

THE MECHANISMS OF VASOMOTOR REGULATION

COMMUNICATION II. REGIONAL VASOMOTOR REFLEXES IN RESPONSE TO ELECTRICAL STIMULATION OF THE AFFERENT FIBERS OF SOMATIC NERVES

V. M. Khayutin and V. L. Tsaturov

From the Experimental Laboratory (Head – Candidate Med. Sci. V. M. Khayutin) of the Institute of Normal and Pathological Physiology (Director – Active Member of the AMN SSSR V. N. Chernigovskii) of the AMN SSSR, Moscow

(Received April 24, 1958. Presented by Active Member of the AMN SSSR V. N. Chernigovskii)

As many authors have shown [1, 8, 9], stimulation of the afferent fibers of the mixed nerves of the lumbosacral or brachial plexuses may cause a reflex fall or rise of the arterial pressure, depending on the parameters of the electrical stimulus. The depressor reflex appearing in response to weak stimulation is replaced by a pressor when the voltage of the electric impulses is raised or their frequency or duration increased. For many years there has been doubt whether the change in the sign of the reflex was due to the presence of special afferent fibers or to intensification of the central summation of afferent impulses of a single pattern, but the first of these views must now be considered as correct.

By the use of several methods of selective blocking of conduction, Gordon [8] observed a connection between the depressor reflex and excitation of the relatively thick and easily stimulated afferent fibers, and between the pressor reflex and excitation of the slender and less easily stimulated fibers. As shown by Molina, Achard and Wiss [9], the appearance of a depressor reflex is accompanied by the development of an action potential in the A β fibers on the electroneurogram of the stimulated nerve, and the appearance of a pressor reflex – in the A δ fibers. This was confirmed by Widen [12] for the celiac and facial nerves. Despite a great deal of research, the problem of the central mechanisms of depressor and pressor reflexes is still unsolved. This depends in particular on the fact that the arterial pressure, by the changes in which the reflex effects are recorded, is only a relative indicator of the state of the vasomotor centers. It may be doubted that the summated hemodynamic effect, as shown by changes in the arterial pressure, can reproduce with sufficient accuracy the changes occurring in individual areas of the vascular system.

The study of the regional vasomotor reflexes must therefore be the best guide to the processes taking place in the vasomotor centers. However, apart from the literature dealing with the so-called Loven reflex, we could find no research devoted to comparison of the systemic and regional vasomotor reflexes arising in response to electrical stimulation of somatic nerves.

EXPERIMENTAL METHOD

The resistance of the vessels of the hindlimbs of cats, anesthetized with urethane (0.5 g/kg) and chloralose (0.03 g/kg), was recorded by means of the method of resistography. The principle of this method, previously described [3] in detail, is stabilization of the minute flow of blood in the vessels of the limb by means of a special perfusion pump [4]. The fluctuating reading gives the pressure in the femoral artery: a fall indicates dilatation of the limb vessels, a rise – constriction. As an anticoagulant we used heparin in doses of 7.5 – 12.5 mg/kg.

The regional reflexes were studied in the vessels of the hindlimb, since the efferent innervation of the vessels of this region has been most fully investigated. The arterial pressure was recorded by a mercury manometer in the carotid artery, and respiration by a Marey's capsule through a tracheal cannula. A series of experi-

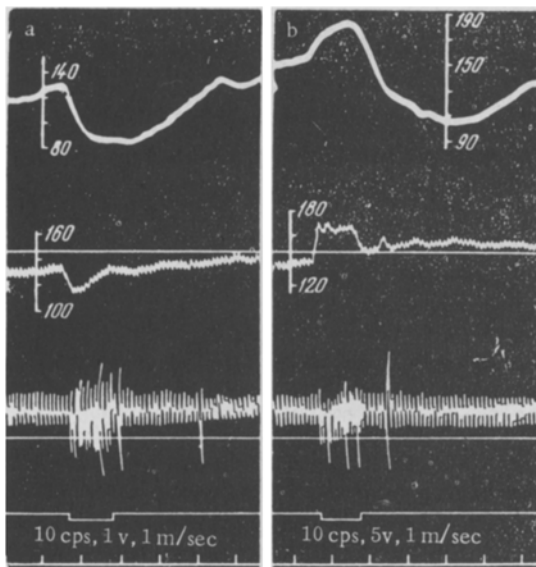


Fig. 1. The change from a depressor systemic reflex and primary regional vasodilatation (a) into a pressor systemic reflex and regional vasoconstriction (b) during intensification of reflex stimulation.

a) Stimulation of the central end of the right sciatic nerve (rectangular impulses; duration — 1 millise, frequency 10 cps, voltage 1 v); b) the same, voltage 5 v. Significance of the curves (from above down): perfusion pressure in the left femoral artery, its base line, arterial pressure, respiration, zero line of the arterial pressure, stimulus marker, time marker (30 sec).

duration of the impulses. Altogether about 70 experiments were performed.

EXPERIMENTAL RESULTS AND DISCUSSION

From our observations, in full agreement with the data in the literature, depressor reflexes arise in the case of stimulation of the afferent fibers with a current of relatively low voltage. These reflexes are more easily revealed and they attain a larger magnitude with shorter impulses of lower frequency. A fall in the arterial pressure usually develops simultaneously with the reflex vasodilatation in the limb (Fig. 1, a; Fig. 3, a). We called this the regional reflex of primary vasodilatation, to distinguish it from the secondary reflex vasodilatation appearing in response to much stronger stimuli. The latter is described below.

The fall in arterial pressure and primary regional vasodilatation arise in response to stimulation of the sciatic (Figs. 1, 2) and tibial nerves of the contralateral limb, or of the tibial nerve (divided at the level of the malleoli) of the perfused limb. These reactions are observed also during stimulation of the main branches of the brachial plexus (Fig. 3) on both contra- and ipsilateral sides. We could not detect any difference in the thresholds of the systemic and regional reflexes. Sometimes the fall in arterial pressure is accompanied by a diminution of the respiratory movements (see Fig. 2, a, b); in other cases respiration is either unchanged or intensified (see Fig. 1, a).

With an increase in the voltage (and also the duration or frequency of the impulses), a characteristic change takes place in the vasomotor reflexes. The depressor reflex becomes less and finally disappears, as a result of which the arterial pressure remains practically unchanged at the time of stimulation, showing as it were a "neutral" reaction. This point in the range of the parameters of stimulation (which is different in individual

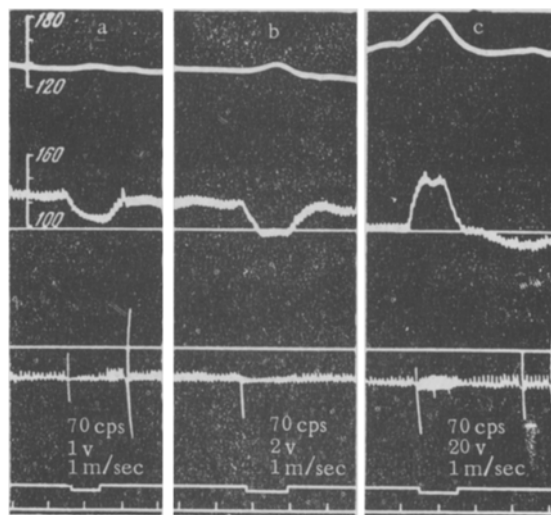


Fig. 2. Gradual strengthening of regional vasoconstriction (left hindlimb) and change from a depressor systemic reflex (a, b) into a pressor (c) with strengthening of the stimulation of the central end of the right sciatic nerve.

Significance of the curves as in Fig. 1.

ments were carried out on animals immobilized with succinylcholine iodide, with maintenance of natural breathing or with artificial respiration. Stimulation of the central segment of the somatic nerves was carried out in some experiments by means of an alternating current of 50 cps, and in others with rectangular unipolar impulses from a specially constructed generator or from a GI-2A apparatus providing independent control of amplitude, frequency and

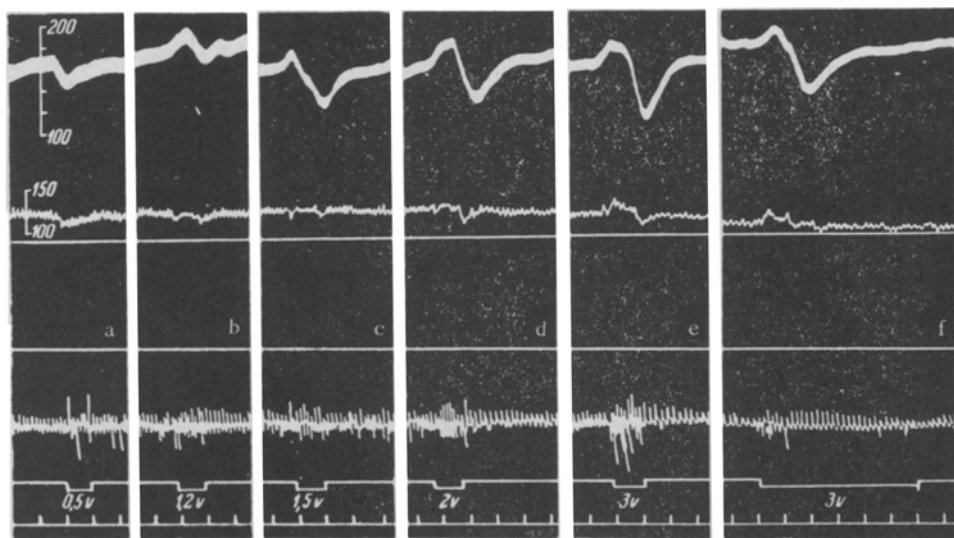


Fig. 3. Change from the depressor systemic reflex (a) through a phase of "neutral" reaction (b, c, d) into a pressor reflex (e, f), and from primary regional vasodilatation (a) into vasoconstriction (b - f) during an increase in the strength of stimulation of the central end of the right brachial nerve [alternating current, 50 cps; a) voltage 0.5 v; b) 1.2 v; c) 1.5 v; d) 2 v; e) 3 v, 30 sec; f) 3 v, 3 min]. Appearance and intensification of secondary regional vasodilatation (c - e). Significance of the curves as in Fig. 1. Autoperfusion of the left hindlimb.

animals) corresponds to the change in the sign of the regional reflex - vasodilatation of the limb changes into vasoconstriction.

Regional vasoconstriction develops in some animals even before the time at which the arterial pressure falls (see Fig. 2, a, b), and in others during the "neutral" reaction (see Fig. 3, b, c). Thus electrical stimulation at some points in the range of parameters leads to vasoconstriction of the limb, while continuing to cause vasodilatation in other organs, for only in this case may the arterial pressure be reduced or maintained at the original level.

Comparison of Fig. 2, a and Fig. 2, b shows that a slight strengthening of stimulation leads to a further increase in both the depressor systemic and the vasoconstrictor regional reflexes; and it is only with still stronger stimuli that a systemic pressor reflex arises (see Fig. 2, c). However, even with a considerable rise in the arterial pressure, the intestinal vessels, as we have seen to our satisfaction, continue to dilate and it is only with even stronger reflex stimulation that these vessels become constricted.

Hence it may be stated that the reflex threshold of vasoconstriction is not the same for all the individual vascular regions. T. S. Lagutina [2] came to the same conclusion from a study of the impulsion in the efferent fibers of various nerves during stimulation of the mechanoreceptors of the urinary bladder.

In a previous communication [5] it was shown that the degree of reflex communication between a number of interoceptive zones and the vessels of the kidney and the small intestine differs. In consequence of these findings, suggesting fractionation of the regional vasomotor reflexes, we put forward the hypothesis of the existence within the confines of the vasomotor centers of "nuclei" (groups of neurones), providing reflex regulation of the vessels of individual organs. The difference in the thresholds of the regional constrictor reflexes for the various vascular regions confirms this hypothesis.

At a definite strength of stimulation, the systemic depressor reflex always changes into a pressor (see Fig. 1, b; Fig. 2, c; Fig. 3, d, e).*

* In this respect our findings differ from Gordon's [8] view of the impossibility of reproduction of the pressor reflexes in case of stimulation of a nerve with impulses about 0.1 millisecond in duration and of any voltage. The

(continued on next page)

At this stage, however, a very distinctive phenomenon develops.

As seen from the kymograms (see Fig. 1,b; Fig. 3,d,e), immediately after the cessation of strong stimulation of the nerve the sign of the regional reflex is suddenly changed – vasoconstriction is replaced by a rapidly developing vasodilatation, the resistance of the vessels being restored only gradually to its original value. An attentive examination showed that secondary regional vasodilatation may arise before the cessation of stimulation. This is clearly shown, in particular, in Fig. 3,c. Specially performed experiments in which the period of stimulation was lengthened (as are shown, for example, in Fig. 3,f) give grounds for the assumption that secondary vasodilatation in these cases always arises during stimulation and not after it has ceased.

This suggests a comparison of the event described with the "perversion" of reflex action discovered by Sherrington and Sowton [6, 10, 11]. This consists of replacement of the reflex contraction of a flexor or extensor muscle by its relaxation in the course of a reflex reaction. It is very characteristic that "perversion" of the spinal motor reflexes develops in response to strengthening of the stimulation of the afferent fibers of the particular nerve [10, 11] or to prolonged stimulation of constant strength [10], i. e. in conditions when contraction of the smooth muscle of the vessels changes into relaxation. According to Sherrington, "perversion" of the reflex effect is due to predominance of inhibition in the motor center of the spinal cord in place of the originally dominant excitation. If this view is correct for the vasomotor centers also, then secondary vasodilatation of the limb must reflect inhibition of the tone of the sympathetic vasoconstrictors.

Another view of the cause of secondary vasodilatation was put forward by Binet and Burstein [7]. They observed this phenomenon in experiments using the same methods as ours, but carried out on dogs. Without any special analysis, these workers postulated that vasodilatation arising immediately after vasoconstriction is caused by vasodilator efferent fibers. In their opinion these are excited secondarily as a result of the increase in the general arterial pressure. Such a view is clearly unsound, as is shown, for example, by the tracing of the reflexes in Fig. 3,c,d. Both phases of the regional reflex develop in this case during negligible changes in the arterial pressure. Experimental denervation of the carotid sinus and aortic zones showed that secondary regional vasodilatation not only does not disappear after denervation of these zones, but in the majority of cases increases.

It must be pointed out that all the types of regional vasomotor reflexes described above are quite independent reactions, unrelated to the reflexes arising at the same time in skeletal muscles. They are observed in experiments on anesthetized animals, when both vasomotor and motor reflexes are carried out, and also in experiments on animals rendered immobile with succinylcholine, when the motor reflexes are abolished.

Hence relatively weak stimulation of the afferent fibers of somatic nerves causes a primary vasodilator reflex in the limb vessels. With an increase in the strength of stimulation this is replaced by reflex vasoconstriction, and with even stronger stimulation the reflex vasoconstriction changes into secondary regional vasodilatation.

In the present communication we can only point out the outward similarity between the change from the vasoconstrictor reflex to the vasodilator with the "perversion" of the spinal reflexes which arises in similar conditions of stimulation. Proof that the processes underlying both these phenomena are identical will be provided in later communications.

SUMMARY

The reflexes on the arterial pressure and on the blood vessels of the posterior extremity elicited by electric stimulation of the afferent fibers of different somatic nerves were studied on anesthetized cats. The reflexes on the blood vessels of the extremity were studied by the method of resistography (perfusion under constant flow). Weak reflex stimulations cause a depressor reflex and dilatation of vessels of the extremity. More intense stimulations cause a vasoconstriction in the extremity with subsequent rise of the arterial pressure, which shows the difference in the thresholds of the regional vasoconstriction for the vessels of different organs. Further increase in the strength of the stimulation is associated with the transition of the regional vasoconstriction into the secondary reflex vasodilatation. The similarity of the latter phenomenon with the "reversal" of the spinal motor reflexes is emphasized.

positive results of our experiments are evidently due not to the different form of the impulses (condenser discharges in Gordon's experiments, rectangular impulses in ours), but to the use of deep barbiturate anesthesia in his experiments. In one of our own experiments on an animal immobilized with succinylcholine, stimuli of a duration of 0.15 millise and a frequency of 50 cps caused a considerable pressor reflex at a voltage of only 0.5 v.

LITERATURE CITED

- [1] M. G. Durmish'yan, Mechanisms of the Effects of Afferent Stimulation, pp. 25 - 28, Moscow, (1955).*
- [2] T. S. Lagutina, The Electrophysiological Characteristics of the Interoceptive Reflex Arc. Author's abstract of dissertation, Moscow, (1958).
- [3] V. M. Khayutin, Fiziol. Zhur. SSSR, 44, No. 7, 645 (1958).
- [4] V. M. Khayutin, V. M. Danchakov and V. L. Tsaturov, Byull. Éksptl. Biol. i Med., 46, No. 2, 117 (1958).**
- [5] V. M. Khayutin, Byull. Éksptl. Biol. i Med. 46, No. 10, 18 (1958).*
- [6] R. S. Creed et al. Reflex Activity of the Spinal Cord, pp. 104 - 108, Moscow - Leningrad, (1935) [Russian translation].
- [7] L. Binet, and M. Burstein, Compt. Rend. Soc. biol. 141, p. 771 (1947).
- [8] G. Gordon, J. Physiol. 102, p. 95 (1943).
- [9] F. Molina, O. Achard and O. Wiss, Helv. acta Physiol., 12, 1, (1953).
- [10] C. S. Sherrington, and Sowton, Proc. Roy. Soc., ser. B, 83, 435 (1911).
- [11] C. S. Sherrington and Sowton, Proc. Roy. Soc., ser. B, 83, 201 (1911).
- [12] L. Widen, Acta Physiol. Scandinav. Supp. 117, 33 (1955).

* In Russian.

** Original Russian pagination. See C.B. Translation.