PHYSIOLOGY

Adrenoreactivity of Rat Pial Arteries under Conditions of Stabilized Systemic Blood Pressure

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Segment-specific characteristics of the reactions of pial arteries of different generations to intravenous injection of norepinephrine were studied under conditions of instrumental stabilization of systemic blood pressure in rats with blocked α- and β-adrenoceptors.

Key Words: *pial arteries; adrenoreactivity; instrumental stabilization of systemic blood pressure; adrenoceptors*

Numerous experiments demonstrated the existence of differentiated adrenoreactivity in various segments of the same blood vessel or described the development of opposite reactions within the vascular network to norepinephrine [6,8-10]. Our previous detailed analysis of the reaction of consecutive arteries in the precapillary subdivision of the meningeal microcirculatory bed in rats to intravenous norepinephrine also showed that this agent provokes both constrictor and dilator vascular responses [5]. The character of the reaction (constriction or dilation) is determined by a number of factors and depends, specifically, on elevation of systemic blood pressure (BP) provoked by injected norepinephrine. This determines indirect effects of norepinephrine on blood vessels due to their mechanical distension and activation of the autoregulatory myogenic flow-stabilizing mechanisms [3,6]. The use of BP stabilization system [5] decreased the total number and magnitude of the dilator responses, but did not eliminate them completely, which can be explained by the dual action of norepinephrine on α_1-adrenoceptors evoking constriction and β_2-adrenoceptors responsible for dilation [6,9,10].

The aim of this study was to assess adrenoreactivity of pial arteries in various segments (generations) under conditions of systemic BP stabilation against the background of α- and β-adrenoceptor blockade and in the absence of this blockade.

MATERIALS AND METHODS

The experiments were carried out on Sprague-Dawley rats (n=11) narcotized with intraperitoneal urethane (190 mg/100 g body weight). Heparin (50 U/100 g body weight) was used as the anticoagulant.

Blood vessels were examined by intravital video microscopy at ×470 [7]. To prevent the reaction of pial vessels to norepinephrine-induced elevation of systemic BP, the latter was stabilized using an original stabilization system [5] at a level equal to BP at the onset of experiment. Under these conditions, the heart rate did not change significantly.

The experiments were performed in two stages. First, the images of intact vessels in the selected part of the pial network were obtained before and 30 sec after intravenous injection of norepinephrine (0.1 ml/100

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g body weight). Second, the recordings were repeated against the background of blockade α- or β-adrenoceptors with prazosin (10^{-4} g/ml; 0.1 ml/100 g body weight) or propranolol (10^{-3} g/ml; 0.1 ml/100 g body weight), respectively. The concentrations of the blockers were chosen by trial-and-error method. The blockade was verified using agonists for α- or β-adrenoceptors phenylephrine (10^{-7} g/ml; 0.1 ml/100 g body weight) and isoproterenol (10^{-9} g/ml; 0.1 ml/100 g body weight), respectively.

The total number of examined pial arteries was 569. These arteries belonged to generation I-IV in the vascular tree of the median cerebral artery. This taxonomy was rather conventional. The first generation (I) corresponded to the arterial segment originating directly under the bone at the edge of the surgical wound. The branches II-V were located sequentially downstream to generation I vessels. The diameter of the examined arteries ranged from 12 to 102 μ. In each artery generation, the relative number of vessels with various diameters was approximately equal. The linear sizes of microvasculature were measured with a stage micrometer and Inspector Matrox software (using calibration coefficients) with an accuracy of 2 μ.

The vascular diameter data were processed statistically with Student's two-sample *t*-test at $p \leq 0.05$. Significance of the difference between two observed frequencies t_d in comparing the numbers of vasomotor reactions was calculated [1].

RESULTS

Intravenous injection of norepinephrine under stabilized systemic BP evoked opposite vascular reactions in all arterial generations: constriction and dilation were observed in 44 and 36% arteries, respectively; in 20% arteries the diameter remained unchanged.

Approximately equal percents (about 33%) of generation I arteries constricted, dilated, or did not change the diameter. The constrictor responses were observed predominantly in generation III-V arteries (50-56%), while dilation took place mostly in generation II arteries (44%) where the relative number of constricted arteries was only 35%. In other groups, 26-33% arteries were dilated (Fig. 1).

Blockade of α-adrenoceptors decreased the number of constrictions in response to norepinephrine only in generation IV arteries. In contrast, the number of constricted vessels increased in generation I-III arteries and did not change in generation V arteries. At the same time, these vascular groups were characterized by increased number of nonreactive vessels (by 10% on the average) and decreased number of dilated arteries (Fig. 2). Thus, under systemic BP stabilization, only generation IV arteries exhibited the expected

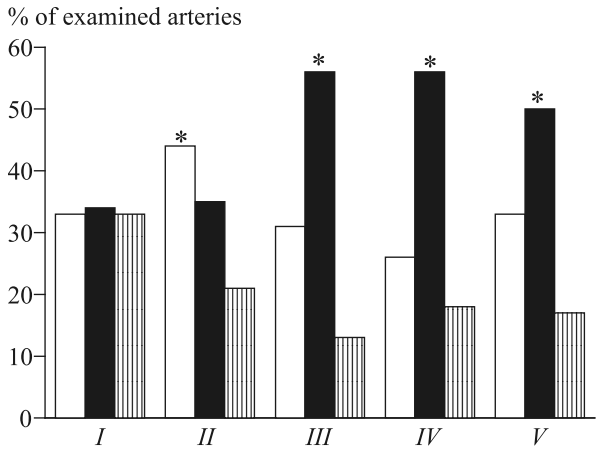

Fig. 1. Effect of norepinephrine (2×10^{-5} g/ml) on vasomotor reactions of pial arteries of various generations. Open bars: dilatation; closed bars: constriction; dashed bars: no responde. Here and in Figs. 2-3: abscissa: artery generation (branching order, I-V); ordinate: percent of responding vessels. *$p \leq 0.05$ compared to the corresponding control group.

reaction to blockade of α-adrenoceptors (decrease in the number of constriction), while the opposite reaction was observed in generation I-III arteries. Probably this means that in Sprague-Dawley rats, generation IV (small) arteries are characterized by maximum density of α-adrenoceptors.

Blockade of β-adrenoceptors significantly attenuated the dilator response to norepinephrine (by 1.4-2.3 times) only in generation I-II arteries, while the number of constricted generation I arteries increased 2-fold. The dilator reactions to norepinephrine prevailed in generation IV-V arteries (54 and 62%, re-

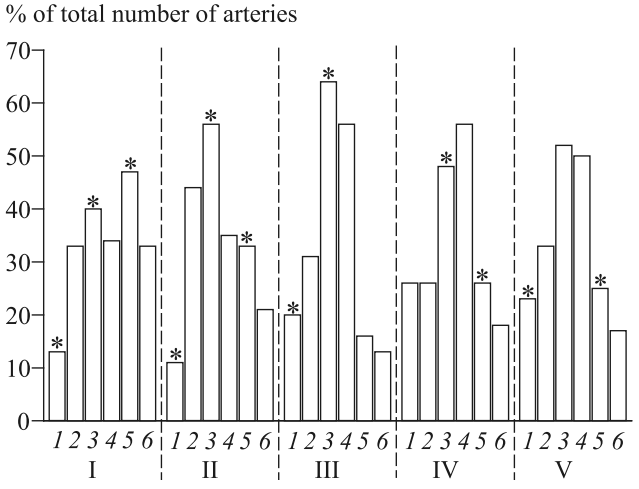

Fig. 2. Responses of pial arteries of various generations to norepinephrine (2×10^{-5} g/ml) against the background of α-adrenoceptors blockade. *1*) dilation against the background of α-adrenoceptor blockade; *2*) dilation before α-adrenoceptor blockade (control); *3*) constriction against the background of α-adrenoceptor blockade; *4*) constriction in the control; *5*) no reaction to norepinephrine against the background of α-adrenoceptor blockade; *6*) no reaction to norepinephrine in the control.

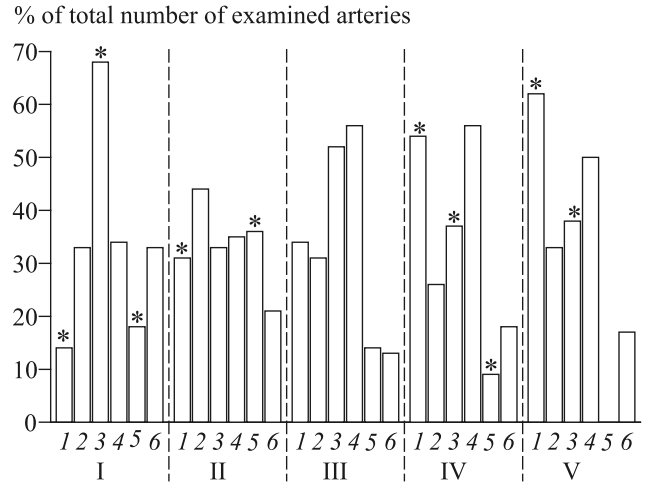

Fig. 3. Responses of pial arteries of various generations to norepinephrine (2×10^{-5} g/ml) against the background of β-adrenoceptors blockade. *1*) dilation under β-adrenoceptor blockade; *2*) dilation before β-adrenoceptor blockade (control); *3*) constriction against the background of β-adrenoceptor blockade; *4*) constriction in the control; *5*) no reaction to norepinephrine against the background of β-adrenoceptor blockade; *6*) no reaction to norepinephrine in the control.

spectively) while the number of constrictor reactions decreased compared to the control. No significant changes were observed in generation III arteries (Fig. 3). Thus, during blockade of β-adrenoceptors under conditions of stabilized systemic BP, the expected reaction to norepinephrine (decrease in the number of dilator responses) was observed only in generation I-II arteries, while generation IV-V arteries demonstrated opposite reaction to this catecholamine. These findings suggest that in Sprague-Dawley rats generation I arteries are characterized by maximum density of β-adrenoceptors.

Thus, experiments with adrenoblockers showed that pial vascular bed of Sprague-Dawley rats is characterized by non-uniform distribution of α-adrenoceptors (available mostly in generation IV arteries, which were predominantly small vessels) and β-adrenoceptors most densely located in generation I arteries. Stabilization of systemic BP made it possible to maintain blood pressure at a constant level thereby blocking the myogenic pathway to affect circulation. However, this approach could not stabilize the cerebral blood flow. Probably, the perturbations in cerebral circulation under stabilized systemic BP triggered the compensatory vascular reactions via activation of the distributive mechanisms of local cerebral blood flow, which in its turn could up-regulate the endothelium-dependent mechanism of vascular tone control [2,4]. As a result, we observed the opposite reactions to norepinephrine in Sprague-Dawley rats: enhancement of constriction in generation I-III arteries during blockade of α-adrenoceptors and augmentation of dilation among generation IV-V arteries during blockade of β-adrenoceptors. The expected decrease in the number of constrictor reactions to norepinephrine under conditions of α-adrenoceptor blockade was observed only in generation IV arteries, while the decrease in the number of norepinephrine-induced dilator responses under conditions of β-adrenoceptor blockade took place only in generation I-II arteries. Therefore, assessment of vascular reactions among the pial arteries of various generations in Sprague-Dawley rats to intravenous injection of norepinephrine under conditions of stabilized systemic BP revealed differences in adrenoreactivity in these arteries at different levels of branching of the pial arterial tree.

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