Scopolamine, amphetamine and light-reinforced responding¹

PETER L. CARLTON

RUTGERS-THE STATE UNIVERSITY

Behavior maintained by response-contingent illumination declines within the session. This decline is reversed by the anticholinergic, scopolamine, but not by the stimulant, amphetamine. These data may be related to earlier findings implicating acetylcholine (ACH) in habituation and in certain functions of the hippocampus.

We have reported (Carlton & Vogel, 1965) data suggesting that the normal activity of the naturally occurring neurotransmitter, ACH, may be required for the process of habituation. That is, the normal loss of stimulus effectiveness consequent to exposure (habituation) appears to be blocked by the anticholinergic scopolamine, which blocks the muscarinic actions of ACH (cf., Carlton, 1965).

Here, we examined this possibility further by capitalizing on the facts that, first, an animal will respond to produce illumination and that, second, such responding declines in the course of the session. This decline may reflect habituation to the initially reinforcing "novelty" of the illumination (see Thompson & Spencer, 1966). If scopolamine, by attenuating the action of ACH, reduces habituation, it should reverse this decline in responding.

In addition to scopolamine, we also studied the effects of amphetamine, a stimulant that shares many of the effects of scopolamine (see Carlton, 1963) but does not attenuate ACH-activity as does scopolamine.

Method

Eighteen adult, male albino rats were randomly assigned to the three groups described below.

We used two operant chambers in which the viewing windows were masked. The sole source of illumination was a single, 15 vac, GE 304 bulb mounted on the back wall of the chamber.

Any depression of the lever in a chamber turned on the light for 3 sec. By continuously depressing the lever for more than 3 sec., however, the animal could keep the light on for the duration of the depression ("holding time").

Eight weekly 3-hr. sessions were given. In sessions 6-8 the animals were removed from the chamber after the first 90 min., given an intraperitoneal injection (1.0 cc/kg) and replaced for the remaining 90 min. Different groups of six rats each were given saline, scopolamine hydrobromide or d-amphetamine sulfate. Three animals in each group worked in each response chamber. Low, medium and high (L, M and H) doses of each drug were given. For scopolamine these were 0.1, 0.3 and 0.5 mg/kg; for amphetamine they were 0.5, 1.0 and 1.5 mg/kg (all doses are in terms of weights of the

salts). The order in which they were given was M, H and L for both drug-groups. These doses of both drugs have profound effects on a variety of operant behaviors (see Carlton, 1963).

All probability statements are based on "within" subjects, nonparametric analyses of variance (Walker & Lev, 1953, p. 438).

Results

Data obtained in Sessions 1-5 were broken down into four categories: holding times and numbers of responses in the first and second halves of the sessions. These categories were separately analyzed for each response chamber. None of the eight analyses indicated a reliable between-sessions effect in Sessions 1-5. Accordingly, the data from Sessions 1-5 were pooled.

Fig. 1. Dose-response curves for amphetamine and scopolamine.

These data indicated a marked within-session decline in responding and complete recovery between weekly sessions. Numbers of responses averaged 52.1 in the first 90 min., and 12.6 in the second 90 min.; the corresponding holding times were 52.4 sec. and 13.7 sec.

The effects of drug injections are shown in Fig. 1; data from the 90-min. post-dose period are plotted. (The "zero" values were obtained from Session 5.) Scopolamine produced a reliable dose-dependent increase in both response frequency and holding-time within sessions 5-8 ($p < 0.02$ in both analyses). In contrast, amphetamine produced a small, reliable ($p < 0.02$) increase in responding but did not reliably alter holding-time. Saline injections affected neither measure.

The tendency for amphetamine to increase only response frequency resulted in a reliable decline ($p < 0.005$) in holding time/response. Neither saline nor scopolamine produced a comparable effect. Average ratios for the saline group ranged from 0.82 to 1.08; the range for scopolamine animals was 0.79 to 1.05. The values for the amphetamine group were 0.87, 0.72, 0.51 and 0.52 in sessions 5-8.

Discussion

Amphetamine, by affecting only response frequency, reliably reduced holding-time/response. This effect is presumably related to the stimulant action of this drug. Scopolamine increased both response frequency and holding-time without reliably changing the ratio of the two measures. These data are in general agreement with two other reports. First, Barry et al (1963) found that amphetamine increased the light-reinforced responding of rats without altering the amount of time the light was on. Second, Tapp (1964) reported increased responding for light due to atropine, a drug qualitatively identical to scopolamine in its effect on ACH-activity.

Scopolamine, but not amphetamine, increased behavior "directed" to illumination of the response chamber; the lack of effect on holding-time/response indicates that the pattern of responding was normal despite an overall increase in response output. Scopolamine restored response-output to levels comparable to or greater than that obtained in the initial portions of the session. The 0.3 mg/kg dose of scopolamine produced an increase to a level roughly the same as that obtained in the first portion of the session. The animals behaved as if they had not had the initial exposure at all. The

high dose not only "reset" the animals to the beginning of the session but reduced the normal within-session decline; levels of behavior following the high dose were thus in excess of those in the initial portion of the session. This effect was not shared by amphetamine and, on this basis at least, cannot reasonably be attributed to a general stimulant action.

These data suggest that attenuated ACH-activity may attenuate habituation, i.e., habituation to the "novelty" of the light/onset. It is of particular interest that this effect of reduced ACH-activity parallels that of lesions of hippocampal areas of the brain (Leaton, 1963).

A possible parallel of attenuated hippocampal function by lesion or by reduced ACH-activity has been pointed out by Douglas & Isaacson (1966) in a report replicating an earlier study by Meyers & Domino (1964). Meyers and Domino also suggested that the effects of altered ACH-activity may involve the hippocampus. Related considerations have been discussed by Carlton (1965).

References

- Barry, H., Johnson, R. N., & Luckey, R. D. Preference for darkness or light was not altered by chlorpromazine or methamphetamine. Paper read at Psychonomic Society, August, 1963.
- Carlton, P. L. Cholinergic mechanisms in the control of behavior by the brain. *Psychol. Rev.*, 1963, 70, 19-39.
- Carlton, P. L. The hippocampus, brain-acetylcholine and habituation. Paper presented at Symposium on Brain, Biochemistry and Behavior, AAAS meetings, 1965.
- Carlton, P. L., & Vogel, J. R. Studies of the amnesic properties of scopolamine. *Psychon. Sci.*, 1965, 3, 261-262.
- Douglas, R. J., & Isaacson, R. L. Spontaneous alternation and scopolamine. *Psychon. Sci.*, 1966, 4, 283-284.
- Leaton, R. N. The effects of hippocampal lesions on reactions to novelty in the rat. Unpublished doctoral dissertation, Yale University, 1963.
- Meyers, B., & Domino, E. F. The effect of cholinergic blocking drugs on spontaneous alternation in rats. *Arch. int. Pharmacodyn.*, 1964, 150, 525-529.
- Tapp, J. T. Cholinergic mechanisms in operant behavior. Paper read at Symposium on Central Cholinergic Mechanisms and Behavior. American Psychological Association meetings, 1964.
- Thompson, R. F., & Spencer, W. A. Habituation: A model phenomenon for the study of neuronal substrates of behavior. *Psychol. Rev.*, 1966, 73, 16-43.
- Walker, H. M., & Lev, J. *Statistical inference*. New York: Henry Holt, 1953.

Note

1. Research supported by Public Health Service grants MH 08340 and MH 08585.