Effects of scopolamine on a "go-no go" avoidance task in rats¹

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After three days of training on an one-way active avoidance task in a shuttle box, rats were injected with scopolamine (0.2 mg/kg) or saline for the next two days and given a random order of active and passive avoidance trials with opposed external cues. Scopolamine did not interfere with passive avoidance training.

Parenteral injection of such anticholinergic agents as atropine and scopolamine, which have potent central and peripheral effects, has been shown to impair performance on passive avoidance (PA) tasks (Bignami, 1966b; Bovet, Robustelli, & Bignami, 1965; Brimblecombe, 1965; Buresova, Bures, Bohdanecky, & Weiss, 1964; Dilts & Berry, 1965; Meyers, 1965; Meyers & Lazarus, 1967). Moreover, it appears that this impairment results from a central anticholinergic action (Dilts & Berry, 1965; Meyers, 1965). It is of interest to note that in only two of these studies, which used highly similar procedures (Bignami, 1966b; Bovet et al, 1965) was a specific external stimulus employed relevant to the PA task.

Since Laties & Weiss (1966) have demonstrated for scopolamine a differential effect on behavior depending upon whether or not an external stimulus is available, it is pertinent to ask if scopolamine will produce the usual deficit in PA when the behavior is externally-cued. The present study attempted to make this determination by first training rats on an externally-cued, one-way active avoidance (AA) task and then interpolating externally-cued, PA trials after scopolamine injection.

Subjects

Twenty male rats of Wistar stock, allowed free access to food and water and ranging in weight from 254-365 g at the beginning of the experiment, were randomly assigned in equal numbers to two groups: (1) saline and (2) scopolamine.

Apparatus

A modified Lafayette shuttle box was used with inner dimensions for each of the two compartments of 12 x 7-3/4 x 8 in. The top of each compartment housed a 25 W incandescent lamp above a section of frosted Plexiglas and could be raised to allow access to the interior. Since the front walls were constructed of one-way glass and the box was used in a darkened room, Ss could be observed covertly. The compartments were separated by a 2 in. high hurdle and a Plexiglas guillotine door. Relay circuitry in conjunction with timers, counters, etc. in an adjacent room were activated by E's closure of a switch to control the then automated presentation of stimuli and the counting of responses. A Standard Electric timer controlled by the relay circuitry and placed next to the shuttle box permitted E to record response latencies to the nearest .01 sec.

Procedure

For three consecutive days all Ss were trained identically on an AA response except that on the first day they were placed in the shuttle box for 5 min with the door raised so that exploration was possible. Training trials followed immediately with S always placed in the right compartment at the start of the trial. A trial was begun by E who simultaneously raised the guillotine door and depressed the switch (controlling the relay circuitry) which resulted in the offset of the house light of the right compartment. If S crossed the hurdle within 10 sec, the trial was terminated and an avoidance response recorded. If S did not respond within 10 sec, a scrambled shock (nominal setting of 1.0 mA, Grason-Stadler 1064GS) was delivered to the grid floor. A response within 10 sec of shock onset terminated the trial and was tabulated as an escape response. If S failed to respond during these 20 sec, the trial terminated. At the end of each trial, S was removed to a mesh cage for the duration of the intertrial interval (mean 60 sec with a range of 30-90 sec). When S reached a criterion of nine avoidance responses out of 10 consecutive trials, his training was discontinued for that day. Rats who did not reach criterion on any of these three days were discarded.

Thirty min prior to the first trial on the fourth and fifth training days, Ss were injected subcutaneously with 0.2 mg/kg scopolamine hydrobromide (as base) or with physiological saline. All injections had a volume of 1.0 ml/kg body weight. On these days, E administered 50 trials of which, in random order, 25 were AA trials as described above and 25 were PA trials. For a PA trial, S was placed in the right compartment in the usual way and the door was raised, but the light in the left compartment went off and shock was made available in that compartment for the 20 sec duration of the trial. If S crossed the barrier, the Standard Electric timer stopped and the latency of this response was recorded. However, the door remained open so that further responses, and therefore shocks as well, were possible. Thus, in order to passively avoid, S had to remain in the right compartment for the duration of the trial.

Results

The findings in terms of response latencies and percentage avoidance are presented in Fig. 1. Since the two groups did not differ³ on AA on Day 3, subsequent behavioral differences can reasonably be attributed to drug effects. In fact, on Day 4, the first day of drug administration, there were no significant differences between Ss injected with saline or scopolamine on either active or passive avoidance. Both groups did, however, display impaired AA on this day compared to Day 3, which prob-

Fig. 1. Median response latencies and percentage avoidance with injections on Days 4 and 5.

ably resulted from the conflict introduced by the PA contingency. On Day 5, the two groups again did not differ on PA, but now the scopolamine group was significantly inferior to the saline group on AA on both latency and percentage avoidance measures. This latter difference resulted from the tendency of the saline group to improve on AA trials on this day relative to Day 4 and the scopolamine group to do worse, although these tendencies reached significance only for the scopolamine group on the latency measure. Both groups showed significant improvement according to both measures on PA over days.

Discussion

Most notable is the fact that the scopolamine Ss were not impaired and performed at a high level on PA, despite the fact that the present dose has been shown to be effective in PA tasks lacking a specific external stimulus (Meyers, 1965; Meyers & Lazarus, 1967). Since during previous training on AA the illuminated compartment was safe and since the "start" compartment remained illuminated and was the safe one during PA, a simple transfer of a light-dark discrimination might have mediated this successful behavior. Indeed, scopolamine

seems not to impair discriminations (Dews, 1955; Herz, 1960). Although no simple explanation is available for the successful PA of these scopolamine Ss compared to the deficient performance of scopolamine Ss in previous externally-cued PA tasks (Bignami, 1966b; Bovet et al, 1965), the difference may lie in the clearly opposed stimuli for active vs passive avoidance in this study or in the difference between the one-way task used here vs the two-way tasks used in those studies (Bignami, 1966a). In any case, it seems clear that scopolamine does not produce a basic inability to passively avoid, but rather only in certain situations.

The effect of scopolamine on the AA task is difficult to assess since the two groups differed on only one of the two drug days. Finally, in view of the fact that many investigators have suggested a hippocampal site of action for anticholinergic drugs (e.g., Meyers, 1965), it is interesting that findings very similar to the above have been reported for hippocampectomized rats (Coscina & Lash, 1967).

References

- BIGNAMI, G. Anticholinergic agents as tools in the investigation of behavioral phenomena. Paper read at 5th Int. Congr. Coll. Int. Neuro-Psychopharmacol., Washington, March, 1966a.
- BIGNAMI, G. Effects of anticholinergic drugs on successive "go-no go" discrimination in the rat. Paper read at 5th Int. Congr. Coll. Int. Neuro-Psychopharmacol., Washington, March, 1966b.
- BOVET, D., ROBUSTELLI, F., & BIGNAMI, G. Étude du conditionnement inhibiteur chez le rat. Action de l'amphétamine, de la chlorpromazine et des agents cholinergiques. *C. R. Acad. Sci. (Paris)*, 1965, 260, 4641-4645.
- BRIMBLECOMBE, R. W. Effects of centrally acting drugs on acquisition of a passive avoidance reaction in the rat. In D. Bente & P. B. Bradley (Eds.), *Neuropsychopharmacology*. Vol. 4. New York: Elsevier, 1965. Pp. 333-336.
- BURES, J., BOHDANECKÝ, Z., & WEISS, F. Effect of atropine on learning, extinction, retention and retrieval in rats. *Psychopharmacologia, (Berl.)* 1964, 5, 255-263.
- COSCINA, D. V., & LASH, L. The effects of bilateral hippocampectomy on a shock vs. shock conflict. Paper read at East. Psychol. Assoc., Boston, April, 1967.
- DEWS, P. B. Studies in behavior. II. The effects of pentobarbital, methamphetamine and scopolamine on performances in pigeons involving discriminations. *J. Pharmacol. exp. Ther.*, 1955, 115, 380-389.
- DILTS, S. L., & BERRY, C. A. Effects of scopolamine in a one-trial learning situation. *Pharmacologist*, 1965, 7, 171. (Abstract).
- HERZ, A. Die Bedeutung der Bahnung für die Wirkung von Scopolamin und ähnlichen Substanzen auf bedingte Reaktionen. *Z. Biol.*, 1960, 112, 104-112.
- LATIES, V. G., & WEISS, B. Influence of drugs on behavior controlled by internal and external stimuli. *J. Pharmacol. exp. Ther.*, 1966, 152, 388-396.
- MEYERS, B. Some effects of scopolamine on a passive avoidance response in rats. *Psychopharmacologia, (Berl.)* 1965, 8, 111-119.
- MEYERS, B., & LAZARUS, M. A. Diminished responsivity on a passive avoidance task to second administration of scopolamine. *Psychol. Rep.*, 1967, 20, 175-178.

Notes

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3. All statistical comparisons between the saline and scopolamine groups were made with the Mann-Whitney U test. The Wilcoxon test was used to compare the performance of a group between days. All tests were 2-tailed and findings were terminated significant if associated with $p < .05$.