EFFECT OF ELECTRICAL STIMULATION OF THE INFERIOR RAPHE NUCLEUS ON SPONTANEOUS AND EVOKED THALAMIC ACTIVITY IN WAKING CATS

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Chronic experiments using a microelectrode technique showed that electrical stimulation of the inferior raphe nucleus inhibits thalamic unit activity, both spontaneous and evoked by radial nerve stimulation. No changes were found in the activity of the same neurons during stimulation of the bulbar reticular formation.

KEY WORDS: electrical stimulation; raphe nuclei; mechanisms of analgesia.

During electrical stimulation of the central gray matter in rats inhibition of behavioral responses evoked by nociceptive stimulation is observed [8, 11]. A similar effect has been obtained in experiments on cats [4, 7, 9]; the strongest analgesia is observed if the stimulating electrodes are located in the dorsal raphe nucleus (DR). Stimulation of DR has been shown to be accompanied by inhibition of spontaneous and evoked activity of neurons in the fifth layer of the dorsal horn of the spinal cord, and this may perhaps be one component of the mechanism of analgesia [4, 5, 7, 9]. Under these circumstances, activity of neurons of the trigeminal nuclei evoked by stimulation of the dental pulp also is depressed [13, 14]. It was subsequently shown that stimulation of the inferior central raphe nucleus (CI) in cats also causes analgesia, to a more marked degree moreover than stimulation of DR [10].

This paper describes a study of the neurophysiological mechanism of electroanalgesia. In chronic experiments on cats the effect of stimulation of CI on spontaneous and evoked thalamic unit activity was studied.

EXPERIMENTAL METHOD

Preliminary operations were performed under general anesthesia: After preliminary intramuscular injection of ketamine (10-15 mg/kg) into the animal and endotracheal intubation, anesthesia was maintained by inhalation of halothane (1-1.5 vols.%).

The cat's head was fixed in the usual way in a stereotaxic apparatus and the bones of the vault of the skull were widely exposed. A metal frame (5 × 5 cm) was fixed with steel screws to the skull parallel to the horizontal axis of the stereotaxic apparatus. Four depressions (two on each side) were drilled on the lateral surfaces of the frame; later, when unit activity was recorded from the waking animal the frame was fixed in the stereotaxic apparatus by mean of rods inserted into these depressions. A mark was made on the upper surface of the frame and its position determined relative to the origin of the coordinates in Jasper and Ajmone-Marsan's atlas [6]. Coordinates for insertion of the microelectrodes were subsequently measured from this mark.

A square hole 1.5 × 1.5 cm was cut out of the cranial bones so that the microelectrode introduced through it could reach the thalamic structures between frontal planes of 0 and +15 [6]. At the edges of the hole a plastic chamber with a lid to prevent injury of the exposed dura was fixed.

Two bipolar concentric stimulating electrodes were inserted in accordance with the coordinates of Berman's stereotaxic atlas [3] at an angle to the vertical axis of the stereotaxic apparatus through holes in the posterior part of the skull: one electrode into CI (P = 8.5, L = 0, H = −8), the second 2 mm laterally, into the structures of the bulbar reticular formation.

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A bipolar silver electrode was implanted subcutaneously into the animal's contralateral (relative to the thalamic nuclei to be studied) forelimb for stimulation of the superficial branch of the radial nerve. The leads from the stimulating and recording electrodes were brought out to a connecting device on the metal frame.

The correct placing of the central stimulating electrodes was verified 3-5 days after the operation: The behavioral responses of the cat to strong nociceptive stimulation (squeezing the animal's paw or tail) were recorded before and during electrical stimulation of the central structures. Square pulses 0.5-5 V in amplitude, 0.2 msec in duration, and with a frequency of 50-300 Hz were applied continuously for stimulation. In all animals stimulation of CI was accompanied by complete analgesia; no analgesia was present during stimulation of the bulbar reticular formation.

During the experiments central structures were stimulated by series of the same pulses as were used to test the correct placing of the electrodes. The duration of the series was 30-50 msec and intervals between them 2 sec. This stimulation caused no changes in the animals behavior.

The superficial branch of the radial nerve was stimulated by single pulses 0.2 msec in duration and with an amplitude of 0.5-1.5 V. In some experiments weak movements of the tip of the cat's limb appeared in response to stimulation of the radial nerve. The interval between conditioning (the last pulse of the series for stimulation of the central structures) and testing (radial nerve stimulation) stimuli was 10-30 msec.

Thalamic unit activity was recorded by means of glass microelectrodes filled with potassium chloride solution and Pontamine blue, with a resistance of 7-11 MΩ. The electrodes were inserted in accordance with coordinates of Jasper and Ajmone-Marsan's stereotaxic atlas [6] with the additions of Robertson and Rinvik [12]. Spike discharges were recorded on still and motion-picture film from oscilloscope screens and also on magnetic tape for subsequent computer analysis.

Experiments were carried out on 5 cats and 28 microelectrode trajectories were verified histologically.

EXPERIMENTAL RESULTS

Activity of 165 neurons was recorded before, during, and after central stimulation. During stimulation of CI the activity of 89 cells was unchanged and the spontaneous activity of 51 cells was suppressed. A depriming effect was observed in the course of 100-300 msec from the end of the series of pulses. In 7 cases spontaneous activity was restored 1-2 min after the end of stimulation. Sixteen cells responded by increased activity to stimulation of CI. Changes in the activity of nine cells were more complex in character: A period of increased activity was followed by inhibition. The results of stimulation of CI on unit activity of the thalamic nuclei are summarized in Table 1.

In the group of neurons responding by inhibition of spontaneous activity to stimulation of CI, 14 responded to stimulation of the radial nerve. The latent period of responses of 12 neurons was 17-25 msec. During stimulation of CI complete inhibition of their evoked activity was observed (Fig. 1A). The responses of two neurons with latent periods of 8 and 11 msec in the posterior ventral nucleus were reduced on account of the later discharges.

TABLE 1. Effect of Stimulation of CI on Unit Activity of Thalamic Nuclei

Name of nucleus	Number of neurons tested				
	total	number of spontaneous activity	inhibition of evoked activity	strengthening of spontaneous activity	"mixed" effect
Pulv.	8	2	—	1	—
SG	11	3	—	1	1
GM-mc	17	3	1	1	1
LP	69	21	5	7	3
VP	2	2	2	—	—
CL	6	1	—	—	—
VL	47	16	6	6	3
VA	5	3	—	—	1

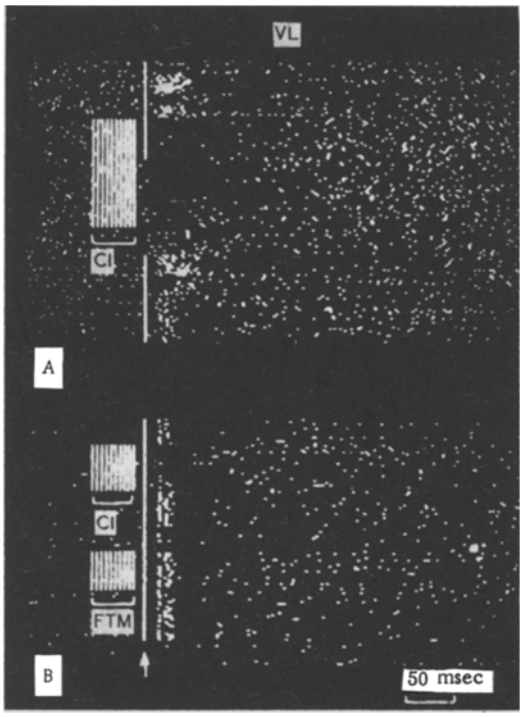

Fig. 1. Effect of electrical stimulation of inferior central raphe nucleus and magnocellular tegmental field on spontaneous and evoked activity of two neurons (A and B) in ventral lateral thalamic nucleus. Discharges of neurons depicted by dot-display method. Oscilloscope beam moved across screen from left to right and from bottom to top successively. Arrow marks stimulation of superficial branch of radial nerve by single pulses (1.2 V, 0.2 msec). CI) Marker of stimulation of inferior central raphe nucleus (duration of series of pulses 40 msec, voltage of each pulse 3 V, duration 0.2 msec). FTM) Marker of stimulation of magnocellular tegmental field (parameters of stimulation the same as for CI).

Neurons responding to stimulation of CI were located in the pulvinar (Pulv.), the suprageniculate nucleus (SG), in the magnocellular part of the medial geniculate body (GM-mc), and in the posterior lateral (LP), posterior ventral (VP), central lateral (CL), ventral lateral (VL), and ventral anterior (VA) nuclei of the thalamus.

Stimulation of the bulbar reticular formation laterally to CI did not affect spontaneous or evoked activity of the neurons tested (Fig. 1B).

Radial nerve stimulation as used in these experiments caused no nociceptive responses in the animals. It is therefore impossible to conclude that stimulation of CI in these experiments blocked the transmission of nociceptive impulses. However, the possibility cannot be ruled out that activity of thalamic neurons evoked by nociceptive stimulation may also have been depressed by stimulation of CI.

Inhibition of evoked activity of the thalamic neurons during stimulation of CI could be the result of strengthening of inhibitory influence on the activity of spinal neurons participating in the conduction of afferent impulses. The depriming effect of electrical stimulation of DR on spontaneous and evoked unit activity in the spinal cord has been demonstrated by other workers [4, 5, 7, 9]. Beall et al. [2] showed that during stimulation of n. raphe magnus (part of CI) activity of neurons of the spinothalamic tract in the first layer of the dorsal horn of the spinal cord is inhibited. The anatomical substrate for influence of this type is evidently formed by descending fibers originating in CI and running to the first, second, and fifth layers of the posterior horn of the spinal cord [1]. Another possibility is that the inhibitory influence may be realized at the supraspinal level.

The region of the bulbar reticular formation stimulation of which in the present experiments did not cause analgesia and did not affect thalamic unit activity corresponds to the magnocellular tegmental field (FTM) in Berman's nomenclature [3]. It was therefore decided to compare the effect of stimulation of CI and of other structures, during stimulation of which analgesia also develops. For this purpose, stimulating electrodes were implanted into DR (P = 0.2, L = 0, H = −0.5) of one of the animals. According to some workers [4, 5, 7, 9], stimulation of this nucleus in cats is accompanied by marked analgesia. In the present experiments the responses of the thalamic neurons to stimulation of DR were identical with changes in activity observed during stimulation of CI. If no changes took place during stimulation of CI, stimulation of DR also was ineffective.

The results thus indicate that changes in activity of some cells of the thalamic nuclei are observed during stimulation of CI, and that the predominant changes are inhibition of spontaneous and evoked activity.

LITERATURE CITED

1. A. I. Basbaum, N. J. E. Marley, J. O'Keefe, et al., Pain, 3, 43 (1977).
2. J. E. Beall, R. F. Martin, A. E. Applebaum, et al., Brain Res., 114, 328 (1976).
3. A. N. Berman, The Brain Stem of the Cat; a Cytoarchitectonic Atlas with Stereotaxic Coordinates, Madison (1968).
4. G. Guilbaud, J. M. Besson, J. C. Liebeskind, et al., C. R. Acad. Sci. (Paris), 275, 1055 (1972).
5. G. Guilbaud, J. M. Besson, J. L. Oliveras, et al., Brain Res., 61, 417 (1973).
6. H. H. Jasper et al., A Stereotaxic Atlas of the Diencephalon of the Cat, Ottawa (1954).
7. J. C. Liebeskind, G. Guilbaud, J. M. Besson, et al., Brain Res., 50, 441 (1973).
8. D. J. Mayer, T. L. Wolfe, H. Akil, et al., Science, 174, 1351 (1971).
9. J. L. Oliveras, J. M. Besson, G. Guilbaud, et al., Exp. Brain Res., 20, 32 (1974).
10. J. L. Oliveras, F. Redjemi, G. Guilbaud, et al., Pain, 1, 139 (1975).
11. D. V. Reynolds, Science, 164, 444 (1969).
12. R. T. Robertson and E. Rinvik, Brain Res., 51, 61 (1973).
13. M. Sasa, K. Munekiyo, and S. Takaori, Brain Res., 101, 199 (1975).
14. B. J. Sessle, R. Dubner, L. F. Greenwood, et al., Can. J. Physiol. Pharmacol., 54, 66 (1976).

PATTERN OF SPREAD OF EXCITATION FROM THE VENTROMEDIAL HYPOTHALAMUS TO LIMBICO-RETICULAR BRAIN STRUCTURES

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The order of appearance of evoked potentials in different parts of the septum, amygdala, and reticular formation in response to gradually increasing stimulation of the ventromedial nucleus of the hypothalamus was studied. Excitation arising primarily in the ventromedial nuclei of the hypothalamus was shown to spread initially to structures of the septum and rostral reticular formation, and only later to the more caudal regions of the reticular formation and amygdala.

KEY WORDS: hypothalamus; limbico-reticular structures; evoked potentials.

In the modern view [2, 5-7], the so-called static emotional excitations are the neurophysiological basis of stable arterial hypertension. These excitations are formed by structures of the limbico-reticular complex, among which the central role is played by the hypothalamic region [1, 2, 8].

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