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Dissociation of the Effects of Scopolamine and d-Amphetamine on a Spontaneous Alternation Task[1]

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KOKKINIDIS, L. AND H. ANISMAN. *Dissociation of the effects of scopolamine and d-amphetamine on a spontaneous alternation task.* PHARMAC. BIOCHEM. BEHAV. 5(3) 293–297, 1976. – The immediate and carry-over effects of scopolamine and d-amphetamine were evaluated in a free running Y-maze spontaneous alternation task. The immediate effect of scopolamine (1.0 mg/kg) or d-amphetamine (5.0 mg/kg) was to reduce alternation to chance or to levels significantly below chance (perseveration), respectively. On a second, non-drug test day alternation decreased in saline treated animals, but increased among mice which received scopolamine on Day 1. In contrast, upon retesting in the non-drug state, the performance of animals initially treated with d-amphetamine resembled that of saline treated mice. Subsequent experiments revealed that these effects could not be attributed to drug effects on peripheral mechanisms, memory consolidation, residual drug action or drug dissociated learning. It was concluded that the behavioral effects of scopolamine and d-amphetamine are qualitatively different. Whereas scopolamine disrupts habituation, d-amphetamine induces perseveration independently of any effects on habituation.

Scopolamine d-Amphetamine Spontaneous alternation Perseveration

IN the absence of response reinforcement, mice and rats permitted to explore a T or Y-maze tend to enter the least recently visited arm, i.e., the animals exhibit spontaneous alternation [2, 7, 9, 10]. Presumably, such behavior is a consequence of habituation to the most recently visited arm, thereby increasing the probability of the relatively novel arm being explored [7,19]. Consistent with such a position anticholinergics (antimuscarinics) which disrupt habituation [6,7] tend to reduce alternation to chance levels [3, 13, 14].

Drug-induced disruption of alternation is not limited to anticholinergics. For example, indirect catecholamine stimulation via d-amphetamine also attenuates alternation performance [1,3]. However, the behavior observed after d-amphetamine treatment is qualitatively different from that seen after administration of scopolamine. In particular, treatment with d-amphetamine results in perseveration, in that animals tend to visit successively the same two arms of the Y-maze [3]. In contrast, after treatment with scopolamine, arm entries occur on a random basis, resulting in chance level alternation. As such, "perseverative risk" is increased [10]; however, rarely do animals exhibit sequences of entries between only two arms of the Y-maze. Since scopolamine does not produce perseveration, even at very high doses, it is unlikely that the behavioral effects of the two drugs simply represent a quantitative difference. Rather, it may be the case that d-amphetamine induces perseverative behavior, quite apart from any effects on habituation.

One technique which may be useful in evaluating the effects of pharmacological treatments on habituation is a transfer paradigm, in which animals initially are tested in the drug state and then retested in the absence of drug treatments. For example, when water-deprived animals are placed into a test chamber containing a water bottle, it is observed typically that those animals pre-exposed to the test chamber (water bottle removed), now approach the water more quickly than naive (unexposed) animals [4, 7, 8]. Pre-exposure presumably resulted in the habituation of exploration or reduction of fear which ordinarily competes with the response of approaching the water source. Consequently, the latency to drink during the subsequent retest was reduced substantially. Predictably, if animals are treated with an anticholinergic during pre-exposure, then these animals subsequently behave like naive animals when tested in the nondrug state [4,7]. The anticholinergic likely attenuated the course of habituation, thereby maintaining the exploratory tendency. A transfer paradigm of this nature was employed to evaluate, and possibly differentiate between the effects of scopolamine and d-amphetamine on spontaneous alternation.

EXPERIMENT 1

Earlier work [19] as well as preliminary experiments in

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this laboratory has revealed that the alternation task is sensitive to the effects of habituation both between and within days. Specifically, within a session alternation declines from about 70% to 55%, whereas between two days the mean levels of alternation decline from approximately 65% to 55%. If a drug treatment attenuates habituation, then the between days decline in alternation should not be observed if animals were initially exposed to the Y-maze in the drug state. In Experiment 1 the carry-over effects of scopolamine and d-amphetamine were examined in free-running Y-maze alternation task. In addition, the peripherally acting agents methylscopolamine and p-hydroxyamphetamine were also employed to evaluate the role of the peripheral cholinergic and catecholaminergic systems.

METHOD

Animals

Twenty-five male and 25 female Swiss-Webster mice bred in our laboratories from stock originally procured from the Bio-Breeding laboratory served as test animals when 60–70 days of age. Mice were housed 3–5 per cage and permitted ad lib access to food and water. Testing was carried out during the light portion of a 12 hour light/dark cycle.

Apparatus

The apparatus consisted of a symmetrical black Plexiglas Y-maze with arms 9.0 cm long, 6.0 cm wide and 7.0 cm high, and covered with a clear Plexiglas roof. The floor of the apparatus consisted of 0.25 cm stainless steel rods spaced 1.0 cm apart. Each arm of the Y-maze had two sets of infrared photoelectric relays mounted in the side walls 1.50 cm above the floor. The first set of relays was positioned at the entrance of the arm while the second set was placed within the arm spaced 7.60 cm from the first. The photocells were wired such that a count, as measured by a deflection of one of three pens of an Esterline Angus recorder, was triggered only after both beams were broken. Once a count was recorded the second beam could not be triggered until the beam at the arm entrance was again broken. Thus the animal was required to enter the chamber at least half-way into the arm in order for an arm entry to be recorded. Each arm of the Y-maze could serve as either a start or goal arm. The apparatus was housed in an illuminated room.

Procedure

Animals were randomly assigned to 5 groups (n = 10/cell) and given intraperitoneal (IP) injections of either saline (10.0 ml/kg), scopolamine hydrobromide (1.0 mg/kg) or d-amphetamine sulfate (5.0 mg/kg). The doses of scopolamine and d-amphetamine were selected on the basis of earlier work in this laboratory [12] which revealed these to be optimal to elicit reduced alternation and perseveration, respectively. To determine whether the effects of scopolamine and d-amphetamine involved the central, as opposed to the peripheral actions of these drugs, 2 groups were treated with equimolar doses of the peripherally acting derivatives of these agents, namely scopolamine methylbromide (0.96 mg/kg) and p-hydroxyamphetamine hydrobromide (3.63 mg/kg). All compounds were dissolved in bacteriostatic water. Fifteen min after injection animals were placed in one arm of the Y-maze and the gate separating the arm from the remaining compartments was removed. The sequence of arm entries were recorded over a 15 min period. A response sequence on which animals entered the arm least recently visited was considered as an alternation (e.g., a sequence of arm entries in this case would be 1, 2, 3, or 1, 3, 2). Nonalternation was considered to be the case in which animals returned to the compartment they had been to most recently (e.g., 1, 2, 1, or 1, 3, 1). The proportion of alternation was computed by dividing the number of alternation by the total number of alternation plus nonalternation. Perseveration was defined as animals alternating at levels which were significantly below chance (50% given two choices). Twenty-four hr following the initial session, mice were tested in a similar manner. However, animals did not receive drug injections on the second day.

RESULTS AND DISCUSSION

The proportion of spontaneous alternations based on the mean proportion of individual alternations are shown in Fig. 1. Alternation data were analyzed through analysis of variance and Neuman Keuls multiple comparisons (α = 0.05) of the group means. In addition, χ^2 analysis of the group proportions were calculated to determine whether the levels of alternation differed from chance. Analysis of variance of the mean proportion of alternation yielded a significant Drug Treatment × Test Day interaction ($F(4,45) = 19.26$, $p<0.001$). In order to be consistent with previous work dealing with spontaneous alternation data, analysis are presented in the absence of arc sine transformations. However it should be noted that analysis of transformed data of Experiment 1 resulted in a Drug Treatment × Test Day interaction ($F(4,45) = 20.30$, $p<0.001$) which was comparable to that observed with the non-transformed data ($F(4,45) = 19.26$, $p<0.001$). Subsequent Newman Keuls multiple comparisons of the simple main effects revealed that Day 1 alternation performance among animals treated with scopolamine or d-amphetamine was significantly lower than that of animals which received saline, methylscopolamine or p-hydroxyamphetamine. Indeed, whereas alternation in the saline and peripheral control groups significantly exceeded chance (χ^2's(1) = 59.44, 51.40, 31.0, $p<0.01$), animals which received treatment with scopolamine or d-amphetamine alternated at levels which were significantly below chance (χ^2's(1) = 7.16, 59.88, $p<0.01$). The finding that perseverative behavior was observed following treatment with d-amphetamine is consistent with previous reports [3]; however, scopolamine typically was not observed to elicit perseveration (see also Experiment 2). Thus, it is likely that the particularly low levels of alternation observed in scopolamine treated animals was a spurious finding. It is noteworthy that in all 3 experiments reported there were not any apparent compartment preferences among scopolamine and amphetamine treated mice (range = .32–.35, .31–.36 and .30–.36 among saline, scopolamine and d-amphetamine groups, respectively). That is, while some animals primarily utilized two particular compartments during the course of a perseverative sequence, other mice employed a different pair of compartments. Moreover, even within animals, more often than not the arms used in the perseverative trains varied within the 15 min test session. Specifically, when the perseverative sequence was interrupted by entry into the relatively

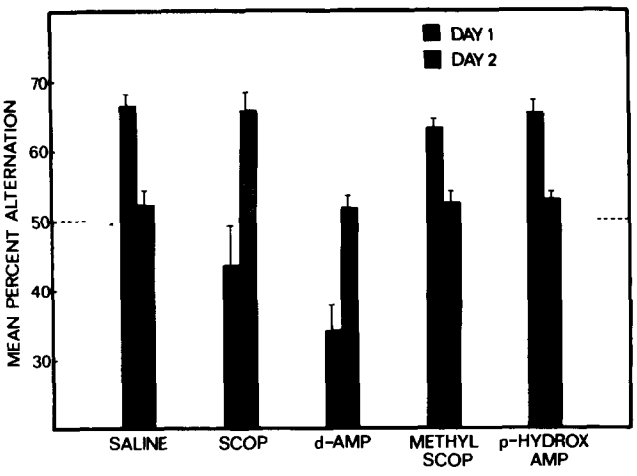

FIG. 1. Mean proportion of alternation responses (± SEM) over 2 consecutive days as a function of Drug treatment with either scopolamine, methylscopolamine, d-amphetamine or p-hydroxyamphetamine. Note: in all cases Day 2 performance was recorded in the nondrug state.

unexplored arm, this arm often was employed in a subsequent train of responses.

Turning to the Day 2 performance it was observed that in saline animals alternation declined significantly between days, although the level of alternation of the second test day exceeded chance ($\chi^2(1) = 5.56$, $p<0.05$). Presumably, habituation to the Y-maze during the initial test session resulted in a decreased tendency to explore novel arms upon subsequent retesting. When mice were initially tested after scopolamine treatment, alternation behavior on the second day was significantly greater than that seen in mice of the saline group, and in fact, alternation levels were well in excess of chance ($\chi^2(1) = 111.34$, $p<0.01$). It is likely that scopolamine attenuated the course of habituation on the initial day of testing, thus permitting high levels of alternation to be manifested upon retesting. In contrast to the effects of scopolamine, animals which received d-amphetamine, scopolamine methylbromide, or p-hydroxyamphetamine on Day 1 did not differ from the saline controls on the second day of testing. Moreover, under these conditions alternation performance did not exceed chance levels (χ^2's (1) = 2.84, 1.24, 1.12, $p>0.05$). If the perseverative effects of d-amphetamine observed in the drug state were the result of the disruption of habituation processes, then high levels of alternation should have been observed upon retesting. Since performance on Day 2 was comparable to that of saline treated mice, it seems likely that d-amphetamine did not deter the course of habituation in a manner comparable to that of scopolamine. Furthermore, since Day 1 and Day 2 performance among the p-hydroxyamphetamine and scopolamine methylbromide groups did not differ from the saline controls, the central acting properties of scopolamine and d-amphetamine are implicated in the mediation of the observed drug effects.

EXPERIMENT 2

The results of Experiment 1 revealed that the effects of scopolamine on habituation were not limited to the drug state, since high levels of alternation were observed in the non-drug state. In contrast, the perseverative effects of d-amphetamine were probably not the result of a disruption of habituation, given that performance on the subsequent retest did not exceed chance. It could be argued that scopolamine did not alter the habituation of the exploratory response, but rather affected the consolidation of the initial experience in the Y-maze [15,18]. That is, in the presence of the drug consolidation occurring over long posttrial periods was hampered, leading to high levels of alternation on Day 2. In the case of d-amphetamine the possibility exists that the drug was still present and exerting an effect (i.e., residual action) thereby modifying Day 2 performance. Accordingly, Experiment 2 was designed first to replicate the findings of Experiment 1, and second to determine whether any residual actions following drug treatments or possible drug-induced modifications of consolidation processes could account for the observed results.

METHOD

Animals

A total of 56 Swiss-Webster mice, 28 male and 28 female, ranging from 60–70 days of age served as test animals. Mice were housed 3–5 per cage and received ad lib access to food and water.

Apparatus and Procedure

The apparatus was identical to that used in Experiment 1. Mice were randomly assigned to 7 groups (n = 8/cell) and given 2 IP injections; one 15 min prior to training (pretrial), and the second immediately after training (posttrial), and the second immediately after training (posttrial). Three groups received pretrial injections of either scopolamine hydrobromide (1.0 mg/kg), d-amphetamine sulfate (5.0 mg/kg) or saline (10.0 ml/kg), followed by posttrial injections of saline. Animals were then tested in the same manner as Experiment 1. To control for drug effects on memory consolidation 2 additional groups were trained in the nondrug state followed by posttrial injections of scopolamine (1.0 mg/kg) or d-amphetamine (5.0 mg/kg). Finally to evaluate potential proactive effects of drug treatments 2 further groups were treated with either d-amphetamine (5.0 mg/kg) or scopolamine (1.0 mg/kg) followed by subsequent injections of saline. These animals were not tested in the alternation task on Day 1 but rather were placed in a carrying cage for the duration of the testing period. Following posttrial injections all mice were returned to their home cages. Mice were retested 24 hours later in the spontaneous alternation task as described in Experiment 1.

RESULTS AND DISCUSSION

Analysis of variance of the mean proportion of alternations of the groups receiving testing sessions on both Days 1 and 2 yielded a significant Drug treatment × Test day interaction ($F(4,35) = 39.80$, $p<0.001$). Consistent with the results of Experiment 1, Newman Keuls multiple comparisons of the simple main effects revealed that relative to saline control animals ($\bar{X}$ percent alternation = .68, .69 and .71 for mice which received saline, amphetamine, or scopolamine posttrial, but saline pretrial), pretrial injections of scopolamine and d-amphetamine substantially reduced alternation on the initial day of testing ($\bar{X}$ percent

alternation = .48 and .36, respectively). Moreover, whereas scopolamine reduced alternation to chance levels ($\chi^2(1)$ = .520, $p>0.05$), treatment with d-amphetamine resulted in perseverative behavior (χ^2 = 68.52, $p<0.01$). As in Experiment 1 alternation among saline treated mice declined significantly between days and under these conditions did not exceed chance ($\chi^2(1)$ = .122, $p>0.05$). As shown in Fig. 2, performance among scopolamine treated animals, on the other hand, was higher on Day 2 relative to the saline controls, and as expected exceeded chance levels. ($\chi^2(1)$ = 44.0, $p<0.01$). Since posttrial scopolamine treatment resulted in chance level performance on Day 2 ($\chi^2(1)$ = 0, $p>0.05$), it is unlikely that pretrial scopolamine treatment affected consolidation, at least not over long posttrial periods.

Consistent with the results of Experiment 1, it was observed that upon retesting, performance of the pretrial d-amphetamine group was at chance levels ($\chi^2(1)$ = 1.92, $p<0.05$) and did not differ from control animals. Inspection of Fig. 2 shows that the chance level alternation displayed by animals in the d-amphetamine condition was not a consequence of residual drug effects. In particular, if animals were not treated with either scopolamine or d-amphetamine, then their subsequent performance was comparable to that seen on Day 1 among saline treated animals (Dunnetts' t's(12,35) = .52, and .96, $p>0.05$ respectively). Predictably, the alternation performance of these groups exceeded chance levels ($\chi^2(1)$ = 54.78, 36.39, $p<0.01$).

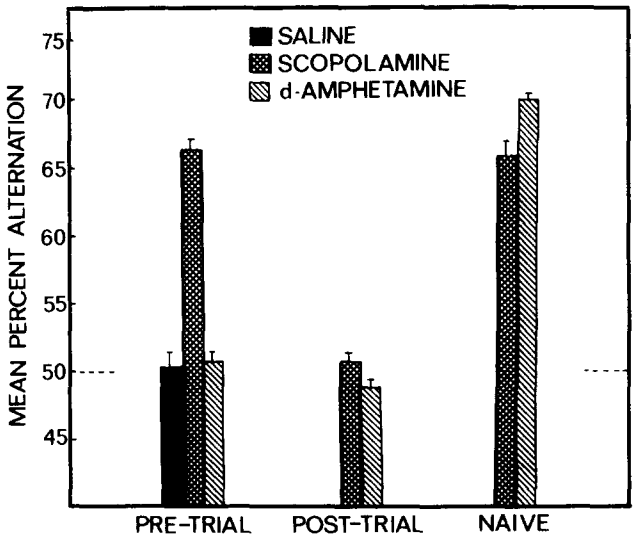

FIG. 2. Mean proportion of alternation responses (±SEM) on Day 2 (nondrug state) as a function of Day 1 Pre-exposure and Drug treatments.

EXPERIMENT 3

While the results of Experiments 1 and 2 suggest that scopolamine disrupts habituation, it could be argued that performance was subject to state dependent (drug dissociated) learning [5, 7, 16, 17]. In particular, the stimulus change exerted by scopolamine during initial training was absent during subsequent retesting. Consequently, the habituation which occurred during initial testing was not transferred to the nondrug state, thus resulting in high levels of alternation on Day 2. It is clear that in the case of d-amphetamine stimulus dissociation was not a cogent factor, since animals which received treatment with saline or d-amphetamine performed at comparable levels on Day 2. The purpose of Experiment 3 was to determine whether the high alternation performance on Day 2, following initial scopolamine treatment, was the result of state dependent processes.

METHOD

Animals

Sixteen male and 16 female Swiss-Webster mice ranging from 60–70 days of age served as test animals. Mice were housed 3–5 per cage and received ad lib access to food and water.

Apparatus and Procedure

The apparatus used in Experiment 3 was identical to that used in the previous experiments. Animals were randomly assigned to 4 groups (n = 8/cell) and tested on two occasions 24 hr apart. Testing was identical to that in Experiment 1. On each day mice received a single IP injection 15 min prior to testing. On Day 1 one-half the mice received injections of scopolamine hydrobromide (1.0 mg/kg) whereas the other half received saline injections. On Day 2 mice were further subdivided (n = 8) and were again treated with an equivalent amount of saline or scopolamine.

RESULTS AND DISCUSSION

Figure 3 summarizes the spontaneous alternation performance as a function of drug treatments. Analysis of variance of the individual alternation scores revealed a significant Drug Treatment × Days interaction ($F(1,28)$ = 5.39, $p<0.05$). Consistent with the results of the previous experiments Newman Keuls multiple comparisons of the simple main effects of this interaction (α = 0.05) along with χ^2 analyses revealed that performance of animals in the saline-saline condition was lower on Day 2 than on Day 1. Whereas alternation during initial testing exceeded chance levels ($\chi^2(1)$ = 30.32, $p<0.01$) performance on Day 2 did not differ from chance (χ^2 = .916, $p>0.05$). As in Experiments 1 and 2, scopolamine reduced alternation to chance levels (χ^2's(1) = .50, .17, $p>0.05$). Furthermore those animals which received scopolamine on Day 1 but saline on Day 2, alternated at higher levels on Day 2 than did animals in the saline-saline condition.

Of particular interest in the present study was the finding that regardless of the drug treatment prior to initial testing, those animals which received scopolamine on Day 2 alternated at chance levels (χ^2's(1) = .192, 0, $p>0.05$). More importantly, since Day 2 performance among animals in the scopolamine-saline condition was significantly higher than that of mice in the saline-scopolamine group, it is unlikely that drug dissociation was a cogent factor in the observed carry-over effects of scopolamine.

GENERAL DISCUSSION

As in previous reports [2,3] the immediate effects of both scopolamine and d-amphetamine was to reduce levels of spontaneous alternation. However, whereas scopolamine simply reduced alternation to chance levels, d-amphetamine produced alternation which was significantly below chance (perseveration). Consistent with a model implicating the

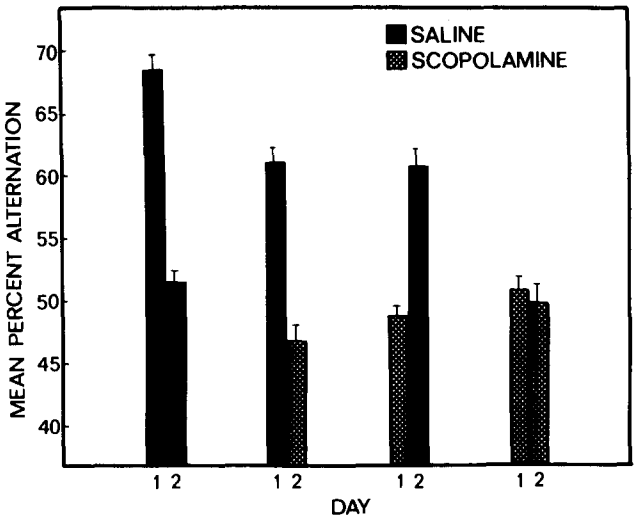

FIG. 3. Mean proportion of alternation responses (± SEM) over 2 consecutive days as a function of Drug Treatment (scopolamine or saline) during pre-exposure, and during subsequent testing.

role of cholinergic activity in mediating habituation processes [7], animals which received scopolamine treatment during initial training behaved like naive animals during subsequent retesting in the nondrug state. It is likely that scopolamine attenuated the course of habituation during the initial testing session, thus permitting high levels of alternation to be manifested upon retesting. Moreover, these findings cannot be attributed to effects of scopolamine on peripheral mechanisms, memory consolidation processes over long posttrial periods, proactive effects of drug treatment, or state dependent learning.

In contrast to the effects of scopolamine, initial treatment with d-amphetamine did not affect Day 2 performance. Although d-amphetamine initially reduced alternation levels in the drug state, when retested in the nondrug state mice performed at a level comparable to that of saline animals. In agreement with Carlton [7], the immediate effects of d-amphetamine quite clearly were not a result of disruption of habituation. In effect the suggestion here is that although both scopolamine and d-amphetamine reduce alternation during initial exposure to the Y-maze, they do so because of different types of biases. Whereas scopolamine seems to disrupt habituation, d-amphetamine produces perseverative tendencies which are not a consequence of effects on habituation.

While the source for the perseverative tendency induced by d-amphetamine is not apparent, it seems clear that response biases (e.g., circling, side preferences or responding on the basis of intrinsic feedback) are not pertinent factors in this respect. In particular, circling elicited by intraventricular injection of d-amphetamine does not elicit perseveration. To the contrary, under these conditions, exceptionally high levels of alternation are observed (Kokkinidis and Anisman, in preparation). On the other hand, modification of stimulus factors affect perseverative behavior. For example, when the novelty value of the apparatus is increased, perseveration typically seen among immature animals is reduced [11]. Conversely, reduction of the novelty value of the apparatus, by pre-exposure, tends to augment perseveration elicited by d-amphetamine [12]. Parenthetically, the latter finding suggests that fear of specific apparatus cues is not responsible for perseveration. After all, prior habituation to the apparatus should have reduced the fear and thus decreased the perseverative effects of the drug treatment. In any event, whether the repetitive behavior elicited by d-amphetamine reflects changes in reinforcement value of novel stimuli or a form of sensitization still needs to be determined.

REFERENCES

1. Adkins, J., J. W. Packwood and G. L. Marshall, Jr. Spontaneous alternation and d-amphetamine. *Psychon. Sci.* **17**: 167–168, 1969.
2. Anisman, H. Dissociation of the disinhibitory effects of scopolamine: effects on activity and habituation. *Pharmac. Biochem. Behav.* **3**: 613–618, 1975.
3. Anisman, H. and L. Kokkinidis. Effects of scopolamine, d-amphetamine and other drugs affecting catecholamines on spontaneous alternation and locomotor activity in mice. *Psychopharmacologia* **45**: 55–63, 1975.
4. Anisman, H., L. Kokkinidis, S. Glazier and G. Remington. Differentiation of response biases elicited by scopolamine and d-amphetamine: effects on habituation. *Behav. Biol.* 1976, in press.
5. Barry, H., III. Classification of drugs according to their discriminable effects in rats. *Fedn Proc.* **33**: 1814–1824, 1974.
6. Bignami, G. Nonassociative explanations of behavioural changes induced by central cholinergic drugs. *Acta neurobiol. exp.* **36**: 5–90, 1976.
7. Carlton, P. L. Brain-acetylcholine and inhibition. In: *Reinforcement and Behavior*, edited by J. T. Tapp. New York: Academic Press, 1969, pp. 286–327.
8. Carlton, P. L. and J. R. Vogel. Studies of the amnesic properties of scopolamine. *Psychon. Sci.* **3**: 261–262, 1965.
9. Douglas, R. J. and R. L. Isaacson. Spontaneous alternation and scopolamine. *Psychon. Sci.* **4**: 283–284, 1966.
10. Drew, W. G., L. L. Miller and E. L. Baugh. Effects of Δ^9-THC, LSD-25 and scopolamine on continuous, spontaneous alternation in the Y-maze. *Psychopharmacologia* **32**: 171–182, 1973.
11. Egger, G. J. Novelty induced changes in spontaneous alternation by infant and adult rats. *Devl. Psychobiol.* **6**: 431–435, 1973.
12. Kokkinidis, L. and H. Anisman. Interaction between cholinergic and catecholaminergic agents in a spontaneous alternation task. *Psychopharmacologia* **48**: 261–270, 1976.
13. Leaton, R. N. and M. J. Utell. Effects of scopolamine on spontaneous alternation following free and forced trials. *Phsyiol. Behav.* **5**: 331–334, 1970.
14. Meyers, B. and E. F. Domino. The effect of cholinergic blocking drugs on spontaneous alternation in rats. *Int. Pharmacodyn. Ther.* **150**: 525–529, 1964.
15. McGaugh, J. L. Drug facilitation of learning and memory. *Ann. Rev. Psychol.* 229–241, 1973.
16. Overton, D. A. State-dependent learning produced by depressant and atropine-like drugs. *Psychopharmacologia* **10**: 7–31, 1966.
17. Overton, D. A. Dissociated learning in drug states (state dependent learning). In: *Psychopharmacology, A Review of Progress* 1957–1967, *Proceedings of the VIth Annual Meeting of the American College of Neuropsychopharmacology, San Juan (Puerto Rico)*, edited by D. H. Efron, J. O. Cole, J. Levine and J. R. Wittenborn. Washington, D. C.: U. S. Government Printing Office (P.H.S. Publication No. 1836), pp. 918–930, 1968.
18. Squire, L. R. Effects of pretrial and posttrial administration of cholinergic and anticholinergic drugs on spontaneous alternation. *J. comp. physiol. Psychol.* **1**: 69–75, 1969.
19. Swonger, A. K. and R. H. Rech. Serotonergic and cholinergic involvement in habituation of activity and spontaneous alternation of rats in a Y-maze. *J. comp. physiol. Psychol.* **81**: 509–522, 1972.