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Role of Mediodorsal Thalamic Nucleus in Olfactory Discrimination Learning in Rats

Abstract. *Severe deficits in the acquisition of an olfactory learning-set task resulted from lesions of the central (olfactory) component of the mediodorsal thalamic nucleus but not from large lesions that destroyed olfactory projections to the amygdala. Complex olfactory learning may be mediated by the olfactory thalamocortical system and not by olfactory projections to the limbic system.*

A prominent projection for olfactory impulses to the central segment of the mediodorsal thalamic nucleus has now been firmly established by experimental anatomical and neurophysiological studies (*1*). This segment of the mediodorsal nucleus projects to several frontal cortical areas including the lateral orbital cortex (*2*). The existence of a thalamic-neocortical projection for olfactory information challenges the traditional view of the olfactory system as a primitive sensory modality having only basal forebrain projections and involved primarily in species-specific or affective behaviors. However, the functional significance of this olfactory cortical projection has not been established (*3*). In behavioral studies we have shown that, when provided with odor cues, rats can acquire learning sets as efficiently as primates trained with visual stimuli do (*4*). We now report that this form of learning in the rat is severely disrupted by lesions of the olfactory thalamic cortical system, but not by lesions of olfactory projections to the limbic system.

Twenty-seven adult male rats were trained on a discrete-trials, "go, no-go" discrimination procedure in a wind-tunnel olfactometer (*4*). On each trial either the positive (S^+) or negative (S^-) stimulus was presented for 3 seconds. Key responses by the subject in the presence of the S^+ stimulus resulted in termination of the trial and delivery of a 0.05-ml water reward; key responses in the presence of the S^- stimulus were not reinforced (*5*). Prior to surgery, animals were trained to discriminate a flashing light (S^+) from a steady light (S^-).

After 10 to 14 days of postoperative recovery, the rats were tested for retention of the visual discrimination problem. On the next day they were trained to discriminate the odor of propyl acetate (S^+) from that of ethyl acetate (S^-). Stimulus concentration for both odorants was approximately 0.05 percent of vapor saturation. Training on this problem was terminated when 90 percent correct responding was achieved in a block of 20 trials. On the next day the positive and negative values of the stimuli were reversed and training was continued until the 90 percent correct responding criterion was achieved. This procedure was continued until six successive discrimination reversals had been completed. Finally, animals were trained to criterion on a simple detection problem in which the odor of amyl acetate (at approximately 0.005 percent of vapor saturation) served as S^+ and no odor served as S^-.

Stereotaxically directed lesions were aimed at the mediodorsal nucleus of 16 rats and at the lateral olfactory tract at the level of the anterior amygdala in four rats. Seven rats with sham lesions served as controls. Histological analysis (*6*) revealed that the amygdaloid lesions bilaterally transected the lateral olfactory tract, destroyed bordering pyriform cortex, and invaded the anterior amygdala (Fig. 1F). Discrete lesions of the central part of the mediodorsal nucleus or of the

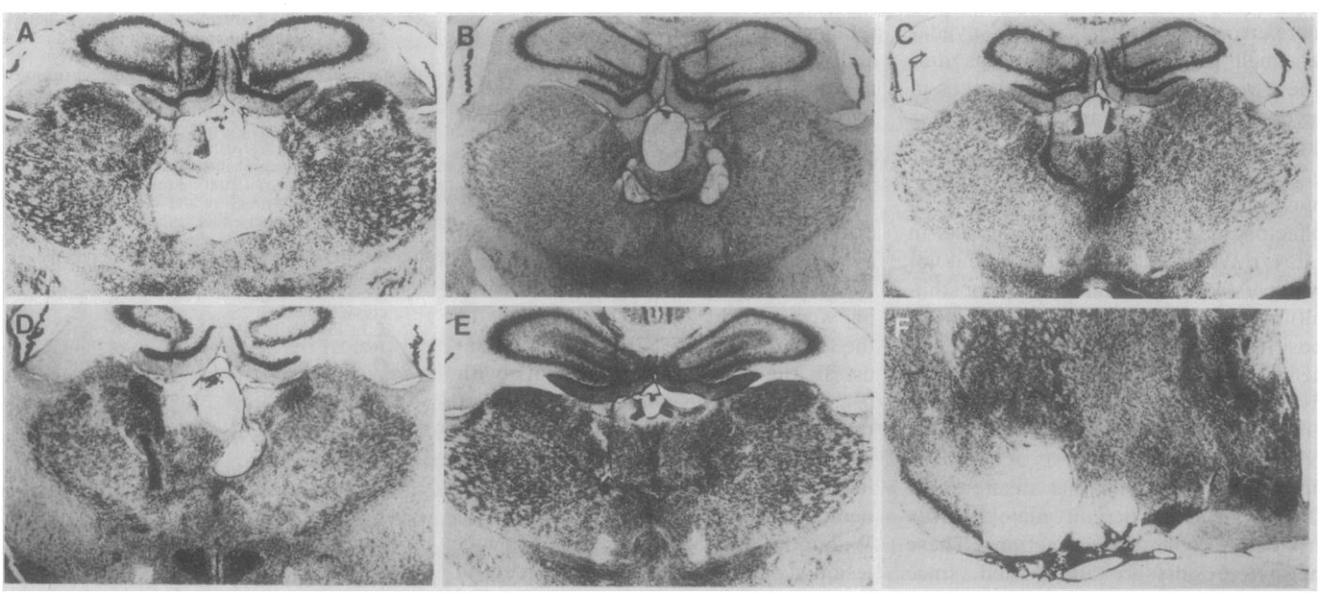

Fig. 1. (A to C) Representative lesions from animals in the large MD group. (D) Thalamic control group. The lesion is located just rostral to the mediodorsal nucleus. (E) Small MD group. Small bilateral lesions are located in the ventral aspect of the central component of the mediodorsal nucleus. (F) Representative lesion in the amygdaloid group. Lesions in this group were bilaterally symmetrical and transected the lateral olfactory tract at the level of the anterior amygdala.

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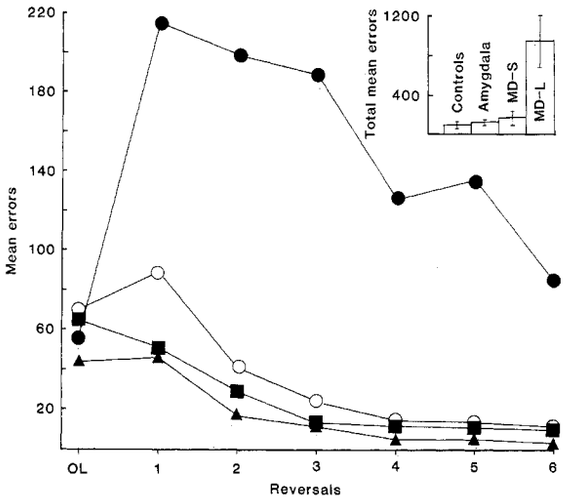

Fig. 2. Errors in original learning and on each of six reversals in the olfactory reversal learning-set task. Because scores for sham-lesioned and thalamic controls were similar, these two groups were combined (control groups) (▲) for purposes of illustration. Symbols: ●, large MD group; ○, small MD group; and ■, amygdaloid group. Inset: Error scores of reversal problems for control and experimental groups. Vertical line is 1 standard deviation.

entire mediodorsal nucleus were produced in six rats (large MD group). Small lesions destroying only ventral or lateral components of the nucleus or asymmetrical lesions involving only part of the central part of the mediodorsal nucleus were produced in five other rats (small MD group). Lesions located anterior, posterior, or ventral to the mediodorsal nucleus, but which did not invade the nucleus, were produced in five rats (thalamic control group).

The results of postoperative tests are illustrated in Fig. 2. No differences were found among groups for retention of the visual discrimination task, acquisition of the two-odor problem, or acquisition of the amyl acetate detection problem (Kruskal-Wallis one-way analyses of variance). However, in the reversal learning task, rats with large MD lesions made significantly ($H = 13.53$, $P < .005$) more errors than animals in the amygdala, small MD, or control groups did. There were no significant differences in reversal performance among these latter groups.

Performance of control rats confirmed our earlier reports of rapid acquisition of olfactory discrimination learning-sets in rats (*4*). When tested with odors (but not when tested with visual or auditory stimuli) most normal animals actually show positive transfer on the first reversal and achieve nearly errorless learning after five or six reversal problems. The present results demonstrate that this same pattern of performance was achieved in animals with lesions that deafferented the amygdala and periamygdaloid cortex from direct olfactory projections. These negative results are unexpected, since these areas receive a massive projection from the lateral olfactory tract (*7*), and electrophysiological studies and clinical reports (*8*) have implicated the amygdala in the sense of smell. The precise role of the amygdala in olfaction has not been established, however.

In contrast to the negative results from large anterior amygdaloid lesions, discrete lesions of the mediodorsal nucleus severely disrupted olfactory reversal learning. Animals in the large MD group made approximately four times as many errors on the first reversal as on initial learning and, although their performance improved in subsequent reversals, only three of the animals in this group made fewer errors on reversal six than in initial learning. The performance of the mediodorsal group is strikingly similar to the successive reversal discrimination performance of normal rats trained with visual cues (*4*).

The deficits obtained in the large MD group may be reasonably specific to complex olfactory learning: these rats retained the preoperatively learned visual discrimination well, performed as well as controls in the initial acquisition of the two-odor problem and in the acquisition of the amyl acetate detection problem. Preliminary data from our laboratory indicate that rats with mediodorsal lesions acquire a visual discrimination reversal as well as sham-lesioned controls do (*9*).

Further, the deficits in reversal learning were related to the specific locus of the lesion within the mediodorsal nucleus. In the small MD group, rats with lesions outside the central component of the nucleus had few or no deficits in reversal learning, whereas those with lesions infringing on the central component of the nucleus performed poorly. Within the large MD group, animals with lesions confined primarily to the central part of the nucleus (Fig. 1C) performed as poorly as those with virtually total destruction of the nucleus (Fig. 1A). Since only the central component of the nucleus seems to receive olfactory projections (*1*), lesions there may be sufficient to produce severe deficits in complex olfactory learning.

Current anatomical and electrophysiological studies have demonstrated that in addition to the pyriform lobe and olfactory tubercle, olfactory impulses project strongly to (i) amygdala, periamygdaloid cortex, and entorhinal cortex; (ii) hypothalamus; and (iii) the mediodorsal nucleus of the thalamus. Available evidence has implicated the hypothalamic olfactory projections in the control of neuroendocrine events (*10*) and the limbic projections as important in species-specific behavior or pheromonal communication (*11*). This study provides evidence for a role of the thalamic olfactory projections. Our results suggest that the thalamic (but not limbic) olfactory projections are important in complex learning involving olfactory clues.

BURTON M. SLOTNICK
Department of Psychology, American University, Washington, D.C. 20016
NAOHIRO KANEKO
Department of Psychology, Keio University, Tokyo, Japan

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