Spontaneous alternation and D-amphetamine

JOEL ADKINS, JAMES W. PACKWOOD, and GEORGE L. MARSHALL, JR.,
University of Oregon, Eugene, Oreg. 97403

Forty male rats were tested for spontaneous alternation in a T maze following doses of d-amphetamine sulfate, ranging from 1.0 to 4.0 mg/kg. Doses of 3.3 and 4.0 mg/kg significantly reduced alternation ($p < .005$), while doses of 2.0 mg/kg or less did not.

Spontaneous alternation, the choice of opposite alleys on successive trials by rats in a T maze, is commonly observed (see Dember & Fowler, 1958). Meyers & Domino (1964) found that the cholinergic blocking drug, scopolamine, reduces spontaneous alternation. Douglas & Isaacson (1966) confirmed this finding and suggested a parallel between the effects of anticholinergic drugs and removal of the hippocampus. Hippocampectomy also reduces spontaneous alternation (Roberts, Dember, & Brodwick, 1962; Douglas & Isaacson, 1964) and, in common with anticholinergic drugs, produces several other symptoms of perseverative responding (see Douglas, 1967; Douglas & Isaacson, 1964; Kimble, 1968).

Gerbrandt (1965) has proposed that there are two opposing neural systems involved in the control of behavioral responses. One is a "response release" system and is thought to include the ascending reticular activating system and associated structures. This first system is said to mediate well established, relatively prepotent responses. The other system, which includes the hippocampus and closely related forebrain limbic structures, is held to inhibit the first in situations requiring response suppression or "control," thus permitting behavioral flexibility in changing situations when the original response becomes inappropriate. Dysfunction of the second system releases the first from inhibition and therefore results in stereotyped and inflexible responding.

Several others also have proposed similar conceptions. Kimble (1968) has described the hippocampus as part of a system giving rise to Pavlovian internal inhibition and acting to inhibit the reticular system. McCleary (1966) also saw the limbic system as affecting response initiation and response inhibition. Douglas (1967) and Douglas & Pribram (1966) have proposed a more explicit model that involves modulation of recurrent and afferent inhibition. The

hippocampus is said to act as an "error detector" that suppresses attention to nonreinforced cues.

It has also been proposed that the two systems are chemically coded, involving different predominant neural transmitter substances (Carlton, 1963; Gerbrandt, 1965). The forebrain inhibitory system may contain a crucial cholinergic link, while the activating system may be mediated at least in part by one or more of the catecholamines—dopamine, adrenalin, and noradrenalin. Therefore, the two systems should be subject to predictable biasing by agents which affect either acetylcholine or the catecholamines. Of specific interest here, similar behavioral effects should result from *facilitating* the catecholaminergic system as from *blocking* the cholinergic system. Dextro-amphetamine apparently mimics the action of one or more of the catecholamines (Goodman & Gilman, 1965) and may act on the reticular activating system (Bradley, 1958). Therefore, it should have similar effects as anticholinergic drugs. Carlton (1961, 1963), in fact, has reported that either scopolamine or d-amphetamine interfered with the performance of a rewarded alternating bar-press task. Since Meyers & Domino (1964) and Douglas & Isaacson (1966) have already extended the finding with scopolamine to spontaneous alternation in a T maze, the present study was done to determine whether d-amphetamine also reduces spontaneous alternation.

METHOD

Forty male albino rats, 4-6 months old, were used. They were raised in the University of Oregon psychology department animal facilities.

The T maze used for testing spontaneous alternation was painted a medium gray and was of approximately the following dimensions: length of stem and goal arms, 24 in.; alley width, 5 in.; height, 6 in. There were Plexiglas guillotine doors between a start box and the stem and between the choice point and each goal arm.

The testing procedure was as follows: S was placed in the start box for 10 sec and all the doors then were raised. When S's whole

body had entered a goal arm, the door was lowered behind it. After about 20 sec in the goal box, S was removed by hand to the start box for the next trial. No reward was used and Ss were not deprived of food or water. All Ss were given three trials. A maximum of 5 min was permitted for each trial. If an animal failed to enter a goal arm within that time, testing was discontinued. Ss earned alternation scores of 0, 1, or 2.

Animals in the drug groups were injected intraperitoneally with d-amphetamine sulfate and control animals were injected with an equivalent volume of physiological saline solution. All injections were done 30 min before testing.

Two experiments were done. In the first, 16 rats were divided into two groups and tested three times in sessions 1 week apart. In the first session, one group was injected with 1.0 mg/kg amphetamine and controls received saline. In the second session, the animals that had served as controls in the first session were injected with 2.0 mg/kg amphetamine while the erstwhile drug group was given saline. In the third session, the Ss were re-divided randomly into two groups. One group received 4.0 mg/kg amphetamine and the other was injected with saline.

In the second experiment, 24 new rats were divided into three groups. Two groups were injected with amphetamine, receiving doses of 1.67 and 3.3 mg/kg, respectively. The remaining group received saline solution. In this experiment, Ss were tested for spontaneous alternation on only 1 day.

RESULTS

The numbers and percentages of alternation for Ss in the first study are shown in Table 1. The alternation performance of the amphetamine groups that received 1.0 or 2.0 mg/kg clearly did not differ from control levels. The animals in the two drug groups, however, had fewer refusals to run, as shown by the greater number of completed trials: 32 as compared to 25 for control Ss. On the other hand, Ss in the 4.0 mg/kg group showed both a reduction in spontaneous alternation and in the number of trials completed. It should be noted, however, that the behavior on uncompleted trials was quite different for control animals and the Ss receiving high doses of amphetamine. Whereas the control animals tended to sit more or less passively, usually at the choice point, the drugged animals were unmistakably hyperactive, with a great deal of stereotyped rearing and

Table 1
Numbers and Percentages of Alternations in Study 1

	1.0*	2.0*	4.0*
Drug	12/16 (75.0%)	14/16 (87.5%)	2/9 (22.2%)
Saline	10/13 (76.9%)	10/12 (83.3%)	9/11 (81.8%)

* Doses of amphetamine in mg/kg

Table 2
Numbers and Percentages of Alternations in Study 2

Saline	Amphetamine	
	1.67 mg/kg	3.3 mg/kg
9/12 (75.0%)	11/15 (73.3%)	5/16 (31.3%)

sniffing at the top of the maze at the choice point.

Table 2 shows the results of the second experiment. As in the first study, there is little apparent effect of the lower doses of amphetamine. Again, there is a reduction of spontaneous alternation at the highest drug dose, but this time without an increase in uncompleted trials.

Since it was apparent from inspection of the data that the lower doses did not affect spontaneous alternation significantly, statistical tests were done only on the difference between the high drug groups and controls. The data from the 4.0 mg/kg group in the first study were combined with those from the 3.3 mg/kg group in the second study and tested against the corresponding control groups by a summed-ranks test. The difference was highly significant ($Z = 2.59$, $p < .005$).

DISCUSSION

The present results show that d-amphetamine in high doses reduces spontaneous alternation. The lack of effect of lower doses was unexpected since comparable doses are known to affect a number of behavioral tasks, including a bar-press task in which reward is contingent upon alternation between two bars (see Carlton, 1963). That the drug actually was systemically active in the present study is suggested by the improvement in the number of trials completed. Furthermore, observation showed a patent increase in sniffing and in locomotor activity in the drugged animals.

The finding that reduction in spontaneous alternation occurs following high doses of d-amphetamine is consistent with the hypothesis of two antagonistic neural systems, one mediated by acetylcholine and the other by the catecholamines. Facilitating a response-release system with d-amphetamine was expected to have behavioral effects similar to those reported for the blocking of a cholinergic response-control system with anticholinergic drugs. Our results thus complement those reported by Meyers & Domino (1964) and Douglas & Isaacson (1966). Unlike the latter study, however, both the one by Meyers and Domino and the present study found alternation rates reduced considerably below chance levels.

Douglas & Isaacson (1964) also found that another anticholinergic drug, atropine,

failed to inhibit alternation in doses of 0.4 or 1.2 mg/kg, as did scopolamine at the lower dose. Carlton (1963) has reported that amphetamine acts synergistically with both atropine and scopolamine in facilitating an avoidance response. It would be of interest to determine whether a similar synergism holds for spontaneous alternation.

The present study, together with those of Meyers & Domino (1964) and Douglas & Isaacson (1966), shows that centrally active drugs can significantly affect choice responses in a task where no specific drives or rewards are known to be present.

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Aversions to grape juice induced by apomorphine¹

KENNETH F. GREEN, *California State College at Long Beach, Long Beach, Calif. 90801*

To find if aversions could be conditioned to the unpalatable taste of grape juice, 12 rats of both sexes were trained to drink for 20 min a day, and, on 3 days, were given grape juice, followed immediately, or in 2 h, by apomorphine. Aversions were formed by all rats. Early injection produced stronger aversions, and sex appeared irrelevant.

Conditioned aversions to flavored foods have been obtained in rats when ingestion is followed by irradiation or by injection of toxic agents. The palatability of the food has appeared to be irrelevant because aversions have been conditioned to preferred flavors such as saccharin or salt, and also to nonpreferred flavors such as quinine or acid (Garcia, Green, & McGowan, in press). However, an exception to the palatability rule might be found with the nonpreferred flavor of grape juice. In experiments on the effects of novelty on the formation of aversions, Revusky & Bedarf (1967) and

Wittlin & Brookshire (1968) had difficulty obtaining aversions to grape juice when it was a novel taste: the former Es found a weak aversion in male rats after a single pairing of novel grape juice with irradiation; the latter Es found no aversion in female rats after three pairings of novel grape juice with injected apomorphine, an emetic agent.

The purpose of the present experiment was to find if an aversion could be conditioned to grape juice at all. Since rats of different sexes were used in the two previous experiments, sex was included as a variable. In addition, injections of apomorphine occurred immediately after drinking in one group, to allow comparison with Wittlin and Brookshire, and were delayed for 2 h in a second group, in order to allow comparison with the delayed irradiation of Revusky and Bedarf.

METHOD

Six male and six female pigmented rats from the psychology department animal facilities were 10 months old when conditioning began. The animals were adapted for more than a month to a schedule where water was available for 20 min each