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The Effects of Scopolamine on Three Different Types of Suppressed Behavior of Rats

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McKIM, W. A. *The effects of scopolamine on three different types of supressed behavior of rats.* PHARMAC. BIOCHEM. BEHAV. 12(3)409–412, 1980.—Twelve albino rats were trained to lever press on a variable-interval one min schedule for sweetened condensed milk reinforcement. While responding on this schedule a two minute tone was presented. For one group it signalled a response contingent shock (Punishment), for another group it signalled the delivery of an unavoidable non-contingent shock at its termination (CER) and for a third group, reinforcement was withheld during the tone (Extinction). In the first experiment scopolamine in doses of 0.8 to 12.8 mg/kg did not alter response rates during the tone for any group. In a second experiment 16 hooded rats were tested with 6.4 mg/kg of scopolamine using a similar procedure, but with different shock levels, apparatus, reinforcement and session duration. For all three groups the drug depressed responding during the tone. It was concluded that when all other aspects of the situation are equated scopolamine will produce the same effect on behavior suppressed by punishment, CER and extinction.

Conditioned emotional response Extinction Operant behavior Punishment Rat Scopolamine Suppressed responding Variable interval schedule

ATTEMPTS have been made to compare the effects of drugs on behavior that has been suppressed by different means and it has been found that a drug effect may depend on whether the behavior being studied has been suppressed by contingent electric shock (punishment), non-contingent shock (conditioned emotional response, CER), or by extinction [4,5].

For example, Miczek [8] has found that scopolamine decreases punishment suppressed behavior of rats, yet it increases responding during periods of discriminated extinction when these two procedures are components of a multiple schedule. A similar effect has also been demonstrated using squirrel monkeys [3]. Other experiments have examined the effect of scopolamine on behavior suppressed by a CER and found the drug to have no effect [9].

One difficulty which arises when comparing drug effects such as these is that it has been shown that changes in procedure can modulate the effect of a drug. McMillan and his colleagues have demonstrated that parameters such as the strength and duration of the aversive stimulus, the schedule of the positive reinforcement and the schedule of presentation of the punisher can modify drug effects on punished behavior [2, 6, 7]. It is also likely that such variables are also important in CER and extinction.

The purpose of this research was to compare the effects of scopolamine on behavior suppressed by punishment, CER and extinction procedures while attempting to reduce as many other differences in procedure as possible.

EXPERIMENT 1

METHOD

Subjects

The subjects, twelve male albino rats, bred at Woodlyn Farms, Guelph, Ontario, were three months old at the start of training. They were deprived to 80% normal body weight for the duration of the experiment.

Apparatus

The rats were tested in Lehigh Valley Electronics animal boxes (model 1316, Lehigh Valley Electronics, Beltsville, Maryland), which were housed in metal, sound attenuating chambers. On one wall of the experimental chamber there were two levers and in the center of the wall there was an opening for the dipper mechanism which delivered approximately 0.1 cc of a mixture of equal parts tapwater and sweetened condensed milk. The levers were located 9 cm on either side of the feeder about 2.5 cm from the floor of the chamber. Only the lever to the left of the feeder was used in this experiment and the remaining lever was retracted.

The floor of the boxes was made of stainless steel rods through which a footshock could be delivered to the rats. Shock was generated by a Grason-Stadler shock generator, model E106GS, (Grason-Stadler Company, Inc., Concord, MA.).

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Procedure

The animals were randomly divided into three groups of four, labelled Extinction (EXT), Punishment (PUN), and Conditioned Emotional Response (CER). One rat was dropped from the CER group (this rat accidentally received a 110 VAC electric shock through the feeder mechanism and refused to respond for many sessions), leaving this group with only three rats.

All rats were trained in the response chamber to depress the lever for a reinforcement of sweetened condensed milk. They were trained on a VI one min schedule for one hr every second day for about three weeks. At this point their response rates showed no indication of any systematic changes. Three 1000 Hz tones, each of two min duration, were then presented to each rat during every session at random intervals. The rates of responding were recorded during each tone (conditioned stimulus, CS), as well as during a two min period preceding the CS (pre-CS). Training was continued until the two rates were consistently equal.

At this point a differential training procedure was initiated during the tone. For EXT group, the feeder mechanism was disconnected for the duration of the tone so that an extinction schedule would be in effect. The PUN group received a scrambled 0.5 mA intensity shock of 0.5 sec duration through the grid floor of the chamber for every response emitted during the CS presentations. The CER group received a shock of the same intensity and duration, but only at the termination of each CS. For the PUN and CER groups the VI Schedule remained in effect during the tone.

Total pre-CS and CS responses were then used to calculate a suppression ration (SR) for each session. The formula for the calculation of the ratio was:

$$SR = \frac{\text{CS response}}{\text{Pre-CS responses} + \text{CS responses}}$$

This formula is the same as the one used by Annau and Kamin [1].

Using this ratio, 0.00 indicates no responding during CS presentations or complete suppression; 0.50 indicates equal responding during the two intervals and ratios greater than 0.50 indicate an increase in responding during the CS.

After several sessions the ratios for the PUN and CER groups were 0.09 and 0.07 respectively, and showed no systematic change, indicating nearly complete suppression of responding during the CS. The EXT group had still not fallen below an average of 0.45 indicating very little suppression during the CS. A special procedure was then initiated in an attempt to lower their suppression ratios.

For ten one-hr sessions the onset of the CS signalled non-reinforcement as usual, however, a Change Over Delay (COD) of 2 min was in effect. Every response reset the timer and delayed the termination of the CS by 2 min. Thus, each subject was required to completely suppress all responding for two min in order to return to the VI one min schedule otherwise in effect.

After ten such sessions the average SR for this group was 0.25 which still indicated considerably less suppression than the other two groups. They were, nevertheless, consistent and apparently reflected stability of responding. The COD schedule was discontinued and the rats were returned to the previously described discriminated extinction schedule. Their SR remained at 0.25 and showed no signs of changing.

After all groups had stabilized, drug injections were started. Each group was run every second day and every second session was a drug session. Scopolamine hydrobromide was given IP immediately before each session in the following doses: 0.8, 1.6, 3.2, 6.4, and 12.8 mg/kg body weight. Each dosage was administered three times to each rat in a random order and each rat was injected with saline before all non-drug sessions.

RESULTS

Figure 1 shows the group means for CS rate, pre-CS rate and suppression ratio (SR) for each drug dosage. Each drug data point is the average for all animals in that group based upon three drug administrations for each rat at that dosage, saline data points are the average of fifteen saline sessions for each rat.

As can be seen from Fig. 1 there was a consistent decline in pre-CS rate of responding in all groups with increasing scopolamine doses. A 3×6 repeated measures analysis of variance was done on these data which showed this decline to be significant, $F(5,38)=14.0$, $p<0.01$. There was no significant difference found for either the groups main effect, $F(2,10)=1.62$, $p>0.05$, or the groups×dosage interaction, $F(10,38)=1.01$, $p>0.05$, showing that this decline was similar for all treatment conditions.

A similar analysis done on the responding during the CS showed a significant groups effect, $F(2,10)=32.20$, $p<0.01$, reflecting the high initial rate of the EXT group, but no significance was found for the dosage, $F(5,38)=0.803$, $p>0.05$, or the groups×dosage interaction, $F(10,38)=0.99$, $p>0.05$.

An analysis of the SR data showed a significant drug-produced increase in SR, $F(5,38)=6.93$, $p<0.01$, which reflects the decrease in pre-CS rate and the lack of change in CS rate. There was a significant group effect reflecting the high initial SR for the EXT group, $F(5,38)=83.8$, $p<0.01$, but the groups×drug interaction was not significant $F(5,38)=0.717$, $p>0.05$.

These data show that the drug decreased the VI response rate in the pre-CS period, but had no effect on any suppressed behavior at any dosage.

DISCUSSION

It might be argued that the EXT group was not really suppressing behavior as a result of extinction because of its previous training with the COD, a form of punishment. Consequently a second experiment was done in which COD was not used.

EXPERIMENT 2

Experiment 2 was similar in design to Experiment 1, different procedures, apparatus and subjects were used. In addition, no dose response data were collected and no COD procedure was employed.

METHOD

Subjects

The subjects in this experiment were 18 male Long-Evans strain hooded rats obtained from the Canadian Breeding Farm and Laboratories, La Prairie, Quebec. They were 90 days old at the beginning of the experiment. The rats were kept on 80% of their 90 day old weight for the duration of the study. Water was always available ad lib in their home cages. The rats were assigned randomly to three groups of 6 rats each. However, two animals died before the experiment could be completed.

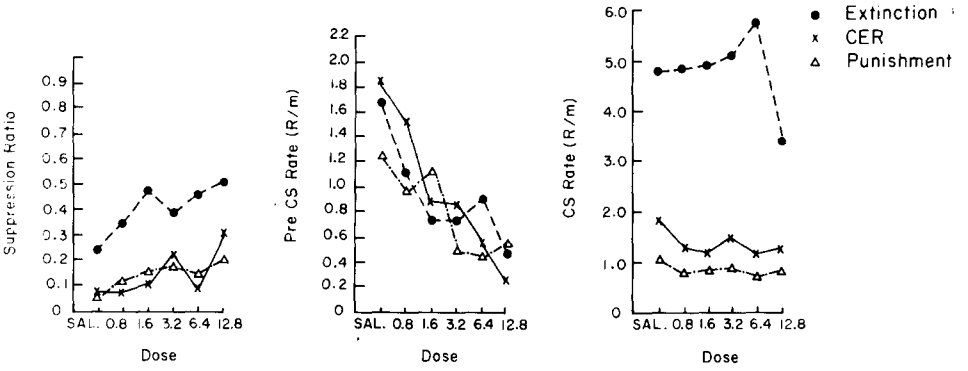

FIG. 1. Mean suppression ratio, CS rate and pre-CS rate at different doses of scopolamine for animals in Experiment 1.

Apparatus

The apparatus used in this experiment was one BRS animal chamber, 24 cm wide, 30 cm long and 20 cm high (BRS Electronics, Beltsville, Maryland). The ceiling and two walls were made of clear Plexiglas; two walls were made of aluminum and the floor consisted of 14 stainless steel rods 0.5 cm in diameter. A small food hopper protruded from the middle of one of the aluminum walls about 1 cm from the floor. Midway between this hopper and the right side of the box was an aluminum lever protruded 3 cm from the wall about 7 cm from the floor.

Presentations of stimuli, food pellets and electric shock were controlled by electro-mechanical equipment located in another room. The animal chamber was housed in an isolation box made of 1.7 cm thick plywood and white noise was used to mask extraneous noises.

Procedure

Once the rats were brought to 80% of their free-feeding body weight they were shaped to depress the lever in the animal chamber. After shaping, the rats were placed on a VI 1 min schedule for approximately 10 to 15 sessions until their rate of responding was stable both within and between sessions. Animals were normally run for one half hour once a day every day.

After their VI rates were stable, a 2 min tone of approximately 1000 Hz was sounded at random intervals twice per session to each rat. Responses emitted during the tone and the two min prior to the tone were recorded and a suppression ratio similar to that used in Experiment 1 was calculated. The tone was presented until response rates during and preceding the tone were equal.

At this point differential training procedures were initiated. The three groups of six animals were treated in a manner similar to Experiment 1 except that the PUN group was shocked at a 0.2 mA level with a duration of either 0.5 sec or the duration of the lever press, whichever was shorter. Another exception was that the shock intensity was set at 0.2 mA for a 0.5 sec duration for the CER group. At this point as well, all animals were injected with 2.5 cc/kg body weight normal saline IP 15 min before being placed in the operant chamber.

The SR's for each group stabilized at the following levels: EXT, 0.14; PUN, 0.06; and CER, 0.16. These means were considered to be similar enough and so no extra training or manipulation of shock levels was considered necessary and drug injection was begun. The COD procedure used in Experiment 1 was not used in Experiment 2.

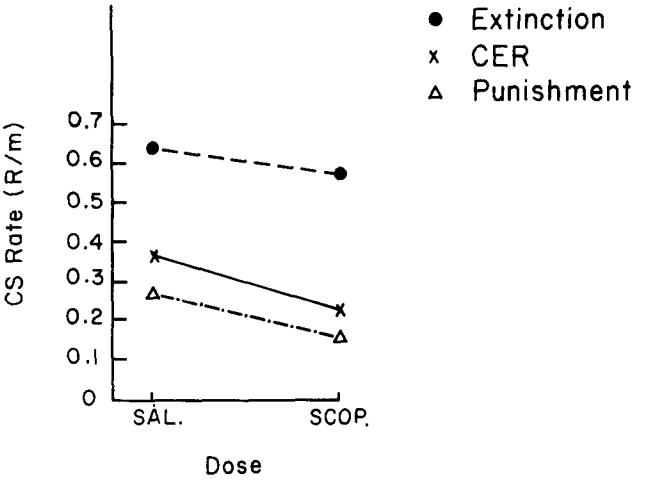

FIG. 2. Mean CS rate after saline and 6.4 mg/kg scopolamine for animals in Experiment 2.

All animals were injected IP with 6.4 mg/kg scopolamine hydrobromide 15 min before each drug session. Three drug sessions were given each animal and two saline control sessions were given between each drug session. The rats were run at approximately the same time every day.

RESULTS

Of the 18 animals who started the experiment, 16 finished the full course of injections. One animal in the CER group died of chronic respiratory disease before he was given any drug injections and subject in the PUN group died of a similar infection after the first injection of scopolamine. The data from this latter rat, however, are included in all graphs and analyses.

As in Experiment 1 the drug produced a decline in the pre-CS rate as determined by a 3×2 repeated measures analysis of variance, but unlike Experiment 1 there was also a significant decline in CS response rate produced by the drug. $F(1,14)=8.74$, $p<0.005$. There was, however, no group×drug interaction, $F(2,14)=1.37$, $p>0.05$, or significant groups main effect, $F(2,14)=3.26$, $p>0.05$, showing that the drug produced an equal decrease in CS response rates for all three groups. Mean CS response rates are presented in Fig. 2.

DISCUSSION

Although scopolamine caused no change in suppressed responding in Experiment 1 and decreased it in Experiment 2 there was never any differential drug effect due to the different treatment conditions. Since there were so many differences between Experiments 1 and 2 it is impossible to suggest which variation in procedure, training, apparatus or strain of subject contributed to the difference in drug effect, but it can be concluded that when other factors are held constant scopolamine will effect behavior suppressed by punishment, CER and extinction in the same way.

Earlier research has indicated that scopolamine increases behavior suppressed by extinction or non-reinforcement, but does not increase behavior suppressed by punishment or CER. Since all three procedures in this experiment were presented in the usual format of a CER, it may be reasonable to suggest that previously noted differential effects may have resulted from different experimented procedures such as intensity or duration of the controlling stimulus, duration of components or the nature of other components in the schedule. The question of which factors are important will have to await further research.

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