The effects of chemical stimulation in dorsal midbrain tegmentum on self-stimulation in hypothalamus and septal area¹

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Abstract

Four rats were implanted with chemical probes in dorsal midbrain tegmentum (DMT). Two of these had an electrode implanted in the septal area, while the other two had an electrode in hypothalamus. Minute quantities of carbachol (around 3 μ gm) placed in DMT depressed self-stimulation in hypothalamus by over 90% and self-stimulation in septal area by 35%. The placement of sodium chloride, choline chloride, or an empty cannula into DMT had no effect on either septal or hypothalamic self-stimulation. It was tentatively concluded that (1) a cholinergic system may exist in DMT, (2) that this system acted to suppress both septal and hypothalamic self-stimulation, and (3) that septal self-stimulation was suppressed less than hypothalamic self-stimulation perhaps because the former, in contrast to the latter, attenuated possible aversive effects of DMT stimulation.

Problem

Recent brain and behavior studies using lesioning and stimulation techniques have shown that it is possible to investigate the interactions between two brain structures in an awake, freely moving animal. Thus, for example, Vanderwolf (1964) has shown that septal lesions reduced impaired shuttlebox performance caused by medial thalamic lesions. Egger & Flynn (1963) have shown that attack behavior elicited by posterior hypothalamic stimulation may either be reduced or increased by electric stimulation depending on the area in amygdala being stimulated. Schiff (1964) has shown that lesions in ventral reticular formation reduce septal self-stimulation. Olds & Olds (1962) have shown that self-stimulation in hypothalamus is markedly reduced by stimulation of dorsal midbrain tegmentum (DMT).

The present study offers another method for the investigation of brain interactions in the freely moving animal. Self-stimulation in hypothalamus and septal area are studied during chemical stimulation of DMT.

Method

Four male Holtzman albino rats were used. Two were implanted with electrodes aimed at septal area, and two were implanted with electrodes aimed at hypothalamus. All four animals had a chemical probe implanted in the boundary region where central grey meets superior colliculus and tegmentum.

The chemical probe consisted of three parts: a guide cannula, a dummy probe, and a chemical injector. The guide cannula and dummy probe were implanted at the time of operation. The chemical injector was used to apply the test chemicals. The dummy probe or the chemical injector could be screwed into the guide

cannula. The former penetrated 4 mm, the latter 5 mm, into the brain.

Chemicals were applied in crystalline form according to the method of Grossman (1962). The inside diameter of the 30 gauge injector was too small (0.15 mm) to accommodate one crystal, so each chemical was powdered with a mortar and pestle. The chemical injector tip was firmly pressed against the powder one time. The tip was then tapped against a clean surface to rid the injector of any excess chemical. With this procedure, and using a microbalance, the weight of the injected chemical was estimated to be no greater than 3 ± 2 μ gm. The following chemicals were used: carbamylcholine chloride (carbachol), choline chloride, and sodium chloride.

Following a one week recovery after implantation, Ss were trained to self-stimulate for brain reward. The training procedures for self-stimulation have been described by Olds (1960). In the present study, the stimulus was a sine wave of 30 μ a and 60 cps. Criterion for self-stimulation was 10 responses/min. Ss were allowed to self-stimulate for 15 min./day until the daily self-stimulation rate was consistent. At this point a chemical was tamped into the chemical injector which in turn was screwed into the guide cannula. Chemical stimulation was alternated with one or two days where no chemical stimulation was given. On the last three days of the study, carbachol, choline chloride, and sodium chloride were successively applied. The treatment sequence was the same for all Ss.

Results

The results may be seen in Table 1. Carbachol stimulation in DMT suppressed hypothalamic self-stimulation but had a minor effect on septal self-stimulation. The other chemical substances applied had little or no effect on septal or hypothalamic self-stimulation. Histology showed that all four chemical probes were in the DMT region. Septal 34 had its electrode in the anterior olfactory nucleus, septal 35 had its electrode in the boundary of medial septum and anterior hippocampus. Both hypothalamic animals had their electrodes in the medial forebrain bundle at the level of the posterior ventromedial nucleus of the hypothalamus.

Discussion

The lack of effect of the empty cannula, sodium chloride, and choline chloride on septal and hypothalamic self-stimulation suggests that the carbachol effect was not the result of tissue destruction or mechanical deformation resulting from the insertion of

Table 1

Animal	Mean Self-Stimulation Scores ¹		Reduction %	Self-Stimulation Scores	
	Control	Carbachol		NaCl	Choline
Septal 34	503 ± 137 (8)	293 ± 162 (5)	42	470	583
Septal 35	679 ± 149 (9)	489 ± 174 (6)	28	812	547
Hypothalamic 37	1008 ± 182 (8)	19 ± 11 (6)	98	1250	1041
Hypothalamic 38	885 ± 222 (8)	142 ± 149 (8)	87	890	989

1. Mean plus or minus one standard deviation. Control scores are based on days when S had the dummy probe or the cleaned and empty chemical injector in the guide cannula. Numbers in parentheses represent the number of times the procedure was applied.

the chemical injector, a bulk or osmotic effect of the chemical itself, or the choline constituent or the hygroscopic properties of carbachol. It may tentatively be concluded that the effect observed is caused by cholinergic stimulation in DMT. Other cholinergic drugs (nicotinic and muscarinic) should be studied to confirm this conclusion.

Olds (1960) found that electrical stimulation in DMT sometimes caused backing up and circling, urination and defecation. This looked like escape behavior and, in fact, Ss would learn to press a bar to terminate DMT stimulation. When carbachol was placed in DMT, Ss of the present study revealed similar behavior to Ss receiving DMT electrical stimulation. It is believed that the reduction in bar pressing seen in septal and hypothalamic Ss may be accounted for, in part, by the general suppressing effects of aversive stimuli on operant behavior.

This explanation cannot account for all the data, since it fails to explain the differential effects of carbachol on septal and hypothalamic self-stimulation. One possible explanation is that septal stimulation alleviates some of the aversive properties of DMT stimulation, while hypothalamic stimulation has no such ameliorative effects. This possibility was suggested by a study (Routtenberg & Olds, 1962) in which it was shown that low levels of septal stimulation attenuated escape behavior caused by DMT stimulation. Low levels of hypothalamic stimulation, on the other hand, somewhat increased escape behavior. It was possible, therefore, that in the present study, septal stimulation, in contrast to hypothalamic stimulation, reduced both the aversive

quality of DMT stimulation and its suppressing effects on behavior.

The present results are relevant to two methodological problems raised by Valenstein (1964) concerning interaction experiments in self-stimulation studies. The first problem concerns the possibility that electrical stimulation in two separate points in the brain might interact in an electrical rather than neurophysiological fashion. The use of chemical stimulation in one area, and electrical in another would seem to eliminate this problem. The second difficulty arises in the interpretation of results. Olds & Olds (1962) have suggested that the reduction in hypothalamic self-stimulation may be explained by assuming the existence of an inhibitory relation between DMT and hypothalamus. Valenstein (1964) has pointed out that the reduction in bar pressing may be the result of a reduction in motor activity or general suppressing influence of aversive stimuli on behavior, rather than neurophysiological inhibition. While not necessarily supporting the latter view, the present study offers some evidence against the notion that DMT stimulation reduces self-stimulation in only a non-specific fashion, since there was a major sparing of septal self-stimulation during DMT chemical stimulation. These results, in fact, suggest fruitful neurophysiological experiments.

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Note

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