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Scopolamine Does Not Affect Footshock Sensitivity in the Rat[1]

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SMITH, R. F. *Scopolamine does not affect footshock sensitivity in the rat.* PHARMAC. BIOCHEM. BEHAV. 8(1) 31–34, 1978. – To test the generality of the finding of Feigley, *et al.* [8] that scopolamine increases sensitivity/reactivity to footshock, rats were tested under either scopolamine or saline conditions for sensitivity to footshock in an automated version of the flinch-jump paradigm. There was no significant trend toward increased sensitivity following scopolamine injection at any of the response magnitudes assessed. Since the previous study included an operant response in the measure of sensitivity, it was suggested that apparent effects of scopolamine on reactivity to footshock are dependent on the inclusion of an operant response in the measure of reactivity, and are not due to changes in sensory thresholds.

Scopolamine Cholinergic inhibitory system Footshock sensitivity

FEIGLEY, Beakey and Saynisch [8] have recently reported that injection of scopolamine hydrobromide increases sensitivity/reactivity to suprathreshold footshock in the rat, particularly in the range of shock amplitude slightly above the detection threshold of the undrugged rat. If confirmed, this finding would have profound implications for interpretation of data including that cholinergic blockade affects performance of rats on several shock-motivated tasks (see [6]). Increased sensitivity to footshock might adequately explain facilitated two-way active avoidance and facilitated bar-press avoidance behavior following injection of cholinergic blocking agents [2, 10, 14, 21]. In addition, confirmation of increased sensitivity after scopolamine would challenge interpretations of altered performance on shock-motivated tasks after limbic lesion (e.g., [12,18]), since limbic lesion has been reported to deplete brain acetylcholine [15]. Carlton [3] has described the effects of anticholinergic compounds on behavior as disinhibiting behavior, and several authors have drawn a widely accepted analogy between the effects of scopolamine and of hippocampal lesion [5, 7, 21]. Some of the effects of either chemical- or lesion-induced blockade of cholinergic function are commonly described as "decreased ability to withhold responses," and the notion that a cholinergic septalhippocampal system is involved in response inhibition has now become widely accepted [6]. The question of whether scopolamine injection produces a deficit in response inhibition, or merely increases sensitivity to stimuli, is therefore an important one.

Feigley, *et al.* [8] used escape latency after shock onset as their measure of reactivity to footshock. A number of authors have demonstrated that reduction of cholinergic activity by drug or lesion increases activity in several types of situations (e.g., [9, 16, 21]). Feigley, *et al.*'s measure of latency to escape thus included an operant activity response (running), known to be affected by changes in cholinergic activity, as part of the measure of reactivity to shock. Changes in latency after scopolamine might therefore be due either to increase sensitivity to footshock, or to increased reactivity to shock of the same perceived intensity.

While Feigley, *et al.* recognized this problem, their efforts to clarify interpretation failed to remove the ambiguity. To estimate changes in activity consequent to scopolamine injection, they randomly interspersed shock and pseudoshock (nonshock) trials. At the intensity where scopolamine had the most pronounced effect (0.07 mA), the drug decreased escape latency in the absence of shock in a dose-related manner on the shock trials. Their control of pseudoshock trials was inadequate in that latency to escape on the pseudoshock trials was latency after no stimulus at all. On the shock trials, latency was taken after a stimulus (shock) which they showed was detected by the animal. Since Graf [9] has shown that differential effects of environmental stimulation on activity are more pronounced in scopolamine-injected animals than in controls, it is plausible that animals with scopolamine injections should be more active after a stimulus (shock trial) than after no stimulus (pseudoshock trial). Because of this lack of comparability between shock and pseudoshock trials, no statement is justified as to whether scopolamine affected sensitivity to the shock, or the operant response (running) to that shock.

The present study, therefore, sought to determine if a

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dosage of scopolamine intermediate between Feigley, *et al.*'s most effective doses would affect sensitivity to footshock as determined by the elicited response to brief inescapable footshock. If sensitivity to footshock is affected by scopolamine, changes in responding to a brief inescapable footshock should be apparent in the same direction as Feigley, *et al.* noted in the operant response to a sustained footshock.

METHOD

Animals

Adult male Sprague-Dawley rats (275–300 g) were randomly divided into saline (n = 10) and scopolamine (n = 9) injection groups. Animals were colony housed on a 12:12 light-dark cycle, with free access to food and water.

Apparatus

A 7 × 7 × 20 cm Plexiglass chamber was equipped with a shock grid floor. The Plexiglass was rigidly connected to a telephone diaphragm, producing a voltage change whenever the cage was moved. This voltage was amplified by an Allied Electronics model MPA-20 20 W audio amplifier, rectified, and delivered to an Esterline-Angus recording milliammeter. A pen deflection was thus produced by a movement of the chamber (i.e., rat), with the deflection proportional to the magnitude of the movement.

For shock delivery, a BRS/LVE SGS-003 shock generator-scrambler was modified to allow external control of shock intensity. Ten rheostats were set to provide shock intensity for 0.2 mA to 2.0 mA in 0.2 mA increments (comparison with the intensities used by Feigley, *et al.* is not possible because of the differences in shock delivery systems). A BRS/LVE stepping switch provided a pre-set ascending, then descending pattern of intensities. An Automated Data Systems 1248A timer-counter with counter slave performed all timing and control functions.

Injection Procedure

Forty min prior to footshock sensitivity testing, each animal received an injection intraperitoneally of either 2.0 mg/kg scopolamine hydrobromide (Burroughs-Wellcome, Tuckahoe, NY) or an equal volume of normal saline.

Testing Procedure

Animals were placed in the Plexiglass chamber and allowed to habituate to the chamber for two min prior to footshock sensitivity testing. They were then administered four series of twenty shocks each, with the first ten shocks in ascending order of intensity, and the second ten in descending order. Fifteen sec elapsed between shocks within a series, and two min elapsed between series.

RESULTS

The animal's reaction to each shock was scored by measuring the deflection on the penwriter record. The scorer had no knowledge of the experimental treatment of the animal. Each animal received a total of eight shocks at each of ten intensities. Following scoring of shocks, the median response at each shock intensity was calculated, and the threshold current for four arbitrarily selected response amplitudes of 5, 10, 20, and 40 mm deflection was calculated by linear interpolation between shock intensities. These response amplitudes roughly covered the range between a medium flinch and a large jump, when compared to rater judgements of the responses. Thus, thresholds for four response amplitudes were obtained and used as the data for statistical analysis.

Figure 1 presents the mean thresholds for each response amplitude for the scopolamine and saline control groups. The lack of meaningful differences between groups was confirmed by a two-way repeated measures analysis of variance. This analysis indicated no significant main effect of drug treatment or significant interaction ($Fs<1$); only the repeated measures effect was significant ($F(3,51) = 34.68$, $p<0.001$), indicating that more current was required to elicit the higher response amplitudes. Thus, these data failed to provide any suggestion of an increase in shock sensitivity following injection of 2.0 mg/kg scopolamine.

DISCUSSION

The present data are clearly incompatible with the notion that scopolamine increases sensitivity to footshock. It is most likely that the obvious procedural differences between the present study and that of Feigley, *et al.* [8] may account for the apparent discrepancy. As mentioned in the introduction, Feigley, *et al.* used latency to move from the shocked compartment during continuous shock as their measure of reactivity, while the present study measured the elicited response from a single brief footshock. Since several reports cited above indicate that scopolamine may increase activity, it seems most probable that changes in responding after scopolamine are contingent on the inclusion of an operant response (e.g. running) in the dependent measure. When no such response is allowed, as in the present study, no trend toward increased reactivity is apparent following scopolamine injection.

Although levels of acetylcholine have been widely linked to the notion of response inhibition, [3], the present study found no significant effects of 2.0 mg/kg scopolamine on footshock sensitivity. Since another putative neurotransmitter, serotonin, has been widely linked to sensitivity to specific footshock [11,20] and auditory [4] stimuli, it may be profitable to make a distinction between emitted and elicited responses with respect to neurochemical systems of response inhibition. Thus, the septal-hippocampal cholinergic system has been largely implicated in control of emitted responses, such as water drinking in a passive avoidance situation [13], bar pressing on high fixed ratio schedules [18], DRL performance [17], Sidman avoidance [3], and spontaneous alternation [7]. Serotonergic mechanisms, on the other hand, appear to inhibit responsiveness to footshock [11,20] and auditory stimuli [4], i.e., to inhibit elicited responses. It is clear from the present data that scopolamine does not disinhibit all responses. Since other data suggest that serotonergic disruption may disinhibit responses to specific stimuli in at least some modalities, I suggest that the distinction between elicited and emitted responses carries the potential of helping to distinguish between the functions of serotonergic and cholinergic systems, each of which may be described as inhibitory. This distinction may reconcile the present data with those of Feigley, *et al.*, who used a response having some operant characteristics, while the present experiment measured only the elicited reaction to inescapable footshock. While scopolamine does not appear to increase sensitivity to footshock, apparent increases in reactivity may be observed if the dependent measure includes an operant response.

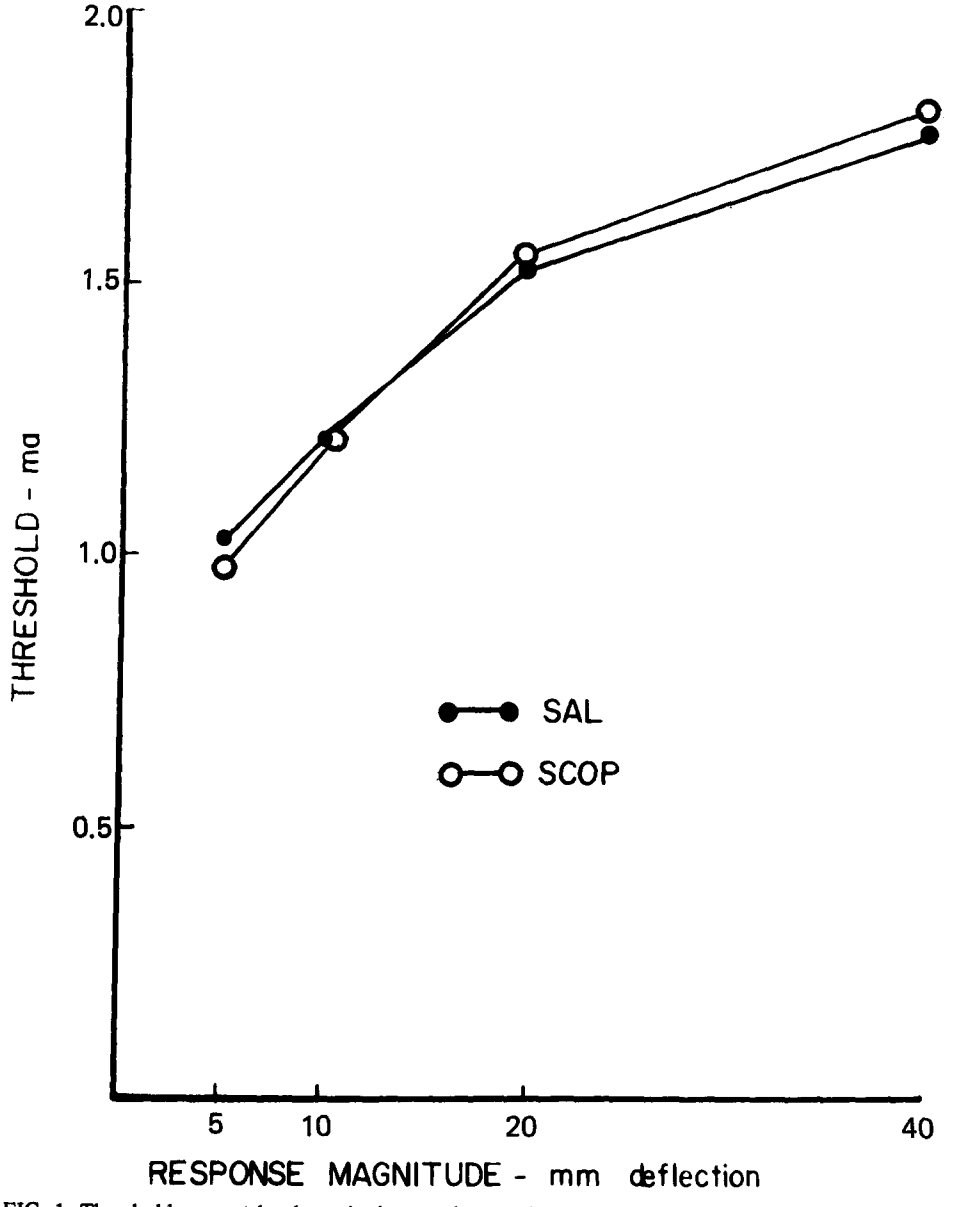

FIG. 1. Threshold current level required to produce each of the response amplitudes scored. There are no significant differences between groups on any response magnitude assessed.

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