# DEPRESSOR RESPONSES TO STIMULATION OF THE NERVE TO THE GASTROCNEMIUS MUSCLE IN INTACT UNANESTHETIZED CATS

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Changes in the blood pressure, heart rate, and respiration rate during stimulation of the nerve to the gastrocnemius muscle before and after intravenous injection of noradrenalin were studied in chronic experiments on unanesthetized cats. Stimulation of the nerve to the gastrocnemius muscle in intact animals caused an increase in the blood pressure and the heart and respiration rates. Similar stimulation of the nerve against the background of noradrenalin-induced hypertension led to a fall of blood pressure and quickening of the heart beat. The depressor response was unchanged by β-adrenergic receptor blockade but it disappeared after blockade of muscarinic cholinergic receptors by methylatropine. In unanesthetized decerebrate animals the phase of the fall of blood pressure did not take place. It is suggested that the depressor response of the latter is due to strong cholinergic vasodilatation arising by a reflex mechanism in response to stimulation of the motor nerve in the intact cat.

KEY WORDS: *somato-autonomic reflexes; baroreceptive reflexes; cholinergic vasodilatation.*

Weak activation of somatic afferents is known to be accompanied by a fall of blood pressure (BP) in anesthetized and decerebrate animals [4, 11]. Its cause is passive vasodilatation, i.e., vasodilatation arising through a decrease in the flow of tonic impulses in the sympathetic nerves [8, 12]. No reference to the possibility of obtaining active vasodilatation in response to stimulation of somatic afferents could be found.

The object of this investigation was to study the depressor response to stimulation of the nerve to the gastrocnemius muscle in intact cats under chronic experimental conditions.

## EXPERIMENTAL METHOD

Twenty experiments were carried out on 11 cats of both sexes weighing from 2.5 to 4.7 kg. Under pentobarbital anesthesia (40 mg/kg) and under sterile conditions a stimulating electrode was implanted on the nerve to the gastrocnemius muscle, a bipolar myographic electrode was inserted into the gastrocnemius muscle, the veins and aorta were catheterized, and, in some cases, a silicone-treated catheter was introduced into the trachea 5-6 days before the experiments began.

The stimulating electrode consisted of two silver wires 0.1 mm in diameter, fixed inside a length (10 mm) of silicone-treated tube by means of KLT-30 silicone sealer. Branches of the nerve from the medial and lateral heads of the gastrocnemius muscle were isolated from the tibial nerve at a distance of 20-25 mm from the muscle and placed inside the electrode. The connecting wires were brought out subcutaneously on the head. The interelectrode distance was 2-3 mm and the resistance 8-12 kΩ.

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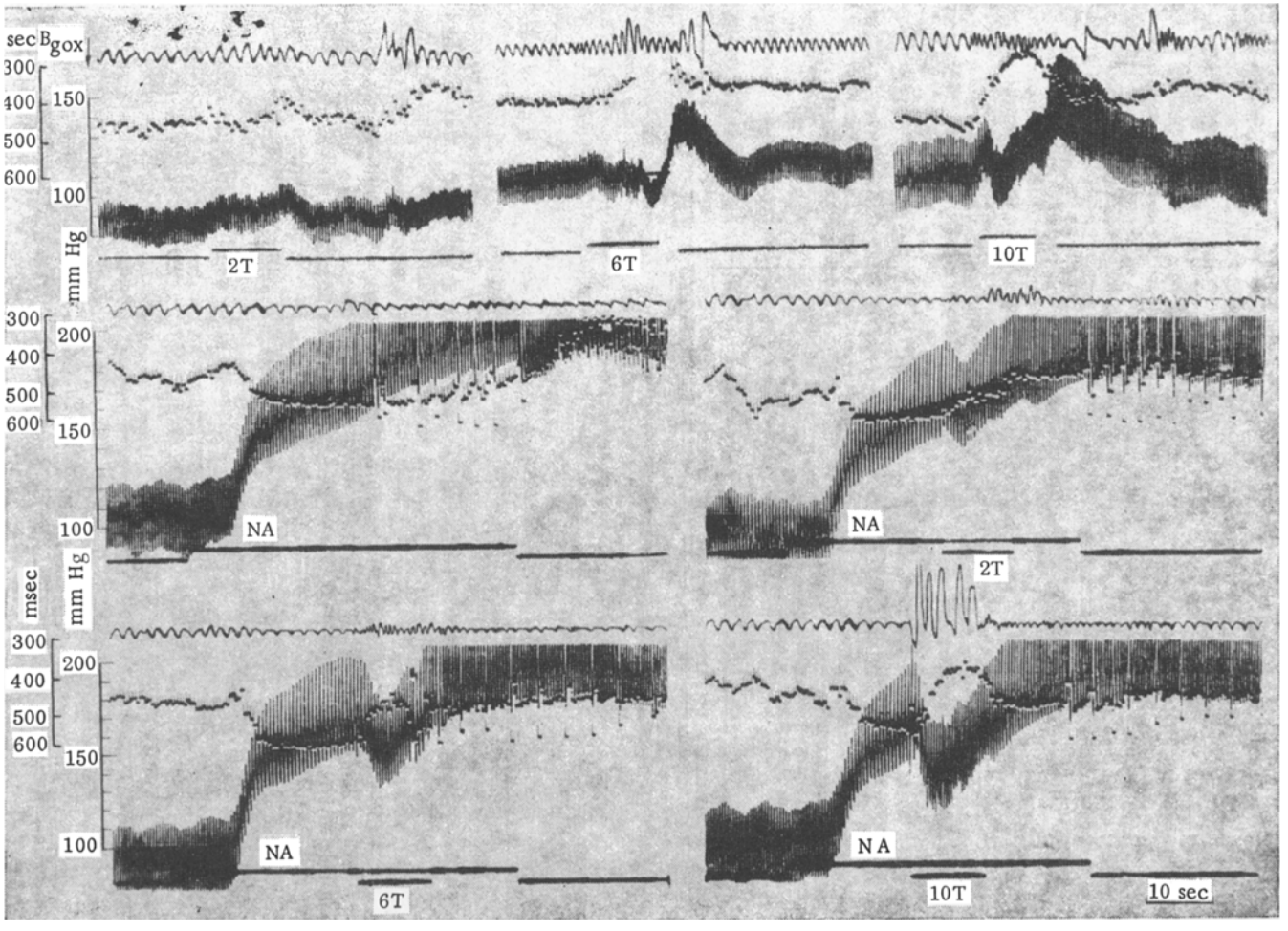


Fig. 1. Changes in BP and heart and respiration rates during stimulation of nerve to gastrocnemius and injection of NA. Top row of records obtained after stimulation of nerve with strength of 2 T, 6 T, and 10 T; middle row after intravenous injection of NA and stimulation of nerve to gastrocnemius with a strength of 2 T after injection of NA; bottom row after stimulation of nerve to gastrocnemius with strength of 6 T and 10 T after injection of NA. From top to bottom curves represent: respiration (change in intratracheal pressure), interval between consecutive cardiac contractions, BP, marker of experimental procedure.

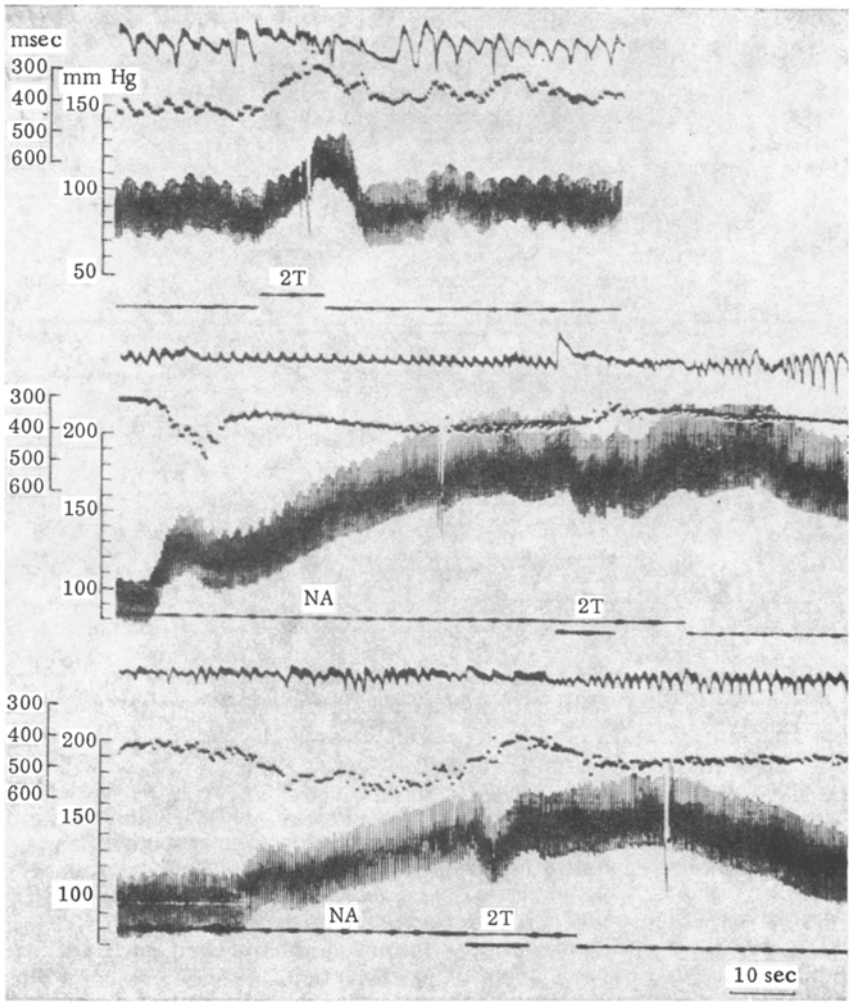


Fig. 2. Autonomic responses evoked by stimulation of nerve to gastrocnemius before (top 2 records) and after (bottom record) intravenous injection of propranolol, 1 mg/kg. Legend as in Fig. 1 (respiration recorded by carbon transducer).

The myographic lead was made from flexible multiple-strand stainless steel wire with vinyl insulation (AS 632 wire, kindly provided by Dr. J. Cooner — "Cooner Sales Co.," USA). At the beginning of each experiment the threshold of excitation of the nerve to the gastrocnemius muscle (T) was determined from the appearance of the M response on the electromyogram (EMG). The mean motor threshold was 0.172 V for a pulse 0.1 msec in duration. Tetanic contractions of the muscle were induced by stimulation of the nerve with square pulses (50 Hz, 0.1 msec, 1-10 T). The voltage of the stimulating pulses at the output of the ÉSL-2 stimulator was set by means of a VK7-10A/1 digital voltmeter.

The method of recording BP was described previously [1]; BP was measured with an EMT-34 electromanometer (Elema-Schonander, Sweden). The heart rate was recorded continuously by means of an analog time interval measurer [2], triggered by the BP pulse wave. The heart rate in the course of the experiment was measured and averaged by the Ch3-34 digital frequency meter.

Artificial raising of BP to activate the baroreceptors was produced by intravenous injection of noradrenalin (NA) from an infuser at the rate of 20 µg/kg/min.

Respiration was recorded by means of a carbon resistance transducer. In a series of experiments respiration was studied relative to the charge in intratracheal pressure measured through a silicone-treated catheter of the EMT-33 electromanometer.

All the parameters studied were recorded on the Mingograph-34 apparatus.

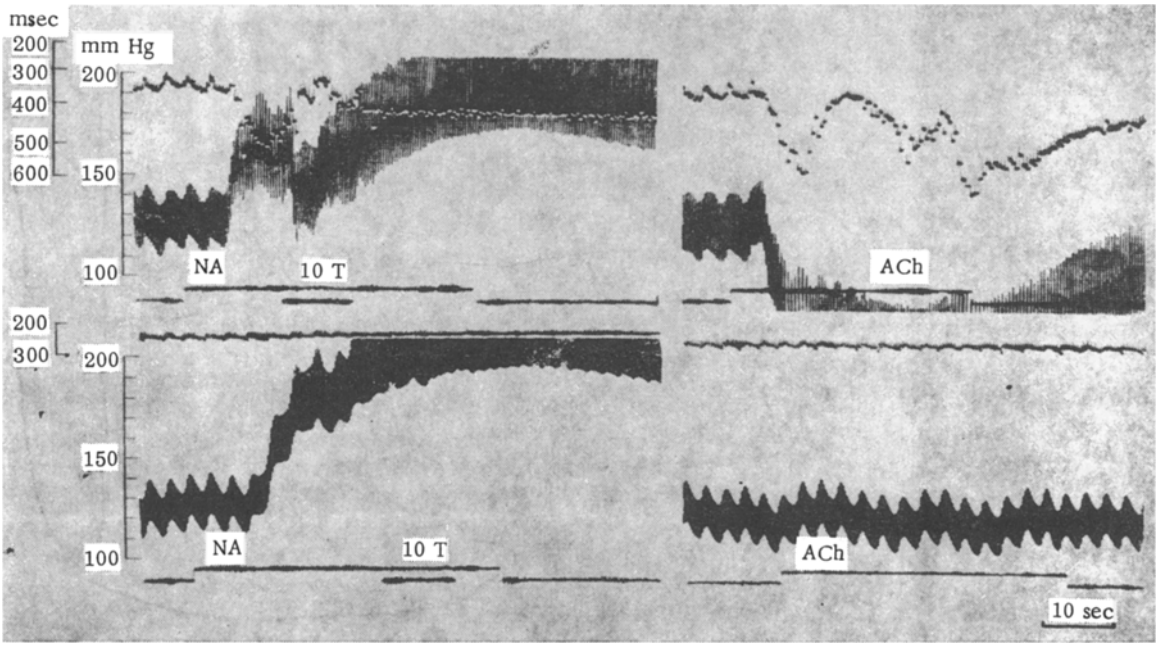


Fig. 3. Autonomic responses caused by stimulation of nerve to gastrocnemius muscle and intravenous injection of 10 μg acetylcholine (ACh) before (above) and after (below) intravenous injection of methylatropine, 1 mg/kg. From top to bottom: interval between consecutive cardiac contractions, BP, marker of experimental procedure.

## EXPERIMENTAL RESULTS

Stimulation of the nerve to the gastrocnemius muscle with a strength of 3-4 T was not accompanied by the appearance of nociceptive responses, but was sufficient to excite the motor axons, as shown by the appearance of a maximal M response on the EMG. Meanwhile BP and the heart and respiration rates were increased (Fig. 1). With a decrease in the frequency of stimulating pulses the amplitude of the pressor response decreased but it never changed to depressor. Increasing the strength of stimulation to 8-10 T as a rule was accompanied by a weak nociceptive response and by augmentation of the autonomic changes.

However, if NA was injected intravenously into the cat and, when BP was high, the nerve to the gastrocnemius muscle was stimulated, a clear phase of depression of BP combined with tachycardia developed (Fig. 1). If the strength of stimulation was increased from 2 to 10 T, the amplitude of the depressor response increased, to reach 40-50 mm Hg in a series of experiments. In similar experiments on anesthetized cats, incidentally, no depressor phase of the change in BP was discovered [13].

The chief causes of the reflex decrease in BP could be passive vasodilatation, active vasodilatation, and inhibition of cardiac activity.

Intravenous injection of NA led to an increase in BP (in these experiments up to 200-250 mm Hg) through activation of the vascular α-adrenergic receptors [5]. Activation of the baroreceptive reflex and depression of the flow of tonic sympathetic impulses in the vascular [14] and cardiac [6] nerves were a result of the elevation of BP. The direct action of NA on the vessels and the almost complete absence under these circumstances of a flow of tonic impulses in the sympathetic nerves rule out passive vasodilatation as the cause of the observed decrease in BP.

The possible role of β-adrenergic vasodilatation [16] was tested by blocking the β receptors with propranolol. Injection of propranolol (1 mg/kg) was followed by slowing of the heart beat. The character of the hemodynamic changes caused by stimulation of the nerve to the gastrocnemius muscle after injection of NA was virtually unchanged: As before BP fell and the heart rate rose (Fig. 2). The results of the experiments with propranolol ruled out not only β-adrenergic vasodilation, but also a reduction of the sympathetic influences on the heart as possible causes of the appearance of the depressor response of BP.

The role of cholinergic processes in the depressor response of BP was tested by injection of methylatropine (1 mg/kg), a substance which does not penetrate into the CNS. In all the experiments injection of methylatropine completely abolished the depressor response and the tachycardia evoked by stimulation of the nerve to gastrocnemius (Fig. 3). The blocking action of methylatropine ruled out the possible effect of working hyperemia, for blockade of muscarinic cholinergic receptors does not change working hyperemia [9]. Under these experimental conditions only the gastrocnemius muscle contracted appreciably, and this could not lead to any significant decrease in the peripheral vascular resistance. During tonic contraction of the gastrocnemius muscle (frequency of stimulation 50 Hz), moreover, the blood flow in it actually decreases as the result of mechanical compression of the vessels [3].

On the basis of our own observations and data in the literature it is impossible to link the depressor response with inhibitory vagal influences on the heart, for stimulation of a somatic nerve against the background of activation of baroreceptors leads to central inhibition of vagal influences [13], as was revealed by the appearance of tachycardia in the intact cats (Fig. 1) and in the cats with blocked β-adrenergic receptors (Fig. 2).

It may be suggested that the observed decrease in BP was attributable to massive cholinergic vasodilatation in the skeletal muscles. The possibility of cholinergic vasodilatation against the background of the action of catecholamines, in principle, is deduced from the results of experiments of Bülbring and Burn [7]. Integration of the depressor response takes place at the suprabulbar and, most probably, at the hypothalamic levels, for in six control experiments on unanesthetized decerebrate cats a phase of lowering of the BP could not be obtained. The fact that a depressor response of BP appeared only during strong activation of the baroreceptors confirms the view that the depressor reflex arc is closed in the hypothalamus, for the role of the hypothalamus in the mechanism of the reflex of the baroreceptors has been demonstrated [10]. Activation of the baroreceptors itself, moreover, facilitates the onset of cholinergic vasodilatation in skeletal muscles [15].

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