Effects of atropine on performance of an S^D-S^Δ discrimination in rats *

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When a buzzer was used as the discriminative stimulus, atropine sulfate impaired performance of an established S^D-S^Δ discrimination by increasing response rates during S^Δ periods. Atropine methylnitrate did not have this effect, suggesting that the behavioral effects of atropine sulfate resulted from its antagonism of a central cholinergic inhibitory system. The importance of selecting a neutral cue in studies of anticholinergic drugs is discussed.

Carlton (1963, 1969) has proposed that anticholinergic drugs interfere with the inhibition of irrelevant or maladaptive responses by antagonizing a central cholinergic circuit. Examination of performance on an S^D-S^Δ discrimination provides a sensitive test of Carlton's hypothesis, since a centrally active anticholinergic would be expected to increase responding during nonrewarded S^Δ intervals, without affecting responding during rewarded S^D periods. Thus, the S^D rate provides a control measure that may reflect general changes in motivation or reactivity to the test conditions. It is especially important to evaluate these influences, since anticholinergics such as atropine and scopolamine alter food and water intake (Stein, 1963; Whitehouse, Lloyd, & Fifer, 1964) and increase reactivity to light (Oliverio, 1968). In a preliminary study in our laboratory, acquisition of an S^D-S^Δ discrimination was studied in rats that received atropine sulfate, atropine methylnitrate, or saline injections. Atropine in either form retarded acquisition primarily by depressing the response rate during S^D periods. This effect may have occurred because of the aversiveness of the light S^D or the unpalatability of the pellet reward (70% of the atropine Ss had difficulty eating). The present experiment examined the effects of atropine on performance of an S^D-S^Δ discrimination under conditions where the influence of the cue could be directly evaluated. Difficulties in ingesting reward were eliminated by using a sucrose solution.

SUBJECTS

Eight female Holtzman rats, approximately 270 days old at the

start of the experiment, were assigned randomly to one of four groups of two Ss each: (A) buzzer-on S^D, buzzer-off S^Δ; (B) buzzer-off S^D, buzzer-on S^Δ; (C) light-on S^D, light-off S^Δ; (D) light-off S^D, light-on S^Δ. The rats were caged singly and maintained at 75% of their ad lib weight by food deprivation. Water was available at all times except during the experimental sessions.

APPARATUS

A Scientific Prototype A 100 chamber was modified to accommodate a rat lever, a cue light (No. 509 K), and a dipper (Lehigh Valley, Model 1351) on the front panel. A buzzer was located outside the chamber. Conventional relay circuitry programmed test conditions and reinforcement and recorded performance. Each rewarded barpress allowed S 3 sec access to an 8% sucrose solution presented in a 0.1-cc cup. The chamber was housed in a Coleman ice chest which contained an exhaust fan.

PROCEDURE

The rats were initially trained to barpress on an VR 10 schedule with S^D cue conditions in effect. They were then trained on the S^D-S^Δ discrimination until they made 85% of their responses during S^D periods for three consecutive sessions. Each 30-min session consisted of 1-min-long S^D and S^Δ periods that were alternated beginning with an S^D interval. Once discrimination had stabilized at the 85% criterion level, drug tests began. Each S received two tests at each of two doses (2 mg/kg, 5 mg/kg) of atropine sulfate, atropine methylnitrate, or volumetric equivalents of saline. Both drug and dosage were counterbalanced; 1-4 days of tests without injections followed each drug session to reestablish baseline performance and insure complete elimination of the drugs. Drugs were injected intraperitoneally 20 min before testing.

STATISTICAL ANALYSIS

Preliminary analyses indicated that

there were no consistent order effects or changes in baseline performance with testing. Accordingly, the data for all noninjected sessions were pooled to provide a baseline measure, and changes in performance due to the independent variables were expressed as difference scores from the noninjected baseline. Mixed-model analyses of variance (Myers, 1966, p. 198) were performed. The valence of the S^D (cue on or cue off) was a between-S variable, and drug and dose were within-S variables. Analyses were done on difference scores for the percentage of responses made during S^D periods and for the S^D and S^Δ rate measures. On each of these three measures, the main effect of drug was further analyzed by the method of linear contrasts (Myers, 1966, p. 330). On each measure, the following set of orthogonal contrasts was tested: (1) performance under atropine sulfate was compared to performance under atropine methylnitrate and saline; (2) performance under atropine methylnitrate and saline was compared. Separate analyses were performed for Ss trained with each type of cue (buzzer or light).

RESULTS

Table 1 summarizes the performance of the rats trained with the buzzer. Since drug dosage did not affect performance significantly on any measure, data from both tests at each of the two doses were pooled. Atropine sulfate, but not atropine methylnitrate, reduced the percentage of responses made during S^D periods by increasing response rates during S^Δ intervals. There was little change in response rate during S^D periods (middle panel of Table 1) due to drug treatment ($F < 1$), but statistical analysis of the percentage of responses made during S^D periods (upper panel of Table 1) revealed significant drug effects. On the percentage measure, performance under atropine sulfate differed from that under atropine methylnitrate and saline ($F = 21.11$, $df = 1/4$, $p < .025$), but there was no significant difference between atropine methylnitrate and saline ($F < 1$). Analysis of the S^Δ rate measure (lower panel of Table 1) revealed a similar pattern of drug effects. Again atropine sulfate differed significantly from atropine methylnitrate and saline ($F = 10.33$, $df = 1/4$, $p < .05$), but the latter two treatments did not differ. The higher dose of atropine sulfate tended to produce greater effects on both the percentage measure and the S^Δ rate measure, but these trends were not reliable. The valence of the cue did not affect performance on any measure.

Performance of the rats trained with the light is shown in Table 2. Analysis of the percentage measure

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Table 1
Performance of Rats Trained with the Buzzer

Group*	Atropine Sulfate	Atropine Methyl-nitrate	Saline	Baseline
	Mean Percent Responses During S ^D Periods			
A	79.2	84.9	87.3	85.8
B	84.8	90.3	90.7	89.2
	Mean Response Rate During S ^D Periods			
A	734.0	729.3	752.0	724.5
B	734.5	723.3	776.3	726.5
	Mean Response Rate During S ^Δ Periods			
A	195.5	137.5	110.3	122.0
B	135.5	74.0	78.5	94.0

*Valence of cue: (A) Buzzer On—S^D, Buzzer Off—S^Δ; (B) Buzzer Off—S^D, Buzzer On—S^Δ.

Table 2
Performance of Rats Trained with the Light

Group*	Atropine Sulfate	Atropine Methyl-nitrate	Saline	Baseline
	Mean Percent Responses During S ^D Periods			
C	86.4	92.1	89.3	89.3
D	84.6	90.3	86.3	85.8
	Mean Response Rate During S ^D Periods			
C	629.4	685.5	718.0	739.9
D	740.9	719.9	767.0	785.0
	Mean Response Rate During S ^Δ Periods			
C	92.4	60.1	85.4	88.1
D	135.9	83.4	128.3	145.8

*Valence of cue: (C) Light On—S^D, Light Off—S^Δ; (D) Light Off—S^D, Light On—S^Δ.

revealed a significant drug effect ($F = 11.81$, $df = 2/4$, $p < .025$) which resulted from a slight impairment in performance under atropine sulfate and a slight improvement under atropine methylnitrate. Subsequent tests revealed significant differences in performance between atropine sulfate and atropine methylnitrate ($p < .05$), but neither atropine treatment differed from saline. Both forms of atropine tended to depress responding during S^D intervals, but these trends were not significant. Neither dose nor valence of the cue significantly affected performance.

DISCUSSION

The performance of rats trained with the buzzer is in close agreement with the expectations of Carlton's (1963) hypothesis. Atropine sulfate impaired performance of a well-established discrimination by increasing the rate of irrelevant responses. Since atropine methylnitrate did not produce these

changes, the behavioral effects of atropine sulfate are clearly central and the data support the existence of a central cholinergic system involved in the inhibition of ineffectual responses. These results also demonstrate that centrally active anticholinergic drugs can produce disinhibition of responses controlled by external stimuli, supporting the conclusions of Heise & Lilie (1970).

The behavior of animals trained with the light stimulus appears to be at variance with the expectations of Carlton's hypothesis. However, it must be recognized that atropine can produce photophobia by preventing pupillary constriction. Photophobia, which would depress responding in the light, could cancel the effects of blocking the central cholinergic inhibitory system. Many, but admittedly not all, of the trends in the response rate data support this interpretation. In any event, the use of light as a discriminative stimulus

introduces unnecessary complications in the study of anticholinergic drugs.

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