PHYSIOLOGY

Discharge Activity of Single Muscle Vasoconstrictor Efferents in Cats during Opposite Changes in Arterial Pressure

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Signals of individual muscle vasoconstrictor efferents of gastrocnemius muscle were recorded in narcotized cat during rise and fall of systemic arterial pressure induced by phenylephrine and sodium nitroprusside, respectively. In control, mean discharge rate of these efferents was 2.0±0.4 Hz. Phenylephrine (45 μg/kg) increased arterial pressure from 120.3±4.2 to 170.7±8.2 mm Hg. This increase was accompanied by a short-term (5-10 sec) decrease in discharge rate of muscle vasoconstrictor efferents to 0.5±0.3 Hz followed by virtually complete recovery of muscle discharge rate against the background of increased arterial pressure. Sodium nitroprusside (30 μg/kg) decreased arterial pressure from 132.8±6.2 to 64.1±4.3 mm Hg. Under these conditions the discharge rate of vasoconstrictor efferents increased to 3.5±0.6 Hz and remained at this level throughout the hypotension period (2-3 min). Unloading of baroreceptors (occlusion of the carotid artery) increased the discharge rate of muscle vasoconstrictor efferents throughout the occlusion period (up to 30 sec). Thus, blood pressure rise and drop induced asymmetric by their duration changes in the discharge responses of muscle vasoconstrictor efferents. Phenylephrine increased asymmetry of the vasoconstrictor component of the baroreflex and induced cumulative rise of discharge rate of muscle vasoconstrictor efferents in response to a series of short-term reversible blood pressure jumps caused by repeated occlusions of the abdominal aorta. Our findings extend our knowledge on the efferent component of the baroreflex regulation and on possible mechanisms of hypertension.

Key Words: *phenylephrine; sodium nitroprusside; muscle vasoconstrictor efferents; baroreflex; C-fibers*

Baroreflex stabilization of blood pressure (BP) belongs to the most important processes in living organisms. The afferent signals of this reflex are generated by baro- and chemoreceptors located predominantly in the carotid sinuses and aortic arch. The views on efferent component of baroreflex originated predominantly from the studies of the effects produced by BP changes on the parameters of cardiac activity and sympathetic discharges in renal nerve [13]. At the same time, the direct data on sympathetic vasomotor baroreflex signals are scanty [8,11]. Specifically, the data on "baroreflex escape", *i. e.* premature termination of baroreflex inhibition of vasoconstrictor discharges against the background of high BP, substantiated the views on baroreflex as a short-term mechanism of BP stabilization. However, there are data on long-term baroreflex inhibition of sympathetic activity in renal nerve [1,9,10]. Therefore, the characteristic temporal

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limits of baroreflex stabilization of BP need more detailed assessment. Our aim was to study the efferent vasomotor signals, which determine the development of baroreflex reactions. To this end, we assessed the duration of changes in discharge activity of individual muscle vasoconstrictor efferents (MVCE) produced by BP rise and fall. Taking into consideration the role of disturbances in the sympathetic regulation during the early stages of hypertension [1,12], it is clear that the study of peculiarities of baroreflex regulation of BP is both of theoretical and practical interest.

MATERIALS AND METHODS

Experiments were carried out on cats weighing 2.9-4.2 kg (n=14) anesthetized with chloralose and urethane (40+600 mg/kg) and artificially ventilated. The end-tidal CO_2 was kept at 4.3% by changing the inspiratory volume. The urinary bladder was catheterized. BP was measured in the left carotid artery with a BMT301 monitor. Fine nerve bundles were teased from gastrocnemius branches of the sciatic nerve isolated in the popliteal space. Preparation of fine nerve bundles and recording from individual C-fibers were described elsewhere [4,5,7]. A fine bundle mounted on a platinum electrode was cut distally, which made it possible to record the efferent discharges only.

The electrical discharges from nerve bundle and signal from BP transducer were digitized using a 12-bit ADC-12m converter (Biola) with sampling rate of 5 kHz and processed using original software. This software used digital data to calculate the mean BP during each cardiac cycle and duration of this cycle. In addition, it automatically recognized spikes of individual nerve fibers and calculated the corresponding mean discharge rate (MDR) curves. We used only bundles containing C-fibers with tonic discharges. C-fiber efferents with tonic discharges were identified as MVCE according to the following criteria: MDR increased during systemic BP drop caused by sodium nitroprusside (SNP) or decrease in regional BP resulting from occlusion of the carotid artery; MDR decreased during systemic BP rise induced by phenylephrine (PE) or occlusion of the abdominal aorta. PE and SNP were dissolved in Ringer solution immediately before the experiment and injected into the right jugular vein. The data are presented as the mean and standard errors.

RESULTS

Bolus intravenous infusion of PE (45 μg/kg in 1 ml Ringer solution) induced a rapid rise of BP from 120.3±4.2 to 170.7±8.2 mm Hg (n=14, Fig. 1, *b*). This rise was not monotonous and lasted for about 1 min from the start of infusion. Then BP slowly returned to the initial level during the following 20-30 min. During the rapid rise of BP, MDR of single MVCE decreased from 2.0±0.4 Hz to 0.5±0.3 Hz (n=17), then MDR returned to the initial level within 10 sec (Fig. 1, *a*), although BP far surpassed the initial level during this period (Fig. 1, *b*). Thus, hypertensive period after PE injection was longer than the period of inhibition of MVCE discharge activity.

By contrast, bolus intravenous injection of SNP (30 μg/kg in 1 ml Ringer solution) induced monotonous BP decrease from 132.8±6.2 to 64.1±4.3 mm Hg. This drop was accompanied by an increase in MVCE discharge rate from 1.8±0.5 Hz to 3.5±0.6 Hz (n=8). Discharge rate remained high throughout the

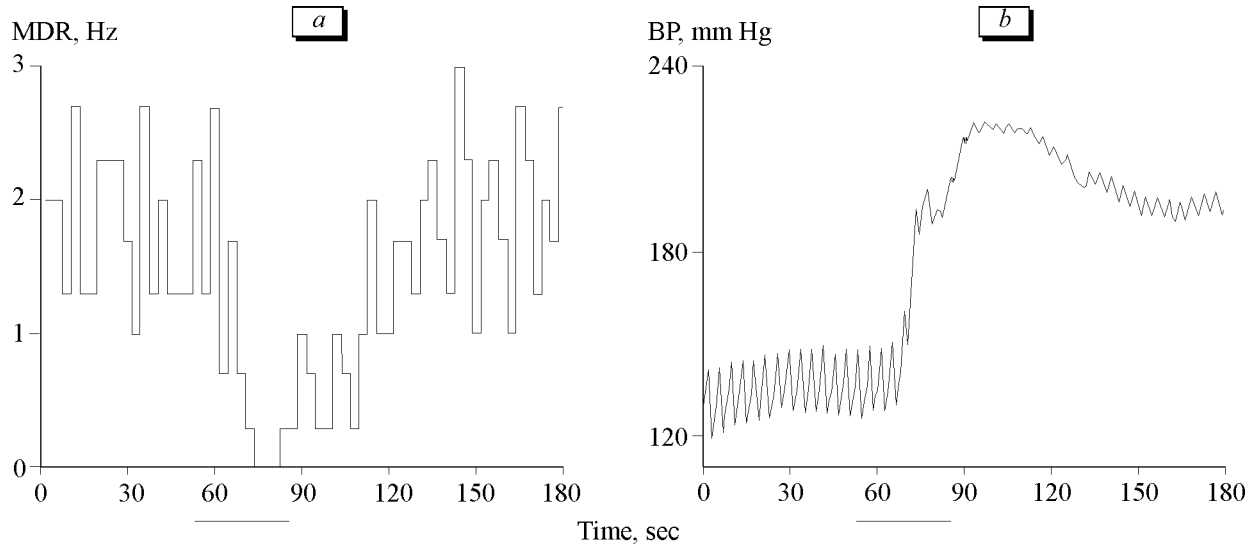

Fig. 1. Effect of phenylephrine (40 μg/kg) on mean discharge rate (MDR) of single vasoconstrictor efferent fibers of gastrocnemius muscle (*a*) and blood pressure (BP) in narcotized cat (*b*). Solid lines: phenylephrine infusion. Sampling period for calculation of MDR was 3 sec.

hypotensive period (2-3 min, Fig. 2, *a*, *b*) and then gradually decreased in parallel with BP recovery. The long-term (up to 30 sec) increase in MDR of MVCE was also observed during unloading of baroreceptors by occlusion of the carotid artery (Fig. 2, *c*). Thus, the duration of baroreflex inhibition of vasoconstrictor discharges was pronouncedly lower than the duration of baroreflex activation of vasoconstrictor firing in response to BP drop.

Injection of PE modified the baroreflex response to BP rise. In the control, the transient BP jump produced by short-term (8 sec) occlusion of the abdominal aorta (Fig. 3, *b*) was accompanied by a similar short-term decrease in discharge rate in vasoconstrictor fibers (Fig. 3, *a*). In PE-treated cat, occlusion of the abdominal aorta also produced a short-term drop of MDR, but after the end of occlusion MDR rapidly returned to normal and even surpassed it despite the fact that BP before and after occlusion were equal. Two or three repeated occlusions produced a pronounced cumulative increase in MDR, which by 1.5–2 times surpassed the initial level (Fig. 3, *c*). Therefore, the reversible changes in the discharges of MVCE produced by short-term BP jumps under normal conditions were replaced by irreversible cumulative rise in MDR after reversible BP jumps in PE-treated cat.

In the control, the discharge rate of MVCE (2.0± 0.4 Hz) was similar to MDR of sympathetic MVCE of feline gastrocnemius muscle (0.5-3 Hz) observed previously in similar experiments [11]. The "asymmetry" in the changes of MVCE activity during BP rise and drop observed in this study seems to be an intrinsic feature of the baroreflex reaction, which does not result from chemical interference with PE or SNP. Indeed, the long-term BP rise in hemodynamically isolated carotid sinus produced without PE resulted in complete inhibition of MVCE only for 10 sec [11]. In our study, the long-term (30 sec) BP drop in the region

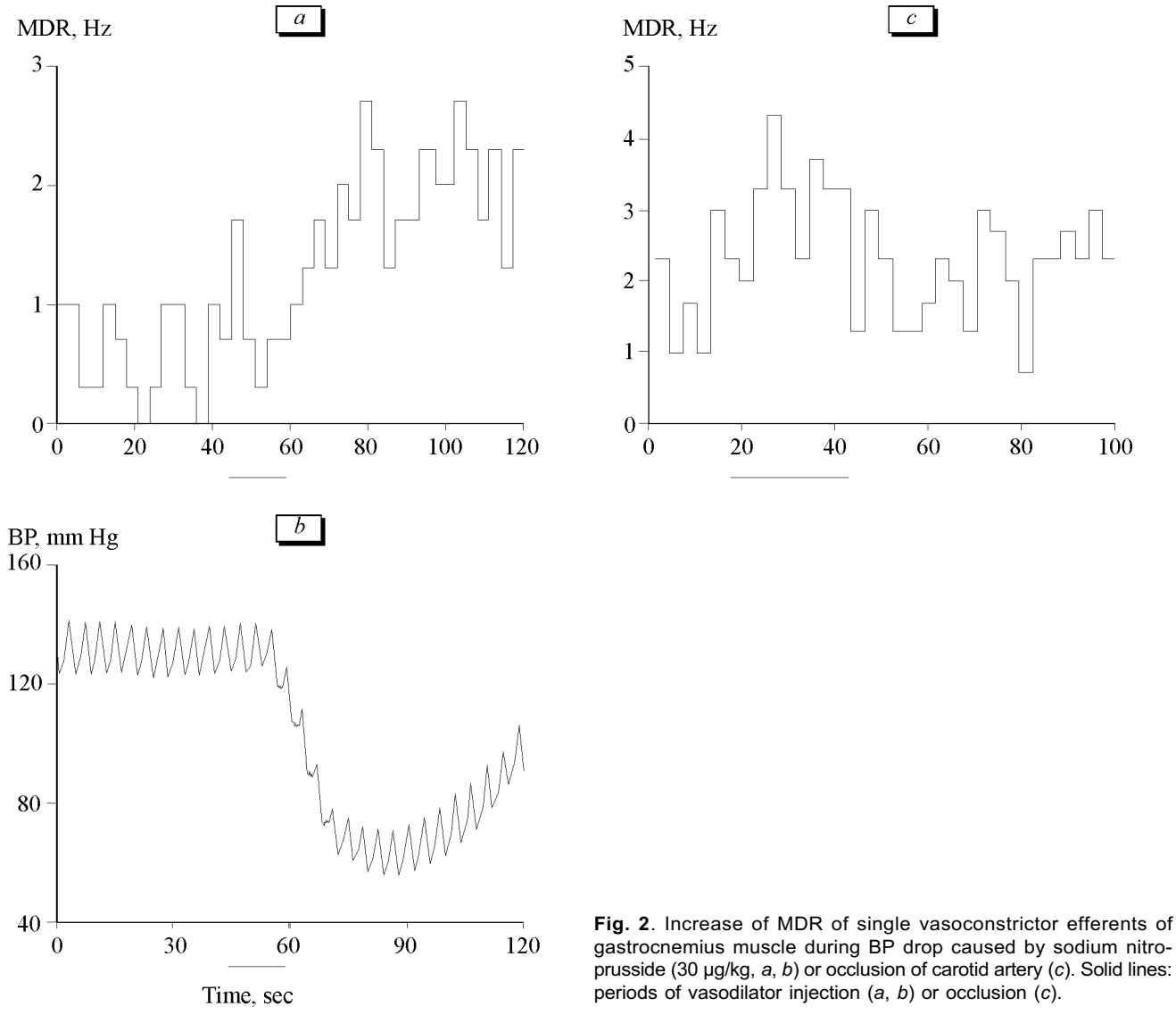

Fig. 2. Increase of MDR of single vasoconstrictor efferents of gastrocnemius muscle during BP drop caused by sodium nitroprusside (30 μg/kg, *a*, *b*) or occlusion of carotid artery (*c*). Solid lines: periods of vasodilator injection (*a*, *b*) or occlusion (*c*).

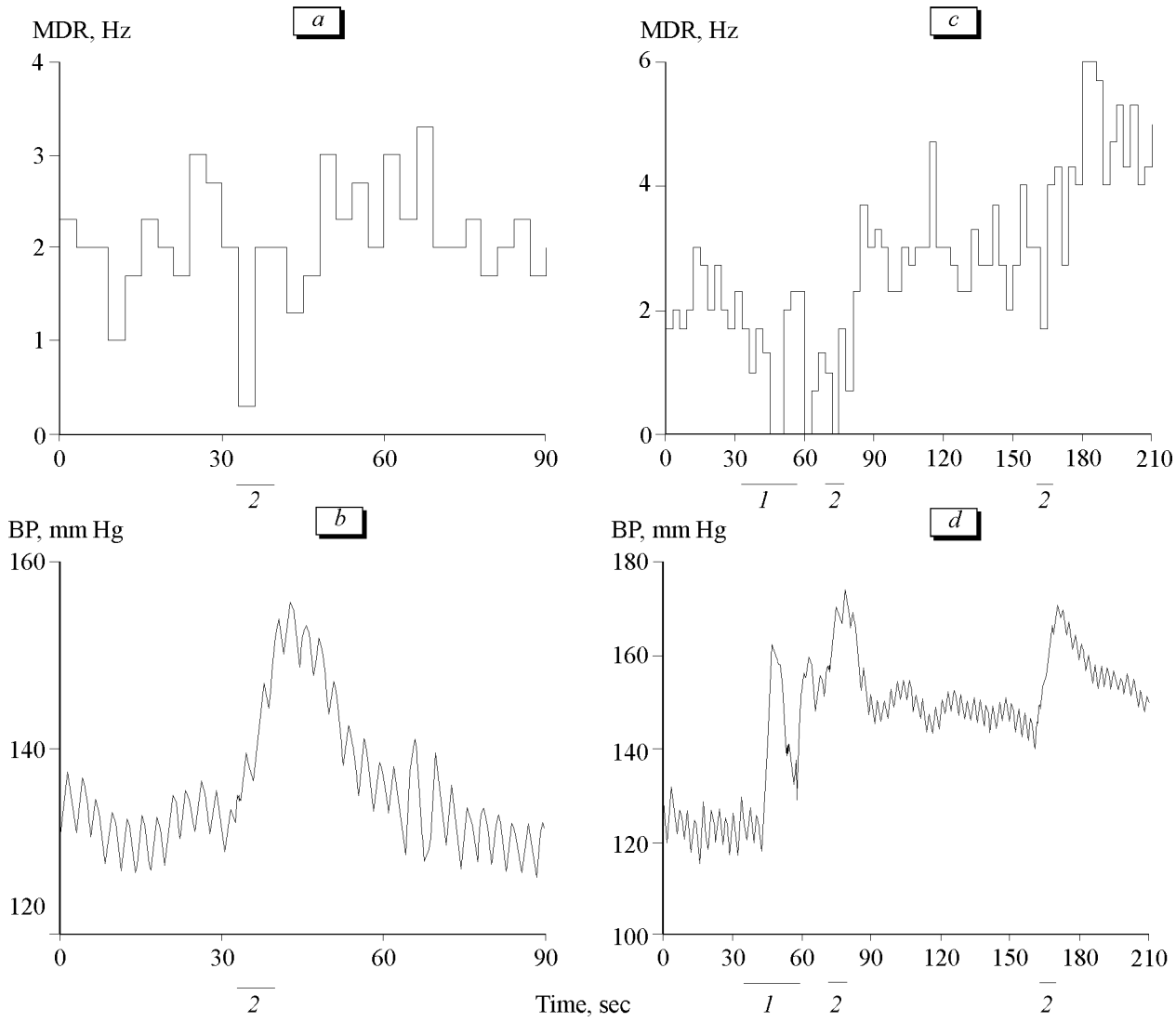

Fig. 3. Effect of short-term occlusion of abdominal aorta on the changes in BP and MDR of single vasoconstrictor efferents of gastrocnemius muscle of narcotized cat in control (*a*, *b*) and under the action of phenylephrine (*c*, *d*). *1* — period of phenylephrine injection; *2* — periods of occlusion of abdominal aorta.

of carotid sinuses induced by occlusion of the carotid artery (performed without SNP) produced a persistent increase in discharge rate of MVCE throughout the occlusion period (Fig. 2, *b*). Therefore, the sympathetic vasoconstrictor branch of baroreflex significantly longer counteracts to BP drop than to its rise irrespective of the factor (chemical or hemodynamic) modulating BP. In other words, asymmetry of baroreflex reactions to opposite changes in BP is an intrinsic feature of sympathetic vasoconstrictor neurons.

This asymmetry of baroreflex vasoconstrictor response to opposite changes in BP was augmented by PE. In the control, inhibition and subsequent recovery of discharge activity of MVCE during BP rise and drop induced by transient occlusion of the abdominal aorta compensated each other. As a result, activity of MVCE returned to the initial level. By contrast, similar opposite perturbations in BP produced asymmetrical changes in discharge activity under the action of PE: the increase in MDR during BP drop surpassed the decrease in MDR observed during BP rise. Thus, a single short-term jump of BP enhanced discharge activity of MVCE, and a train of such jumps resulted in cumulative enhancement of this activity.

Augmentation of asymmetry of sympathetic vasomotor system induced by α_1-agonist PE is probably related to the effect of α-agonists on the central component of the baroreflex [2,3,6,9]. Cumulative enhancement of MVCE discharge activity during repeated perturbations of BP under the action of PE can be considered as a mechanism of hypertension induced by stress stimulation, which is typically accompanied by the rise of blood epinephrine content and unstable BP. This effect can be especially pronounced during

surgery and can potentiate constriction of muscle arterioles and restriction of regional blood flow. These peculiarities of PE action can explain its efficiency during acute hemorrhage.

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