Differences in Adrenoreception in the Microcirculatory Bed of the Pia Mater in Normotensive and Spontaneously Hypertensive Rats

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Adrenoceptors in pial vascular bed of normotensive Wistar-Kyoto rats are distributed unevenly during stimulation of the superior cervical ganglion, their density was maximum in the 5th-generation arteries. In spontaneously hypertensive rats (SHR) the density of adrenoceptor is lower than in normotensive rats and their number is maximum in the 1st-generation arteries.

Key Words: *pial arteries of different generations; α- and β-adrenoceptors; spontaneously hypertensive rats*

Different reactivity of pial arteries in hypertensive and normotensive rats is determined by peculiarities of the neurogenic mechanism of vascular tone regulation at different levels of the pial arterial system [1,2]. This phenomenon can be explained by abnormal density of adrenoceptors (AR) in pial arteries of this or that generation in hypertensive animals.

We studied the distribution of α- and β-AR in different parts of the arterio-arteriolar component of the pia mater vascular network in normotensive Wistar-Kyoto (WKY) and spontaneously hypertensive rats (SHR). We also evaluated the vasoconstrictor responses of 1st-5th generation (order of branching) pial arteries of the middle cerebral artery basin to electrical stimulation of the superior cervical ganglion (SCG) under conditions of AR blockade and without it.

MATERIALS AND METHODS

Experiments were carried out on 25 WKY (250-290 g) and 28 SHR rats (240-280 g). Blood pressure measured on the tail by the cuff method was 120-130 mm Hg in conscious WKY and 185-195 mm Hg in SHR animals.

The animals were narcotized with urethane (125 mg/100 g intraperitoneally). A hole (~1 cm^2) was drilled in the parietal area of the skull, the dura mater accessible through the hole was removed. The pial vascular network was scanned in reflected light by life-time television microscopy [1]. The reaction of arteries (changes in diameter) to electrical stimulation of SCG was evaluated by changes in the width of erythrocyte flow in a vessel. The diameter of each portion of a vessel was measured in a series of photographs before and after SCG stimulation.

In experimental series I, the reaction of vessels to SCG stimulation was studied after prazosin blockade of α-AR and without blockade. In series II, the reaction of pial arteries to SCG stimulation was studied after propranolol blockade of β-AR and without blockade. The blocker concentrations were selected experimentally. Propranolol was used in a concentration of 1×10^{-3} g/ml in both rat strains. Prazosin was used in a concentration of 1×10^{-5} g/ml in WKY and 1×10^{-4} g/ml in SHR rats. Receptor blockade was verified by injection of the agonist: phenylephrine (1×10^{-7} g/ml) for α-adrenoblocker and isoproterenol (1×10^{-9} g/ml) for β-adrenoblocker.

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The superior cervical ganglion (ipsilateral to the studied hemisphere) was stimulated with a series of rectangular electric pulses applied via bipolar silver electrodes to the nerve plexus for 20 sec. The sympathetic tract below SCG was not crossed. Threshold parameters of nerve stimulation were experimentally selected for each animal strain. WKY rats were stimulated with pulses of 10 Hz frequency, 6.1 V, and pulse duration 0.5 msec. The stimulation threshold for SHR rats was higher (10 Hz frequency, 9.1 V, and 1 msec pulse duration).

Arteries of the 1st-5th generation of the middle cerebral artery (10-106 μ in diameter) were studied: 902 in WKY and 1034 SHR rats. The portion of artery emerging directly from under the bone at the edge of the operation field was considered as the first generation artery. Branches of the 2nd-5th generations were located in succession (along the bloodflow) after the 1st generation vessel.

Constriction reactions of vessels of different generations in response to SCG stimulation were analyzed. The number of constricted vessels was evaluated every 10 sec over 40 sec after the end of stimulation under conditions of AR blockade and without it.

RESULTS

The number of constricted vessels in SHR animals increased from 28% among the 1st-generation vessels to 38% in the 4th-5th-generation vessels (Fig. 1), while in WKY rats the number of constricted arteries was about the same in all groups of vessels, the increase in the number of constricted vessels in the direction from 1st to 5th generation did not surpass 5-6%.

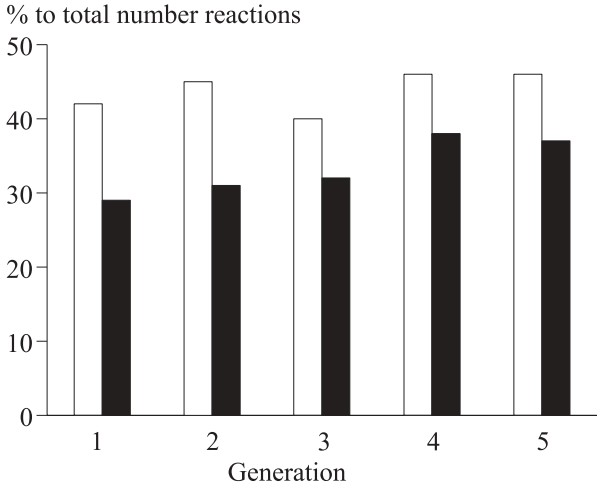

Fig. 1. Incidence of constrictor responses of pial arteries to SCG stimulation in WKY rats (light bars) and SHR (dark bars).

The incidence of constrictor reactions to SCG stimulation in WKY rats decreased significantly under conditions of α-AR blockade (except the 3rd generation vessels) and was most pronounced in the 5th-generation arteries (by 33% in comparison with the stimulatory effect without blockade). The number of constrictor reactions in the 2nd-generation vessels decreased by 24%, of the 1st- and 4th-generation vessels by 17% (Fig. 2, *a*). In SHR rats the number of constricted 1st-generation pial arteries decreased by 48% in comparison with the effect without blockade (Fig. 2, *b*). Under conditions of α-AR blockade, the number of constrictor reactions of the 3rd-5th-generation arteries in SHR rats increased by 40, 23, and 89%, respectively, in comparison with the effect without blockade, the number of constricted 2nd-generation vessels remained unchanged.

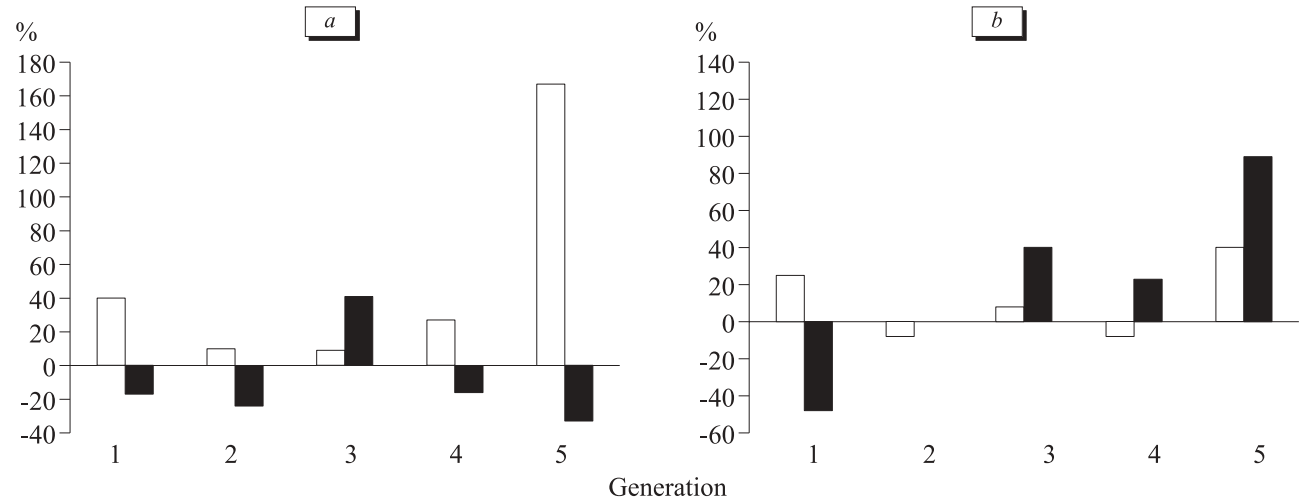

Fig. 2. Changes in vasoconstriction in response to SCG stimulation in WKY rats (*a*) and SHR (*b*) under conditions of α-AR (light bars) and β-AR blockade (dark bars). The number of constrictions without blockade is taken for the zero.

The number of constricted vessels in response to SCG stimulation under conditions of β-AR blockade increased in WKY rats in comparison with the effect without blockade. This increase was most pronounced in the 5th-generation arteries (by 167%) and for the 1st- and 4th-generation vessels (by 40 and 27%, respectively). The increase in the number of constricted 2nd- and 3rd-generation vessels was about 10%. In SHR with β-AP blockade the number of constrictor reactions to SCG stimulation increased only for the 1st- and 5th-generation arteries (by 25 and 40%, respectively) in comparison with the constrictor effect of stimulation without blockade; the increase in the number of constricted 2nd-4th-generation arteries did not surpass 8% (Fig. 2, *b*).

Hence, in WKY rats constriction of arteries of all generations in response to SCG stimulation was similarly expressed. From these results, even distribution of AR along the vascular tree in the pial vascular system of WKY rats could be expected. However, under conditions of α-AR blockade the number of constrictor reactions to SCG stimulation decreased differently in vessels of different generations. The decrease in the number of constricted vessels was more pronounced for the 5th-generation vessels (33%), while for arteries of other generations it was 20% on average. The increase in the number of constricted vessels in response to SCG stimulation under conditions of β-AR blockade was detected for arteries of all generations, being most pronounced for arteries of the 5th branching order (2.7 times). These data indicate that AR are distributed unevenly in the pial vascular bed of WKY rats and are more abundant in vessels of higher generations, mainly in the group of precortical arterioles. Presumably, higher density of AR on 5th-generation arteries underlies the sympathetic regulation of rapid redistribution of blood and its delivery to the smallest areas, which is essential for blood pressure regulation in the distal vascular segments of the pia mater and intracerebral vessels.

In contrast to WKY rats, in SHR the number of constrictor responses to SCG stimulation increased from the 1st- to the 5th-generation vessels. Stimulation under conditions of α-AR blockade decreased in the number of constrictions in only 1st-generation arteries. Blockade of β-AR, similarly as in WKY rats, mainly affected the number of constrictor responses to SCG stimulation in the 1st- and 5th-generation arteries. It is also worthy of note that no expected changes in the number of constrictor reactions to stimulation were detected in arteries of the 2nd-4th branching order under conditions of α- and β-AR blockade (decrease in the number of constrictions in α-AR blockade and increase in β-AR blockade). This can indicate the absence or very low density of AR in this area of the pial vascular network. In this case the detected increase in the number of constrictions of pial arteries of higher generations in response to SCG stimulation in SHR can result from redistribution of intravascular pressure and flows. Presumably, neurogenic vasoconstriction in the most reactive parts of the vascular network of the pia mater (1st-generation arteries) is associated with bloodflow redistribution which, in turn, can lead to passive reduction of the diameter of less reactive capillaries.

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