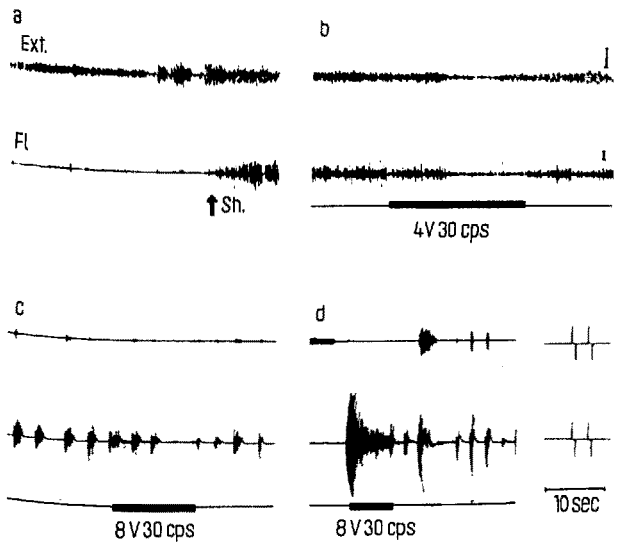
tion on the extensor activity. When the foot pad was stimulated during shivering, an inhibition was seen, demonstrated by a decrease activity of both types of muscles. The inhibitory effect was not fully developed until late in the period of stimulation, Figure (b). Figures (c) and (d) are examples from another experiment. In figure (c) is shown the inhibition of shivering when stimulated with 8 V. In Figure (d) the animal was stimulated in the absence of shivering as demonstrated by silence of flexor activity, against a slightly tonus of the extensors on the EMG record. In this situation the stimulation evokes a striking activation of the flexors without any response of the extensors. In a few cases there was a rebound effect with facilitation of shivering after the period of stimulation. This is also illustrated in the Figure (d).



EMG records from extensor (Ext) and flexor (Fl) muscles. Anaesthetized dog with nembutal (33 mg/kg, i.p.) (a) Note that silence of flexor muscles was present before shivering (Sh.). (b) Inhibition of shivering by stimulation of the foot pad. (c) The same inhibitory effect obtained in one other experiment. (d) Flexor reflex activation obtained by stimulating the foot pad as in (c) in the absence of shivering. (a, b) Recorded from the foreleg muscles; (c, d) recorded from the hindleg muscles. Calibration 100 μV.

Conclusions. It is concluded that peripheral stimulation inhibits the EMG activity produced by the shivering attack. This muscular influence is a generalized one and affects both flexor and extensor muscles. It differs from the flexor activation observed when stimulation was performed in absence of shivering. The characteristica of the late phenomenon suggest a process occurring at a spinal level and a simple reflex in nature. The inhibition of shivering, on the contrary, could be an inhibitory process set up by afferent inputs on the hypothalamus or the reticular formation[5].

Résumé. La stimulation de la patte chez le chien anesthésié, inhibe l'activité musculaire enregistrée pendant les attaques de frisson. Cet effet peut dépendre de l'action inhibitrice des influx nerveux agissant sur l'hypothalamus ou même sur la formation réticulaire, et peut se distinguer des influences inhibitrices d'origine médullaire qu'on observe quand la patte est stimulée en dehors des attaques de frisson.

L. D'Anna

Instituto de Fisiología, Facultad de Medicina, Universidad de Buenos Aires (Argentina), 9th September 1966.

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Mechanisms of Sympathetic Regulation of Arterial Smooth Muscle

According to recent data[1-3], sympathetic nerve endings have been shown at the border line between the adventitia and the media; only exceptionally do they penetrate into the superficial layers of the media. Several layers of vascular smooth muscle have been shown to be at a considerable distance from the adrenergic nerve endings. It has been evidenced[4-5], however, that conduit vessels with several smooth muscle layers, free of adrenergic nerve endings, constrict to sympathetic stimulation induced either reflectively or directly; and the range of the sympathetic control of the radius of the conduit vessel has been formulated[6].

The question then arose by which mechanism is excitation of the smooth muscle, particularly of the layers free of adrenergic endings, realized? Theoretically 2 possibilities must be considered: (a) conduction of excitation from cell to cell, or (b) diffusion of the transmitter released from nerve endings to the effective smooth muscles. The present study is designed as an attempt to prove the second possibility.

Method. In a series of tests on 7 dogs, anaesthetized with thiopental (70 mg/l kg b.w.) the range of the sympathetic control of the diameter of dorsal pedal artery was followed. The arterial diameter was recorded by means of a differential inductive transformer[7]. Stimulation of the peripheral stump of the cut sympathetic trunk by bipolar platinum electrodes was applied (between LG_3–LG_4) by means of square wave pulses of 5 msec duration, at a frequency of 0.5–15 c/sec. The reproduction of original recordings (Figure 1) represents contraction (diameter decrease) of the dorsal pedal artery at various frequencies of sympathetic stimulation.

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The relation of the size of contraction to the stimulation frequency (mean values and standard deviations) for the whole series of tests is shown in Figure 2.

Maximum contraction (taken as 100% in the construction of this curve) ranged between 105.0 and 420.0 microns, i.e. an average of 14.08% of the resting diameter. The frequency-response curve is similar to that described for the femoral artery[6] and for resistant vessels[8]. Mathematical analysis proved that this frequency-response curve does not differ from the hyperbola (interrupted line) of the given formula.

In a second series of experiments on 9 dogs, monoamines in the wall of the dorsal pedal artery were studied

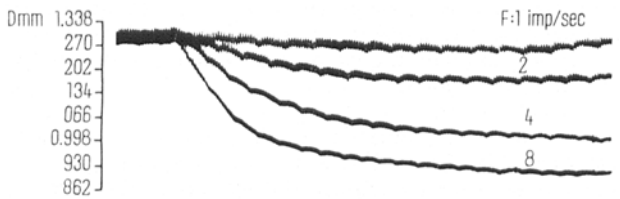

Fig. 1. Decrease of diameter of dorsal pedal artery during stimulation of the right sympathetic trunk (square wave impulses, supramaximal intensity, 5 msec duration) with various frequencies.

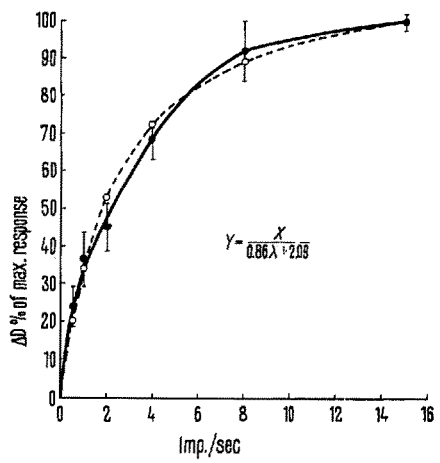

Fig. 2. Frequency-response curve of sympathetic control of dorsal pedal artery (full-line); abscissa-impulses/sec, ordinata-decrease of diameter in % of maximal response. Dotted line: hyperbola of the given formula.

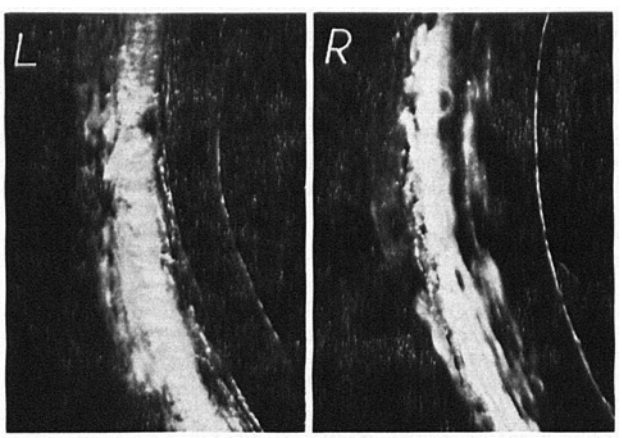

Fig. 3. Section of dorsal pedal artery. *L* left control, *R* right during stimulation.

histochemically, according to FALCK[1]. To prevent catecholamine degradation, both monoaminooxidase (MAO) and catechol-*o*-methyltransferase (COMT) were inhibited by pyrogallol (200 mg/kg) and nialamide Pfizer (100 mg/kg) pretreatment respectively. At the moment of maximum contraction produced by stimulation of the peripheral stump of the sympathetic trunk, the artery was frozen (propanbutan mixture at the temperature of liquid nitrogen) and a segment of about 15 mm length was excised. Under similar conditions but without sympathetic stimulation, the contralateral artery was excised. The tissue was lyophilized and examined histochemically according to the method referred to above. 30 μ thick paraffin sections were mounted in liquid paraffin on a single glass plate and photographed in immediate succession in a fluorescent microscope.

It was shown that (1) the dorsal pedal artery belongs to the type of vessels where adrenergic fibres penetrate some upper layers of the media; they have never been found, however, within the inner half of the media next to the intima. (2) Fluorophore cloudlets may be noticed around the nerve endings. Occasionally the media was entirely or partially diffusely infiltrated with fluorescent material.

In 66% of vessels excised during sympathetic stimulation, the level of diffusively dispersed fluorophore was considerably higher as compared with the contralateral (non-stimulated) sections.

These findings are illustrated in Figure 3. The control left dorsal pedal artery was excised 30 min after cutting the left sympathetic chain. The right dorsal pedal artery was removed (30 min after transsection of the right sympathetic chain) during stimulation of the sympathetic trunk – as described above (frequency 15 imp/sec).

The results strongly support the hypothesis that smooth muscle layers considerably remote from the adrenergic nerve endings are activated by diffusion of catecholamines released at nerve endings – with postganglionic stimulation.

Conclusions. (1) The sympathetic control of the radius of the dorsal pedal artery has been investigated and the range of this control established. The stimulation frequency-response relationship (similar to other vascular segments hitherto studied) has been stated to have a hyperbolic character. (2) Evidence is presented that monoamine transmitters, released by sympathetic stimulation, diffuse from the nerve endings to smooth muscle layers remote from the nerve terminals[9].

Zusammenfassung. Der Wirkungsbereich der Querschnittsregulation der A. dorsalis pedis durch den Sympathikus bei Hunden wurde erfasst und die Relation Reizerfolg-Reizfrequenz durch eine Hyperbel charakterisiert. Mittels Fluoreszenzmethode gewonnene Befunde weisen darauf hin, dass die durch Sympathikusreizung freigesetzen Monoamine zu den nervenfreien Mediaschichten diffundieren.

M. GEROVÁ, J. GERO and S. DOLEŽEL

Institute for Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava (Czechoslovakia), 19th March 1967.

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[9] For the supply of Nialamide we are indebted to Pfizer Corporation, Eastern Europe Division.