Adrenergic Reactions in Microcirculatory Bed of Pia Mater in Rat Brain

A. V. Kostylev, V. N. Shuvaeva, O. P. Gorshkova, and D. P. Dvoretsky

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Differential characteristic of the reaction of pial arteries of various generations to intravenous administration of norepinephrine was obtained in experiments on rats under artificially stabilized systemic blood pressure.

Key Words: *pial arteries; adrenoreactivity; artificial stabilization of blood pressure*

Most methods examining the neurogenic regulation of blood supply to the brain are based on the use of pharmacological drugs. For evaluation of the peculiarities of adrenergic regulatory mechanisms, the researchers use sympathomimetic amines such as norepinephrine (NE). However, this agent can induce ambiguous reactions [4-6]. The character of the vascular reaction and even its directivity (dilation or constriction) are determined by a number of factors depending on experimental paradigm (species, dosage, the mode of drug administration, specificity in the response of individual segments of vascular bed, *etc*.) [6-8]. A serious obstacle to assess the direct effect of intravenous NE on cerebral vessels is elevation of systemic blood pressure (SBP) induced by this drug. Under these conditions, NE exerts indirect effects on the blood vessels via their mechanical extension and triggering the intrinsic myogenic mechanisms of blood flow stabilization [1,2].

Our aim was to compare the reactions of pial arteries of various segments to intravenous NE in experimental rats with and without artificial stabilization of blood pressure.

Laboratory of Blood Circulation Physiology, I. P. Pavlov Institute of Physiology, Russian Academy of Sciences, St. Petersburg, Russia. ***Address for correspondence:*** vshuv@kolt.infran.ru. V. N. Shuvaeva

MATERIALS AND METHODS

The experiments were carried out on Sprague--Dawley rats (n=9) narcotized with intraperitoneal urethane (150 mg/100 g body weight).

Pial vessels were observed using vital TV-microscopy [3] at total magnification ×470.

At the first stage, the background image of selected pial vascular net and the reaction to NE (0.1 ml/100 g body weight) 30 sec postinjection (the time corresponding to maximum elevation of SBP induced by the drug) were recorded. At the second stage, the procedure was repeated using blood pressure stabilization system (BPSS). This system prevents responses of pial vessels to NE-provoked elevation of SBP by stabilizing it at the initial level (Table 1); heart rate remained unchanged under these conditions.

BPSS is a pressure buffer consisting of air compressor, air reservoir, mercury manometer, donor blood reservoir, tubes and valves (Fig. 1). This system supplied donor blood into the vascular bed of the rat or drew the blood from it, respectively, during SBP fall or rise in the experimental rat. The vascular system of the rat was connected to BPSS and PDP-400 pressure transducer of an electromanometer via a catheter passed into abdominal aorta to continuously monitor and control the level of SBP. The beat-to-beat SBP values were calcu-

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TABLE 1. Effect of Intravenous NE (2×10^{-5} g/ml) on SBP ($M\pm m$, n=10)

Conditions of experiments	Baseline	NE	Maximum response
BPSS-off	70.3±4.0	101.1±6.9*	134.8±8.2*
BPSS-on	78.5±4.7	79.5±4.6	89.6±5.3

Note. *p<0.05 compared to the baseline.

lated by the formula $P_{mean}=P_{diast}+{}^1/_3(P_{syst}+P_{diast})$, where P_{diast} and P_{syst} are diastolic and systolic pressure values, respectively. In each experiment, the electromanometer was calibrated with a mercury manometer.

A total of 297 pial arterial vessels were examined. The first-order (A1) to fifth-order (A5) branches of the middle cerebral artery were tested. This classification is arbitrary. The arterial segment emerging directly from under the bone at the edge of the operational field was considered as the first segment of arteries (A1). The successive downwards branches were classified as A2 to A5. The diameter of examined vessels was 17-168 μ. In each arterial segment, the vessels of various diameters were presented in equal proportion. The linear size of microvessels was measured with a routine stage micrometer operated under an Inspector Matrox software with the use of calibration coefficients. The accuracy of these measurements was 2 μ.

The data were processed statistically using Student's t test.

RESULTS

Intravenous NE produced opposite effects in pial arteries. In BPSS-free (BPSS-off) experiments, approximately equal number of vessels were constricted (38%) or dilated (39%), while other vessels (23%) were unresponsive. When SBP was stabilized, the number of dilated arteries decreased, whilst that of unresponsive ones significantly increased. The use of BPSS did not significantly change the number of arteries constricted by NE (Table 1). Stabilization of SBP with BPSS significantly decreased the range of dilation and constriction of pial arteries (Table 2). In BPSS-off experiments, the number of NA-constricted arteries was similar for arteries of all segments (28% on the average) with a single exception of A3 arteries, where this number amounted to 51% ($p\leq0.05$). In this group, dilation was minimum (27% vessels *vs.* 40-60% in other groups).

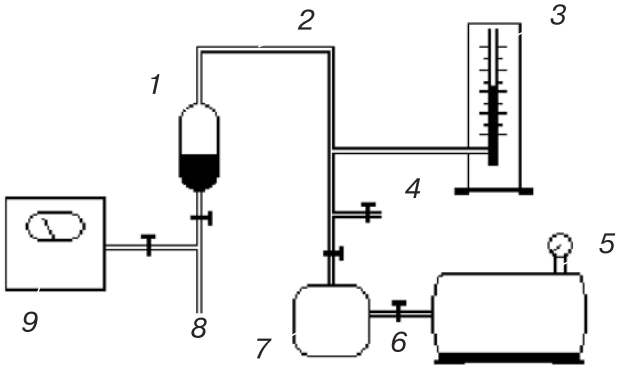

Fig. 1. The scheme of BPSS. *1*) reservoir with donor blood; *2*) tubing; *3*) mercury manometer; *4*) relief valve to release air into atmosphere; *5*) compressor; *6*) valve; *7*) air reservoir; *8*) connection of BPSS to rat vascular bed; *9*) electromanometer coupled with a recorder.

BPSS decreased the number of NE-constricted A3-arteries from 51% (in BPSS-free experiments) to 33% ($p\leq0.02$). However, it did not significantly change the number of constricted arteries in other groups, so the total number of such reactions in all groups remained approximately the same. Stabilization of blood pressure with BPSS decreased the number of NE-dilated arteries in A1 and A2 groups approximately by 2.0 ($p\leq0.02$) and 1.5 ($p\leq0.05$) times, respectively. In group A3 and A4 arteries, the number of dilated vessels remained approxima-

TABLE 2. Effect of Intravenous NE (2×10^{-5} g/ml) on Pial Arteries ($M\pm m$, n=10)

Conditions of experiments	Constriction		Dilation		Number of unresponsive arteries, %
	number of arteries, %	amplitude of reaction in percentage to diameter prior to NE	number of arteries, %	amplitude of reaction in percentage to diameter prior to NE	
BPSS-off	38	18.8±2.6	39	22.6±3.6	23
BPSS-on	33	10.6±1.0*	31**	13.8±1.4*	36***

Note. *p<0.05, **p<0.01, ***p<0.002 compared to BPSS-off data.

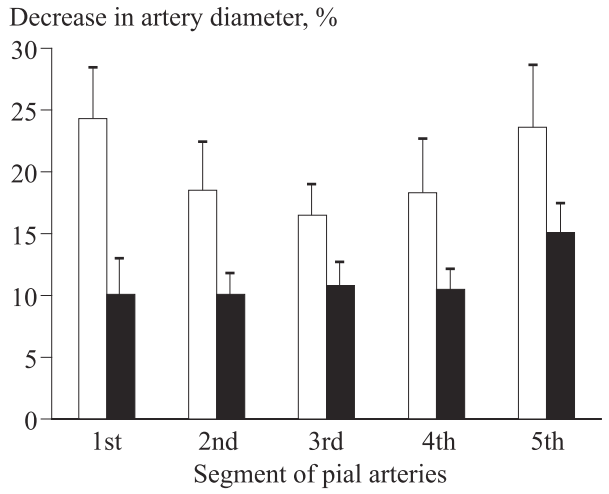

Fig. 2. Amplitude of constrictor reactions in pial arteries of various branch order induced by intravenous NE (2×10^{-5} g/ml) assessed by the changes in diameter relatively to prior NE value (%). The open and filled bars show BPSS-free (control) and BPSS-on data, respectively.

tely the same (30% on the average), while in group A5 it increased from 50 to 65% ($p \leq 0.05$).

In addition, BPSS significantly decreased the amplitude of NE-induced constrictor reactions in pial arteries of all segments (Fig. 2).

The use of BPSS decreased the total number and amplitude of dilator reactions induced by intravenous NE, although it did not eliminate them entirely, which can be related to NE-induced activation of β_2-adrenoreceptors responsible for dilation in addition to routine activation of α_1-adrenoreceptors that trigger vasoconstriction [2,5,6]. Since stabilization of SBP did not suppress the mechanisms of local redistribution of blood supply to the brain, the dilation in one segment of the pial vascular network could be compensatory to constriction of arteries located in other segments of this network. The present data on the reaction to NE in arteries of various segments suggest that the greatest role in redistribution of cerebral blood flows is played by the arteries of segments 1-3.

Thus, stabilization of SBP with BPSS provides conditions for more precise assessment of NE action on pial arterial vessels.

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