SYMPATHETIC INNERVATION OF THE CEREBRAL ARTERIAL SYSTEM STUDIED USING ANTEROGRADE LABELLING WITH WGA-HRP

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SUMMARY :

The exact anatomical pattern of sympathetic innervation of the cerebral arteries is not clearly understood. In the present study the anterograde labelling of sympathetic nerve fibers originating from the superior cervical ganglion was achieved by a neurotracer; WGA-HRP, in order to demonstrate the nerve fibers and their terminals on the arterial wall. The plexus of sympathetic nerve fibers on the arterial wall were classified into two main patterns; circular and mesh-work. On the other hand sympathetic innervation of the intracerebral small arterioles could not be observed.

KEY WORDS :

Cerebral arteries, Sympathetic System, WGA-HRP.

INTRODUCTION

Many studies concerned with the sympathetic innervation of the cerebral blood vessels demonstrated that the noradrenergic nerve plexus, originating from the cervical sympathetic ganglia, developed on the wall of the cerebral arteries (8, 10, 13, 14, 15, 18). Since fluorescent histochemical staining techniques were used in these studies, the exact anatomical pattern and manner of the sympathetic innervation of the cerebral blood vessels were not fully understood. There are still many unsolved important problems, for instance; laterality and intensity of the innervation, innervation of the small pial arteries and the intracerebral arterioles by the peripheral sympathetic nerve; relation between the difference in the pattern of nerve plexus and controuing the tonus of the cerebral blood vessels (1, 5, 10, 11, 12, 13, 18, 20). These promlems are still obscure because the objective nerve fiber and nerve plexus could not be directly observed, and a fine nerve fiber and its terminals could not be traced clearly. Wheat germ aggulutinin conjugated horse radish peroxidase (WGA-HRP) has been used as a highly sensitive neuronal tracer which is able to label the entire course of the axon, from neuron to its terminal (4, 22). In the present study, we used anterograde labelling of the sympathetic nerve fibers originating from the superior cervical ganglion (SCG) in rats in order to demonstrate the nerve fibers and their terminals on the arterial wall. The goals of our study are to clarify the problem of the laterality of the innervation, the difference in the mode of nerve plexus on each arterial level, and extension of the peripheral sympathetic innervation to the arterial trees in the brain.

MATERİAL AND METHOD

Twenty albino Sprauge-Dawley rats weighing 200 to 250 g were anesthetized with an intraperitoneal administration of sodium pentobarbital (50 mg/Kg). Each animal was fixed supinely in a stereotaxic apparatus. The right SCG was exposed and 2 to 3 % of WGA-HRP (Toyobo) dissolved in 1M KCI, colored with Brilliant blue, was injected into the ganglion via a glass micropipette. The amount of WGA-HRP solution was 2 to 3microliter for full distribution into the ganglion. Two or three days after the injection, the rats were deeply reanesthetized with sodium pentobarbital and perfused transcardially with physiological saline followed by a fixative solution (2 % paraformaldehyde, 0.5 % glutaraldehyde, 0.1M phosphate buffer). Immediately after the perfusion fixation, the brain was taken out, and the main arteries of the base of the brain were carefully dissected out en bloc under an operative microscope. The arteries were reacted with the TMB method (16) and observed as a whole mount preparation.

RESULTS

The internal carotid nerve originating in the SCG ascended along the internal carotid artery (ICA) and

entered the neurocranium. The internal carotid nerve consisted of several bundles, some of which were running in the caudal direction and others advanced to the rostral circulation of the circle of Willis. Although thick bundles and fine fibers forming the nerve plexus were usually observed on the wall of the arteries in the ipsilateral side of the the circle of Willis and their branches, dual innervation was also observed on the anterior cerebral artery and superior cerebral artery bilaterally. The posteriorly directed sympathetic nerve fibers coursed along the posterior communicating artery to innervate the basilar artery (BA). The labelled fibers and plexus were observed on the wall of the lower part of the BA and bilateral vertebral artery (VA). In only approximately one third of the animals, were the labelled fibers and plexus observed on the wall of the upper part of the BA (Fig. 1)

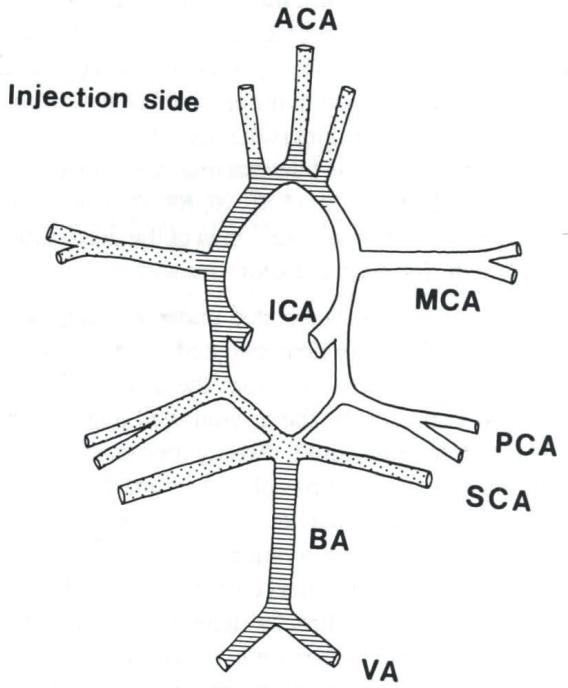

Fig.1 : Distirubiton of the labelled sympathetic nerve fibers on the cerebral arterial all after WGA-HRP injection into the right superior cervical ganglion. In the parts of oblique lines, bundles of nerve fibers were running parallel and fine nerve terminals were running perpendicular to the long axis of the vessel in a circular pattern of nerve plexus. In the parts of dots, nerve bundles and fine nerve fibers formed a mesh work pattern. ICA; internal carotid artery; ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; SCA, superior cerebellar artery; BA, basilar artery VA; vertebral artery.

The plexus of sympathetic nerve fibers on the arterial wall were classified into two main patterns depending on our observations. a- circular pattern perpendicular of the long axis, b-mesh-work pattern. Whilst the first pattern was observed in the ICA the proximal part of the ACA (A1 portion), middle cerebral artery (MCA) and posterior cerebral artery (PCA), BA and VA, (Fig. 2A, B), in the distal part of the

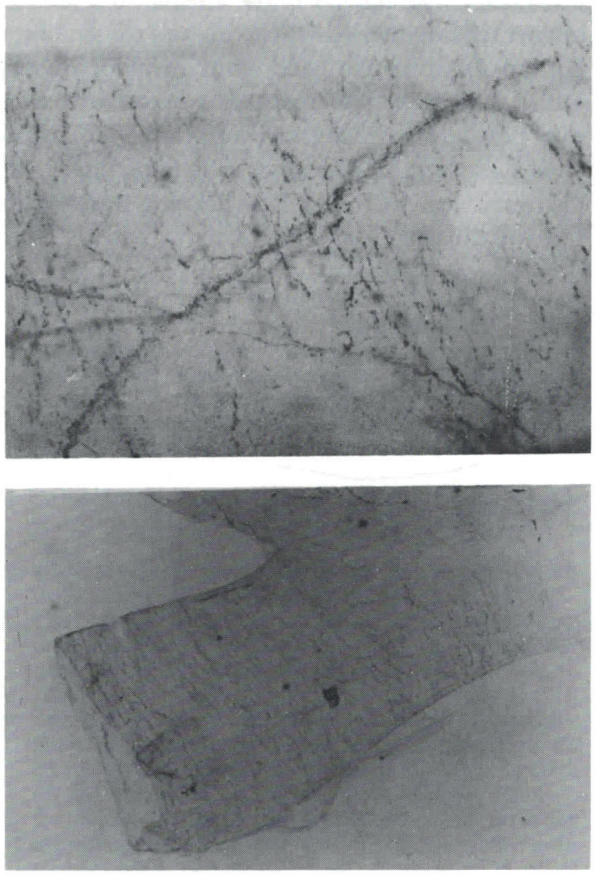

Fig.2 : A circular pattern of the nerve plexus on the wall of a - the anterior cerebral artery (10x40 magnification) b - The internal cerebral artery (10x10 magnification)

MCA, ACA, PCA and SCA, a mesh-work pattern of nerve plexus was seen (Fig. 3). The density of nerve plexus with a circular pattern was greatest in both the BA and VA. The mesh-work of nerve plexus on

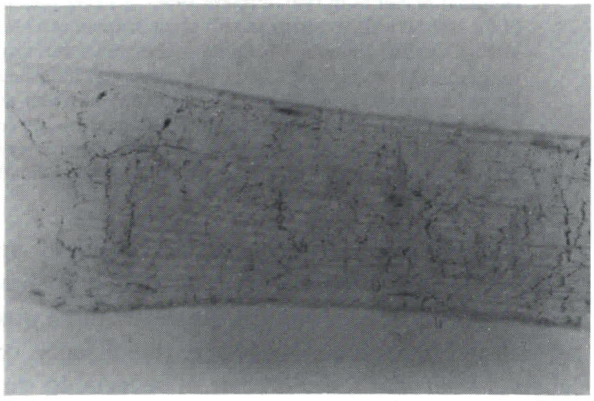

Fig.3 : A mesh work pattern of the nerve plexus on the wall of the middle cerebral artery (10x20 magnification).

each artery became weaker with the increase in the distance from the circle of Willis. On the wall of the proximal part of the ACA which usually showed a

fine nerve bundle was running almost parallel to the long axis of the vessel and terminal branches were branched perpendicular to the arterial long axis at almost regular intervals appearing as a rib-structure pattern. On the other hand, on the wall of arteries with a mesh-work pattern, the fine nerves were running parallel to the long axis of the artery and branched a few terminal branches as to innervate small districted area. A Camera lucid drawing of these patterns is illustrated in (Fig. 4A, B).

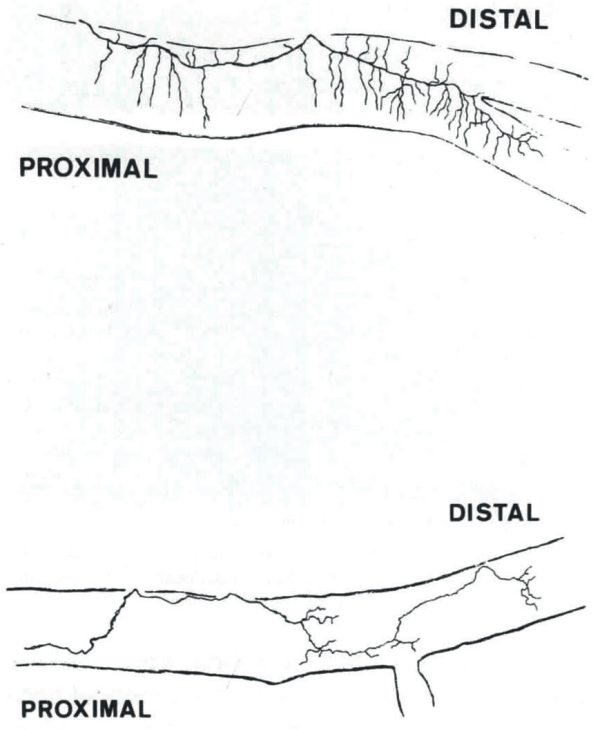

Fig.4 : Camera lucida drawing of the delicate nerve fibers and the terminal branches in two different types of nerve plexus of the arterial wall. A: proximal part of the anterior cerebral artery. A fine bundle of nerve fibers was running longitudinally to the long axis of the artery and branched nerve terminals perpendicularly to the nerve fibers at regular intervals. B: middle cerebral artery. Fine nerve fibers were running parallel to the long axis of the artery and branched a few terminal branches to innervate a small restricted area.

The labelled sympathetic nerve could be observed in the wall of the small arterial branches derived from the main arteries. However, there was no parallel correlation between the density of labelled fiber and the diameter of vessels. In the branches from the MCA or ACA, scanty or no labelled fibers were observed, although a more densely labelled plexus could be observed on the wall of arterial branches derived directiy from ICA. These findings indicated that the degree of the sympathetic innervation of small branches from the main arteries should be dependent on the density of the plexus of the parent artery and the distance from the ICA. The labelled sympathetic nerve on the small pial arteries of diameter of 20 to 30 micrometer, derived from ACA or PCA, were rarely observed on the cortex of cerebral longitudinal fissure or in the deep located cisterns. On the other hand, in the pial arteries originating from the branches of MCA over the cerebral hemisphere, no labelled fibers were observed. Furthermore, no sympathetic innervation of the intracerebral small arterioles could be observed.

DISCUSSION

In the previous reports, it was demonstrated that the main arteries belonging to the circle of Willis and its branches were commonly innervated by the ipsilateral side of SCG, and the arteries of the posterior circulation were overlappedly innervated by SCG and the stellate ganglion (STG) (10, 14, 15, 18, 20). In addition to this common manner, some of the arteries were described to be innervated by bilateral SCG, but distributed area of the bilateral innervation were different in each study (18, 14, 15, 20, 10). This discrepancy may suggest the technical limits of the denervation study with fluorescent histochemistry.

This and previously reported studies(21) using WGA-HRP in our laboratory demonstrated the entire course of the sympathetic nerve from the SCG to the fine terminal branches on the arterial wall (Fig. 4). This tracing technique could directly demonstrate the running course of the peripheral sympathetic nerve to the cerebrovascular vessel and the anatomical distribution of the innervation. Furthermore, observation of the labelled nerve fibers on each level of small vessels could directly demonstrate limitation of the peripheral sympathetic nerve innervation to the small arteries or arterioles. In this study the absence of labelled fibers on the intracerebral vessels could prove the previous studies performed by denervation technique that the peripheral sympathetic nerve did not innervate intracerebral small arterioles or capillaries (7, 8).

It has been reported that sympathetic nerve endings display a tonic adrenergic activity to constrict the cerebral blood vessels, although the significance of sympathetic nerves in regulation of cerebral blood flow is still controversial (2, 5, 9, 19). We suggested that the strength and quality of the vasoconstriction observed on the different cerebral vessels might be explained by these differences in the distribution pattern and density of the nerve plexus in each level of the cerebral arterial tree.

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