ROLE OF THE GIGANTOCELLULAR NUCLEI OF THE RETICULAR FORMATION IN MECHANISMS OF ANALGESIA IN AURICULAR ELECTROACUPUNCTURE AND THE ACTION OF MORPHINE

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Descending systems of the spinal cord play an essential role in the group of antinociceptive mechanisms. Altogether three bulbospinal pathways [4] are known to be involved in the conduction of inhibitory influences on primary pain afferents. One of them arises from neurons of the gigantocellular nuclei (GCN) of the reticular formation and runs in the posterior funiculus of the spinal cord. The other two pathways arise mainly from neurons of the nucleus magnus raphe and the paragigantocellular nuclei (PGCN) of the reticular formation and descend into the spinal cord in the tractus dorsolateralis.

Participation of GCN, PGCN, and the nucleus magnus raphe in the mechanisms of analgesia has been demonstrated experimentally. For instance, injection of morphine into these brain zones or their electrical stimulation is accompanied by marked analgesia [1, 2, 7]. It has also been shown that the development of analgesic effects, in particular during stimulation of GCN, depends on activation of noradrenergic systems.

The role of GCN in the development of analgesia in different types of pain relief, in auricular acupuncture (AEA) and during the action of morphine, for example, has still not been explained.

EXPERIMENTAL METHOD

Experiments were carried out on 32 rats weighing 200-250 g, divided into two groups. In the rats of group 1, GCN were coagulated under chloral hydrate anesthesia (360 mg/kg, intraperitoneally) through a bipolar electrode, inserted into the brain at coordinates AP = 10.0, VD = 10.0, and L = ±0.8. A direct current of 5 mA was applied for 25-30 sec. Rats of the control group underwent a mock operation. The extent of coagulation was verified in frontal brain sections cut on a freezing microtome from the rat brain fixed beforehand in 10% neutral formalin.

Nociceptive sensation (NS) was assessed by the length of the latent periods (LP) of the hot-plate (HP) and tail-flick (TF) responses. In the first case the rats were placed on a hot plate at 55°C [5], in the second the tail was subjected to temperature stimulation by the focused beam of light of a 150-W projection lamp [3]. LP were measured at definite time intervals before and after stimulation.

The following techniques were used for analgesia: a) AEA — in this case NS was depressed by stimulation of regions in the zone of acupuncture points of the lung on the auricle of the ear [8] through electrode clips, using a biphasic current (0.6-1.0 mA, 4 Hz), with pulse duration of 0.4 msec for 15-20 min; b) intraperitoneal injection of morphine in a dose of 10 mg/kg. All the results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The morphological control showed that the zone of coagulation (Fig. 1) was located in the region of GCN, and in the rostrocaudal direction it extended over a length of 1.5-2 mm.

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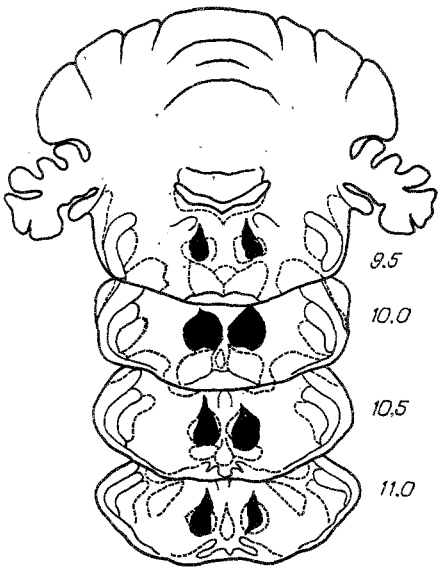

Fig. 1. Reconstruction of brain sections with localization of lesions of GCN. Numbers denote levels in accordance with the atlas.

Measurement of LP 12-15 days after the operation showed that the initial level of LP of HP and TF in the control and experimental series did not differ significantly. For instance, LP of HP in the control group was 12.0 ± 1.2 sec and in the experimental group 10.7 ± 1.9 sec. LP of TF in rats after coagulation of GCN was 3.1 ± 0.2 sec, compared with 3.0 ± 0.1 sec in animals undergoing the mock operation. These results are evidence that bilateral destruction of GCN has no effect on regulation of NS in the resting state.

In the experiments of series I the effect of GCN of the reticular formation on LP of nociceptive responses was studied before and after stimulation by AEA. AEA caused an increase in LP of HP in the control and experimental groups compared with the background level for 20 min of the recovery period (Table 1), and this can be taken to indicate that the development of the analgesic effect after AEA actually took place in the animals of both groups. Comparison of LP of HP between the groups showed that this parameter was shorter in rats of the experimental group than in the control for 10 min of the recovery period (Table 1). These results are evidence that activity of the antinociceptive mechanisms is partly inhibited in rats subjected to bilateral destruction of GCN.

Evaluation of NS by measuring LP of TF showed that this parameter in the control was higher than initially for 20 min after the end of electrical stimulation (Table 1). In the experimental animals AEA caused only a temporary (for 1 min after the end of stimulation), but significant, increase in LP of TF. Comparative analysis of the groups showed that LP of TF was shorter in the experimental rats after 5 and 10 min.

It can be concluded from comparison of the results of measurement of LP of HP and TF responses that bilateral coagulation of GCN of the reticular formation is accompanied by depression of activity of the antinociceptive mechanisms, which are activated under normal conditions by the action of AEA.

In the experiments of series II the degree of development of antinociceptive responses was studied in rats with destruction of GCN and in the control in response to injection of morphine. Systemic injection of morphine caused an increase in LP of HP in the control and experimental rats starting with the 20th minute, and it remained at a higher level than initially until the 40th minute. Statistical analysis of LP of the experimental and control groups revealed no difference between these parameters. Similar results also were obtained when NS was measured by the tailflick test (Table 1). Morphine lengthened LP of TF in both groups: from the 10th to the 50th minute in the control, from the 10th to the 40th minute in the experiment. Comparison of TF responses showed that differences in the duration of LP after injection of morphine were not statistically significant.

It can be concluded from these results that destruction of GCN of the reticular formation does not affect analgesia induced by morphine. Similar conclusions were drawn in other investigations [6, 9], when PGCN were inactivated.

TABLE 1. Changes in LP (in sec) of HP and TF Responses in Rats with Destruction of Group A10 of Neurons in Ventral Tegmental Region and in Animals Undergoing Mock Operation, after Action of Morphine and AEA

Procedure	Test	No. of animals	Initial value of LP	Time after procedure, min						
				0	5	10	20	30	40	50
Injection of morphine	HP									
	Control	7	13,2±1,4	—	—	5,0±4,0	9,3±3,5*	13,1±3,7*	11,3±4,1*	7,8±4,8
	Experim.	7	10,2±2,1	—	—	4,1±2,9	7,8±2,1*	11,3±2,2*	8,3±2,3*	2,4±1,2
	TF									
	Control	7	3,4±0,2	—	—	1,5±0,5*	1,9±0,7*	1,9±0,6*	2,0±0,8*	1,5±0,5*
	Experim.	7	3,9±0,3	—	—	1,5±0,5*	0,6±0,5	1,3±0,6***	1,9±0,5*	1,0±0,6
AEA	HP									
	Control	9	1,2±1,2	6,2±0,5*	5,0±0,7*	4,1±0,8*	3,1±0,7*	0,3±0,7	—	—
	Experim.	9	10,7±1,9	3,2±0,3*,**	2,0±0,8**,***	2,0±0,4*,**	1,7±0,8***	0,7±0,5	—	—
	TF									
	Control	9	3,0±0,1	2,4±0,6*	1,7±0,5*	1,9±0,4	1,0±0,4*	0,1±0,3	—	—
	Experim.	9	3,1±0,2	1,2±0,4*	0,2±0,3**	0,01±0,2**	0,3±0,36	0,1±0,1	—	—

Legend. Data given above are differences between parameter determined after procedure and its initial value. *$p < 0.05$ Compared with initial value, **$p < 0.05$ compared with control, ***$p < 0.05$ for 1α compared with control.

Neurochemical systems of GCN thus are involved in the formation of antinociceptive mechanisms associated with AEA, whereas under the influence of morphine, analgesia is realized without the participation of GCN. Accordingly, it must be concluded that the mechanisms of pain suppression due to AEA and the action of morphine differ from one another in their morphological and functional structure.

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