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BRIEF COMMUNICATION

Increased Acquisition of a Complex Appetitive Task After MSH and MIF[1]

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STRATTON, L. O. AND A. J. KASTIN. *Increased acquisition of a complex appetitive task after MSH and MIF.* PHARMAC. BIOCHEM. BEHAV. 3(5) 901–904, 1975. – After daily injections of melanocyte stimulating hormone (MSH), MSH-release inhibiting factor (MIF), or diluent albino rats ran a 12 choice Warden maze for a palatable food reward. Rats receiving the hormones had shorter latencies and made fewer errors than controls during learning but, unlike results with simple tasks, there were no differences during extinction. The results demonstrated that both MSH and MIF-I could facilitate the acquisition of an appetitive task which seemed of sufficient complexity to emphasize differences in performance.

Complex appetitive learning MSH MIF Warden maze

MELANOCYTE-stimulating hormone (MSH) produces resistance to extinction in relatively simple behavioral situations such as active and passive avoidance and appetitive T-maze problems [6]. However, less is known about the effect of MSH on extinction of complex tasks or on the learning process itself. Rats learned a simple brightness discrimination reversal faster after receiving MSH [14], but a complex conditional brightness habit was acquired more slowly by rats given the same pituitary hormone [15]. Sandman *et al.* [13] found that MSH tended to facilitate appetitive learning in a simple T-maze, but the degree of improvement was not statistically significant. We previously proposed [6] that MSH might have a differential effect on learning depending on the difficulty and type of problem.

Several hypotheses have been offered to explain the behavioral effects of MSH [6]. There is some evidence that MSH increases motivation or emotion [15,16] and attention [14]. These explanations might predict that rats receiving MSH would learn a complex maze faster than controls. The present investigation used a 12 choice maze to study the effects of MSH and Pro-Leu-Gly-NH_2, an MSH-release-inhibiting factor (MIF-I), on acquisition and extinction of a complex habit for food reward. MIF-I, a tripeptide found in the hypothalamus, may influence learning in a manner similar to that of MSH [12]. MIF-I exerts extra-endocrine effects upon the central nervous system of the rat, mouse, monkey, rabbit, and man [8, 9, 11].

METHOD

Animals and Apparatus

Twenty-one male albino Sprague-Dawley rats weighing between 250 and 280 g were obtained from ARS Laboratory. They were housed individually and provided free access to water in their cages. The rats were handled frequently to achieve gentling which might facilitate the appetitive nature of the task. All animals were deprived of food until they reached 85 percent of their original body weight. The 85 percent level was maintained throughout the experiment by pairing each rat with a nondeprived rat of similar weight to obtain a growth-weight norm. Each rat

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was ear-marked and assigned a number in 1 of 3 groups according to a series of computerized random numbers.

The apparatus was a 12 choice, 10 cul-de-sac Warden modular maze with a start box and a goal box manufactured by Lafayette Instrument Co. The food reward was a wet mash, prepared daily, which consisted of ground rat chow, sugar, and powdered milk mixed with water.

Procedure

After the rats were deprived of food for 24 hr they were placed in the goal box of the maze and allowed to eat for 1 min on Day 1, 2 min on Day 2, and 3 min on Days 3 and 4. An additional 10 g of rat chow were provided in the home cage, or an adjusted amount was given if rats fell below 82 percent or above 88 percent of the body weight of their matched pairs. Starting with the fifth day 7 rats received daily intraperitioneal injections of α-MSH (40 μg/kg), 7 received MIF-I (Pro-Leu-Gly-NH_2; 800 μg/kg), and 7 received an equal volume of diluent (0.01 M acetic acid in 0.9 percent saline). The solutions were coded so that the experimenter did not know which animals were receiving the hormones. Each day the rats were given daily injections of the designated solution 15 min before running the maze. They ran 2 trials on the first day and 4 trials every day during the next 9 days of training. At the end of each trial the animals were allowed 1 min to eat in the goal box before being transferred to the start box for the next trial. Total running time from start box to goal box (latency), and initial and repeated errors were recorded for each trial. Initial errors were recorded when a rat entered any cul-de-sac. Repeated errors were recorded when a rat entered the same cul-de-sac more than once during the same trial. Retracing errors were not counted unless a rat entered a cul-de-sac. Percentage weight gain from the first to the last day of study was calculated for each rat. Since only 2 rats required adjustment in supplemental feeding, and they were from different groups, this procedure was not considered to be a significant factor in testing for weight differences among groups. On Days 11 and 12 extinction trials were run by removing the wet mash from the goal box while keeping all other conditions constant. Identical hormone injections were continued during extinction. Time and total error scores were recorded.

RESULTS

A three-way analysis of variance (hormone X days X trials) was performed on the time it took rats to run from start box to goal box (latency) during Days 2–10 of acquisition. There was a significant decrease in running time over days, $F(8,144) = 56.36$, $p<0.001$, and trials, $F(3,54) = 4.87$, $p<0.01$, and a days by trials interaction, $F(24,432) = 10.45$, $p<0.001$. No other interactions were significant. Rats receiving hormonal injections took less time to reach the food reward than controls, $F(2,18) = 6.66$, $p<0.01$; Fig. 1. There were no differences between groups receiving MIF-I and MSH. A similar three-way analysis of variance of the initial errors showed that fewer errors were made by rats receiving MSH or MIF-I, $F(2,18) = 3.63$, $p<0.05$; Table 1. The effect of days, $F(8,144) = 65.98$, $p<0.001$, and the days by trials interaction, $F(24,432) = 5.61$, $p<0.001$, were significant. The small differences among the groups in repeated errors and all measures recorded during extinction were non-significant. An analysis for weight gain over the 12-day period showed no differences among groups.

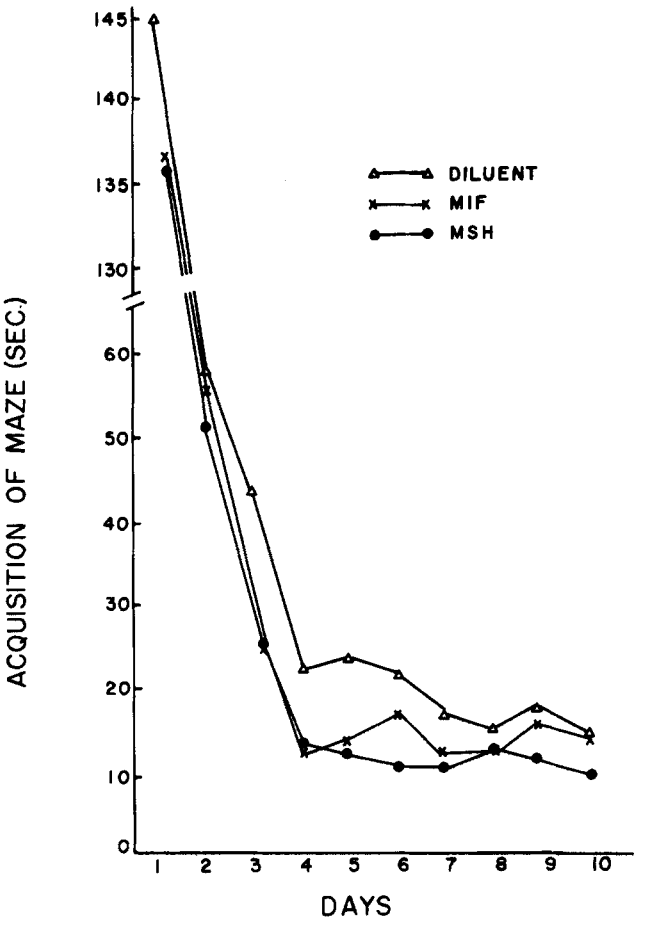

FIG. 1. Mean number of seconds to run the maze for hormonal and control groups during each day of acquisition.

DISCUSSION

Rats that received MSH and MIF-I had shorter latencies and made fewer errors than controls in learning a complex appetitive task. Sandman *et al.* [13] reported a nonsignificant decrease in latency when rats were given daily MSH before learning a simple T-maze for food. MSH also increased acquisition of visual discrimination and reversal learning problems using albino rats, but there were no differences between hooded groups [12]. Stratton and Kastin [16] found that MSH increased the number of avoidance responses made by rats at low but not at high levels of shock motivation. These findings suggest that MSH and related hormones affect acquisition as a function of task complexity as well as kind and degree of task motivation. Complex tasks offer a greater range of response possibilities and may be more sensitive in detecting differences in performance.

ACTH and MSH share a common polypeptide core ($MSH/ACTH_{4-10}$) which is the active agent necessary to increase resistance to extinction of a conditioned avoidance task [2]. Like MSH, ACTH has a differential effect on avoidance learning depending on the level of extrinsic motivation, although ACTH appears to be maximally effective at high levels of shock [1], whereas MSH is most effective at low shock levels [16]. In a study by Gray *et al.*

TABLE 1

TIME, ERRORS, AND WEIGHT GAIN (MEAN ± S.E.) DURING LEARNING AND EXTINCTION

Treatment	Total Time Acquisition (sec)	Initial Errors Acquisition	Repeated Errors Acquisition	Total Time Extinction (sec)	Total Errors Extinction	Weight Gain Days 1–12 (g)
MSH	820.00 ± 53.99†	60.71 ± 4.03*	13.57 ± 1.85	610.00 ± 77.92	32.43 ± 3.68	26.00 ± 2.85
MIF-I	902.00 ± 57.54†	67.14 ± 6.93*	16.29 ± 3.23	550.00 ± 25.36	32.00 ± 1.36	22.86 ± 1.60
Diluent	1139.57 ± 147.40	82.71 ± 5.64	20.29 ± 4.60	560.00 ± 99.72	31.71 ± 2.12	22.29 ± 4.07

*$p<0.05$ as compared with controls (Duncan Multiple-Range Test) †$p<0.01$ as compared with controls

[5] 2 I.U. of ACTH decreased running time to a food reward in a straight alleyway, and learning curves showed a pattern similar to that of the present study. Experimental groups in both studies reached and maintained shorter latencies more rapidly than controls. However results of studies with ACTH usually are confounded by the release of corticosterone from the adrenal cortex.

In contrast to earlier studies [6], MSH did not produce resistance to extinction; however, only one experiment involved running to a food reward and this was a simple appetitive task [13]. Gray *et al.* [5] reported that ACTH also had no differential effect on extinction of a simple appetitive task, and we observed a similar lack of delayed extinction after administration of MSH to rats tested in a shuttle box avoidance problem (unpublished observation). In the study using MSH [13] rats learned the maze for only 4 days before extinction as compared to 10 days in the study by Gray *et al.* [5] and the present study. Resistance to extinction first increases and then decreases with continued training [10]; therefore, treatment differences in the rate of extinction may become possible only with shorter training periods. More important may be the fact that extinction of complex tasks does not follow the same pattern as extinction of simple tasks where only one alternative response is available to the animal. Since MSH has been associated with adaptive behavior it could be argued that exploration during extinction is adaptive in a maze containing numerous blind alleys that might possibly contain food. In partial corroboration of the study of Sandman *et al.* [13], Garrud *et al.* [3] reported that $MSH/ACTH_{4\text{-}10}$ (which does not have adreno-cortical effects) increased resistance to extinction of a simple appetitive task when injected during extinction. Thus, complexity of the task, defined as the number of possible response alternatives, may be an important factor producing differential effects during both learning and extinction of problems modified by hormone injections.

In agreement with Sandman *et al.* [12] the effects of MIF-I on learning were not distinguishable from those of MSH. Although MIF-I has been found in bovine hypothalamic tissue it does not appear to inhibit MSH release under usual physiological conditions [8]. Also, knowledge of differential functions of these hormones in some assay systems does not necessarily imply their opposition in behavioral systems. It is possible for hormones mediating color changes in lower vertebrates to operate antagonistically in the periphery and affect behavioral processes in a similar way in the CNS.

Previous studies have reported evidence consistent with the view that injections of MSH increase motivation and attention in treated animals [14,16]. In addition daily injections of polypeptide hormones might produce a more distinctive physiological state in hormone-treated animals than controls, which could facilitate memory of previous training (state dependency). Presence of a distinctive internal state during learning could improve day-to-day memory retrieval leading to more rapid acquisition of the task. In a recent study Gray [4] found direct evidence that ACTH causes state-dependency; therefore, this explanation of the behavioral action of these hormones should not be ruled out. The results of this particular experiment are also consistent with the explanations previously proposed that MSH increases motivation, attention, and adaptation to the environment [6,15].

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