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Effects of Apomorphine on Punished and Unpunished Responding in the Rat

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McMILLAN, D. E. AND R. L. EVANS. *Effects of apomorphine on punished and unpunished responding in the rat.* PHARMACOL BIOCHEM BEHAV **30**(3) 753–754, 1988.—Apomorphine has been reported to increase shock-suppressed drinking, which suggests that it might have antianxiety activity. Because some drugs that increase shock-suppressed drinking are not active in other punishment procedures, the effects of apomorphine on punished and unpunished responding maintained by a multiple fixed-interval, fixed-interval schedule of food presentation were studied in rats. At doses from 3.125 to 100 μg/kg, apomorphine failed to increase punished or unpunished responding. In contrast, pentobarbital produced large increases in punished responding maintained by a fixed-interval schedule of food presentation.

Apomorphine Punished responding Unpunished responding Rats

THERE have been suggestions that dopaminergic mechanisms may be involved in the effects of some drugs on punished responding [3,5]. Recently, Hjorth *et al.* [1] reported that low doses of the dopamine agonist, apomorphine, increased rates of shock-suppressed drinking [6]. Because of concern about the specificity of this test [4], the effects of apomorphine were studied in rats under a multiple fixed-interval, fixed-interval punishment schedule under conditions matching those used by Hjorth *et al.* as closely as possible. Under this schedule, apomorphine failed to increase either punished or unpunished responding.

METHOD

Subjects

Five male rats of the Sprague-Dawley strain served as subjects. The rats weighed approximately 300 g at the beginning of the study, but were then reduced to 80% of this weight for the remainder of the experiments. The rats had water available freely in the home cage. Body weight was maintained by food pellets delivered during the experiments and by supplemental feeding in the home cage immediately after testing.

Procedure

Rats were trained to lever press in a Gerbrands test chamber to produce food pellets (90 mg Noyes pellets), after which they were gradually stabilized under a multiple fixed-interval, fixed-interval schedule (mult FI FI) of food presentation. During one 90-sec FI component only the houselight was on, while during the other 90-sec FI component a light above the key was turned on and a sonalert sound stimulus was added. If no responses occurred within 30 sec after either 90-sec FI elapsed, the schedule automatically switched to the other FI component. After responding stabilized under the mult FI FI, every 5th response during the component signalled by the sonalert and the key light produced a scrambled electric shock of 0.25 mA intensity and 100 msec duration scrambled across the grid floor. Punishment reduced rates of responding to about 25% of the rates seen during the nonpunishment component (see figure legends).

After responding stabilized under the mult FI FI with punishment schedule, two dose-effect curves were obtained for apomorphine. The effects of several doses of pentobarbital sodium were also determined. Apomorphine was prepared (apomorphine hydrochloride dissolved in 0.9% saline with abscorbic acid) and administered (subcutaneously) as specified by Hjorth *et al.* [1]. Injections were administered 10 min before a session of approximately 60 min in duration. Three rats received an ascending dosage series and two a descending dosage series. The entire dose-effect curve was determined once and then replicated. One rat was slow to develop baseline stabilization and was not used in the determination of the first dose-effect curve. After determination of the apomorphine dose-effect curves, sodium pentobarbital dissolved in 0.9% saline was administered 30 min before a session to establish that the procedure was sensitive to the effects of drugs known to increase punished responding. Drug injections were given on Tuesdays and Fridays. Saline control injections were given on Thursdays and were used to estimate baseline variability.

Because our 60-min test sessions were much longer than the 10-min sessions of Hjorth *et al.* [1], several months after completion of the studies described above, the experiments with apomorphine were repeated in the same rats using 10-min session durations which were initiated 10-min after injections.

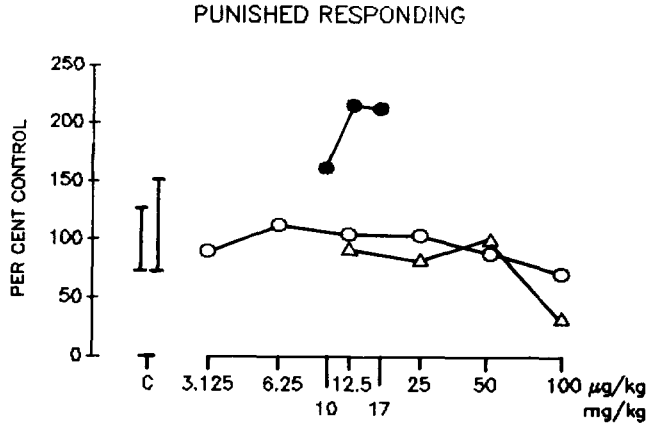

FIG. 1. Effects of apomorphine and pentobarbital on punished responding. Unfilled points represent means of duplicate observations in 5 rats receiving apomorphine before 60-min sessions, unfilled triangles represent means of single observations in these same rats for apomorphine effects during the 10-min sessions, and filled points represent means of single observations in the same rats receiving pentobarbital 10 min before the 60-min session. The first bracket represents the range of 15 determinations of the group mean on control days for the one-hour sessions and the second bracket represents the range of 9 determinations of the group mean on control days for 10-min sessions. The overall mean control rate of punished responding was 0.07 responses/second for 60-min sessions and 0.12 responses/second for 10-min sessions. Doses are μg/kg for apomorphine and mg/kg for pentobarbital.

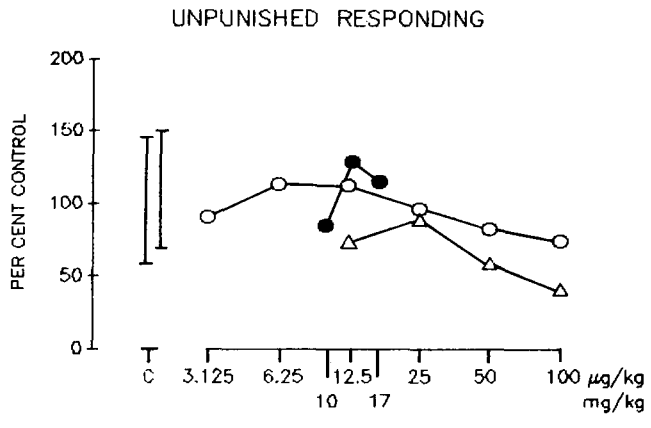

FIG. 2. Effects of apomorphine and pentobarbital on unpunished responding. Unfilled points represent means of duplicate observations in 5 rats receiving apomorphine before 60-min sessions, unfilled triangles represent means of single observations in these same rats for apomorphine effects during the 10-min sessions, and filled points represent means of single observations in the same 5 rats receiving pentobarbital 10 min before the 60-min sessions. Brackets represent the range of 15 determinations of the group mean on control days for the one-hour sessions and the second bracket represents the range of 9 determinations of the group mean on control days for 10-min sessions. The overall mean control rate of unpunished responding was 0.23 responses/second for 60-min sessions and 0.27 responses/second for 10-min sessions. Doses are μg/kg for apomorphine and mg/kg for pentobarbital.

RESULTS

Figure 1 shows the effects of apomorphine on punished responding. Across a range of doses from 3.125 to 100 μg/mg, apomorphine failed to increase punished responding (unfilled circles), either during the original observation or during the replication with shorter sessions (triangles). In contrast, all doses of pentobarbital produced clear increases in punished responding (filled circles).

Figure 2 shows similar data for unpunished responding. Apomorphine failed to increase unpunished responding across the dosage range studied at both session durations. Pentobarbital also failed to increase unpunished responding (triangles).

DISCUSSION

Apormorphine did not increase punished responding in the rats maintained under the mult FI FI with punishment schedule at the doses where Hjorth *et al.* [1] reported an increase in punished drinking. This was not because of a lack of sensitivity of the FI punishment baseline to drugs that increase punished responding, since pentobarbital produced clear increases in punished responding. Procedural differences between the present study and that of Hjorth *et al.* [1], such as the presence of a nonpunishment component and the use of intermittent punishment in the present study, may have contributed to the differential findings in the two studies, although such differences have not previously been shown to be important determinants of whether or not drugs increase punished responding [2].

As Seppinwall [4] has pointed out, a number of drugs that increase punished drinking (e.g., buspirone, tracazolate and PK 9084) are inactive or weak in increasing shock suppressed lever pressing in rats. Apomorphine may fall into this class of drugs.

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