Increased pain thresholds following combined lesions of thalamic nuclei centrum medianum and centralis lateralis*

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In this experiment, cats were trained to escape from footshock in a shuttlebox. Current applied to the feet was varied in ascending and descending sequences for each animal according to the psychophysical method of limits, and each animal was trained until stable thresholds for escape responding were achieved. Animals then had bilateral lesions made in thalamic nuclei centrum medianum and centralis lateralis, were given 8 days to recuperate, and were retrained to a stable level of escape responding. The results showed that aversive thresholds were significantly elevated for all animals for up to 90 days following thalamic lesions, indicating that the midline thalamus plays a role in the perception of pain derived from footshock.

Experimental evidence in both humans and nonhuman mammalian animals has suggested that there are at least two different types of pain sensations. Discrete pain, frequently called discriminative pain or bright pain, is thought to take different anatomical pathways from diffuse pain, which is frequently called nondiscriminative pain or dull pain. The discrete pain pathway is associated with the lemniscal system, has few synapses, and has a specific projection nucleus at the level of the lateral thalamus in the ventrobasal nuclear complex (Bowsher, 1957; Carpenter & Hanna, 1961; Poggio & Mountcastle, 1963). The diffuse pain pathway is an extralemniscal system, has many synapses, and has thalamic termination sites in the medial thalamus in the intralaminar nuclei (Kerr, Haugen, & Melzack, 1955; Bowsher, 1957; Nauta & Kuypers, 1958). The suspected thalamic nuclei of termination for diffuse pain include centrum medianum, centralis lateralis, parafascicularis, and subparafascicularis. The present experiment is the first in a series designed to assess the role of the thalamus in modulating the perception of both discrete and diffuse pain. The purpose of this particular experiment was to determine the extent to which the medial thalamus influences the perception of bright pain.

PROCEDURE

Eight adult cats served as Ss in this experiment. Each animal was trained to a stable level of escape responding

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from footshock in a shuttlebox, had lesions made in the medial thalamus, was given 8 days to recover, and was retrained to a stable level of escape responding. The shuttlebox was 2 ft wide, 6 ft long, and 3 ft deep, with a 6-in.-high barrier on the floor which divided the box into two equal parts. The floor of the shuttlebox consisted of a grid across which current could be applied to elicit escape behavior. On each testing day each animal was placed in one end of the shuttlebox, the grid on that end of the box was electrified, and the animal was required to escape to the other end of the box by jumping over the small barrier in the middle of the box. This procedure was repeated until the values of current required to elicit stable escape responding could be determined. For each animal on each testing day, current values were varied in both an ascending and descending sequence according to the psychophysical method of limits, which permitted the computation of ascending and descending current thresholds for escape responding, as well as the average ascending-descending current threshold. The amount of current delivered to the animals was continuously monitored, and current values associated with escape responding were measured in milliamperes. The current was carried by rectangular stimulus pulses that were 7 msec in duration and occurred at a rate of 50 pulses/sec.

Each animal had bilateral lesions made in thalamic nuclei centrum medianum (CM) and centralis lateralis (CL). Lesions were made with concentric bipolar electrodes at two or three levels in each nucleus by applying 25 mA of radio frequency current for 30 sec. At the end of the experiment, animals were sacrificed and the brains perfused, fixed in 20% sucrose-formal solution, sectioned at

25 microns, and stained in alternate sections with Klüver and cresyl violet stains. Lesions were reconstructed for all animals in the experiment.

RESULTS

Figure 1 illustrates the effects of lesions in thalamic nuclei CM and CL on escape behavior. The average current thresholds for the eight cats for the last 10 days before thalamic lesions are shown on the left of the figure, and the average thresholds for the first 10 days following the lesions are shown on the right. Statistical analysis of the average ascending-descending thresholds indicated that thresholds were significantly elevated during the first 10 days following lesions of the intralaminar nuclei ($t = 31.79$, $df = 158$, $p < .001$).

The essential features of escape behavior for individual animals following thalamic lesions are illustrated for two animals in Fig. 2. The average ascending-descending current thresholds for the last 10 days before thalamic lesions and throughout postoperative training are shown on the left and right, respectively. As was the case for all eight animals, current thresholds were elevated following thalamic lesions but returned to preoperative levels with continued testing. As illustrated in Fig. 2, current thresholds for Animals IL-10 and IL-7 returned to preoperative levels after 40 and 48 days, respectively. Although current levels for all animals eventually returned to preoperative levels, the rate of return varied from 6 ($N = 1$) to 90 days ($N = 2$).

Histological reconstruction of the lesions revealed that damage was largely restricted to thalamic nuclei CM and CL in all animals and was confined exclusively to these nuclei in Animals IL-10 and IL-7.

DISCUSSION

This experiment has demonstrated that the medial thalamus plays a role in modulating the perception of pain—in this instance, pain produced by shocks to the foot pads of cats. In particular, it has shown that current thresholds for escape responding were elevated following bilateral lesions of thalamic nuclei centrum medianum and centralis lateralis. As was the case in earlier experiments following midbrain lesions in nonhuman Ss (Orlowski & Glusman, 1969) and people (White, 1966), the elevated pain thresholds that followed surgical damage of the central nervous system were temporary. In all animals in the present experiment, current thresholds for escape responding returned to normal within 90 days following lesions in the midline thalamus.

The recovery of aversive thresholds in the present animals indicates a

Fig. 1. Average aversive thresholds for all animals for the last 10 days prior to thalamic lesions and the first 10 days following the lesions. Ascending, descending, and average ascending-descending thresholds are expressed in milliamperes.

return of sensitivity to aversive or painful stimuli. While there is no clear explanation for this phenomenon, a number of nonsensory factors can be eliminated. For example, recovery cannot be explained on the basis of some nonspecific effects due to surgical intervention, because lesions in some other parts of the thalamus have no significant effect on aversive thresholds (Anderson, unpublished observations). Nor can the elevations and subsequent recovery be accounted for by some general impairment of activity or unspecified involvement of motor functions, because all animals in this experiment responded as smoothly and efficiently on the first postoperative day as on the last and because maintaining thresholds required the same basic response regardless of the level maintained. Since the animals maintained threshold responding even on the first postlesion testing day, the reduction in sensitivity cannot be due to extinction and relearning of escape contingencies.

The recovery of aversive thresholds may be related to the nature of the nociceptive stimulation used to elicit escape behavior. It has been suggested by Bowers (1957) that discrete sharp pain, which lasts only as long as the provoking stimulus is applied, is mediated primarily by a direct spinothalamic pathway whose termination is in the lateral thalamus. On the other hand, diffuse, poorly localizable, excruciating pain that persists for some time after withdrawal of the initiating stimulus may be

mediated primarily by a spino-reticulo-thalamic pathway whose termination is in the medial thalamus. The nociceptive stimulus used in the present experiment consisted of shocks to the foot pads, which is most likely a stimulus that would most effectively activate the spinothalamic system. If the medial thalamus is primarily involved in mediating

nondiscriminative or diffuse pain, it would, perhaps, not be surprising that lesions in centrum medianum and centralis lateralis would fail to produce lasting elevations in aversive thresholds to footshock. Experiments are now under way to determine the extent to which the medial thalamus influences the perception of nociceptive stimuli that activate the diffuse pain system.

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Fig. 2. Aversive thresholds for two individual animals before and after thalamic lesions. Thresholds, in milliamperes, for the last 10 days prior to thalamic lesions are shown on the left; thresholds obtained throughout postoperative training are on the right.