EFFECT OF NUMBER OF STIMULATED NERVE FIBERS AND IMPULSE FREQUENCY ON CHARACTER OF VASOMOTOR RESPONSES

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In experiments on cats the character of the vasomotor effects was found to depend on the frequency of stimulation of the sympathetic chain and on the number of stimulated nerve fibers, which was varied by stimulating different levels of the chain and by stimulating it in the stage of degeneration of its nerve fibers. The writers consider that vasoconstriction and vasodilatation are the result of excitation of different numbers of nerve fibers of the same type.

It has long been known that stimulation of the same vasomotor nerve can give rise to both vasoconstrictor and vasodilator effects [8, 16, 18]. This difference in the character of the effects is usually attributed to differences in the quantatiative parameters of stimulation. These facts, like many others, are customarily explained by the presence of specific vasoconstrictor and vasodilator fibers in these nerves [20]. However, not all the experimental results so far obtained can be explained on the basis of this concept [8].

The experimental results described in this paper provide another explanation for the different effects of stimulation of the sympathetic chains, which contain vasomotor fibers for the hind limbs.

EXPERIMENTAL METHOD

Experiments were carried out on 52 cats in which, under ether-urethane anesthesia, recordings were taken of the pressure in the carotid artery by a mercury manometer and the resistogram of the right and left femoral arteries. Unilateral division of the sympathetic chain was carried out on 32 cats 3-25 days before the investigation, under sterile conditions at the level between the 3rd and 4th lumbar ganglia. The responses of the limb vessels were studied to electrical stimulation of the sympathetic chain at the level between the 4th and 5th lumbar ganglia in the 32 cats after the preliminary operation at various stages of degeneration of the nerves, and at levels from the 1st to the 5th lumbar ganglia in the remaining 20 animals, immediately after decentralization of the sympathetic chains. The vasomotor nerves were stimulated electrically by pulses from a type ES-103 (Japan) stimulator, with the following parameters (frequency 1-40 Hz, amplitude 1-10 V, duration of pulse 3 msec, and of stimulation 5-20 sec).

EXPERIMENTAL RESULTS AND DISCUSSION

Responses of the vessels of the cats' hind limbs to stimulation of the sympathetic chain at different levels after its division in the inferior thoracic region, immediately before stimulation, are shown in Fig. 1.

Simultaneous stimulation of the segments of both chains between ganglia L_1 and L_2 at a constant voltage (2 V) and at all the frequencies used (1-20 Hz) in this experiment led only to vasodilatation of both limbs (Fig. 1A). The effect of stimulation of the chains at the same voltage but at a lower level (L_3) was sub-

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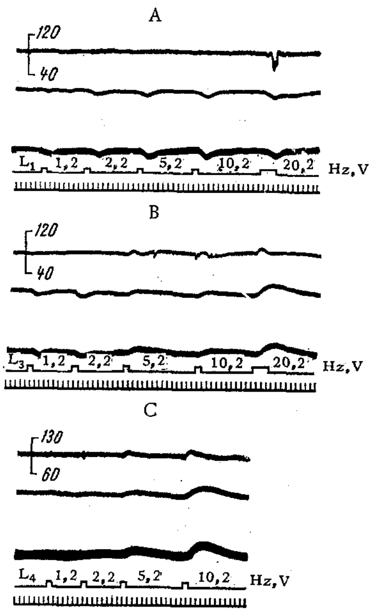

Fig. 1. Vasomotor response of cat's hind limbs in relation to frequency of stimulation of sympathetic chain at levels L1 (A), L3 (B), and L4 (C). From top to bottom: arterial pressure; resistograms of left and right femoral arteries; marker of stimulation with indication of frequency and strength; time marker (5 sec).

stantially different: dilator effects remained only to stimulation at relatively low frequencies, and high frequencies of stimulation gave rise to constriction (Fig. 1B). Stimulation with unchanged parameters at a still lower level of the sympathetic chain (L_4) produced only constriction (Fig. 1C).

Results similar to those described above were observed not in all experiments, but only in 70%, but the transition from dilator to constrictor effects observed in the same animal as the level of stimulation of the chain and the frequency of stimulation were changed was regular in character.

In the case of those segments of the chain whose stimulation evoked both types of effects, vasodilatation invariably took place at low frequencies and changed to constriction only at relatively high frequencies of stimulation. Since the strength of the stimuli remained constant, the change from dilator responses to constrictor would be difficult to explain on the basis of the concept of specificity of dilator and constrictor fibers differing in their excitability. Dilatation as the sole effect of stimulation of the upper lumbar levels likewise cannot be explained from this point of view, for the threshold strength of stimulation at these levels was 2 V, and the same stimulation applied to lower levels of the chain gave rise to different effects depending on the frequency of stimulation.

The effects of stimulation of the sympathetic chain at different stages of degeneration of its fibers are shown in Figs. 2 and 3. The effect of stimulation of the left sympathetic chain at level L_4 on the 5th day after its division continued to be dilator at all frequencies of stimulation from 2 to 20 Hz (Fig. 2A). It remained unchanged whatever the strength of stimulation (Fig. 2B). The impression was gained that, as a result of the degeneration, only the vasodilator fibers remained intact. However, increasing the frequency of stimulation to 40 Hz while leaving its strength unchanged (5 V) produced a definite constrictor effect (Fig. 2C). An increase in the frequency characteristic of stimulation was thus followed by an opposite vasomotor effect, despite the fact that in this case also all the fibers remaining after degeneration were stimulated.

All frequencies of stimulation of the left chain at levels L_4 and L_5 on the 7th day after division gave purely dilator effects (Fig. 3A, C). However, the effects became constrictor if the chain was stimulated at both levels simultaneously (Fig. 3B).

What are the characteristics of the nervous effect of combined stimulation of the sympathetic chain at two levels? It is difficult to accept that the constrictor effect of combined stimulation at L_4 and L_5 was due to the activation of vasomotor fibers of a different type from those fibers which were excited by stimulation of these segments of the chain separately at the same frequencies and strengths. On the contrary, it could certainly be considered that the same vasomotor neurons were excited by both types of stimulation. Since activation of the fibers forming the chain at the levels L_4 and L_5 separately was invariably followed by vasodilatation of the limb, it could be supposed that vasoconstriction in response to stimultaneous stimulation of the chain at these two levels was due to excitation of the same fibers. The difference between the effects in these cases could only be the result of quantitative differences in the flow of vasomotor impulses. From the writers' point of view the only possible assumption can be that during combined stimulation some changes took place in the frequency characteristic of the nervous effect, with a larger number of fibers simultaneously activated than when the two levels of the chain were stimulated separately.

This view is supported by the results shown in Fig. 1, when stimulation of the intact chain at level L_3 produced different effects depending on its frequency. Since the strength of stimulation was kept constant, in this case also it is impossible to consider excitation of fibers of different types.

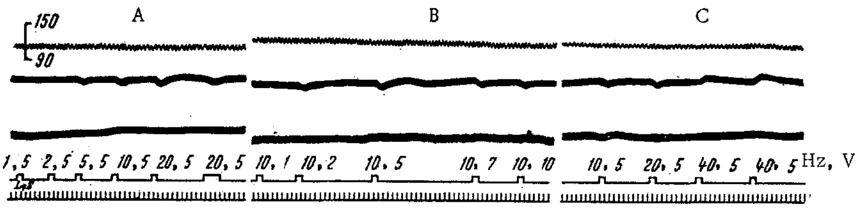

Fig. 2. Effect of the parameters of stimulation on vasomotor responses to stimulation of the left sympathetic chain in the stage of degeneration of its fibers. Legend as in Fig. 1.

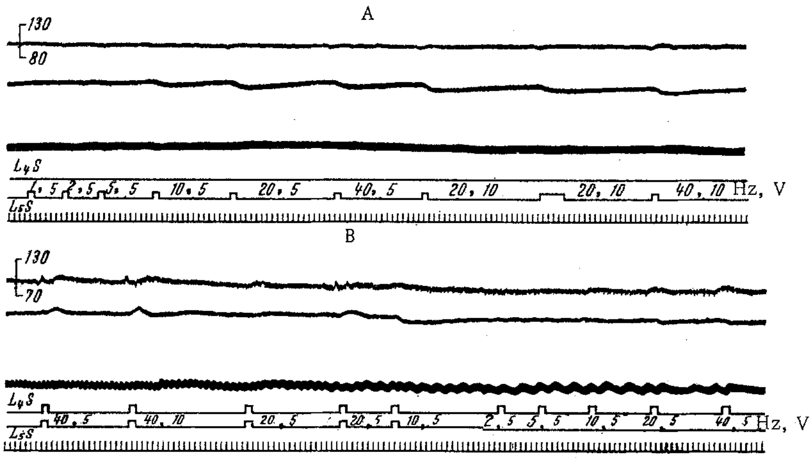

Fig. 3. Vasomotor responses of cat's hind limbs to separate (A, level L_5; C, level L_4) and combined stimulation (B, levels L_4 and L_5) of two levels of the left sympathetic chain in the stage of degeneration of its fibers. Legend as in Fig. 1

The effect of replacement of the vasodilator response by constrictor with an increase in the frequency of stimulation above the physiological level during stimulation of segment L_4 of the chain after preliminary degeneration of some of its fibers is particularly interesting from this point of view (Fig. 2C). The replacement of dilatation by constriction on an increase in the frequency of stimulation in this case suggests that the impulse frequency is functionally equivalent to the number of vasomotor fibers. Under these conditions the frequency of stimulation evidently compensates for the fibers in this part of the chain lost through degeneration at the level L_4, stimulation of which usually evoked a constrictor effect when all the fibers were intact (Fig. 1C).

Since it is impossible to explain convincingly all the results obtained on the basis of the hypothetical specificity of vasoconstrictor and vasodilator nerve fibers, the writers claim that a more satisfactory explanation can be obtained from the quantitative point of view [9].

Morphological analysis indicates an increase in the number of fibers in the lower segments of the sympathetic chain supplying the vessels of the lower limb, as the result of the entry of fibers from the white rami communicantes from spinal roots T_{11} to L_4 into the chain [4, 6]. It can be seen how, with the same parameters of stimulation, the dilator effect at level L_1 is replaced by a constrictor effect at level L_4 (Fig. 1). The absence of qualitative heterogeneity of the nerve fibers in the sympathetic chain is confirmed by the findings of Bayliss and Bradford [13], who showed that stimulation of individual groups of white rami communicantes entering the sympathetic chain does not give rise to differences in vasomotor effects.

The hypothesis that the number of nerve fibers is the factor which determines the character of the vasomotor response is also confirmed by the experiments of Rodionov [7], who observed conversion of the vasoconstrictor effect into vasodilator after division of some fibers of the stimulated sympathetic chain.

This view also explains the relationship between the time elapsing after division of the nerve and the character of the vasomotor responses to stimulation of the nerve. It can naturally be assumed that as degeneration proceeds the number of active, functioning fibers becomes progressively smaller. Accordingly, a strength of stimulation which previously excited a large number of fibers will be capable of exciting the residual smaller number of fibers prsesent 3-5 days after division, and evidently as a result of this, the vasoconstrictor effect observed is replaced by a vasodilator effect.

This hypothesis is also supported by the results of morphological investigations of the vasomotor pathways, for no structural differences have been found between vasodilator and vasoconstrictor nerve elements [2]. No effector fibers differing in their rate of degeneration after division of the nerve can be demonstrated morphologically in the walls of blood vessels [11].

Direct experimental tests likewise do not confirm the view that vasoconstrictor and vasodilator fibers differ in their excitability [17, 19]. The pharmacological tests which are usually used in attempts to demonstrate qualitative differences between types of vasomotor nerve elements cannot now be regarded as sufficiently convincing [8, 9].

From the quantitative point of view, a more satisfactory explanation is provided by results indicating differences in effects at different stages of development. Vasodilatation in the rabbit's ear in young animals during stimulation of the cervical sympathetic nerve [1], and also the exclusively dilator effects on the limb vessels of puppies [14] during stimulation of the lumbar sympathetic chain are explained by the relatively small number of nerve elements in the early stage of development, whereas the constrictor effects found in adult animals during stimulation of the same nerves can be attributed to excitation of a larger number of fibers.

Furthermore, changes in the effects after denervation of the nerves may also be dependent on profound functional changes taking place in the tissues of the vessels after denervation. For instance, changes in metabolic processes in the denervated muscle [3] and in the flow of afferent impulses in the decentralized sympathetic chain [5] have been demonstrated. Changes in the character of the vasomotor responses observed at different times after division of the nerves can also be related to changes in the tissue reserves of mediators [10], for after degeneration of the sympathetic nerves the reserves of catecholamines [15] and of acetylcholine [12] in the body are depleted. These factors may lead to changes in the reactivity of the blood vessels to nervous influences.

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