixed order of dosages (0.1–1.0 mg/kg) on Wednesday of the experimental week. Following the establishment of the dose response function each dosage was replicated. Phencyclidine hydrochloride was supplied by the National Insttitue on Drug Abuse. Saline control injections were given on the other days of the experimental week.

Data Analysis

Average bite and lever press responses and standard error of the mean were calculated for each saline control baseline. For each drug dosage a percent change from the immediately preceding four day saline control was calculated. A *t* test for determining the significance of a discrepancy between one observation and the sample mean was computed [16]. Since few responses were recorded on control days on the spontaneous aggression procedure any large increase or decrease in responding would result in an extraordinarily large percent change and not fairly represent the results. Therefore the difference from the immediately preceding saline control was calculated.

RESULTS

The fixed-time, response-independent shock delivery schedule generated post-shock hose bites and pre-shock lever responses. Only occasional responses were recorded on the "no shock" spontaneous aggression procedure.

Figure 1 illustrates the results on four monkeys on the shock elicitation procedure. Across the dosages tested (0.01–0.4 mg/kg) during the first dose effect determination three of the four subjects show a consistent or episodic increase in biting. Upon replication of the dose effect function all four subjects demonstrate a decrease in this effect and an increase in lever press responses. Table 1 presents the statistical significance of the drug effects. Some significant tests would be expected by chance but the large number of significant results (40% of all *t*'s significant at <0.05) and the trends observed in the dose response curves lend confidence in these data. Figure 2 presents cumulative records of bite responding on saline control and on the first administration of 0.4 mg/kg PCP for two subjects. The bottom record of each pair illustrates bite responding during saline control conditions. For both MC-70 and MC-81 bite responding at 0.4 mg/kg PCP has a totally different temporal distribution than during control sessions. In the case of MC-70 biting is essentially continuous throughout the session.

Effects of PCP on spontaneous aggression are illustrated in Fig. 3. Few responses were recorded for these subjects, however at 0.4 and 1.0 mg/kg responding did increase during the experimental session.

DISCUSSION

Phencyclidine has unique effects on shock-elicited aggression. The dose response function is relatively flat until the high dosages (the welfare of the subjects prohibited increasing dosage further and continuing testing of the animals in a procedure which employs restraint). Although this disjunctive dose response function is unique when compared to other drugs tested in this procedure, it seems to be characteristic of phencyclidine as demonstrated by results reported by other investigators [2, 3, 10, 14, 17]. An additional unique feature of phencyclidine is the fact that subsequent drug testing did not produce similar responding to initial testing. In previous research in drug testing on this procedure in this laboratory a shift in responding has not been seen. This effect although unique to PCP in this testing paradigm may be characteristic of PCP and has been observed by other investigators using other testing procedures [13,14].

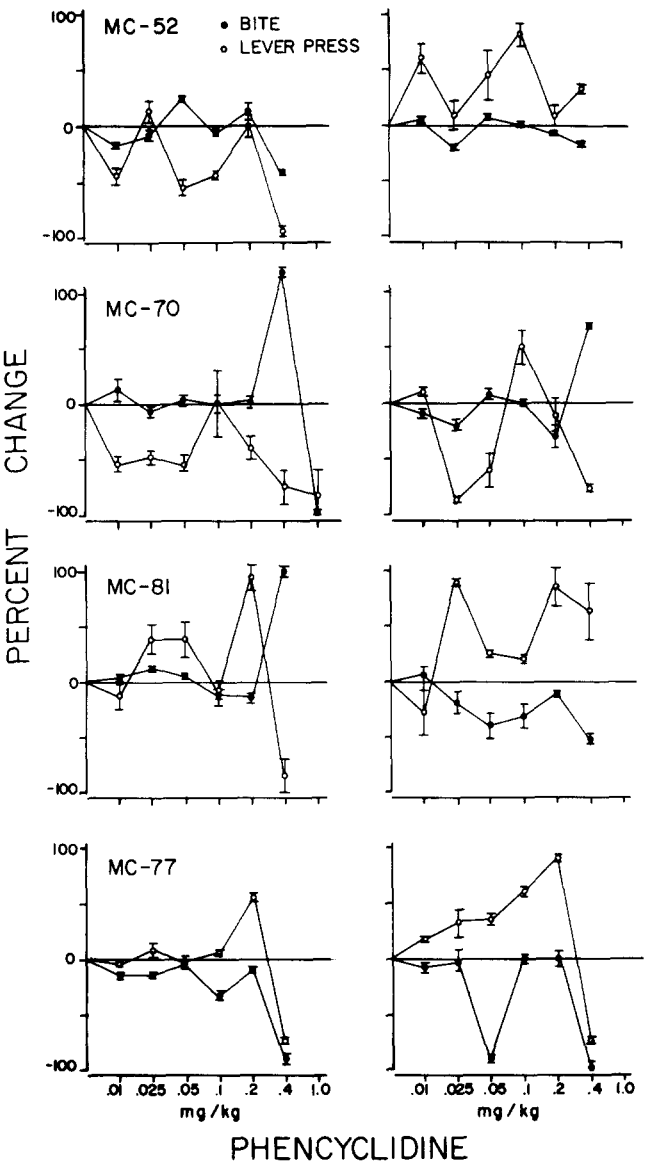

FIG. 1. Effect of PCP on bite and lever press responses for 4 squirrel monkeys on the fixed-time, response-independent shock schedule. Bites and lever presses are presented as the percent change from the immediately preceding saline control. The standard error of the mean for the control brackets the drug point. The initial dose-effect curve is on the left, the replication is on the right.

TABLE 1

RESULTS OF t-TESTS FOR EFFECTS OF PCP ON BITE AND LEVER RESPONDING FOR 4 SUBJECTS ON THE FIXED-SHOCK PROCEDURE

mg/kg		0.01	0.025	0.05	0.1	0.2	0.4	1.0
Bites								
MC-52	No. 1	<0.001		<0.01			<0.001	—
	No. 2		<0.02			<0.05		—
MC-70	No. 1						<0.001	<0.001
	No. 2		<0.05				<0.001	<0.001
MC-81	No. 1		<0.01				<0.01	—
	No. 2						<0.01	—
MC-77	No. 1	<0.05	<0.02		<0.01	<0.05	<0.01	—
	No. 2			<0.001			<0.01	—
Lever Presses								
MC-52	No. 1	<0.05		<0.02	<0.05		<0.01	—
	No. 2	<0.05			<0.01			—
MC-70	No. 1		<0.02				<0.001	—
	No. 2		<0.001	<0.05			<0.001	—
MC-81	No. 1					<0.01	<0.01	—
	No. 2							—
MC-77	No. 1					<0.01	<0.01	—
	No. 2	<0.05		<0.01	<0.001	<0.001	<0.01	—

Number 1 represents the first dose response curve.
Number 2 represents the second dose response curve.

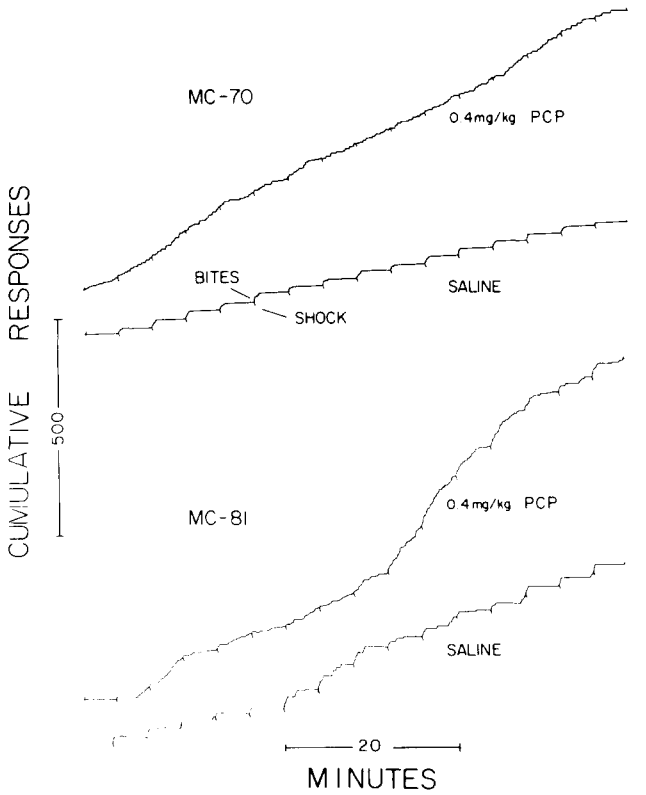

FIG. 2. Cumulative bite records for MC-70 and MC-81 at 0.4 mg/kg PCP. The bottom record of each pair is the record for the saline control day preceding 0.4 mg/kg drug day.

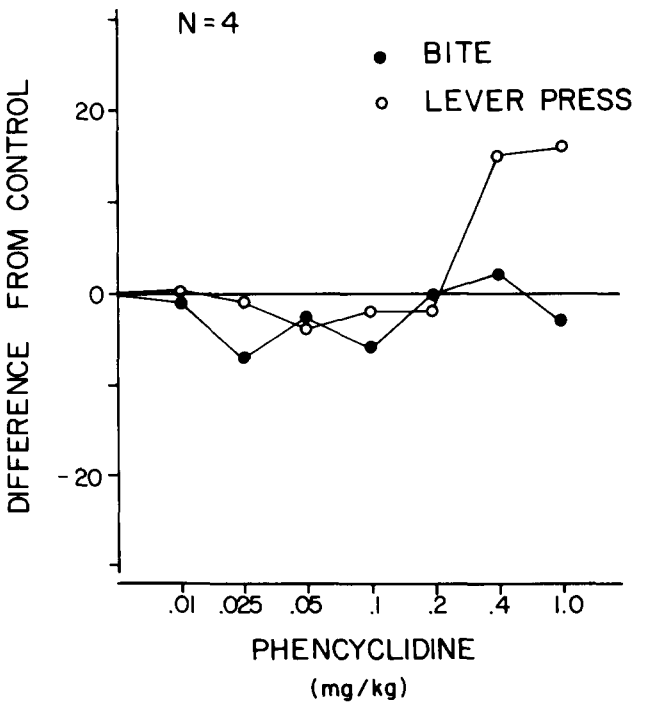

FIG. 3. Effect of PCP on bite and lever press responses for 4 squirrel monkeys on the spontaneous aggression procedure. Bites and lever presses are presented as the difference from saline control.

The effects of phencyclidine on aggression as reported previously [1, 5, 12] differ from the results reported in this experiment. Although changes in aggression with PCP have been reported, procedural differences as well as the species-specific effects of phencyclidine make comparisons between these studies difficult. Although a dose dependent decrease in target biting and an increase in panel pressing in individual rats has been reported [5] and is similar to the effects noted in the second dose effect curve in the present experiment, the temporal relationship to shock presentation of target bites and panel presses is not described such that a comparison between hose bites and lever presses of the present experiment can not be easily made.

The present finding that aggressive responding was increased more in a shock-elicited aggression procedure than in a spontaneous aggression procedure may be a reflection of basic processes as expressed in natural settings [15]. PCP intoxicated individuals, when kept in a deprived environment did not exhibit the aggressive-hyperexcitable effects, whereas, individuals in an environment such as a police station or party were sometimes triggered to aggressive reactions [15].

The results of this experiment demonstrate individual differences in response to phencyclidine, a difference in effect with repeated dosing and a difference in response when noxious stimuli are presented or not presented. The results from the current procedures correlate well with reports of human aggression and may be useful for further study of phencyclidine and other drugs.

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