Brief Communications

Memory-enhancing effect of posttraining epinephrine is not blocked by dexamethasone

JAMES L. McGAUGH, M. CATHERINE BENNETT,
K. C. LIANG, RONALD G. JULER, and DAVID TAM
University of California, Irvine, California

There is extensive evidence that stress-related hormones administered shortly before or after training on a variety of tasks can influence retention (de Wied, 1984; McGaugh, 1983). Such evidence suggests that hormones released by learning experiences may serve as endogenous modulators of memory storage (Gold & McGaugh, 1984).

Recently, Tilders, Berkenbosch, Vermes, Linton, & Smelik (1985) reported that a number of hormones, in addition to corticotrophin releasing factor (CRF), induce the release of adrenocorticotrophic hormone (ACTH) from the pituitary cortex *in vitro*. The hormones found to release ACTH include epinephrine, norepinephrine, arginine vasopressin, oxytocin, angiotensin II, vasoactive intestine polypeptide (VIP), and histidine isoleucinamide. Since several of these hormones have been found to influence memory, these findings suggest that a common action by which the hormones affect memory storage might involve the release of ACTH from the anterior pituitary.

Many studies have shown that posttraining administration of epinephrine alters retention: Low doses generally enhance retention, whereas high doses impair retention (McGaugh, 1983; McGaugh & Gold, *in press*). Epinephrine is known to stimulate the release of ACTH *in vivo* (Berkenbosch, Vermes, Binnekade, & Tilders, 1981; Reisine, Heisler, Hook, & Axelrod, 1983; Tilders, Berkenbosch, & Smelik, 1982) as well as *in vitro*. Epinephrine is released from the adrenal medulla and is a ligand for both α - and β -receptors in the periphery. Available evidence indicates that epinephrine crosses the blood-brain barrier poorly, if at all (Weil-Malharbe, Axelrod, & Tomchick, 1959). The effects of epinephrine on retention are blocked by a variety of α - and β -adrenoreceptor antagonists (Sternberg, Korol, Novack, & McGaugh, 1986). Considered together, such findings suggest that epinephrine may influence memory storage through effects initiated at peripheral receptors.

In the present study we sought to determine whether the effect of epinephrine on memory storage is mediated

by the release of ACTH through activation of pituitary adrenoreceptors. It is well established that dexamethasone blocks the release of ACTH (Sakakura, Yoshioka, Kobayashi, & Takebe, 1981). We examined the question of whether dexamethasone administered prior to training might block the memory-enhancing effect of posttraining epinephrine.

METHODS

Male Sprague-Dawley rats (Harlan), 60 days old on arrival, were maintained under standard laboratory conditions (light:dark 12:12 with lights on at 7:00 a.m.) for 1 week prior to training. Training and testing were conducted between 1:00 p.m. and 5:00 p.m. The animals were given a single training trial in an inhibitory avoidance apparatus (Bennett, Liang, & McGaugh, 1985). The animals received a 0.6-mA 0.5-sec footshock immediately after leaving a white, well-lit compartment and entering (with all four paws) a darkened chamber. At 24 h and 4 h prior to training, the animals were given either dexamethasone (2.0 mg/kg s.c.) or the vehicle (10% ethanol, 40% propylene glycol, and 50% isotonic saline). Immediately posttraining, animals from each of these groups received either epinephrine (0.10 mg/kg s.c.) or physiological saline. The dose of epinephrine was selected on the basis of previous dose-response studies. Response latencies (ceiling of 600 sec) on the retention trial given 24 h later were used to assess retention.

Approximately 1 week later we examined the effects of dexamethasone on shock sensitivity. The rats were injected with dexamethasone (2.0 mg/kg s.c.) or the vehicle solution both 24 h and 4 h prior to testing. Each rat received six series (three ascending, three descending) of discrete shocks (.05-sec duration, 30-sec inter-shock interval, and 2-min intervals between series) ranging from 100 to 1,000 μ A in increments of 100 μ A.

RESULTS

The retention performance findings are shown in Table 1. Posttraining epinephrine significantly enhanced the retention of dexamethasone-treated animals as well as vehicle controls. In the groups given posttraining sa-

Table 1
Effect of Posttraining Epinephrine (0.1 mg/kg s.c.) and
Pretraining Dexamethasone (2.0 mg/kg s.c.) Administered
(24 and 4 h) Prior to Training on Retention of an
Inhibitory Avoidance Response

Treatment		Interquartile		N
Pretraining	Posttraining	Median	Range	
Vehicle	Saline	193.9	180-283	13
	Epinephrine	544.1*	221-600	14
Dexamethasone	Saline	370.3	224-600	10
	Epinephrine	600†	600-600	12

Note—Both groups given epinephrine differed significantly (* $p < .02$, † $p < .05$, two-tailed Mann-Whitney U tests) from their respective saline control groups. The saline controls given dexamethasone or the injection vehicle prior to training did not differ significantly ($p > .05$).

This research was supported in part by USPHS Grant MH12526 and Office of Naval Research Contract N00014-84-K-0391. K. C. Liang is now at The National Taiwan University, Taipei, Taiwan 107, Republic of China. Address correspondence to James L. McGaugh, Center for the Neurobiology of Learning and Memory, University of California, Irvine, CA 92717.

Table 2

Flinch and Jump Thresholds (in μ A) of Rats Given Dexamethasone (2.0 mg/kg s.c.) or Injection Vehicle 24 h and 4 h Prior to the Tests

	Flinch		Jump	
	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>
Vehicle	265	29	577	29
Dexamethasone	204	18	515	28

Note—*N* = 9 per group. The vehicle controls and dexamethasone groups did not differ significantly (*p* > .05, *t* tests) in either flinch or jump thresholds.

line, the retention performance of animals pretreated with dexamethasone did not differ significantly from that of vehicle-pretreated animals. Furthermore, as is shown in Table 2, the dexamethasone- and vehicle-treated animals did not differ significantly in either flinch or jump thresholds.

DISCUSSION

These findings indicate that posttraining epinephrine enhances retention in animals given dexamethasone prior to training as well as in vehicle control animals. The findings also indicate that the effect of the dexamethasone in the present study was not due to an influence on sensitivity to the footshock: Dexamethasone did not significantly affect retention of animals given posttraining saline and did not affect flinch or jump thresholds. Since the dose of dexamethasone used was greater than that required for the suppression of both basal levels and stimulated release of ACTH (Weidenfeld, Siegel, Conforti, & Chowers, 1983), these findings strongly suggest that the memory-enhancing effect of epinephrine is not mediated by ACTH released from the pituitary. Although it remains to be determined whether the effects of other hormones on memory are mediated by the release of ACTH, the present findings indicate that the release of ACTH is not the common mediator of the memory-modulating effects of endogenous hormones that are known to stimulate ACTH release.

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