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BRIEF COMMUNICATION

The Effects of Apomorphine on Leverpress Shock Escape Learning in Rats[1]

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MATTINGLY, B. A. *The effects of apomorphine on leverpress shock escape learning in rats.* PHARMACOL BIOCHEM BEHAV 25(3)693–695, 1986.—Four groups of rats (n=10 each) were tested on a discrete trial leverpress shock escape task 15 min following an intraperitoneal injection of either 0 (saline), 0.5, 1.0, or 2.0 mg/kg apomorphine hydrochloride. The results indicated that all doses of apomorphine produced a severe disruption in escape performance. This disruption was temporary, however, as all apomorphine groups were responding as quickly as the saline control rats by the end of the training session. A comparison of the effects of apomorphine with the previously reported effects of scopolamine and septal lesions on shock escape learning revealed both similarities and differences. These findings suggest that a septal lesion-induced reduction of acetylcholine levels does not simply "unleash" an antagonistic dopaminergic system.

Rats Shock escape learning Apomorphine Dopaminergic mechanisms Scopolamine Cholinergic mechanisms Septal lesions Acetylcholine Dopamine Acetylcholine-dopamine balance

FOLLOWING septal damage there is a significant reduction in the levels of several forebrain neurotransmitters (see [3,9]). Over the past few years we have been studying the potential involvement of these secondary neurochemical changes in the behavioral effects of septal lesions in certain aversive learning tasks [4–7]. We have found, for example, that the cholinergic antagonist, scopolamine, but not methyl-scopolamine, produces a disruption in discrete trial leverpress shock escape learning very similar to that produced by septal lesions [4]. In contrast, a depletion of brain serotonin produced by para-chlorophenylalanine (PCPA) does not affect the performance of rats on a leverpress shock escape task [6]. Likewise, increasing brain serotonin levels via 5-hydroxytryptophan does not affect the shock escape performance of either normal or septally-lesioned rats [6]. Hence, these findings suggest that a lesion-induced reduction in brain acetylcholine, but not serotonin, levels may be involved in the deficient shock escape performance of rats with septal lesions.

Although our previous studies suggest the involvement of cholinergic mechanisms, because of the interaction among various neurotransmitters in many central "pathways," many neurotransmitters probably play some functional role in any complex response pattern of the organism. For example, in some areas of the brain (e.g., striatum), acetylcholine and dopamine have been found to function in precise balance such that decreasing the activity of one has more or less the same effect as increasing the activity of the other (see [1] for review). Moreover, recent evidence has been presented supporting a cholinergic-dopaminergic interaction in various limbic structures including the septum (e.g., [8]). It is possible, therefore, that the disruption of shock escape learning produced by scopolamine and septal lesions may be the result of an imbalance between acetylcholine-dopamine mechanisms. If so, then increasing dopaminergic activity should have an effect on leverpress shock escape performance in rats similar to that produced by decreasing acetylcholine activity with scopolamine or septal lesions. The purpose of the present study, therefore, was to determine whether the leverpress shock escape performance of rats would be disrupted by a drug-induced facilitation of dopaminergic activity. Consequently, groups of rats were injected with either saline (control) or the central dopaminergic agonist, apomorphine (0.5, 1.0, or 2.0 mg/kg) and then tested on a discrete trial leverpress shock escape task.

METHOD

Subjects

Forty male Wistar albino rats were experimentally naive and approximately 90 days old on the day of testing. All rats were housed individually and maintained on ad lib food and water. A 12 hour light-dark cycle was held constant throughout the experiment.

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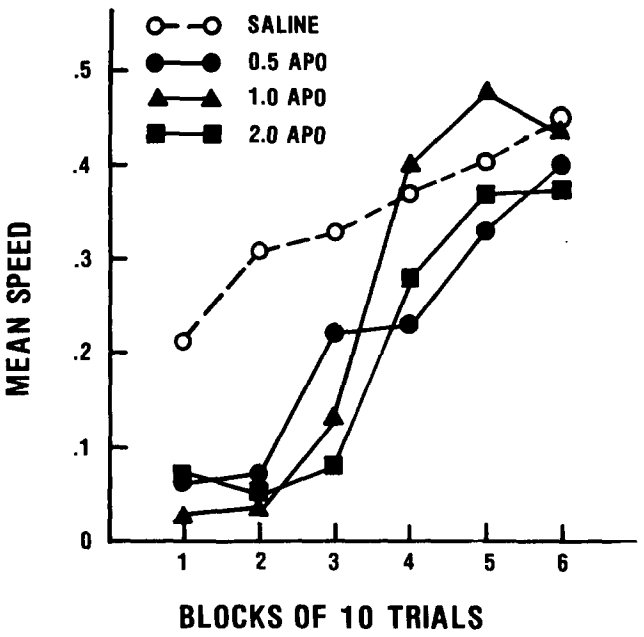

FIG. 1. Mean speed scores (1/(latency+1)) for the four groups across blocks of 10 escape trials.

Apparatus

Behavioral testing was conducted in two Grason-Stadler operant conditioning chambers (Model IIII) housed individually in sound attenuated research chests. These chambers had grid floors, and a house light (GE 1820) and response lever mounted on one wall. Grason-Stadler constant current shock generators (Model 700) equipped with grid scramblers were used to deliver footshock.

Design and Procedure

Prior to initiation of testing, the rats were randomly assigned, in equal numbers, to one of four drug condition groups. Three groups were injected intraperitoneally (IP) with doses of 0.5, 1.0, or 2.0 mg/kg of apomorphine hydrochloride and the fourth group was injected IP with an equivalent volume of the saline vehicle. All injections were given 15 min before the shock escape training session. All doses were calculated based on the salt weight of the drug and dissolved in isotonic saline just prior to administration. Also, all doses were administered in a volume of 1 ml/kg and treatment conditions were coded so that group assignments were unknown to the experimenter during injection and testing procedures. Following the injection all rats were returned to their home cage.

Shock escape training was initiated 15 minutes following the drug injection. In the test session, the rat was placed into one of the chambers and 90 sec later a 1.0 mA footshock was delivered to the grid floor. This shock continued for 1 min or until the rat pressed the lever. The shock trials were separated by 90 sec intervals and the test session consisted of 60 discrete shock escape trials. During the test session, response latencies to the nearest 0.001 sec were recorded. These response latencies were converted to speed scores by adding the integer one to each latency (in sec) and then taking the reciprocal (i.e., 1/(Latency+1)). This transformation prevents very short or very long latencies scores from making a disproportionate contribution to the mean performance scores. The possible range of transformed scores is from zero to one, with larger numerical scores representing faster speeds. Besides response latencies, the total number of leverpresses (barpresses) and the total amount of time the lever was depressed (bartime) during the session was recorded.

RESULTS

The mean speed scores for the four groups across six blocks of 10 shock escape trials are plotted in Fig. 1. As may be seen in this figure, the escape performance of the apomorphine-injected rats was severely disrupted across the first three trial blocks as compared to the saline-injected control rats. The apomorphine-injected rats, however, displayed a marked improvement in performance across the last three blocks and consequently, their performance differed little from the saline control rats on the final block of ten trials. An analysis of variance performed on these data revealed, as expected, a significant drug effect, $F(3,36)=3.64$, $p<0.05$, block effect, $F(5,180)=60.40$, $p<0.0001$, and also a significant Drug × Block interaction, $F(15,180)=3.52$, $p<0.0001$. Subsequent analysis of the Drug × Block interaction indicated that the three apomorphine groups responded significantly more slowly than the saline groups on the first two trial blocks, Newman-Keuls tests, $p<0.05$ in each case, but did not differ from each other, $p>0.05$ in each case. On trial block 3, the apomorphine groups again responded significantly more slowly than the saline groups, $p<0.05$ in each case, but the 0.5 mg/kg apomorphine rats responded significantly faster than the 2.0 mg/kg apomorphine rats, $p<0.05$. On trial block 4, only the 0.5 and 2.0 mg/kg apomorphine groups differed significantly from the saline group, $p<0.05$ in each case, and no significant differences in escape speed were found among the groups on the final two blocks of trials, $p>0.05$ in each case.

As might be expected from the speed score data, the apomorphine groups made significantly fewer leverpresses than did the saline group, $F(3,36)=3.34$, $p<0.05$. The three apomorphine groups, however, did not significantly differ from one another, Newman-Keuls tests, $p>0.05$ in each case. In contrast, the apomorphine groups did not significantly differ from the saline group in the total amount of time the lever was depressed during the session, $F(3,36)=1.68$, $p>0.05$. Consequently, the apomorphine rats displayed significantly more bartime per barpress than did the saline control rats, $F(3,36)=4.19$, $p<0.05$.

DISCUSSION

It is evident from these results that apomorphine produces a severe disruption in the leverpress shock escape performance of rats. This apomorphine-induced disruption in escape performance is similar to that produced by septal lesions [6] and scopolamine treatments [4]. These findings, therefore, are consistent with the view that the septal nuclei are involved in central dopamine-acetylcholine interactions (e.g., [2,8]). It should, of course, be recognized that since apomorphine in the present study and scopolamine in an earlier study [4] were administered systemically, it cannot be concluded that the similar behavioral effects of these two drugs are mediated exclusively by the septum. Moreover, a comparison of the incidental behaviors produced by apomorphine in the present study with those produced by

scopolamine and septal lesions in previous studies [4,6] suggests that the disruption in shock escape performance resulting from these three treatments may be related to different behavioral mechanisms. That is, previous studies of leverpress shock escape learning [4,6] have shown that "normal" rats learn to escape shock quickly by staying near the lever and holding it down during the intertrial intervals. Consequently, escape speed is usually directly related to the amount of time the lever is depressed (bartime). Rats with septal lesions [6] and scopolamine-treated rats [4], however, have difficulty remaining near the lever during the intertrial intervals, and therefore, display significantly less bartime and much slower escape latencies than do normal rats [4,6]. In contrast, apomorphine-treated rats did not differ from the saline control rats in bartime and actually held the lever down significantly longer per leverpress than the saline control rats. Thus, the slower escape responding of the apomorphine-treated rats, unlike scopolamine-treated and septally-lesioned rats, does not appear to be secondary to an inability to remain near or on the response lever during the intertrial intervals.

These differences in incidental behavior between apomorphine- and scopolamine-treated rats suggest that acetylcholine and dopamine do not act in a reciprocally coordinated fashion with respect to shock escape learning. Moreover, these findings suggest that while a reduction in acetylcholine levels may be involved in the effects of septal lesions, a septal lesion-induced reduction of acetylcholine levels does not simply "unleash" an antagonistic dopaminergic system.

REFERENCES

1. Butcher, L. L. (Ed.) *Cholinergic-Monoaminergic Interactions in the Brain*. New York: Academic Press, 1978.
2. Carey, R. J. Septal lesions augment locomotor hyperactivity induced by amphetamine and not scopolamine. *Psychopharmacology (Berlin)* **76:** 96–97, 1982.
3. Gage, F. H., R. G. Thompson and J. J. Valdes. Endogenous norepinephrine and serotonin within the hippocampal formation during the development and recovery from septal hyperactivity. *Pharmacol Biochem Behav* **9:** 359–367, 1978.
4. Mattingly, B. A. Scopolamine disrupts leverpress shock escape learning in rats. *Pharmacol Biochem Behav* **24:** 1635–1638, 1986.
5. Mattingly, B. A., H. Chandler, E. B. Applegate and M. Brunelle. Activity during a conditioned aversive stimulus in rats treated with para-chlorophenylalanine. *Psychol Rec* **34:** 389–396, 1984.
6. Mattingly, B. A., J. E. Gotsick and E. B. Applegate. Serotonin, septal lesions, and shock escape learning in rats. *Psychol Rep* **59:** 3–9, 1986.
7. Mattingly, B. A., F. H. Osborne and J. E. Gotsick. Activity changes during a conditioned aversive stimulus in rats with septal lesions. *Physiol Behav* **22:** 521–525, 1979.
8. Megens, A. A. P. H. and A. R. Cools. Involvement of the septum in central dopamine-acetylcholine interactions in morphine-treated cats. *Pharmacol Biochem Behav* **18:** 761–767, 1983.
9. Sethy, V. H., M. J. Kuhar, R. A. Roth, M. H. VanWoert and G. K. Aghajanian. Cholinergic neurons: Effect of acute septal lesion on acetylcholine and choline content of rat hippocampus. *Brain Res* **55:** 481–484, 1973.