# GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

# Effects of Dopamine and Sodium Nitroprusside on Myocytes of Regional Arteries and Veins during Whole-Body Hypothermia and Hypoxia

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In experiments on cats, dopamine induced constriction, while sodium nitroprusside dilation of arteries and veins perfused with a constant volume of autoblood in the decentralized gastrocnemius muscle and small intestine. Vascular responses to both test substances were reduced under the effect of hypothermia and especially under the effect of hypoxia alone. During combined exposure to hypoxia and hypothermia the decrease in the amplitude of vascular responses to dopamine and sodium nitroprusside was similar to that observed during hypoxia alone.

**Key Words**: *constriction and dilation of arteries and veins; gastrocnemius muscle*; *small intestine*; *dopamine*; *sodium nitroprusside*; *hypoxic hypoxia*; *hypothermia*

Vasoconstrictor and vasodilator pharmacological agents (*e.g.*, dopamine and sodium nitroprusside) are widely used in clinical practice for correction of systemic blood pressure. However, the mechanisms of their effects on regional veins are still poorly studied. Little attention is paid to the role of the venous bed in the maintenance of systemic blood pressure compared to the role of the arterial bed [5,7]. Most studies were performed on vascular segments [8,9,11], and only few works were carried out on regional arteries and veins perfused with autoblood [7]. We found no direct experimental data on responsiveness of vascular myocytes to vasoactive substances during combined exposure to potent external stimulus such as hypoxia and hypothermia. Combined exposure to hypoxia and hypothermia is typical of surgical operation on blood-free and artificially cooled organs.

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Our aim was to study the effects of dopamine and sodium nitroprusside on the tone of arteries and veins in the gastrocnemius muscle and small intestine during separate and combined exposure to hypoxia and hypothermia in cats.

## MATERIALS AND METHODS

Experiments were carried out on 14 random-bred male and female cats weighing 2.5-4.0 kg anesthetized with sodium pentobarbital (Nembutal). Heparin (1500-2000 U) was used as the anticoagulant. The gastrocnemius muscle (GM) and small intestine (SI) were hemodinamically and neurally isolated and perfused with autoblood at a constant flow. The shifts in arterial and venous resistance in the muscle and intestine induced by intraarterial bolus infusion of dopamine (5 μg) or sodium nitroprusside (10 μg) dissolved in 0.1 ml 6% dextran (Poliglyukin) were measured by resistography [1,2,10].

Arterial and venous responses were measured under normal conditions and during hypoxia (on mi-

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nute 10 of inhalation of $N_2$+10% $O_2$ mixture), whole-body hypothermia (30°C, cooling rate 0.07±0.02°C per min), and hypoxia+hypothermia.

The data were statistically processed using Student's *t* test. The differences were considered significant at $p<0.05$.

## RESULTS

Under normal conditions, dopamine increased arterial ($PP_A$) and venous ($PP_V$) perfusion pressures in GM by 34.0±5.0 and 3.3±1.0 mm Hg, and in SI by 25.0±2.0 and 2.2±0.1 mm Hg, respectively. The exposure to acute hypoxia at normal temperature decreased vasoconstriction of regional arteries and veins induced by humoral adrenergic stimulus. In GM, $PP_A$ and $PP_V$ decreased by 19.0±5.0 and 2.3±0.4 mm Hg, and in SI by 13.7±1.2 and 1.10±0.12 mm Hg, respectively. Thus, acute hypoxia 2-fold reduced the sensitivity of vascular smooth muscles to dopamine (Fig. 1, *a*, *b*). After termination of hypoxic exposure (*i.e.* under condition of normoxia) hypothermia also decreased dopamine-induced vasoconstriction in both organs (Fig. 1, *a*, *b*). Dopamine infused during hypoxia-hypothermia (30°C) and hypoxia alone induced similar constrictor responses of regional arteries and veins (Fig. 1, *a*, *b*).

Thus, both individual and combined exposure to hypothermia and hypoxia reduced the sensitivity of vascular smooth muscles to dopamine. Hypoxia and hypothermia changed arterial and venous constriction in both organs in a similar manner, although the reactivity of GM vessels to dopamine was always higher than in SI (Fig. 1, *a*, *b*).

In the absence of hypoxia and hypothermia, sodium nitroprusside decreased $PP_A$ and $PP_V$ by 57.0±8.6 and 6.8±1.5 mm Hg in GM, and by 47.5±5.2 and 3.8±

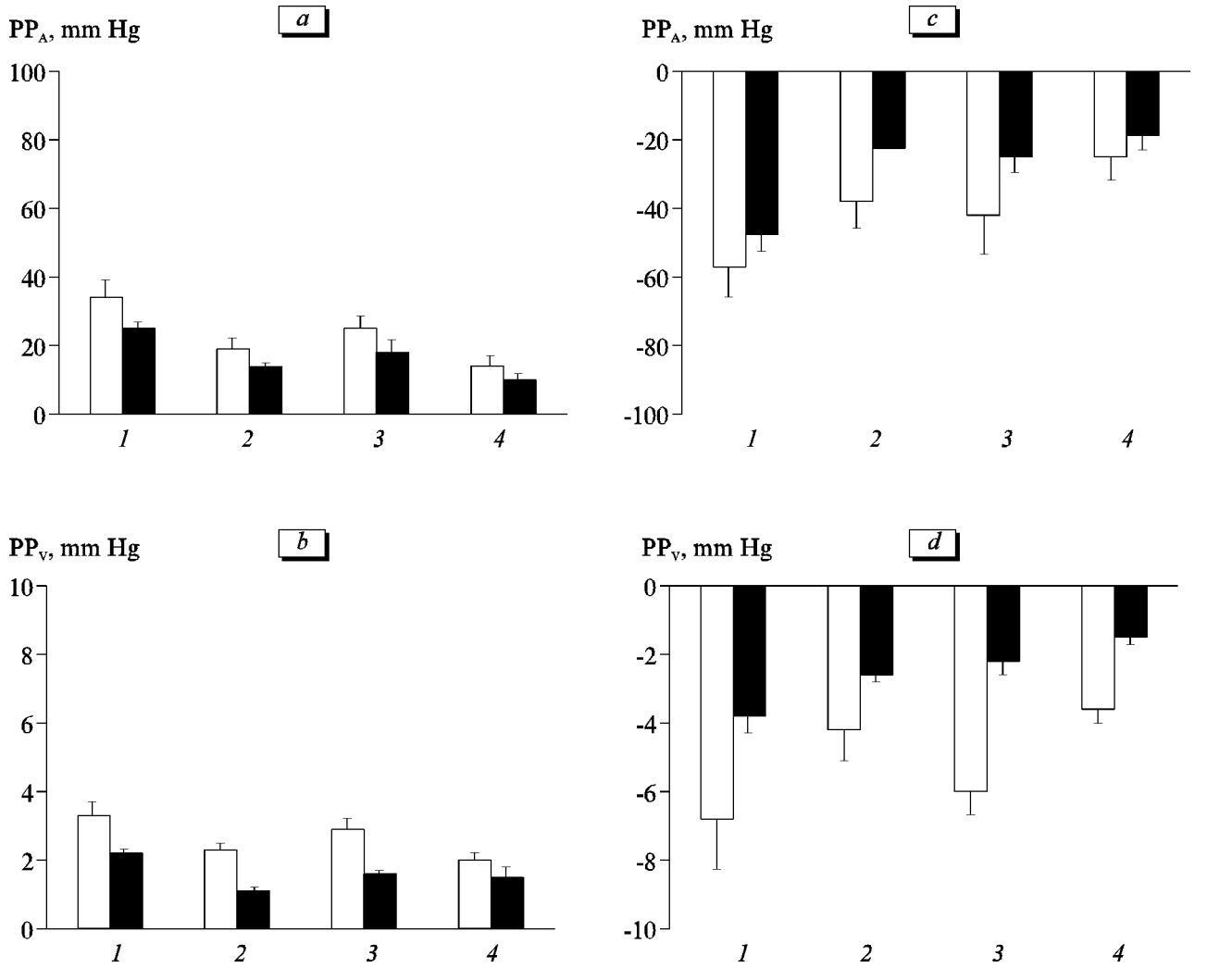


**Fig. 1.** Vasoconstrictor responses to dopamine (*a*, *b*) and vasodilator responses to sodium nitroprusside (*c*, *d*) of arterial (*a*, *c*) and venous vascular bed (*b*, *d*) in the gastrocnemius muscle and small intestine during separate and combined exposure to hypoxia and hypothermia. *1*) baseline responses; *2*) hypoxia; *3*) hypothermia; *4*) hypothermia+hypoxia. $PP_A$ and $PP_V$ are arterial and venous perfusion pressures, respectively.

0.5 mm Hg in SI, respectively. Acute hypoxia alone decreased the vasodilatory responses of regional arteries and veins induced by the agent. In GM, $PP_A$ decreased by 38.0±8.0 and $PP_V$ by 4.2±0.9 mm Hg, while in SI these parameters decreased by 22.5±3.2 and 2.6±0.2 mm Hg, respectively (Fig. 1, *c*, *d*). Cooling to 30°C diminished the decrease in dilator responses of arteries and veins to the agent compared to hypoxia in both organs (Fig. 1, *c*, *d*). When hypoxia and hypothermia were applied simultaneously, the dilation of GM and SI vessels in response to sodium nitroprusside also decreased (Fig. 1, *c*, *d*).

Thus, no functional differences were revealed between regional arteries and veins in constrictor and dilator responses in different organs: hypoxia and hypothermia applied separately and in combination significantly reduced the reactivity of vascular myocytes. Hypoxia produced a more profound effect on myocytic responsiveness than hypothermia. Moreover, hemodynamic effects of combined exposure to these factors were similar to those produced by hypoxia alone. This agrees with the hypothesis [6] that the shifts in vascular responses induced by combination of two external stimuli are determined predominantly by the strongest stimulus. Our study did not confirm the earlier evidence on the protective effect of hypothermia against hypoxia-induced vascular damage [3,4]. The discrepancy can be explained by different mechanisms of action of dopamine and sodium nitroprusside, on the one hand, and norepinephrine and isoproterenol used in previous studies, on the other, on vascular myocytes [3,4].

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