EFFECT OF NEMBUTAL ON ARTERIAL PRESSURE RESPONSES EVOKED BY STIMULATION OF THE HYPOTHALAMUS, MEDULLA, AND LATERAL HORNS OF THE SPINAL CORD

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Small doses of Nembutal (3-10 mg/kg) increase the amplitude of pressor responses evoked by stimulation of various structures of the hypothalamus, medulla, and lateral horns of the spinal cord. Meanwhile, the degree of the effects of Nembutal on cyclic changes in arterial pressure differed very considerably, depending on the nature of the structure stimulated. The investigated doses of Nembutal had no effect on the initial arterial pressure level.

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In the modern view [3], nervous structures responsible for regulation of the arterial pressure participate both in maintenance of the initial level of the arterial pressure and in the production of cyclic changes in vascular tone. It has now been shown that barbiturates inhibit the response of the arterial pressure to stimulation of various elements of the vasomotor center [6, 9, 10]. However, precisely which regulatory mechanisms are influenced by barbiturates and the localization of their action have not yet been finally settled.

The object of the present investigation was to study the character of the action of Nembutal on arterial pressure responses to stimulation of central structures performing different functional roles in the general system of arterial pressure regulation.

EXPERIMENTAL METHOD

Altogether 48 experiments were carried out on cats. In 19 experiments the effect of Nembutal was studied on the arterial pressure responses to electrical stimulation of the hypothalamus, medulla (0.2-5 V, 1 msec, 100/cps) and lateral horns of the spinal cord (3-7 V, 1 msec, 60/cps). Some observations were made on animals after division of the brain at the level of decussation of the optic tracts. The other experiments were performed on cats with an intact nervous system, immobilized with Listhenon (1-1.5 mg/kg). The position of the electrodes was determined on histological sections by the method adopted in our laboratory [7]. Nembutal was injected intravenously as a 1% solution in doses of 1-15 mg/kg. Statistical analysis was carried out by the formulas recommended by L. S. Kaminskii [5] and M. L. Belen'kii [1].

EXPERIMENTAL RESULTS

Stimulation of most structures of the hypothalamus and medulla causes changes in arterial pressure. In our experiments mainly pressor responses were observed (Table 1). Depressor responses were observed if the electrode was situated in the preoptic region, the dorsal portions of the posterior hypothalamus, the motor nucleus of the vagus nerve, and in some cases in the gigantocellular and ventral reticular nuclei. During stimulation of the lateral horns of the spinal cord, pressor changes always developed.

After administration of Nembutal the amplitude of all the evoked pressor responses diminished. Different doses of Nembutal inhibited these responses to a different degree, depending on the structure whose stimulation produced them (Table 1).

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TABLE 1. Effect of Nembutal on Pressor Changes of Arterial Pressure Caused by Stimulation of Hypothalamus, Medulla, and Lateral Horns of Spinal Cord

Structure stimulated	Number of observations	Mean amplitude of response (in mm Hg) before injection of Nembutal	Mean amplitude of response (in mm Hg) after injection of Nembutal in doses of (in mg/kg)	
			3-5	7-10
Posterior hypothalamic region (ventral portion)	12	31.7	5.5±2.7	P<0.001
Medial mammillary nucleus	5	33	28±6.5	P<0.05
Ventro-medial nucleus	3	42	20±8.5	3.7±1.3
			P>0.05	P<0.02
Dorso-medial	3	30	0	0
				P<0.001
Lateral hypothalamic region	3	25	0	0
				P<0.001
Gigantocellular nucleus	6	35.7	15±3.5	1.7±1.2
			P<0.01	P<0.001
Parvocellular nucleus	4	37.5		18±9
				P<0.05
Nuclei of vestibular complex	4	27.5	2±2.1	0
			P<0.02	
Caudal nucleus of pons	5	35	29±8.8	
			P<0.05	
Lateral horns of spinal cord	6	50		40.5±10.5
				P>0.05

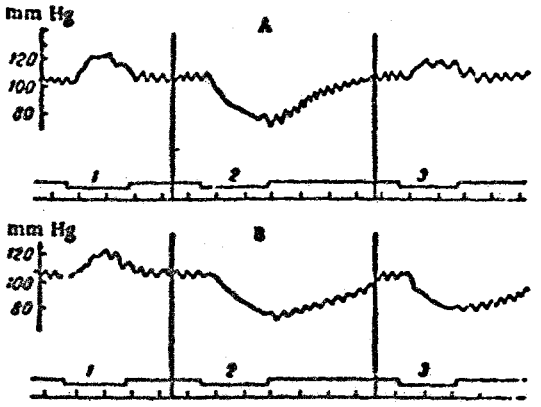

Fig. 1. Effect of Nembutal on responses of arterial pressure to stimulation of posterior hypothalamic region (1), motor nucleus of vagus nerve (2), and to combined stimulation of these structures (3). A) before injection of Nembutal; B) after injection of Nembutal in dose of 3 mg/kg. From top to bottom: trace of arterial pressure, marker of stimulation, time marker (5 sec).

Inhibition of the pressor responses which developed after administration of Nembutal also was manifested by lengthening of the latent period of the response. As little as 0.5-1.5 sec after injection of small doses of Nembutal (1-3 mg/kg), the latent period of the responses to stimulation of the posterior and lateral hypothalamic regions and nuclei of the vestibular complex was increased. Probably these structures contain more synapses along their path to the preganglionic sympathetic neurons than the structures of the medial hypothalamus (ventromedial and medial mammillary nuclei).

As Table 1 shows, after injection of Nembutal in a dose of 7-10 mg/kg, responses of the arterial pressure to stimulation of suprasegmental structures were inhibited by 80-100%. However, the initial level of the arterial pressure in our experiments was practically unchanged after injection of Nembutal in a dose of 7-10 mg/kg, namely 103 (96.3-119.7) before and 98 (79.1-116.1) mm after injection of Nembutal. Consequently, the depressing action of nembutal in small doses was exhibited with respect to the functional activity of the structures participating in cyclic changes of arterial pressure to a much greater degree than with respect to structures responsible for maintaining the initial level of the arterial pressure.

Neurotropic drugs are known to modify the arterial pressure response not only by acting on vasomotor structures, but also by disturbing the intracentral communications with other structures. To clarify the character of action of Nembutal we carried out a series of experiments in which combined stimulation was applied to the hypothalamic structures and bulbar and spinal structures.

In response to combined stimulation of the hypothalamus and medial bulbar structures or the lateral horns of the spinal cord, the responses of the arterial pressure were greater in amplitude than the responses evoked separately. Combined stimulation of the hypothalamus and the parvocellular reticular nucleus led to the appearance of a response which was smaller in amplitude than the changes evoked separately. This was evidently because of activation of elements inhibiting the initial level of the arterial pressure and directed either toward the effector reticular neurons or directly toward the sympathetic neurons of the spinal cord [2]. We observed that the inhibitory elements were more resistant to the action of Nembutal than the pressor structures. In addition, Nembutal in small doses can facilitate manifestation of function of inhibitory structures. As can be seen in Fig. 1, injection of Nembutal in a dose of 3 mg/kg distorted the arterial pressure response to combined stimulation of the posterior hypothalamic region and motor nucleus of the vagus nerve. Since the amplitude of the separately evoked responses remained unchanged after injection of Nembutal, the primary activation of the inhibitory elements can be assumed to have taken place, leading to distortion of the pressor response of the arterial pressure.

This investigation showed that quantitative and qualitative differences exist in the action of Nembutal on the central structures producing cyclic changes in arterial pressure. Small doses of barbiturates can ultimately depress the increased excitability of the suprasegmental structures without influencing the initial vascular tone. This therapeutic effect of barbiturates in hypertensive states is possibly connected with precisely this action. This is all the more probable because, in the opinion of some investigators [4, 8], hypertensive states may arise in association with functional or organic disturbances of the hypothalamic region.

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