Scopolamine effects on forced exercise to exhaustion*

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Three days after training, scopolamine-injected animals were found to exhaust sooner than similarly trained saline-injected and control groups. No differences in running times were found among groups 1 week after training. It is suggested that recently trained animals show greater reliance on a cholinergic system.

Scopolamine is reported to have greater central neural effects than such similar acting anticholinergic drugs as atropine and has been used in psychopharmacological studies of central acetylcholine activity (Goodman & Gilman, 1956). Behavioral changes observed in scopolamine-drugged animals vary and have been reported to include increased general locomotor and specific exploratory activity (Walters & Block, 1969), learning deficits in delayed matching and conditioned avoidance responses (Glick & Jarvik, 1970; Gruber et al, 1967; Herz, 1960), facilitation of moderate self-stimulators (Olds, 1970), and attenuation of conditioned suppression responses (Berger & Stein, 1969a, b). Therapeutic doses in humans usually cause drowsiness, euphoria, amnesia, and sleep, although, in some cases, excitement, restlessness, hallucinations, and delirium are evidenced (Goodman & Gilman, 1956). More recently, Safer (1970) found that, for humans, the psychotomimetic effects (mental and motor impairment) of scopolamine hydrobromide were enhanced by the combined effects of work (treadmill walking) and temperature stress. Although the precise neural mechanisms involved in the mediation of the above mentioned responses remain obscure, all are thought to be related to the attenuation of central acetylcholine activity.

It has been suggested that use of neuronal pathways may give rise to increased function by enhancing the manufacture and availability of transmitter substance (Eccles, 1964). Few studies have been devoted to the problem of scopolamine effects on motor activity in trained animals. It was the purpose of the present study to determine the effects of

scopolamine hydrobromide on forced treadmill running in exercise-trained animals.¹

SUBJECTS

The Ss were 32 male Sprague-Dawley rats obtained from a local supplier. They were housed four per cage and maintained on lab chow ad lib. The Ss were approximately 6 weeks of age at the onset of the experiment.

APPARATUS

The exercise apparatus was a motor-driven Quinton treadmill (Model 18-49B) equipped with an overlying floorless rectangular exercise unit having 15 individual running compartments. Shock (18-20 mA, dc) was administered through vertical electrodes located posteriorly in each compartment to animals not keeping pace with the treadmill belt. Shock was provided by a Grass stimulator, Model 54G.

PROCEDURE

The Ss were trained over a 9-day period (one 5-min session per day) to avoid shock by running on a treadmill at speeds progressing from 1.0 to 1.4 mph. They were then given six strenuous exercise sessions at 1.4 mph

on alternate days in which each S ran for 90 min or to exhaustion, whichever occurred sooner. Since most Ss showed such marked improvements in running times over four sessions, as noted by a sudden increment in criterion time scores, running speed in Sessions 5 and 6 was increased to 1.5 mph in order to assure sufficient exercise stress for further training adaptation. In a seventh and final session, all Ss ran to exhaustion. This latter running time is subsequently referred to as the preinjection time to exhaustion.

Three days or 1 week after Session 7, the animals were again exercised to exhaustion 15 min after an IP injection of either 1 mg/kg of scopolamine hydrobromide (N = 11) or an equal volume of saline (N = 10). The rationale for this procedure was to test the effects of scopolamine on Ss during the early and late stages of training deadaptation, during which different levels of cholinergic enhancement might be suspected. Another control group (N = 11) was given a needle wound only.

Individual preinjection and postinjection running times are listed in Table 1 according to subgroups, i.e., each group is further divided on the basis of whether the postinjection running time occurred 3 days or 1 week after training. Combined group scores based on running time to exhaustion are plotted in Fig. 1 by using the median of the difference scores (preinjection time to exhaustion minus postinjection time to exhaustion). Also shown in Fig. 1 are medians of the difference scores determined for the 3-day delay groups and the 1-week delay groups.

Using a procedural modification

Table 1
Running Times to Exhaustion*

Group	3-Day Delay		1-Week Delay	
	Pre-Injection	Post-Injection	Pre-Injection	Post-Injection
Control	28.5	36.0	25.5	22.0
	40.5	25.5	77.5	48.0
	44.0	56.0	127.0	60.0
	56.0	53.0	40.5	32.0
	58.5	51.0	45.5	35.0
	76.0	80.0		
Saline Injected	7.0	6.5	65.0	32.5
	35.5	51.5	90.0	66.0
	38.5	45.0	54.5	27.5
	41.0	60.0	116.5	90.5
	47.5	64.0	42.5	24.5
	49.5	22.0	38.0	46.5
Scopolamine Injected	111.0	53.5	41.5	35.5
	113.0	47.5	36.0	14.0
	65.0	36.0	6.0	9.5
	67.5	62.5	42.5	20.0
			53.5	14.0

*Times expressed to nearest .50 min.

*This work was assisted by Public Health Service Grant MH 5 T1 6415-13 awarded to the senior author, and facilities were provided by the Department of Physical Education, University of California, Los Angeles.

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Fig. 1. Combined group, 3-day delay, and 1-week delay subgroup median differences based on preinjection minus postinjection time to exhaustion.

suggested by Bradley (1968), the Kruskal-Wallis (K-W) one-way ANOVA and Wilcoxon rank-sum test (WR-S) were administered to test for main effects and interactions of the two treatment variables, drug and time after training. All analyses were done on difference scores. The upper limit of significance was set at the .05 level.

RESULTS

The scopolamine-injected Ss had lower performance scores, i.e., they exhausted sooner. In testing for main effects of the drug treatment, the K-W H value was significant at the .01 level. Using the WR-S test for main effects of time after training, the Wn value was significant at the .05 level. A K-W test for interaction was also significant at the .05 level.

By administering a K-W test to subgroup scores categorized according to time of postinjection testing, i.e., 3 days or 1 week, the H value for main effects of the drug treatment 3 days after training was significant at the .01 level, but it was not significant at the .05 level 1 week after training. Using the WR-S test, it was further noted that the difference among the 3-day postinjection subgroup scores was accounted for by the scopolamine-injected group, i.e., the saline and control subgroup scores (3-day delay) differed from the scopolamine subgroup scores but not from each other.

DISCUSSION

The finding that scopolamine effects were differentiated over time after training might be related to training adaptation of a central neural cholinergic system. Although this notion is speculative, it should be noted that Eccles & Westerman (1959) have provided indirect evidence for training adaptation involving cholinergic mechanisms. It was shown that excess use of hind-limb neural pathways (through exercise) in cats resulted in enhanced monosynaptic function. It was suggested that synaptic action might have been rendered more efficient by "increased size of presynaptic terminals or alteration in number." Inherent in this hypothesis is the assumption of an increased amount of neurotransmitter substance and release. Should training be accompanied by an increased synthesis of central cholinergic neurotransmitter substance, scopolamine as an anticholinergic could eliminate or minimize this effect. Why there was no observed difference among groups after 1 week of deconditioning was not clear. One possible explanation might be that scopolamine may exert a larger effect on cholinergic systems as acetylcholine synthesis is enhanced. Should increased neurotransmitter substance resulting from excess use of neural pathways appear during training, then the effects of scopolamine on running time might be expected to be less after a deadadaptation period. Of course, this assumes that cholinergic depletion plays a major role during the exhaustive phase of exercise, and the evidence from this investigation suggests that this might be true for

recently trained animals.

More experimental controls are needed, such as a methyl-scopolamine-injected group, in order to support the above speculations and to determine to what degree peripheral neural effects of scopolamine could have contributed to the present results. These preliminary results suggest, however, that neuropharmacologic techniques may prove to be useful in determining possible neuronal adaptations with exercise training.

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NOTE

1. Since this investigation was an adjunct to a learning study conducted by the same authors, it should be noted that all Ss utilized in this study had been previously trained on a maze task.