# DIFFERENTIAL INTERACTION BETWEEN HYPOTHALAMIC AND BULBAR MECHANISMS IN BLOOD FLOW REGULATION IN SKELETAL MUSCLES

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In the last decade much experimental evidence has been obtained of close interaction between hypothalamic and bulbar levels of regulation of the activity of the cardiovascular system [3-7, 9, 14]. According to facts obtained by some workers, interaction of this kind is manifested as inhibition of the cardiac and vascular components of the baroreceptor reflex during excitation of the hypothalamic center for defensive reactions [3, 4, 6, 7]. Other workers consider that inhibitory influences from the hypothalamus are limited to reflex bradycardia [5, 11]. In most investigations regions of the hypothalamus related to the defensive center were stimulated; interactions of other hypothalamic structures with mechanisms of baroreceptor regulation of the circulation have hardly been studied at all.

It was accordingly interesting to study the role of baroreceptor reflexes in the development of cardiovascular responses to stimulation of different zones of the hypothalamus. For this purpose changes in the blood flow and vascular resistance were studied in hind-limb muscles in response to stimulation of various hypothalamic structures before and after acute blocking of the principal reflexogenic zones — the carotid sinus, heart, and arch of the aorta.

## EXPERIMENTAL METHOD

Acute experiments were carried out on seven mongrel dogs of both sexes weighing 9-16 kg under chloralose-pentobarbital anesthesia (40 and 15 mg/kg respectively), with the use of suxamethonium (2-5 mg/kg) and artificial respiration. The animals were fixed in a stereotaxic apparatus and concentric bipolar electrodes with a tip 0.1 mm in diameter were inserted into different hypothalamic structures whose coordinates were calculated by reference to an atlas of the dog's brain [10]. The hypothalamus was stimulated by a pulsed current (4-10 V, 50-400 μA, 2 msec, 50 pulses/sec) for 30-60 sec. At the end of the experiments the locations of the points of stimulation were verified in histological brain sections. The velocity of the blood flow was recorded in the leg muscles by a photoelectric drop method using a tachometer, and the arterial and venous pressure in the femoral vessels also was determined by an EMT-31 electromanometer (Elema-Schönander). The vascular resistance was calculated from the difference between the arterial and venous pressure and the velocity of the blood flow. Receptors of the carotid sinus and cardioaortic reflexogenic zones were blocked by bilateral division of the vagus nerves in the neck and compression of the common carotid arteries during stimulation.

## EXPERIMENTAL RESULTS

Depending on the location of the stimulating electrodes the responses observed were divided into two groups: responses to stimulation of the anterior hypothalamus (supraoptic, dorso- and ventromedial nuclei) and responses to stimulation of the posterior hypothalamus (mammillary nuclei, chiefly the lateral mammillary nucleus).

The initial values of the parameters studied were: arterial pressure 156 ± 4.7 hPa, pressure in the femoral vein 6.3 ± 0.3 hPa, blood flow in the leg muscles 12 ± 0.4 ml/min,

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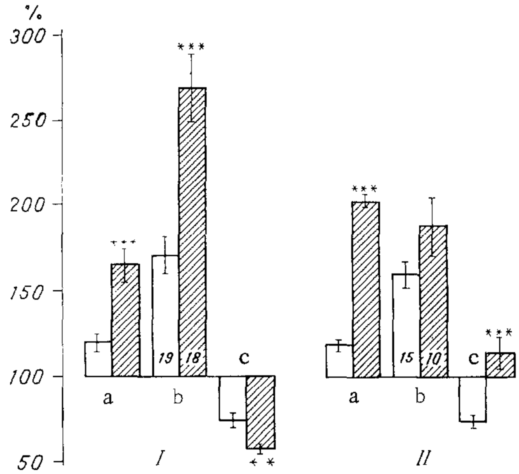


Fig. 1. Changes in circulation in skeletal muscles during stimulation of various hypothalamic structures before and after blocking of baroreceptors of carotid sinus and aortic arch (M ± m). Mean values (in % of initial level, taken as 100) of arterial pressure (a), velocity of blood flow (b), and vascular resistance (c) in leg muscles shown in response to stimulation of structures of anterior (I) and posterior (II) hypothalamus. Empty rectangles denote initial responses, shaded rectangles — responses after baroreceptor blocking. Numbers in rectangles denote number of responses observed. *P < 0.05, **P < 0.01, ***P < 0.001.

vascular resistance 9.8 ± 0.2 conventional units. Electrical stimulation of the various hypothalamic zones caused marked changes in the values of these parameters. In most cases qualitatively similar responses occurred: The arterial and venous pressure rose on average by 26 and 31% respectively, and muscular blood flow increased by 64%, and the vascular resistance decreased by 22% of the initial level. The most marked changes in these parameters were caused by stimulation of the dorso- and ventromedial nuclei.

Acute blocking of the principal reflexogenic zones led to a significant change in the response to hypothalamic stimulation; the effect, moreover, was largely determined by the site of stimulation. For instance, stimulation of structures in the anterior hypothalamus after vagotomy and compression of both carotid arteries was accompanied by a significantly greater rise of arterial pressure, a greater increase in the muscular blood flow, and a greater decrease in vascular resistance than when the baroreceptors were intact (Fig. 1, I). Stimulation of the posterior hypothalamus against the background of blocking of the principal reflexogenic zones also gave a stronger pressor response, but the blood flow increased by only a little more than before blocking of the baroreceptors, and the vascular resistance, instead of decreasing, began to increase (Fig. 1, II).

Data from one experiment illustrating averaged values of the parameters shown in Fig. 1 are given in Fig. 2. Whereas blocking of baroreceptor influences and simultaneous stimulation of the dorsomedial nucleus caused a much greater increase of arterial pressure and blood flow in the leg muscles (Fig. 2b) than the corresponding values in response to isolated stimulation of the same nucleus (Fig. 2a), a combination of the same blocking of the principal reflexogenic zones with stimulation of the region of the lateral mammillary nucleus was accompanied by very weak changes in the muscular blood flow, but by a considerable rise of pressure and of vascular resistance (Fig. 2d). The fact that such different effects can be observed in the same experiment suggests that they are due not to differences in the depth of anesthesia or in the state of the cardiovascular system, but mainly to the site of stimulation.

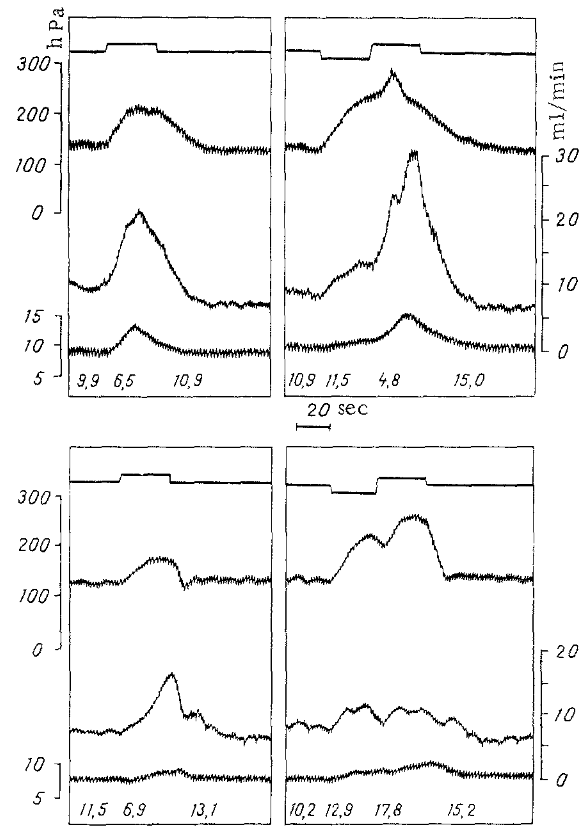


Fig. 2. Effect of blocking of principal reflexogenic zones on changes in muscular blood flow in response to stimulation of dorsomedial (a, b) and lateral mammillary (c, d) nuclei. a, c) Initial responses: b, d) responses after blocking reflexogenic zones. Legend from top to bottom: marker of stimulation (above) and compression of carotid arteries (below), arterial pressure, muscular blood flow, venous pressure. Recordings of integral parameters are shown. Numbers beneath trace of venous pressure show vascular resistance (in hPa·min/ml). On left — scale of pressure (in hPa); on right — velocity of blood flow (in ml/min).

It can thus be concluded that different hypothalamic structures interact differently with the baroreflex mechanisms of the medulla. In one case there is partial occlusion, as a result of which the vasomotor responses to stimulation of the anterior hypothalamus are inhibited by baroreceptor reflexes, but in the other case, on the contrary, these mechanisms somehow or other facilitate the course of vasodilator responses in skeletal muscles. A similar phenomenon was observed previously [2] during a study of responses of the total peripheral resistance to stimulation of various parts of the hypothalamus. The results of the present series of experiments, conducted on a different object, confirm previous findings and shed some light on the mechanism of this phenomenon. In an investigation by Coote et al. [4], unequal inhibition of the vasomotor and cardiac components of the baroreceptor reflex by different hypothalamic structures was observed, and this also points to differential relations between the hypothalamic and bulbar structures.

Enhancement of the pressor responses and vasodilator effect in skeletal muscles discovered in these experiments during anterior hypothalamic stimulation after blocking of the principal reflexogenic zones agrees with data of other workers who observed a decrease in responses to hypothalamic stimulation during activation of baroreceptors [3, 14] or an increase in these responses after blocking of reflexogenic zones [15], and it can be explained on the grounds that certain hypothalamic regions receive impulses from baroreceptors of the carotid sinuses and aortic arch, and they probably participate in the closing of baroreceptor reflexes [1, 8, 13]. It can therefore be accepted that blocking of baroreceptors increases the excitability of some groups of hypothalamic neurons and increases their responses to stimulation.

The decrease in the vasodilator response to stimulation of the posterior hypothalamus after deafferentation of the reflexogenic zones of the cardiovascular system, observed previously [2], and even the appearance of vasoconstriction in skeletal muscles in the present series of experiments evidently differ in nature. Vasodilation in skeletal muscle in response to stimulation of the lateral mammillary nucleus is probably due to some degree to reflex inhibition of vascular tone. Blocking of baroreceptors abolishes the reflex component of the vasodilator response to posterior hypothalamic stimulation, and in that case a sympathoactivating effect of this stimulation is exhibited — the vessels of the hind limbs constrict. This explanation is supported by the fact that in the experiment whose results are shown in Fig. 2 the vasodilator response to stimulation of the lateral mammillary nucleus was not blocked by atropine.

In the present investigation blocking the carotid sinus receptors was produced by temporary occlusion of the common carotid arteries. As special investigations have shown [12], occlusion of the carotid arteries causes the same effect in the vasomotor center as division of the sinus nerves. The same conclusion is reached by comparison of the results of the present investigation with those of a previous study [2], which were qualitatively similar, although the receptors in that case were blocked by surgical denervation of the carotid arteries and carotid sinuses. Since only baroreceptors are blocked by occlusion of the carotid arteries (the chemoreceptors continue to function), and since there are virtually no chemoreceptor fibers [1] in the depressor nerves divided at vagotomy, the procedure of blocking the principal reflexogenic zones used in those experiments is regarded by the present writer as being mainly baroreceptor deafferentation.

The results of the present investigation thus indicate differential effects of baroreflex mechanisms on vasomotor responses to stimulation of different hypothalamic regions.

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