EFFECT OF ELECTROACUPUNCTURE ON NEURONAL ACTIVITY OF THE CENTRAL GRAY MATTER OF THE MIDBRAIN

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The mechanisms of acupuncture analgesia have been intensively studied in recent years. Data now available indicate that acupuncture analgesia arises as a result of a disturbance of formation of the high-threshold afferent flow at various levels of the CNS [2-6, 9, 10], and as a result of activation of the analgesic antinociceptive structures of the brain, namely the central gray matter (CGM), nuclei raphe, caudate nucleus, hypothalamus, etc. [1, 4, 5, 12, 15, 16]. However, it is not known to what degree the antinociceptive systems participate in the realization of acupuncture analgesia developing in response to activation of local-segmental and general analgesic points of application.

It was therefore decided to study the effect of acupuncture at different points on spontaneous spike activity of CGM neurons and on their activity evoked by nociceptive stimulation.

EXPERIMENTAL METHOD

Experiments were carried out on cats anesthetized with chloralose (50 mg/kg) and curarized with tubocurarine. The preliminary operation consisted of tracheostomy, trephining of the skull, partial ablation of the cerebral cortex, isolation of the infraorbital nerve, and implantation of electrodes into the dentine of the upper canine teeth. Unit activity was recorded from CGM neurons by extracellular glass microelectrodes (diameter of tip 1-2 μ, resistance 6-10 MΩ), filled with 3M potassium citrate solution. The region of recording was bounded by coordinates A 1-2 mm, L 1.5-2 mm, and H not more than 6 mm from the dorsal surface of the brain stem, in accordance with coordinates from the atlas of Snider and Neimer [11].

The microelectrodes were inserted with the aid of a microapplicator with step motor and digital indication of the depth of insertion. The location of the microelectrode tip in CGM was verified in serial brain sections. Spontaneous unit activity and responses of the neurons to single electrical stimulation of acupuncture points, the cutaneous surface of the forearm outside the zone of acupuncture points, and above-threshold stimulation of the dental pulp and infraorbital nerve, were evaluated. Electroacupuncture was carried out for 20-30 min at analogs of human acupuncture points with a local segmental effect (Hsia-kuan, E-7) and with a general analgesic action (Hê-ku, Gi-4), by means of standard acupuncture needles, with square pulses with a frequency of 1 Hz, duration 0.5 msec, and amplitude 5-10 V, which, under chromic experimental conditions, inhibited emotional-behavioral and autonomic motor manifestations of pain in animals [2, 4].

EXPERIMENTAL RESULTS

Activity of 46 CGM neurons responding to stimulation of acupuncture points were recorded. Most neurons possessed low-frequency (1-3 Hz) spontaneous spike activity: 48% of cells responded to stimulation at acupuncture points and the rest to electrical stimulation of acupuncture points, the dental pulp, the infraorbital nerve, and the cutaneous surface of the forearm. These neurons, with a wide convergent afferent input, were distributed uniformly in the dorsal part of CGM, whereas neurons (62%) responding selectively to activation of

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TABLE 1. Location and Character of Neuronal Responses in Dorsal Part of CGM

Serial No.	Coordination			Responses to stimulation							
				Hsia-kuan		Hê-ku		cutaneous surface	infraorbital nerve	dental pulp	
	AP	L	H	I	II	I	II			I	II
1	1	1,5	0,8	+	+	+	+	+	−	+	+
2	1,3	1,5	1,2	−	+	+	+	−	−	−	−
3	1,5	1,5	1,4	−	+	+	−	+	−	−	−
4	1	1,5	1,5	−	−	−	+	+	−	−	−
5	2	1,5	1,5	+	+	+	+	+	+	−	−
6	2	1,5	1,7	+	+	+	+	−	−	−	−
7	2	1,5	1,8	+	+	+	+	−	−	−	−
8	2	1,5	1,9	+	+	−	−	−	−	−	−
9	1	1,5	2	−	−	+	+	+	−	−	−
10	1,5	1,5	2,1	−	−	−	+	−	−	−	−
11	2	2	2,1	−	−	+	+	−	−	−	−
12	1	1,5	2,2	+	+	+	+	−	+	+	+
13	1	1,5	2,2	−	−	−	+	+	−	−	−
14	1	1,5	2,2	−	−	−	+	+	−	−	−
15	1,5	1,5	2,4	−	+	−	+	−	−	−	−
16	2	2	2,4	−	−	+	+	−	−	−	−
17	2	1,5	2,4	−	−	+	−	−	−	−	−
18	1	1,5	2,4	−	−	−	+	−	−	−	−
19	1,5	1,5	2,4	−	+	−	+	−	−	−	−
20	2	2	2,5	−	−	+	+	+	−	−	−
21	2	2	2,6	−	−	+	+	+	−	−	−
22	2	1,7	2,7	−	−	+	+	−	−	−	−
23	1	1,5	2,8	−	−	+	+	−	−	−	−
24	2	1,5	3,0	−	−	+	+	−	−	−	−
25	2	2	3,1	+	+	+	+	+	+	+	+
26	1	1,7	3,1	−	−	+	+	−	−	−	−
27	1	1,7	3,2	+	+	+	+	−	−	−	−
28	2	1,5	3,2	+	+	+	+	+	+	+	−
29	2	2	3,2	−	−	+	+	−	−	−	−
30	2	1,7	3,4	−	−	+	+	+	+	+	+
31	2	1,5	3,5	−	−	+	+	−	−	+	+
32	2	1,5	3,6	+	+	+	+	−	−	−	−
33	2	1,5	3,6	+	+	+	+	−	+	−	−
34	2	1,7	3,7	−	−	+	+	−	+	+	+
35	2	1,7	4	−	−	+	+	+	+	−	−
36	1	1,7	4,1	−	−	+	−	+	−	−	−
37	2	2	4,1	+	+	+	+	+	+	+	+
38	2	1,5	4,2	+	+	−	−	+	+	+	+
39	1	1,5	4,2	+	−	+	+	+	+	+	+
40	1	1,7	4,3	−	−	+	−	+	−	−	−
41	2	1,7	4,6	−	−	+	+	+	+	−	−
42	1,5	1,5	4,6	−	−	+	+	−	−	−	−
43	1,5	1,5	4,7	+	+	+	+	+	+	+	+
44	1	1,7	5,2	+	−	+	+	+	−	−	−
45	2	1,5	5,4	+	+	+	+	+	+	−	−
46	1	1,7	5,5	+	+	+	+	−	−	−	−

Legend. I) Ipsilateral side; II) contralateral side. +) Presence, −) absence of response to corresponding procedure.

acupuncture points, were located mainly in its most superficial regions (Table 1).

Electrical stimulation of acupuncture points evoked single or grouped neuronal discharges without any regular pattern in their character of response depending on the point stimulated. The majority of neurons (55%) responded to activation of an acupuncture point with general analgesic action or to electrical stimulation at both points (38%), and only 7% of cells responded to stimulation of acupuncture points with a local-segmental action.

The majority of convergent neurons (over 50% of cells) responded to stimulation at one of the acupuncture points and to cutaneous stimulation in the region of the forearm. This may be due to the fact that, in the present investigations a fairly extensive region was involved by stimulation of the cutaneous surface, due to the great distance between the stimulating electrodes (Fig. 1). Continuous stimulation of acupuncture points for 20-30 min did not significantly change the spontaneous spike activity of most neurons. A decrease in the spontaneous discharge frequency was observed in 13% of cells and an increase in 8%. Responses of neurons to single stimulation of acupuncture points were clearly reproduced for a long time (up to 30 min).

Electroacupuncture inhibited responses of convergent neurons to nociceptive stimulation which began 5-10 min after the beginning of stimulation and reached maximal intensity after

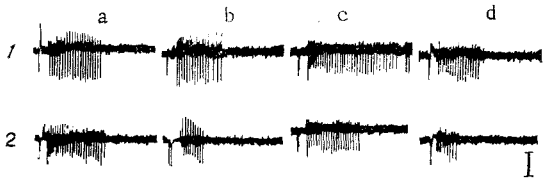

Fig. 1

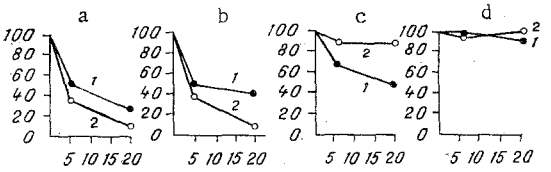

Fig. 2

Fig. 1. Response of CGM neuron to stimulation of different modalities. Traces show responses of neurons to stimulation of infraorbital nerve (a, 1), cutaneous surface of forearm (a, 2), dental pulp on ipsilateral and contralateral sides (b, 1 and b, 2, respectively) and points Hsia-kuan and Hê-ku on ipsilateral and contralateral sides (c, 1; c, 2; d, 1; and d, 2, respectively). Calibration: 100 μV, 10 msec.

Fig. 2. Effect of electroacupuncture on neuronal responses evoked by stimulation of different modalities: a) infraorbital nerve; b) dental pump; c, d) cutaneous surface of forearm, with nociceptive and non-nociceptive stimulation, respectively. 1, 2) Electroacupuncture at points Hê-ku and Hsai-huan, respectively. Abscissa, time (in min); ordinate, changes in number of discharges in neuronal response, in % of control (before acupuncture).

20-30 min. The number of discharges in the response of the neuron to nociceptive stimulation was sharply reduced against the background of electroacupuncture, or even disappeared completely, but the character of responses evoked by non-nociceptive cutaneous stimulation was virtually unchanged. These data make the results of clinical observations [7], according to which acupuncture causes selective suppression of pain sensitivity without changing other types of sensory modalities, clear and understandable. Electroacupuncture at points with a local-segmental effect inhibited by a greater degree (by 80-90%) neuronal responses evoked by stimulation of the dental pulp and infraorbital nerve, compared with the effect of electroacupuncture at a point of general analgesic action. However, electroacupuncture at a point of general analgesic action inhibited neuronal responses evoked by nociceptive stimulation of the cutaneous surface of the forearm more effectively (by 60-70%) (Fig. 2).

The results of these investigations thus indicate that the Hê-ku acupuncture point, with a general analgesic effect, has greater afferent representation on CGM neurons than the Hsia-kuan point, with a local-segmental action. The results are in agreement with existing views according to which stimulation of the point with general analgesic action is accompanied by activation of efferent fibers of several nerve trunks at once, in particular during acupuncture at the Hê-ku point, involving the radial, ulnar, and median nerves [4]. It can also be postulated on the basis of these findings that activation of antinociceptive structures and, in particular, of CGM, plays the key role in the realization of the analgesic effect of acupuncture, arising in response to stimulation of points with a general analgesic action, compared with local-segmental points. Acupuncture analgesia, during activation of local points, is due in all probability mainly to inhibition of conduction of nociceptive information at the level of the first relay neurons [2, 9, 10, 12]. Involvement of the antinociceptive systems of the brain in the realization of the analgesic effect of acupuncture from points with general analgesic action can explain the fact well known to acupuncture practitioners that the analgesic effect of acupuncture at these points is more widespread than that at local-segmental points, whose activation is accompanied by weakening of pain sensitivity in certain, quite well localized, regions of the body.

Very probably the dorsal and ventral divisions of CGM play different roles in the realization of acupuncture analgesia.

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EFFECT OF THYMALIN ON PROTEIN SYNTHESIS IN THE BRAIN AND ON CONDITIONED-REFLEX ACTIVITY OF THE OFFSPRING OF NEUROSENSITIZED RATS

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Experimental studies in recent years have revealed a number of important aspects of the pathogenesis of congenital diseases of the CNS connected with neuroimmunologic conflict between mother and fetus [6]. Besides a progressive neuroautoimmune process in the offspring of neurosensitized female rats, marked changes in protein synthesis in the CNS [7] and disturbance of ability to learn [2] have been found. A very important problem is that of the action of immunoregulators and, in particular, of the Soviet preparation thymalin, which has been successfully used in recent times in the combined treatment of several of the diseases mentioned above [9], on the brain. Restoration of ability to form an instrumental reflex to food in rats after injection of thymus extract was reported in [3]. The remaining experimental studies have been devoted mainly to the effect of thymalin on the immune system and on processes of regeneration [5, 8].

The aim of this investigation was to study the characteristics of protein synthesis in various parts of the brain and also the formation and preservation of a conditioned passive avoidance reflex (CPAR) in the offspring of intact and neurosensitized rats after treatment with thymalin.

EXPERIMENTAL METHOD

Four groups of animals aged 1.5-2 months (altogether 134 noninbred albino rats) were used in the experiments: group 1 consisted of offspring of intact mothers (control); group 2 was the offspring of intact mothers receiving thymalin at the age of 2 weeks (0.3 mg/100 g intramuscularly, daily for 5 days); group 3 consisted of offspring of mothers sensitized 2 weeks before mating with a 20% saline extract of cerebral cortex of allogeneic brain (0.5 ml intraperitoneally, three times at intervals of 1 day); group 4 was the offspring of neurosensitized mothers receiving a course of thymalin treatment at the age of 2 weeks.

In the study of protein synthesis (40 rats) ^{3}H-leucine (200 μCi per animal, intraperitoneally) was used as the precursor. Rats were decapitated 1 h later and four brain structures

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