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A Reappraisal of Scopolamine Effects on Inhibition[1]

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MILAR, K. S., C. R. HALGREN AND G. A. HEISE. *A reappraisal of scopolamine effects on inhibition.* PHARMAC. BIOCHEM. BEHAV. 9(3) 307–313, 1978.—A series of related experiments was conducted to examine the effects of scopolamine on discrimination performance in the presence or absence of a stimulus signalling non-reinforcement. In Experiment 1, rats trained to respond on 1 of two levers in the presence of a 1000-Hz tone and on the other lever in the presence of a 3000-Hz tone were not reinforced when white noise was added to 1 of the tones. Pairing white noise with the other tone during an extinction session demonstrated that the white noise had become a conditioned inhibitory stimulus. In Experiment 2, scopolamine decreased responding and discrimination accuracy on the excitatory (reinforced) trials, and increased responding on the inhibitory (non-reinforced) trials. The magnitude of the drug's effect was similar on excitatory and inhibitory trials. Using combinations of visual and auditory discriminative stimuli, Experiment 3 confirmed the results of Experiment 2. These experiments show that scopolamine disrupts animals' ability to discriminate, and that scopolamine-induced increases in non-rewarded responses cannot be attributed solely to a disinhibitory effect of the drug as Carlton (1969) and others have claimed.

Scopolamine Inhibition Conditioned inhibition Combined cue test Visual discrimination Auditory discrimination

SCOPOLAMINE, an anticholinergic drug, increases responding on nonrewarded trials in a number of experimental situations. Carlton attributed a scopolamine-induced increase in non-reinforced responding to a "disinhibitory" effect of the drug [4]. He maintained that anticholinergics interfere with behavioral inhibitory processes engendered by non-reward so that unrewarded responses which are normally inhibited intrude into the animal's repertoire.

A major problem in assessing possible disinhibitory effects of anticholinergic drugs has been the variety of experimental procedures classified as inhibitory and therefore the variety of behavioral changes considered disinhibitory. In his review, Carlton [5] includes as examples of anticholinergic disinhibitory action, (a) reduction of habituation to a novel environment [6], (b) repeated preference of drugged animals for the arm of a maze containing objects to explore [14] and (c) enhanced two-way avoidance acquisition [16].

Hearst, Besley, and Farthing [11] define an inhibitory stimulus as ". . .a stimulus that develops during conditioning the capacity to decrease response strength below the level occurring when that stimulus is absent." (p. 376). This definition includes both an associative operation to establish the stimulus as inhibitory and a behavioral effect. The authors state that a behavioral decrement alone is not a sufficient condition for inhibition. For example, behavior decrements due to extinction, changes in deprivation or changes in S+ may more parsimoniously be attributed to changes in excitation.

In contrast to the claim that anticholinergics have disinhibitory action, Warburton attributes the increase in non-reinforced responding produced by cholinergic blocking agents to disruption of stimulus discrimination rather than to disinhibition [20]. Brown and Warburton [3,21] applied a signal detection analysis to differential reinforcement of low rates (DRL) performance following treatment with scopolamine and demonstrated that the drug reduced the signal-to-noise ratio. These authors concluded that scopolamine reduced detectability but did not alter the response criterion (i.e., did not disinhibit responding).

A satisfactory experimental evaluation of the response disinhibition and stimulus discrimination hypotheses of scopolamine action required a test procedure in which: (1) response inhibition is demonstrated under non-drug conditions; and (2) the effects of scopolamine upon performance in this situation are evaluated. In the analysis of drug action, free operant procedures confound drug-induced changes in discrimination with drug-rate interactions. A discrete trial procedure minimizes rate-dependent drug effects [12], and, therefore, was used in the present experiments.

One clear form of response inhibition is conditioned in-

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hibition [17]. The combined cue test is one test for conditioned inhibitory properties of a stimulus [10] and is readily adaptable for use in operant discrimination situations [2]. This procedure as employed by Brown and Jenkins [2] consisted of first reinforcing pigeons for pecking the left side of a split key if the key was green and the right side if red. A tone was then established as a conditioned inhibitor by pairing it with 1 of the 2 visual cues (e.g., tone+green); responding to this combination was never reinforced although correct responding to either of the visual cues alone continued to be reinforced. Testing in extinction demonstrated that the tone has become a conditioned inhibitory stimulus: (1) responding to the visual cues alone was maintained at a high rate, (2) there was a low rate of responding to the trained combination of tone+green and (3) a similarly low rate responding occurred to the novel combination of tone+red.

In the present experiments, a combined cue test was used to assess the relative effects of scopolamine on inhibition and discrimination in rats. Experiment 1, carried out under nondrug conditions, consisted of conditioned inhibition training followed by the combined cue test. The animals from this experiment and additional subjects were trained and then tested with scopolamine in Experiments 2 and 3. Disinhibition under drug in Experiments 2 and 3 would be indicated if responding increased primarily on those trials during which the conditioned inhibitory stimulus was present (no-go trials) rather than on those trials during which the conditioned inhibitory stimulus was absent (go trials). Drug-induced discrimination deficits would be indicated if responding increased on no-go trials and decreased on go trials.

EXPERIMENT 1: CONDITIONED INHIBITION TRAINING AND COMBINED CUE TEST

METHOD

Animals

Seven male Sprague-Dawley derived albino rats approximately 90 days old at the time of testing were obtained from Murphy Farms, Indianapolis, Indiana. They were housed two to a cage and placed on a 23 hr water deprivation schedule. Nine percent sucrose solution was used as the reinforcer. All animals had been used in a preliminary experiment ([13], Experiment 3) in which they learned a visual discrimination and had been given scopolamine and saline.

Apparatus

Two two-lever operant chambers 25×24×20 cm were used for experimentation. Each chamber contained two Gerbrands response levers, requiring 25–30 gm force to operate, which were mounted 10 cm above the grid floor of the chamber and displaced 6.5 cm to the right and left of the center line. Three white 6 W panel lights were mounted 15 cm above the floor, one over each lever and one on the center line. Only the center light was used in this experiment. The spigot for dispensing single drops of sucrose solution reinforcer (ca. 0.05 cc/drop) was mounted 5.5 cm above the floor on the center line of the chamber. Tones and white noise were delivered through a 10 cm, 4-ohm speaker mounted on the top of the chamber. Tones were generated by a Hewlett Packard 200 ABR oscillator. White noise was generated by a Grason Stadler 901A noise generator. Intensity of tones, noise and tone-noise combinations was measured with a B & K Instruments sound level meter and adjusted such that all auditory stimuli were presented at 70–71 db SPL. Electromechanical controlling equipment for control of the experiments and recording of data was located in an adjacent room.

Procedure

For all phases of this experiment, trial duration was a maximum of 5 sec, intertrial interval (ITI) duration was 9 sec, and there was a 1 sec pretrial delay at the end of the ITI such that each response during this delay interval postponed trial onset for an additional second. Experimental sessions were held 5 days a week and lasted 1 hr or until the animal had received 100 reinforcers. All animals experienced the 3 phases of this experiment as diagrammed in Table 1.

Phase I: Auditory discrimination training (go/go). Animals were trained to press the left lever in the presence of a 1000 Hz tone and the right lever in the presence of a 3000 Hz tone. Tones were presented in random order. A correct response on a trial terminated the trial, delivered the reinforcer, and initiated the ITI. Incorrect responses terminated the trial and initiated the ITI. In the event of an error or no response, a correction procedure was employed such that a trial was repeated until a correct response occurred. The criterion for termination of Phase I was correct responses on 85% of the trials for two consecutive sessions.

Phase II: Conditioned inhibition training. All animals re-

TABLE 1
PROCEDURE

	Reinforcement Contingencies			
	Go Stimuli		No-Go Stimuli	
	Tone A	Tone B	Tone A+Noise	Tone B+Noise
Phase I: Discrimination Training	Right	Left	Not presented	Not presented
Phase II: Condition Inhibition Training	Right	Left	Extinction	Not presented
Phase III: Combined Cue Test	Extinction	Extinction	Extinction (No-go Familiar)	Extinction (No-go Novel)

ceived equal numbers of each of 3 types of trials in this phase, the 2 excitatory (go/go) trials from Phase I and a no-go trial (tone+white noise). For 4 animals white noise was paired only with the 1000 Hz tone (Tone A in Table 1) and for the other 3 animals only with 3000 Hz (Tone A in Table 1). Responding in the presence of this tone-noise combination was never reinforced. In contrast to a response on a go trial (tone only), a response on a no-go trial (tone+noise) did not terminate the trial; such trials always lasted for 5 sec. The criterion for proceeding to Phase III was responses on 85% of the go trials and responses on no more than 20% of the no-go trials. No correction procedure was used in Phases II or III. Percent response measures were computed as the number of trials on which at least one response occurred.

Phase III: Combined cue test for conditioned inhibition. Animals received equal types of each of four types of trials in this phase: the three types of trials from Phase II (2 types of tone-only go/go trials and the tone-noise combination on which they had received training—no-go familiar trials); plus trials on which white noise was paired for the first time with the other tone (no-go novel trials). All 4 trial types were presented in random order to each animal in a single extinction session. The session continued until either 20 consecutive trials had occurred without a response or until 200 trials had been presented. The percent response measure was computed for each trial type.

RESULTS

Three conditions necessary for demonstrating conditioned inhibition [2] were realized in the results of the combined cue test (Phase III): (1) the excitatory (go/go) discrimination was maintained, (2) the animals exhibited a lower percentage of responding to the inhibitory combination of tone and noise originally trained (no-go familiar) than to either of the tones alone, and (3) there was a similar low percentage of responding to the tone-noise combination never experienced by the animal until the test (no-go novel).

For the Phase III test, mean percent accuracy on the go/go discrimination trials was 87.6%. Data from animals initially trained on 1000 Hz+noise or 3000 Hz+noise were combined since inspection of the data revealed no consistent differences in responding. One animal had to be discarded from this analysis (n=6) due to an equipment failure which resulted in the loss of the data. A one-tailed t test for matched samples showed that there was a significant difference between responding on the go trials and on each of the two types of no-go trials. Mean percent responses on the go (tone-only) trials of Phase III was 45.3% and for the no-go familiar trials 13.5%, $t(5)=5.58$, $p<0.005$. Mean percent response for the no-go novel trials was 22% (compared to go trials, $t(5)=11.1$, $p<0.0005$). There was, however, no significant difference between percent responding on the no-go familiar trials and the no-go novel trials, $t(5)=1.62$, $p>0.20$. These results indicate that white noise had acquired conditioned inhibitory properties which transferred to the novel combination.

A pseudo-discrimination measure of performance on no-go trials was used to examine two possible alternatives to the conclusion that noise was a conditioned inhibitory stimulus in this experiment. This measure reflected whether the animal responded correctly to the tone stimulus when it responded on a no-go trial. For example, on a 1000 Hz+noise trial, a response to the left lever was correct and a response to the right lever was incorrect.

If the animal could not discriminate the tones in combination with white noise and therefore perceived the no-go familiar and no-go novel trials as identical (Alternative 1), then the distribution of responses over the two levers on no-go trials should have been essentially random. If animals were generalizing from the trained tone-noise combination to the untrained combination (Alternative 2), more errors should occur to the novel that to the familiar combination stimulus due to a decrement in generalization of inhibition (cf. [18]). Percent correct in Phase III was 76% on the no-go familiar trials and 78.1% on the no-go novel trials. Clearly, neither alternative explanation is viable: the pseudo-discrimination measure shows that the two combinations were differentiated from each other and that no more errors occurred to the novel than to the familiar combination. Therefore, according to the combined cue test, white noise was a conditioned inhibitory stimulus.

EXPERIMENT 2: SCOPOLAMINE EFFECTS ON CONDITIONED INHIBITION

METHOD

Experiment 2 was designed to assess the effects of scopolamine on conditioned inhibition as defined by Experiment 1. Animals and apparatus were the same as in Experiment 1 with the exception that the data from the animal not included in the results of Experiment 1 are included in the results of this experiment (n=7).

Methylscopolamine, a quaternary compound that does not pass the blood brain barrier and therefore has minimal central nervous system effects [7] was included as a control on Experiment 2 to separate peripheral from central effects of the anticholinergic.

Procedure

All animals were retrained on the go/no-go discrimination of Experiment 1 with equal numbers of both types of go trials (1000 and 3000 Hz) and both types of no-go trials (1000+noise and 3000+noise) presented in random order. No correction procedure was used. Criterion performance was 85% response on the go trials and no more than 20% response on the no-go trials. Drugs were administered intraperitoneally 10 min prior to each drug session. Experimental sessions were held daily, Monday through Friday. Drug sessions occurred on Tuesday and Friday if criterion performance had been attained on the previous day. Doses of 0.125, 0.25, and 0.50 mg/kg scopolamine hydrobromide, 1.0 mg/kg methylscopolamine (scopolamine methyl bromide) and 0.9% saline solution were given once to each animal in a random order.

RESULTS

Mean percent response for go and no-go trial responding is presented in Fig. 1. The control (no treatment) data shown in the figure are taken from the session prior to the drug session for each drug dose. An analysis of variance appropriate for a repeated measures experimental design indicated that there was a significant drug induced decrease in go responding, $F(6,36)=3.898$, $p<0.004$, and increase in no-go responding, $F(6,36)=3.26$, $p<0.012$. Subsequently, a Newman-Keuls test for paired comparisons on repeated measures revealed that there were significant differences be-

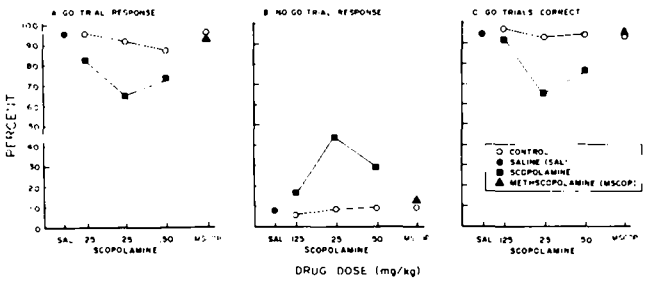

FIG. 1. Performance on go and no-go trials under non-drug and drug conditions in Experiment 2.

tween saline and 0.25 mg/kg scopolamine for both go and no-go trial responding ($p<0.05$), but not between saline and any other dosage of scopolamine. The lack of a significant effect of 0.50 mg/kg scopolamine was due, in part, to the increase in variability of performance with this dose. There was no treatment effect of methylscopolamine and, as is apparent from Fig. 1, responding under both saline and methylscopolamine control conditions was not different from the non-treatment control days.

Because go as well as no-go trial percent responses were affected, scopolamine cannot be considered a solely disinhibitory drug: it impaired the discrimination between go and no-go trials. Additionally, Fig. 1 shows that scopolamine also impaired discrimination of the go/go (tone only) trials. Percent accuracy in responding was consistently high for all control conditions (see Fig. 1C). Mean percent correct for nondrug control days was 94%; for saline 94.3%; and for methylscopolamine 94.6%. As is evident in Fig. 1C, scopolamine disrupted go/go discrimination performance. Newman-Keuls tests showed that this effect was significant at 0.25 mg/kg and 0.50 mg/kg ($p<0.01$). It appears then that scopolamine not only disrupted the go/no go discrimination but additionally produced a decrement in the accuracy of the go/go discrimination.

Scopolamine might nevertheless be considered disinhibitory if, in addition to affecting discriminability, the drug increased no-go trial responses more than it decreased go trial responses or the accuracy of the go/go discrimination. In order to compare percent go response, percent go trial accuracy and percent no-go response, it was necessary to use 100% minus percent no-go response for the no-go measure. An analysis of variance for each dose of scopolamine indicated that although the drug increased no-go responding at 0.25 mg/kg ($p<0.002$) and 0.50 mg/kg ($p<0.058$), there was no selective drug effect on any type of responding for any dosage (drug×response interaction: 0.25 mg/kg, $p=0.623$; 0.50 mg/kg, $p=0.772$). In other words, there was no greater drug effect on no-go trial percent response than on go trial percent response or go/go percent accuracy. Any disinhibitory effects of scopolamine that may have occurred were too small to be detected over the drug's substantial effects on discriminability. Thus, the results of Experiment 2 indicate that scopolamine impaired discrimination.

EXPERIMENT 3

METHOD

Experiment 3 was designed to confirm and expand the findings of Experiment 2. In addition, Experiment 3 addressed itself to two possible limitations of Experiment 2: (1) Discrimination performance may have been facilitated by the fact that the tone-noise combinations set the occasion only for no-go or inhibitory trials. If, instead, combination stimuli had signalled go or excitatory trials, both discrimination accuracy and drug effects might have differed from the previous results. (2) A second question raised by Experiment 2 concerns the generality of the results obtained from the particular auditory stimuli employed in that experiment. Tones and white noise are not orthogonal stimulus dimensions and although the pseudo-discrimination measures of Experiment 1 indicated that tones were discriminable in combination with the white noise, it is possible that animals did not perceive the tones+white noise as compound stimuli but rather as some distortion of the tones. The use of cross-modal (e.g., visual and auditory) stimuli in combination would obviate this problem. It is possible that the obtained results may apply only to auditory inhibitory stimuli; therefore, Experiment 3 also examined drug effects on an auditory excitatory stimulus.

In Experiment 3 animals were trained on a visual discrimination: steady light vs. flashing light, or an auditory discrimination: 1000 Hz vs. 3000 Hz. Effects of scopolamine on responding cued by cross-modal compound stimuli, either tone-light or light-tone combinations, were examined for possible discriminatory and/or disinhibitory effects as defined in Experiment 2.

Animals

Thirteen male Sprague-Dawley derived albino rats approximately 90 days old were obtained from Hormone Assay, Chicago, Illinois. They were maintained on a 23 hr water deprivation schedule. Nine percent sucrose solution was used as the reinforcer.

Apparatus

Four operant chambers identical to those described in Experiment 1 were used for experimentation.

Procedure

Session length, trial length, intertrial intervals and experimental procedure were the same as those in Experiment 1 except for minor differences in the correction procedures. The animals first received go/go discrimination training followed by go/no-go training.

Go/go discrimination training. Seven animals were trained to press the left lever on discrete trials if the center cue light was flashing at a 0.5-sec repetition rate and the right lever if the center cue light was steady. For the remaining six animals, right lever trials were signalled by a 1000 Hz tone and left lever trials by a 3000 Hz tone. Discriminative stimuli were presented in random order. A correct response on a trial terminated the trial, delivered the reinforcer and initiated the ITI. Incorrect responses terminated the trial and initiated the ITI. Correction trials followed an error or no response. This phase terminated after 19 sessions by which time the animals trained on the visual discrimination were responding correctly on 70% of the trials and animals trained on the auditory discrimination were responding correctly on 80% of the trials.

Go/no-go discrimination training. Animals were divided into three subgroups for this phase: tone excitatory, tone

TABLE 2
STIMULUS CONDITIONS FOR EXPERIMENT 3

	Groups		
	Tone Excitatory	Tone Inhibitory	Light Inhibitory
Go Stimuli	steady light + 1000 Hz	steady light	1000 Hz
	flashing light + 1000 Hz	flashing light	3000 Hz
No-Go Stimuli	steady light	steady light + 1000 Hz	1000 Hz + steady light
	flashing light	flashing light + 1000 Hz	3000 Hz + steady light

inhibitory, and light inhibitory. All animals received two types of go trials and two types of no-go trials (see Table 2). Session length was increased to 90 min or 100 reinforcers and a correction procedure was introduced for both go and no-go trials. All no-go trials lasted 5 sec whether or not the animal responded. Go trials were repeated until the rat made a correct response; a response to a no-go trial programmed a repeat of that trial until an appropriate failure to respond occurred.

Tone inhibitory. Three animals that had been trained on the visual discrimination continued to be reinforced for correct responding to the steady light/flashing light discrimination trials from the previous phase. In addition, they received trials in which either the steady light or the flashing light was accompanied by a 1000 Hz tone inhibitory stimulus. Responses in the presence of a light-tone combination were never reinforced.

Tone excitatory. The remaining four animals originally trained on the visual discrimination were reinforced for correct responses to steady light or flashing light trials only if those trials were accompanied by a 1000 Hz tone excitatory stimulus. Responding on the steady light or flashing light trials was never reinforced.

Light inhibitory. The six animals originally trained on the 1000 Hz vs. 3000 Hz discrimination continued to be reinforced for correct responding to these tones. No-go trials were signalled by one of the tones accompanied by a steady center panel light. Responses to either of these tone-light combinations were never reinforced.

After 17 sessions of training on this go/no-go discrimination the correction procedure was discontinued, and the two types of go trials and the two types of no-go trials were presented in a predetermined random order with no trial repetition after errors. The reinforcement contingencies did not change.

When responding had stabilized, animals were drugged on Fridays. Doses of 0.0625, 0.125, 0.25 and 0.50 mg/kg of scopolamine and 0.9% saline solution were given intraperitoneally 10 min prior to each drug session. Animals received each dose at least once and the majority of animals received two injections of scopolamine at each dose level in a random sequence. Illness precluded the second dosing for several animals.

RESULTS

Figures 2 and 3 show effects of the graded doses of scopolamine on mean percent response on go and no-go trials and mean percent accuracy on the go trial discrimination (correct go trial responses/go trials responded to) for two tasks in Experiment 3. Go/no-go discrimination performance reflected in the percent response measures, apparently did not differ among the three discrimination tasks under nondrug conditions. Animals on all three tasks responded on 90% of the go trials and less than 20% of the no-go trials. Go/go discrimination accuracy was also high for all three groups under nondrug conditions. Mean percent accuracy on the go trial discrimination was 85% or better for each group. The type of discriminative stimuli—visual with auditory excitatory or auditory inhibitory stimulus and auditory with visual inhibitory stimulus—does not seem to have affected task performance. The performance of animals on these three auditory-visual tasks was comparable to the performance of subjects in the auditory discriminations of Experiment 2 (see Fig. 1).

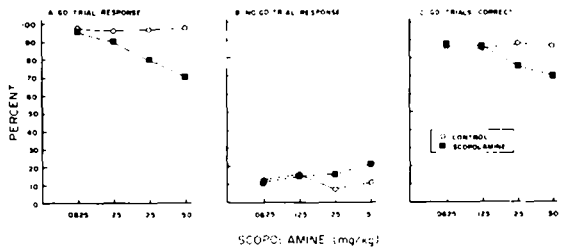

FIG. 2. Performance on go and no-go trials under non-drug and drug conditions for the light inhibitory group in Experiment 3.

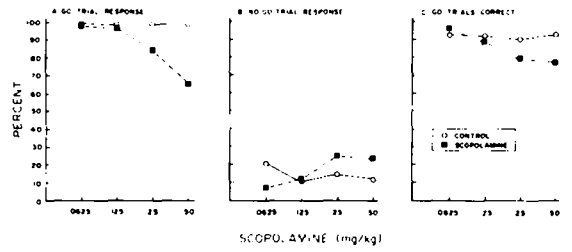

FIG. 3. Performance on go and no-go trials under non-drug and drug conditions for tone excitatory group in Experiment 3.

Saline injections produced no change in task performance for any animals; therefore, the control (non-drug) data shown in the figures are taken from the session immediately preceding the drug sessions. An analysis of variance for each dose of scopolamine was used to facilitate separation of disinhibitory and discrimination deficits. Due to the number of

animals that did not receive two injections at each drug dose, the data analysis was confined to the results of the first injections.

Light Inhibitory

Scopolamine significantly affected responding at doses of 0.25 mg/kg, $F(1,5)=10.14$, $p<0.024$, and 0.50 mg/kg of scopolamine, $F(1,5)=45.11$, $p<0.001$, on the light inhibitory task. Comparison of drug and nondrug responding with Newman-Keuls tests showed that at 0.25 mg/kg the drug significantly increased no-go responding ($p<0.05$). At the 0.50 mg/kg dose all three dependent measures were significantly disrupted by the drug: go responding decreased ($p<0.05$); no-go responding increased ($p<0.05$) and go discrimination accuracy decreased ($p<0.01$) (see Fig. 2). However, there were no significant drug×response interactions (again, 100% minus percent no-go response was used as the no-go measure) at either of the doses (for 0.25 mg/kg: $F(2,10)=0.108$, $p=0.899$; for 0.50 mg/kg: $F(2,10)=0.058$, $p=0.944$, indicating that scopolamine did not selectively affect any one type of responding. That is, the drug effect on no-go responding was not greater than the effect on go trial responding or on go/go discrimination accuracy.

Tone Excitatory

A significant drug effect on responding on the tone excitatory task was produced at 0.50 mg/kg of scopolamine, $F(1,3)=37.5$, $p<0.009$ (see Fig. 3). Go responding decreased significantly under the drug ($p<0.05$) and no-go responding increased ($p<0.10$). There was no significant drug response interaction, $F(2,6)=1.635$, $p=0.271$, indicating no selective effect of scopolamine on no-go trial responding.

Tone Inhibitory

Scopolamine decreased go responding and increased no-go responding on the tone inhibitory task. However, there were no statistically significant drug effects at any doses for this group, probably due to the small number of animals (n=3).

The results of Experiment 3 confirm and extend the findings of Experiment 2. Performance comparable to that obtained in Experiment 2 was obtained with different discriminative stimuli and cross-modal compound stimuli. Additionally, neither drug effects nor responding under nondrug conditions were different when the compound stimulus set the occasion for excitatory (go) trials rather than inhibitory (no-go) trials. When scopolamine produced a substantial change from nondrug responding, the change occurred on at least two dependent measures. Thus Experiment 3, like Experiment 2, provides evidence that scopolamine produces discrimination deficits.

GENERAL DISCUSSION

Scopolamine prolongs extinction [9], attenuates habituation to novel stimuli [6,14], enhances two-way avoidance and impairs one-way avoidance [8]. Findings such as these were interpreted by Carlton [4,5] and others as evidence that scopolamine disinhibits nonrewarded responses. Using an experimentally validated paradigm for conditioned inhibition the present research examined possible disinhibitory effects of scopolamine.

The argument that scopolamine has a disinhibitory action is based on experiments that showed that nonrewarded responses increased under drug conditions. However, these experiments did not ascertain whether the pretreatment baseline involved inhibitory stimulus control. The combined cue procedure of Brown and Jenkins [2] was used here as a test of the inhibitory properties of a stimulus signalling nonrewarded responses. We found that scopolamine increased responding on no-go trials cued by a conditioned inhibitory stimulus. However, the drug also decreased go trial responding and disrupted go/go discrimination accuracy, and there were no significant differences in the magnitude of the drug's effect on the three measures.

We have shown that our results are robust, i.e., they were observed under several different stimulus conditions. Thus the scopolamine effects in the present experiments are compatible with the hypothesis that scopolamine affected discrimination [12, 19, 20]. Scopolamine action is not exclusively disinhibitory.

It is, of course, possible that scopolamine could have produced disinhibitory effects that were not detectable in our experimental situation. A signal detection experiment is one way to detect and to separate the disinhibitory effects from the discrimination effects of the drug. Signal detection procedures have been used to characterize drug-induced performance changes as changes in sensitivity (discrimination process) or bias (response tendency) [1]. Warburton and Brown [21] applied signal detection analysis to DRL performance and demonstrated that scopolamine affected sensitivity rather than bias. In a recent series of signal detection experiments Milar [15] found that scopolamine decreased sensitivity but had no effect on bias (i.e., did not disinhibit responding). In view of these recent findings it is clear that scopolamine acts on discrimination processes and probably has no disinhibitory action.

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