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Drug Effects Under Automaintenance and Negative Automaintenance Procedures[1]

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POLING, A. AND J. B. APPEL. *Drug effects under automaintenance and negative automaintenance procedures.* PHARMAC. BIOCHEM. BEHAV. 9(3) 315–318, 1978.—Three food-deprived pigeons were initially exposed to an automaintenance procedure in which brief periods of response key illumination were followed by food delivery without regard to the subject's behavior. Keypecking occurred at a high rate while the key was illuminated and was reduced in dose-dependent fashion by acute administration of LSD (0.05–0.45 mg/kg), quipazine (1.0–8.0 mg/kg), haloperidol (0.08–0.32 mg/kg), and pentobarbital (4.0–16.0 mg/kg). The animals were then exposed to a negative automaintenance procedure in which food delivery followed key illumination only if the lighted key was not contacted. Keypecking occurred at a low rate under this procedure, with no responses occurring during the majority of key illuminations and was decreased or unaffected by LSD, quipazine, and haloperidol; pentobarbital increased responding at doses of 4.0 mg/kg and 8.0 mg/kg and reduced responding at a dose of 16.0 mg/kg.

Automaintenance Negative automaintenance LSD Quipazine Haloperidol Pentobarbital Keypeck Pigeons

IF a food-deprived pigeon is occasionally presented with food preceded by illumination of a response key, keypecking is reliably engendered and maintained despite the lack of any programmed dependency between key-pecking and food delivery or key illumination (e.g., [5, 9, 18, 19]). Such automaintained keypecking, which is known to differ from operant keypecking in both topography [11] and duration [20], seems to occur at a high rate [11,18] and, probably as a consequence of this rate, is reduced by acute administration of the CNS stimulant *d*-amphetamine [18]. The effects of other compounds under this procedure have not, however, been reported. Thus the present study analyzed the effects of two psychotomimetic agents [23], LSD (0.05–0.45 mg/kg) and quipazine (1.0–8.0 mg/kg), the neuroleptic haloperidol (0.08–0.32 mg/kg), and the barbiturate sedative pentobarbital (4.0–16.0 mg/kg). Within these dose ranges, each of these compounds, like *d*-amphetamine, has been reported to reduce high-rate responding [1, 8, 16, 21] and therefore might also be expected to reduce automaintained responding. Two psychotomimetics were administered since recent investigations (e.g., [16,23] have indicated LSD and quipazine to have similar discriminative properties, to affect schedule-controlled behavior similarly, and to have similar pharmacological mechanisms of action; the present study assessed whether the compounds would also produce similar effects under an automaintenance (respondent conditioning) procedure.

A second part of the experiment was concerned with the effects of these drugs on behavior under a negative automaintenance procedure. In this procedure, food follows key illumination unless the lighted key is contacted; if a contact response occurs, food is not delivered. Depending on specific experimental parameters, responding may (e.g., [24]) or may not (e.g., [10]) be well maintained. In nearly all cases permitting comparison, however, responding occurs less frequently under a negative automaintenance procedure than under an automaintenance procedure.

The negative automaintenance procedure involves responding which appears to be evoked by respondent conditioning and suppressed by an operant contingency [2, 13, 17]. This operant contingency is paradigmatically negative punishment: response-dependent nondelivery (or, removal) of a stimulus results in a decrease in the probability of responding. Responding suppressed by positive punishment (i.e., response-dependent delivery of a stimulus) has been useful in selectively classifying drugs [14]. However, drug effects under negative punishment procedures have seldom been evaluated and it is not clear whether procedures involving negative punishment are useful for demonstrating selective drug effects, or whether drug effects under positive and negative punishment procedures are similar. Poling and Appel [15] did report that drug effects under a negative automaintenance procedure were similar to those found under procedures involving response-dependent electric

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shock punishment: atropine, d-amphetamine, and morphine reduced, while diazepam increased, rate of keypecking. If drug effects under negative automaintenance and other punishment procedures are in fact similar, it might be expected that appropriate doses of pentobarbital, but not of LSD, quipazine, or haloperidol, would increase responding under a negative automaintenance procedure, since responding suppressed by electric shock is generally increased by barbiturates (and other antianxiety agents) but not by these other compounds [21].

METHOD

Animals

Three experimentally-naive adult male White Carneaux pigeons were used. They were maintained at approximately 85% of free-feeding weights.

Apparatus

Two BRS/LVE (Model 143–05) operant conditioning chambers were used. Each was equipped with a 2.5 cm diameter response key horizontally centered 24 cm above the floor. Key illumination was provided by a 7 W red bulb located behind the key. Key operation required a force of approximately 0.05 N. A 15 W white houselight provided continual ambient illumination. The grain magazine, filled with mixed grain, was located below the response key. A 7 W white bulb illuminated the magazine opening when the magazine was raised. Electromechanical and solid state programming equipment was located in a room adjacent to the chambers.

Procedure

Animals were initially magazine trained for ten 60-min sessions during which the grain magazine was presented every 45 sec for a duration of 4 sec. After magazine training, each animal was exposed to a fixed trial autoshaping (automaintenance after acquisition) procedure similar to that described by Brown and Jenkins [5]. The response key was darkened during a variable intertrial interval (mean=30 sec; range=10–120 sec) and then illuminated for a 10-sec trial. At the offset of key illumination the magazine was raised and illuminated for 4 sec independently of the animal's behavior. Keypecks during each trial and intertrial interval were recorded separately. Each daily session terminated after 32 trial presentations. Sessions were typically conducted 7 days a week at about the same time each day.

After 5 sessions of relatively stable trial responding as indicated by no graphically-obvious trend in mean response rate across sessions (post hoc analyses indicated that in all instances where this stability criterion was used the mean response rate during sessions, N, N+1, and N+2 was within ± 5% of the mean response rate during sessions N+2, N+3, and N+4), an injection regimen was begun in which animals received an intramuscular injection of isotonic saline (1.0 ml/kg), LSD (0.05, 0.15, or 0.45 mg/kg), quipazine (1.0, 4.0, or 8.0 mg/kg), haloperidol (0.08, 0.16, or 0.32 mg/kg), or sodium pentobarbital (4.0, 8.0, or 16.0 mg/kg) 15 min prior to each session. LSD, quipazine, and haloperidol were dissolved in 0.9% sodium chloride solution prepared so that the volume injected was always 1 ml/kg of body weight. A commercially-prepared sodium pentobarbital injection (Lilly), diluted with distilled water to a 1 ml/kg injection volume, was used. Drugs were given prior to every fifth session, with sodium chloride injections preceding all other sessions. Each animal received each drug dose twice, in an irregular order.

Following the final drug session, all animals were exposed to a negative automaintenance procedure. This procedure was identical to the automaintenance procedure with one exception: food delivery followed only those key illuminations (trials) in which responding did not occur. Thus keypecking prevented food delivery although it did not affect key illumination or forthcoming trial presentations. The negative automaintenance procedure was in effect until the mean response rate showed no graphically-obvious trend across 5 consecutive sessions. At that time, an injection regimen similar to the one described above was instituted. However, due to a fire which rendered our laboratory inoperable, bird P-111 received each dose of LSD on only one occasion, P-273 received each dose of haloperidol on one occasion, and P-817 received each dose of pentobarbital on one occasion.

RESULTS

For the combined data of all birds, one-way repeated-measures analysis of variance [12] indicated that response rate and percentage of trials with responding did not vary significantly ($p>0.05$) across the blocks of five saline control sessions that immediately preceded drug injections under either the automaintenance or negative automaintenance procedures; post hoc analyses (above) also indicated no trend toward increased or decreased response rates across blocks of control sessions. Further, under both procedures, there was no significant difference (Dunn's procedure, $p>0.05$; [12]) between the rate of responding or the percentage of trials with responding during the first and second administration of a particular drug dose, regardless of whether the comparison was made across all drugs and doses, all doses of a single drug, or a single dose of a particular drug. Thus data are presented as a simple comparison of response rate and percentage of trials with responding during the saline control sessions immediately preceding drug administrations and these measures during drug sessions; to facilitate comparison, both administrations of a given drug dose are combined, as are all saline control sessions. Following saline, animals responded during virtually all (over 90% of) trials under the automaintenance procedure; no responding occurred during most (over 75% of) trials under the negative automaintenance procedure (Fig. 1). For all pigeons, the mean control response rate during trials in which pecking occurred was also much higher under the automaintenance procedure (over 1.2 responses/second) than under the negative automaintenance procedure (less than 0.2 response/second) as shown in Fig. 2.

Under the automaintenance procedure, all doses of LSD, quipazine, haloperidol, and pentobarbital decreased both the percentage of trials (Fig. 1) during which responding occurred and the mean response rate during such trials (Fig. 2). The magnitudes of these decreases were generally directly related to dose.

Under the negative automaintenance procedure, the 4 mg/kg and 8 mg/kg doses of pentobarbital increased both the percentage of trials with responding (Fig. 1) and the mean response rate during such trials (Fig. 2), while the 16 mg/kg dose decreased both of these measures relative to saline control values. Neither LSD, quipazine, nor haloperidol had any clear effects on responding under a negative auto-

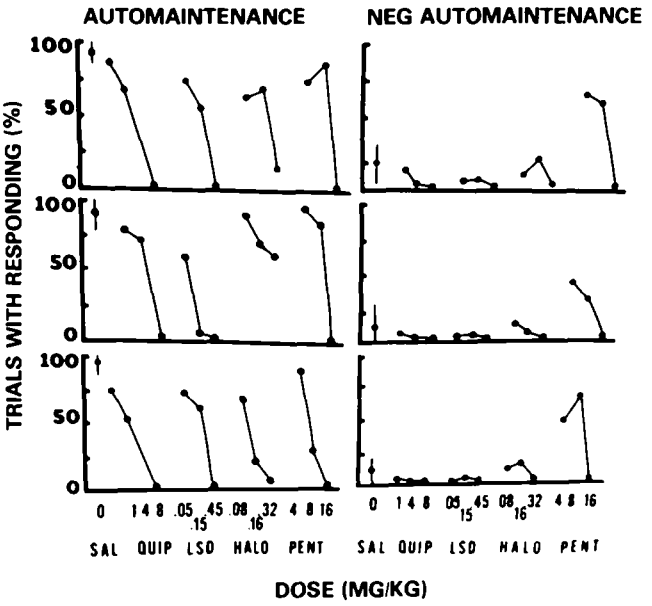

FIG. 1. Percentage of key illuminations (trials) in which responding occurred under all experimental conditions. With the exceptions described in text, each bird received each drug dose twice and saline injections preceded all other sessions. Each saline control point represents the control sessions which immediately preceded drug injections (24 sessions under the automaintenance condition, 21 sessions under the negative automaintenance condition); the vertical lines represent the range across individual control sessions.

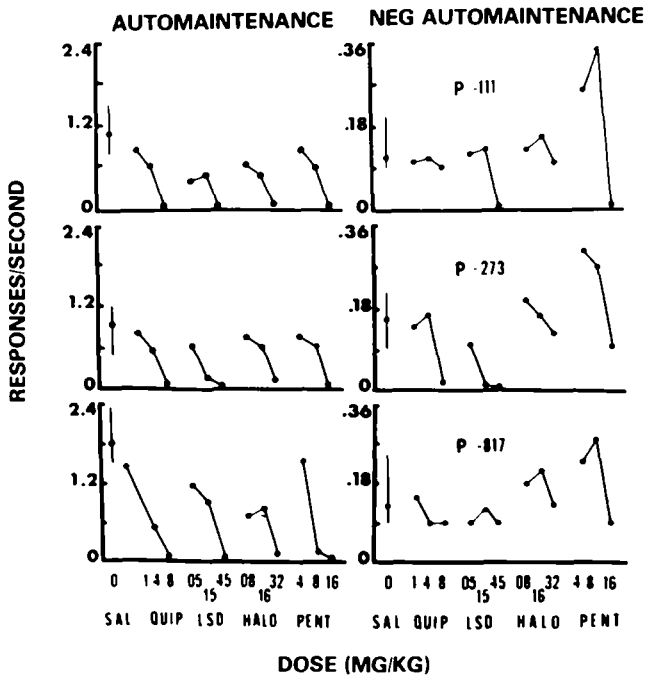

FIG. 2. Response rates of each animal during all experimental conditions. Rates represent only those key illuminations (trials) in which responding occurred. Thus the lowest possible rate is 0.10 responses/second (1 response/10 seconds). Each saline control point represents the control sessions which immediately preceded drug injections (24 sessions under the automaintenance condition, 21 sessions under the negative automaintenance condition); the vertical lines represent the range across individual control sessions.

maintenance procedure, although the higher doses of each of these compounds seemed to decrease responding to below the control level, which was in itself quite low.

DISCUSSION

The fact that pecking was reliably maintained under an automaintenance procedure is consistent with many earlier studies (e.g., [5, 9, 19]). That the negative automaintenance procedure strongly reduced the frequency of responding is also consistent with many earlier reports (e.g., [10, 13, 15, 17]), although some studies (e.g., [22,24]) have found responding to be little suppressed by the institution of this procedure. Griffin and Rashotte [7] have demonstrated that the effects of negative automaintenance may depend critically on the specific experimental parameters employed.

All doses of LSD, quipazine, haloperidol, and pentobarbital decreased the relative frequency of responding under the automaintenance procedure. Despite different pharmacological mechanisms of actions, psychotomimetics (LSD, quipazine), neuroleptics (haloperidol), and barbiturate sedatives (pentobarbital) previously have been demonstrated to decrease responding maintained by operant reinforcement schedules at overall rates similar to those maintained under the automaintenance procedure of the present study [1, 8, 16, 21]. Thus, their ability to reduce the frequency of responding under an automaintenance procedure is not surprising: most behaviorally-active compounds reduce responding occurring at a high rate irrespective of the conditions under which such responding is maintained (see [6]).

Under the negative automaintenance procedure, LSD, quipazine, and haloperidol decreased or had no obvious effect on the relative frequency of responding. However, since little responding occurred during nondrug sessions under this procedure, drug-induced decreases in responding would not be readily apparent. This floor effect may have contributed to the apparent lack of effect of certain doses of LSD, quipazine, and haloperidol, and it would be interesting to determine the effects of these compounds under a negative automaintenance procedure in which a higher frequency of responding occurred.

In contrast to these drugs, the lower (4 mg/kg and 8 mg/kg) doses of pentobarbital increased the relative frequency of responding. The 16 mg/kg dose of this compound generally incapacitated the birds (i.e., they adopted a hunched, ruffled posture and did not fly when dropped), and thus little or no responding could occur.

At doses comparable to those used in the present study, LSD, quipazine, haloperidol, and pentobarbital have been found to increase responding maintained by operant reinforcement schedules at low rates similar to those which occurred under the negative automaintenance procedure [1, 8, 16, 21]. All of these drugs therefore might be expected to increase responding under the negative automaintenance procedure. However, an earlier study [15] reported that diazepam, but not d-amphetamine, atropine, or morphine increased responding under a negative automaintenance procedure. Each of these compounds, like those used in the present study, increases low-rate operant responding. Diazepam, but not d-amphetamine, atropine, or morphine, also generally increases operant responding suppressed by response-dependent electric shock [21]. Thus, across several drug classes, drug effects under a negative automaintenance procedure resembled those reported under more conventional punishment procedures. This was also the case in the

current study, since pentobarbital regularly increases responding suppressed by response-dependent shock delivery, while LSD, quipazine, and haloperidol have not been reported to have such effects [21]. Since the negative automaintenance procedure is in fact a negative punishment procedure (above), the general similarity between drug effects under this procedure and other punishment procedures raises no obvious conceptual difficulties, even though drug effects under positive and negative punishment procedures are not always similar [4].

However, it must be emphasized that the extent of the similarities between drug effects on responding suppressed by negative automaintenance and other punishment procedures remains to be determined. Previous research has compellingly demonstrated that drug effects on responding suppressed by punishment are far from simple. For example, while amphetamines generally decrease responding punished by electric shock delivery, this effect can be qualitatively reversed by altering shock intensity [14] or the behavioral history of the animal [3]. It is to be expected that drug effects under a negative automaintenance procedure are also modifiable, although the extent of this modifiability is presently unknown.

Data collected to this point do suggest that the negative automaintenance procedure, like other procedures that suppress responding [21] and unlike the automaintenance procedure, may be of value in differentiating the behavioral effects of diverse classes of drugs, since some but not all compounds increased responding under this procedure and those drugs which increased responding are those which generally increase (or disinhibit) responding suppressed by other procedures.

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