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BLOOD PRESSURE REFLEXES TO STIMULATION OF TIBIAL NERVE A FIBERS IN MESENCEPHALIC AND BULBAR CATS

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The role of the various subgroups of A fibers of the tibial nerve (pulse frequency of electrical stimulation 10/sec) in the formation of reflex changes in blood pressure (BP) was investigated in unanesthetized cats with total transection of the brain stem at the level of the pontomedullary junction (bulbar animals) or at the rostral border of the mesencephalon (mesencaphalic animals), and also in anesthetized cats with an intact brain. The lowest thresholds for the reflexes were found in anesthetized animals with an intact brain, the highest in bulbar cats. Excitation of A fibers in anesthetized cats with an intact brain evoked only depressor reflexes. In some bulbar and mesencephalic animals only pressor reflexes appeared. In the experiments of this group excitation of fibers with a conduction velocity of over 15 m/sec in mesencephalic cats evoked reflexes of near maximal strengths, whereas in bulbar cats excitation of thinner A fibers also was necessary. In unanesthetized animals disconnection of the suprabulbar structures thus lowers the sensitivity of the central mechanisms of vasomotor regulation to impulses in low-threshold A fibers. No such effect was found in another group of experiments in which depressor reflexes appeared in response to stimulation of fast-conducting A fibers only. In these experiments, if slower A fibers also were stimulated, the reflexes became pressor but the difference between their magnitude in the bulbar and mesencephalic cats was not significant.

KEY WORDS: *decerebration; somatic afferents; blood pressure reflexes; general anesthesia.*

In the classical view reflex responses of the blood pressure (BP) to somatic nerve stimulation remain normal (i.e., the same as in animals with an intact brain) provided that connections are preserved at least with the pontobulbar region of the brain [4, 11]. This view is supported by the absence of changes in these reflexes after decerebration not only in acute [9, 10] but also in chronic experiments [13]. In these cases reflexes in anesthetized animals with an intact brain were regarded as "normal." However, other workers [1, 2, 5-8]

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reported significant changes in BP reflexes after transection of the brain stem at various levels above the medulla.

To study the effects of suprabulbar regions of the brain on reflex processes in the bulbospinal systems for regulation of the circulation, in the investigation described below reflex responses of BP to impulses in different subgroups of afferent A fibers of the tibial nerve were compared in unanesthetized cats subjected to free collicular decerebration (mesencephalic animals), unanesthetized cats in which the medulla was separated from higher structures (bulbar animals), and in anesthetized cats with an intact brain.

EXPERIMENTAL METHOD

In 10 experiments the animals were anesthetized with chloralose and urethane (30 and 500 mg/kg, intravenously), and in 23 experiments they were decerebrated. For this purpose, under ether anesthesia a wire electrode 0.4 mm in diameter, with an uninsulated tip 2.5 mm long, was inserted into the brain as far as the base of the skull. A second (lamellar) electrode was fixed to the temporalis muscle. A stabilized high-frequency current generator [15] was connected to the electrode and, 15 sec after switching on the current (30 mA, 20 V) the electrode began to be withdrawn from the brain at a speed of about 0.1 mm/sec. The width of the coagulated layer of tissue in sagittal sections was 3-4 mm and in frontal about 3 mm. For complete transverse destruction of the brain stem the thermocoagulation was repeated at steps of 2-3 mm. Precollicular decerebration was performed on 11 animals (dorsally, immediately anteriorly to the tectum, ventrally, through the mamillary bodies). In another 12 cats the medulla was separated from the pons (the electrode was inserted through the cerebellum). At the end of decerebration the administration of ether was stopped and, 2-4 h later, under artificial ventilation in accordance with the nomogram in [12] the study of BP reflexes began in animals immobilized with flaxedil or myorelaxin (suxamethonium). The left tibial nerve was stimulated with square pulses (0.1-3 V, 0.1 msec, 10/sec). The threshold of excitation (1 T) of A_β fibers of the tibial nerve, determined from the record of its electrical activity [3], was taken as the unit of strength (amplitude) of the stimuli. BP was recorded in the right femoral or carotid artery by means of the electromanometer with KSP-4 recorder.

EXPERIMENTAL RESULTS

General Characteristics of BP Reflexes. The threshold of appearance of reflex changes in BP (Table 1) in the mesencephalic cats was a little lower than in bulbar cats (1.5-3 T in the 1st case, 2-7 T in the 2nd). After both precollicular and bulbar decerebration, threshold reflexes in some animals were pressor (experiments of group I), whereas in others they were depressor (experiments of group II). In the experiments of group II the reflexes became pressor in response to stimuli within the range 3-10 T, whereas in all the anesthetized animals they remained depressor up to a strength of 30 T (Fig. 1). The amplitudes of the pressor reflexes in the mesencephalic animals were greater than in the bulbar cats, and this difference was particularly great in the experiments of group I in response to stimuli under 10 T in strength. The difference between the results of the experiments of groups I and II was not connected with the BP level: in both bulbar and mesencephalic cats in both groups of experiments its values were similar, averaging about 140 mm Hg at the beginning of recording of the reflexes and about 120 mm Hg at the end of the experiments.

Effect of Stimulation of Different Subgroups of A Afferents of the Tibial Nerve on Magnitude and Character of Reflex Changes in BP. According to previous observations [3], during stimulation of the tibial nerve at a strength of 1-1.5 T only the lowest-threshold A_β fibers are excited; all A_β fibers are excited at 2.5-3 T, but at 2-2.5 T the A_δ fibers with a conduction velocity of over 20 m/sec are already being excited also. This fraction of A_δ fibers may be designated $A_{\delta 1}$, to distinguish them from the $A_{\delta 2}$ group of fibers which begin to be excited when the amplitude of stimulation is 3-5 T, and whose conduction velocity is 15-22 m/sec and also from the group $A_{\delta 3}$ of fibers with threshold excitation of 15-30 T and with a conduction velocity of under 15 m/sec [3].

Stimulation of the tibial nerve with a strength of 1-1.5 T caused no change in BP in any of the bulbar cats, and only in one of the 11 mesencephalic animals was BP lowered by 2 mm Hg. Meanwhile, in anesthetized cats with a whole brain, impulses in the most excitable A_β fibers caused a reduction of BP in 50% of the experiments (Table 1). Consequently, in unanesthetized decerebrate cats impulses in this fraction of A_β fibers of the tibial nerve were

TABLE 1. Direction of Reflex Changes in BP in Decerebrate and Anesthetized Animals During Stimulation of Low-Threshold A Fibers of Tibial Nerve

	Mesencephalic cats						Bulbar cats							Anesthetized cats with intact brain					
	strength of stimulation (in T for A_β fibers)																		
№ expt.	1,5	2	3	5	7	10	№ expt.	2	3	5	7	10	15	№ expt.	1	1,2	1,5	2	2,5
1	O	P	P	P	P	P	12	P	P	P	P	P	P	24	D	D	D	D	D
2	O	P	P	P	P	P	13	O	P	P	P	P	P	25	O	D	D	D	D
3	O	O	P	P	P	P	14	O	O	P	P	P	P	26	O	D	D	D	D
4	O	O	P	P	P	P	15	O	O	P	P	P	P	27	O	O	D	D	D
5	D	D	D – P	P	P	P	16	O	O	P	P	P	P	28	O	O	D	D	D
6	O	D	D	D	P	P	17	O	O	P	P	P	P	29	O	O	O	D	D
7	O	D	D	D	D	P	18	O	O	O	P	P	P	30	O	O	O	D	D
8	O	O	D	P	P	P	19	O	D	P	P	P	P	31	O	O	O	O	D
9	O	O	D	D	P	P	20	O	D	D – P	D – P	D – P	P	32	O	O	O	O	D
10	O	O	D	D	P	P	21	O	D	D	P	P	P	33	O	O	O	O	D
11	O	O	D	D	D	P	22	O	D	D	P	P	P						
							23	O	O	D	P	P	P						

Legend. O) Reflex absence, D) depressor reflex, P) pressor reflex.

unable to change the intensity of discharge of vasoconstrictor neurons to a sufficient degree to be reflected in BP.

In the anesthetized cats the depressor reflexes reached their maximal value in response to stimulation with a strength of 2-3 T (Fig. 1C), i.e., during excitation of all A_β and $A_{\delta 1}$ fibers. At this strength of stimulation, in all the group II experiments (in both mesencephalic and bulbar cats) depressor reflexes developed, but they were substantially smaller in magnitude than in the anesthetized animals with an intact brain. This could indicate a latent excitatory action of the relatively high-threshold fraction of the A_β and $A_{\delta 1}$ fibers, not discovered in the anesthetized animals, or a less marked effect of the inhibitory component of the action of these fibers under conditions of decerebration and absence of anesthesia. The first hypothesis is supported by the experiments of group I, in which impulses in these same fibers evoked only pressor reflexes; in the mesencephalic animals, moreover, they were highly significant: the magnitude of the reflexes in these experiments in response to stimulation with a strength of 3 T averaged 50.5% of maximal.

The addition of impulses in $A_{\delta 2}$ fibers (stimulation of the tibial nerve with a strength of 3-5 T) to the afferent flow in the experiments of group I led to a marked increase in the pressor reflexes (Fig. 1A). In response to stimulation with a strength of 5 T, in the mesencephalic animals they reached an average of 71% of the maximal amplitude, compared with 29% in the bulbar cats (the difference is statistically significant). In the experiments of group II the switch to stimulation of this strength was accompanied by a decrease in the depressor reflexes and by the appearance of pressor reflexes (Fig. 1B; Table 1), whereas in the anesthetized animals with an intact brain there was only a decrease in the depressor reflexes (Fig. 1C). The flow of impulses in afferent $A_{\delta 2}$ fibers evidently substantially modifies the relationship between inhibitory and excitatory influences on preganglionic vasomotor neurons toward their excitation; in the decerebrate animals the excitatory action of these fibers was more marked than in the anesthetized cats with an intact brain, and more marked in the mesencephalic than in the bulbar cats.

The addition of impulses in $A_{\delta 3}$ fibers (an increase in the strength of stimulation to 15-30 T) to the afferent flow in anesthetized cats usually caused a reduction of the depressor reflexes (Fig. 1C), whereas if the anesthesia was superficial, it changed them into pressor [3]. In the decerebrate animals impulses in $A_{\delta 3}$ fibers potentiated the pressor reflexes, which reached their maximal value in the experiments of group I at a strength of stimulation of 20-25 T, and in the experiments of group II at 30 T.

The difference between the amplitude of the maximal reflexes and the reflexes at 10 T in the experiments of group I was only 20% in the mesencephalic cats, but 33% in the bulbar cats. In the experiments of group II this difference was greater: 60 and 63% respectively. Consequently, in the experiments of group II the inhibitory components of the action of A_β and $A_{\delta 1}$ afferent fibers (and also, perhaps, $A_{\delta 2}$) on preganglionic vasoconstrictor neurons was expressed more strongly. This phenomenon conceals the difference between the magnitudes

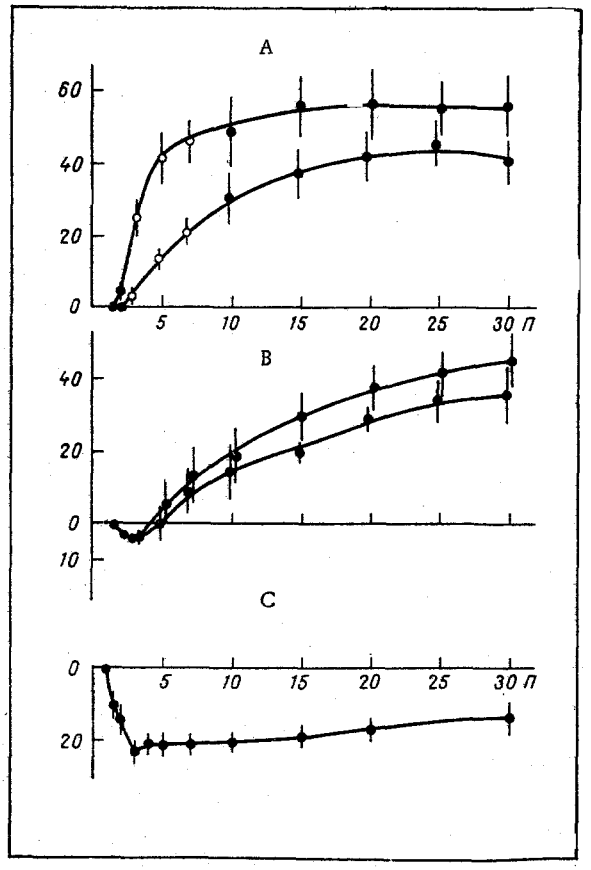

Fig. 1. Magnitudes of reflex changes in blood pressure, averaged for group of experiments, as functions of intensity of tibial nerve stimulation. Abscissa, amplitude of electrical stimuli (0.1 msec, 10/sec) measured relative to threshold of most excitable tibial nerve fibers; ordinate, reflex change in blood pressure (in mm Hg). A (experiments of group I): top curve represents unanesthetized mesencephalic cats (4 experiments), bottom curve unanesthetized bulbar cats (7 experiments). Empty circles denote mean values of reflexes, difference between which, to the same strength of stimulation, is statistically significant in bulbar and mesencephalic animals (at strengths of stimulation of 3, 5, and 7 T, $P < 0.001$, 0.01, and 0.02, respectively); B) (experiments of group II): top curve represents unanesthetized mesencephalic animals (7 experiments), bottom curve unanesthetized bulbar animals (5 experiments); C) experiments on anesthetized animals with intact brain (results of 10 experiments).

of the pressor reflexes in the mesencephalic and bulbar animals, which was clearly demonstrable in the experiments of group I.

It seems likely that there is a common basis for the three phenomena: 1) the appearance of depressor reflexes only in response to stimulation of A fibers of the tibial nerve in the animals with an intact brain with the ordinary depth of anesthesia; 2) the higher threshold of the pressor reflexes in the decerebrate animals in the experiments of group II than in those of group I; 3) the substantially smaller value of the pressor reflexes to stimulation of $A_\beta + A_{\delta 1} + A_{\delta 2}$ fibers in the bulbar animals of group I than in the mesencephalic animals of the same group. This common basis may be the total or partial inhibition of mechanisms generating the so-called very late A response [14]. This investigation of reflex changes

in electrical activity of the vasoconstrictor fibers showed that this response is of the greatest, if not decisive, importance in the production of pressor reflexes to stimulation of A fibers of somatic nerves. At the ordinary depth of anesthesia the activity of the neuron systems generating the very late A response is suppressed, and in that state tetanic stimulation of A fibers of the tibial nerve (at least with a frequency of not more than 10/sec) does not cause pressor reflexes. The difference between the thresholds of these reflexes in the experiments of groups I and II also probably reflects a difference in the sensitivity of the mechanisms of generation of the very late A response, which is most probably due to individual differences between the animals. Finally, it can be postulated that the appearance of large pressor reflexes in the mesencephalic cats in the experiments of group I, in response to comparatively weak (3-5 T) stimulation was due to the very high sensitivity of the mechanisms of generation of the very late A response, created by the facilitatory influences of the mesencephalon. It is impossible to state in which experiments — those of group I or II — the reflexes are "normal," but it will be evident that, in principle, the mesencephalon can exert powerful facilitatory influences on the reflex activity of the bulbospinal mechanisms controlling the circulation.

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