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PAPER

CHANGES IN JEJUNAL ARTERIES IN SPONTANEOUSLY HYPERTENSIVE AND NORMOTENSIVE RATS FOLLOWING NEONATAL TREATMENT WITH CAPSAICIN

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ABSTRACT
The relationship between blood pressure and jejunal artery morphology was examined in spontaneously hypertensive rats (SHR) rendered normotensive with capsaicin treatment. At two days after birth SHR and normotensive rats were treated with a subcutaneous injection of capsaicin, a substance P-releasing undecapeptide. At 4 and 12 weeks after treatment the animals were anesthetised and their blood pressures recorded through a femoral cannula. The animals were then sacrificed, and jejunal vessels removed and processed for electron microscopy. It was found that although the blood pressure of the SHR had been controlled by the capsaicin treatment at normotensive levels, wall thickening was present, similar to that seen in uncontrolled hypertensive rats. It was concluded that the morphology of the jejunal artery appears to be related to strain-linked factors other than blood pressure.

INTRODUCTION

During the development of hypertension a thickening of the arterial media occurs in both hypertensive animals (Bevan 1976, Ichijima 1969,

Mulvaney et al 1978, Warshaw et al 1979), and hypertensive patients (Pickering, 1968; Cook and Yates, 1972). The medial hypertrophy is considered by some authors to be either the cause or the result of increased arterial pressure (Cox, 1982; Folkow, 1978; Pfeffer et al, 1974; Tobia et al, 1974). In this study we examine the relationship between blood pressure and arterial wall structure in rats which normally develop hypertension, but which were rendered normotensive by neonatal administration of an antihypertensive agent. Since we have demonstrated that capsaicin, a substance P-releasing undecapeptide, has a marked hypotensive effect on adult SHR and an antihypertensive effect when administered to neonatal rats (Scott and Pang 1982), it was used as the antihypertensive agent in this study.

MATERIALS AND METHODS

Twelve SHR and twelve normotensive Wistar Kyoto rats were treated at two days after birth with a subcutaneous injection of capsaicin (Sigma), 50mg/kg. At 4 and 12 weeks after treatment, six treated, and an equal number of untreated rats of the same age and strain were anesthetised with pentobarbital (35mg/kg), and their blood pressures were recorded through a femoral cannula. The animals were then sacrificed by perfusion through the heart with a formaldehyde/glutaraldehyde fixative (Pang and Scott, 1981), at a pressure of 120mmHg. The jejunal arteries were removed and the proximal part of each, from its origin at the superior mesenteric artery to the point of branching, processed for electron microscopy. Transverse sections lum thick were cut from resin embedded arteries and photographed. From the negatives, wall thickness and lumen diameter were measured. The wall thickness measurements were taken at the thinest point. The lumen diameter measurements were made across the narrowest diameter. Transverse sections were also cut for electron microscopic examination. Random photographs were

taken of those sections at a magnification of 11,600 times and prints made at a final magnification of 35,000 times. Estimations of the percentage volume of elastin, smooth muscle and collagen were made from the photograhs using an overlaid one-hundred point grid.

RESULTS

The blood pressure of the treated rats was lower than that of the untreated rats, in both strains, at both 4 and 12 weeks after treatment. The values obtained are given in table 1.

Despite preventing the development of hypertension in the SHR, wall thickening similar to that seen in uncontrolled hypertensive rats occurred. As shown in table 2, the wall thickness of jejunal arteries from the treated and untreated SHR was not significantly different.

An examination of the percentage composition of the arterial wall at twelve weeks of age in treated and untreated rats showed only minor alterations in the amounts of collagen, elastin and smooth muscle (table 3).

Table 1. Mean arterial pressure in mmHg of untreated and capsaicin treated 4 and 12 week old normotensive (WKY), and hypertensive (SHR) rats. (± SD).

		4 weeks	12 weeks
Untreated	WKY	81.6±4.8	91.2±4.7
	SHR	82.3±3.0	136.0±3.4
Treated	WKY	62.3±6.3	62.1±6.8
	SHR	79.2±3.5	101.0±5.2

DISCUSSION

Following capsaicin treatment the blood pressure of the genetically hypertensive rats did not rise to hypertensiv levels. Despite the control of blood pressure at normotensive levels, wall thickening similar to that seen in uncontrolled hypertensive rats occurred.

The antihypertensive effect of capsaicin treatment in genetically hypertensive rats was reported by Scott and Pang (1982), following treatment of neonatal rats. The effect of this agent is related to its ability to release substance P from storage sites.

Table 2. Lumen diameter and wall thickness of jejunal vessels, in um, of untreated and capsaicin treated 12 week old normotensive (WKY) and hypertensive (SHR) rats. (± SEM).

		Lumen diameter	Wall thickness
Untreated	WKY	309.7±26.3	8.5±0.8
	SHR	223.0±29.0	11.3±0.9
Treated	WKY	260.9±19.8	10.1±1.9
	SHR	281.1±20.0	13.2±1.4

Table 3. The volume density of collagen, elastin and smooth muscle in jejunal vessels of untreated and capsaicin treated 12 week old normotensive (WKY) and hypertensive (SHR) rats. (± SEM).

		Collagen	Elastin	Smooth Muscle
Untreated	WKY	17.4±1.4	2.9±0.7	78.0±2.0
	SHR	16.6±0.9	3.5±0.5	80.1±1.4
Treated	WKY	12.3±1.9	2.5±0.8	74.2±2.0
	SHR	20.3±1.8	4.2±0.7	75.4±2.1

It has been demonstrated that treatment of neonatal rats with capsaicin results not only in a depletion of certain stores of substance P, but in the permanent loss of certain substance P-containing neurons (Jancso et al 1977). There have been no reports of a direct effect of capsaicin on the development of vascular structures.

The development of hypertrophy of the jejunal arterial wall in the genetically hypertensive rat, despite the control of blood pressure at normal levels, suggests that some factor other than blood pressure is responsible. Recent evidence has suggested that the sympathetic innervation of the jejunal arteries of the SHR is increased above control levels from two weeks of age onwards (Scott et al 1982). It seems likely that the factor responsible for the development of medial hypertrophy in the jejunal arteries is related to the sympathetic innervation, particularly since it has been demonstrated that the sympathetic innervation can have a trophic effect on vascular smooth muscle (Abel and Hermsmeyer 1981, Bevan et al 1975).

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