Intravital studies on cerebral arteries in hypertensive and normotensive rats

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Summary

1. The diameters of main cortical surface branches of the middle cerebral artery were continuously monitored through a closed cranial window in spontaneously hypertensive rats (SHR) and in normotensive Wistar Kyoto (WKY) rats by aid of a multichannel video-angiometer under resting conditions and under maximal vasodilatation induced by hypercapnia.

2. Initial mean arterial pressure was 172 ± SEM 9 mmHg in SHR and 103 ± 5 mmHg in WKY rats; during hypercapnia the corresponding values were 183 ± 9 and 127 ± 7 mmHg.

3. The resting diameter of the arteries was 55 ± 1 μm in SHR (n = 53) and 87 ± 1 μm in WKY rats (n = 53; P < 0.001). The percentage increase in diameter during vasodilatation (Paco₂ 70 mmHg) was larger in SHR (54%) than in WKY rats (36%). However, the maximum lumen diameter remained significantly smaller in SHR (84 ± 2 μm compared with 117 ± 5 μm in WKY rats; P < 0.001). No significant further dilatation was seen in either group after α-adrenoceptor blockade.

4. The smaller diameter of cortical arteries during vasodilatation is consistent with the concept that hypertensive vascular hypertrophy encroaches on the lumen in vivo. The larger percentage increase in diameter of cortical arteries in hypertensive rats corroborates Folkow’s hypothesis on the haemodynamic consequences of an altered media/lumen ratio in hypertension.

5. There is no evidence that an enhanced sympatho-adrenergic tone prevents maximum vasodilatation during hypercapnia in SHR.

Key words: cerebral arteries, cortical arteries, hypercapnia, vasodilatation.

Introduction

It is well established that chronic hypertension leads to an increased thickness of the arterial vessel wall although the magnitude of this alteration varies with the vascular bed and hypertension model studied. The haemodynamic consequences of such structural vascular changes are controversial [1–5]. With the method described by Furuyama [6] we observed an increased vessel wall to lumen ratio in extra-parenchymatous cortical arteries in SHR [7, 8]. Moreover, the cerebral blood flow measured during maximum vasodilatation at the same perfusion pressure in normotensive and hypertensive rats was markedly reduced in SHR compared with WKY rats [9]. Unless the vessel density was considerably reduced in SHR this would indicate a decreased internal radius. The aim of the present study was to determine the diameters of defined branches of the middle cerebral artery on the brain surface at various levels of smooth muscle tone up to complete relaxation.

Methods

Six SHR and six WKY rats (age 6 months) were initially anaesthetized with pentobarbitol (30 mg/kg intraperitoneally), tracheotomized and mechanically ventilated with air. Catheters were inserted into the aorta from a femoral artery for continuous blood pressure recording and sampling of blood for blood gas analyses, and in a jugular vein for injection of drugs. Mean arterial pressure (MAP) was continuously registered and the body temperature maintained between 37° and 38°C by the aid of an electric heating pad. After placing the animal in the prone position the head was fixed into a stereotoxic head-holder and a closed cranial window was inserted in the parietal region on the left side [10]. A TKX 29 Philips video camera was attached to a Leitz...
intravital microscope and the calibre of the main cortical branches of the middle cerebral artery was continuously monitored by aid of a multi-channel video-angiometer device [11]. Single experiments were recorded on videotape. Hypercapnia was induced by adding CO₂ to the breathing air until maximum dilatation of the arteries was obtained. At the end of the experiments, first yohimbine (5 mg/kg) and then phenoxybenzamine (1 mg/kg) was given intravenously to evaluate a possible sympathoadrenergic influence on vessel tone during hypercapnia. Student's t-test was used for statistical evaluation.

Results

Initial MAP, MAP during maximum hypercapnic vasodilatation and MAP after yohimbine and phenoxybenzamine were 172 ± SEM 9, 183 ± 9, 180 ± 9 and 147 ± 17 mmHg in SHR; corresponding values for WKY rats were 103 ± 5, 127 ± 7, 125 ± 10 and 106 ± 12 mmHg. Resting arterial diameter at PaCO₂ 30 mmHg was 55 ± 1 μm in SHR (n = 53) and 87 ± 1 μm (n = 53) in WKY rats (P < 0.001). Maximum vasodilatation was obtained at PaCO₂ 70 mmHg. During hypercapnia the percentage increase in diameter was 54% in SHR and 36% in WKY rats. The absolute increase was similar in the two groups. The diameter during vasodilatation thus remained significantly smaller in SHR (84 ± 2 μm compared with 117 ± 5 μm in WKY rats; P < 0.001). No significant further dilatation was seen in either group after adrenoceptor blockade.

Discussion

The present results show that arteries on the brain surface have a smaller lumen in SHR than in WKY rats at resting tone as well as during maximum vasodilatation. No lumen reduction at resting tone was observed in arteries of similar size in the cremaster muscle of SHR [2, 3]. The discrepancy illustrates that results obtained from one vascular bed are not necessarily valid for another. The difference in lumen diameter during dilatation between SHR and WKY rats is consistent with the concept that hypertensive vascular hypertrophy encroaches on the lumen. A sympatho-adrenergic influence on vessel tone preventing maximum vasodilatation during hypercapnia was ruled out by α-adrenoceptor blockade. The reason for first giving the α₁-antagonist yohimbine was twofold. First, there is evidence that blockade of presynaptic α₁-receptors may unmask an effect on postsynaptic α₁-receptors. Second, a recent report [12] indicates that there may be postsynaptic α₁-adrenoceptors in cerebral arteries. The failure of α-adrenoceptor antagonists to modify the diameter of cerebral arteries during pronounced hypercapnia is in agreement with an earlier study on normotensive animals [13]. The prompt response to hypercapnia of arteries in hypertensive animals indicates that there is no decreased vessel reaction to hypercapnia in these animals. The larger percentage increase in diameter during vasodilatation in SHR agrees with Folkow's hypothesis about the haemodynamic consequences of an altered media/lumen ratio in SHR.

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References