The “Richness” of Sympathetic Innervation
A Comparison of Cerebral and Extracerebral Blood Vessels

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SUMMARY The number of adrenergic nerves was quantified, on both cerebral and femoral blood vessels. No difference was found between the two vascular beds. The data failed to establish a “richer” innervation of cerebral vessels. This is in agreement with my previous, extensive, subjective and unpublished impression. Consequently, the suggestion of others, which ascribes certain features of cerebrovascular behavior to an unusually rich vascular innervation, remains unproved.

IT HAS BEEN SUGGESTED that cerebral blood vessels may be less responsive to norepinephrine (NOR) or to sympathetic stimuli than other vascular beds because they have a richer innervation.1 2 It is postulated that the rich innervation in some way protects the cerebral vessels from the effects of NOR. I have presented evidence that cerebrovascular nerves may not release NOR as readily as other vascular nerves when exposed to reserpine.3 4 However, it remains to be seen whether this phenomenon is related to unusually avid binding of NOR and, if so, whether this binding is responsible for the diminished responses of cerebral vessels to NOR or to sympathetic stimuli. In fact, in the resting state, the concentration of NOR in individual varicosities does not seem greater in cerebrovascular nerves than in nerves to other vascular beds.5 6 In any case, it must be stated that the concept of a “richer” innervation for cerebral vessels appears to imply a greater number of nerves than would be seen adjacent to extracerebral vessels. No evidence has ever been presented to support such a claim.1 2 In my experience, I have not been able to substantiate such suggestions. This brief report quantifies my observations concerning numbers of nerves, and consequently strengthens my previous subjective and unreported observations.

Methods

Male rats weighing 150 to 400 gm were used. Stretch preparations were made of vessels at the base of the brain and their adherent branches. These were compared with femoral artery stretch preparations similarly prepared from the same rats. The preparations were stretched on coverslips, dried overnight in a vacuum at room temperature and exposed to paraformaldehyde vapor according to the technique of Falck and Hillarp.6 This technique reveals NOR in nerves by producing a characteristic fluorescence. The preparations were evaluated by dark field, reflectance fluorescence microscopy using appropriate filters for the exciting light and emitted light and a monochromator to further analyze the emitted light. The monochromator was set at the wavelength of maximum emission of the fluorescent NOR. Use of the monochromator, together with a pinhole mask, has been described previously.3 5 The present study connected a photocell in series with the monochromator to a chart recorder. Each time a fluorescent nerve appeared in the aperture of the pinhole mask, it was recorded by the photocell and reflected as a spike on the chart recorder. The specimen was driven across the field by a motorized microscope stage, and in this way an entire width or length of a vessel branch could be scanned. Since the chart speed was known and the speed of the motorized stage was known, the number of spikes per linear millimeter of scanned vessel could be calculated. Each spike represented either a new nerve fiber or a varicosity on a fiber. A side-arm viewing tube carrying 20% of the light permitted the observer to directly monitor the nerves as they slowly entered and left the field under the mask aperture. Another observer simultaneously watched the pen on the recorder. In this way, it became clear that all nerves passing the aperture were “seen” by the photocell and recorded as a deflection of the pen. The system did not provide time responses sufficiently rapid to relate the amount of fluorescence to the height of the pen deflection or the area under the curve. In other words, some deflections appeared as blips on the shoulders of other deflections.

Results

Sixteen preparations of cerebral vessels were scanned from five rats, and 19 preparations were scanned from femoral vessels of the same rats. Four to 40 nerves or varicosities (peaks on the chart paper) were recorded from each preparation. The number of spikes per linear millimeter of cerebral vessels was 41 ± 16 per millimeter of vessel; femoral = 44 ± 16, mean ± SD. At no time during the course of the investigation was there ever a suggestion that nerves on the cerebral vessels were more numerous.

Discussion

The results failed to display any difference between the average number of adrenergic nerves on cerebral vessels and the average number on femoral vessels. They confirm my previously subjective impression. They do not substantiate suggestions of a “richer” innervation on cerebral vessels.1 2 Of course, they do not rule out the possibility that cerebral vessels are better innervated than some extracerebral bed other than the femoral. However, the present data, plus my earlier studies on the intensity of fluorescence,2 4 made it unlikely at this point that absolute numbers of nerves or absolute amount of NOR explained the relative insensitivity of cerebral vessels to exogenous or endogenous sympathomimetic stimuli.7

Suggestions of a “richer” innervation3 engendered some discussion at the recent Seventh International Congress on
Cerebral Blood Flow. It was suggested that the term "richer" might imply an unusually large number of nerve fibers in relation to the relatively low volume of smooth muscle around cerebral vessels. Such an extension of the "richer" hypothesis, of course, is not tested by the present data.

References


Clinical Implications of the Doppler Cerebrovascular Examination: A Correlation With Angiography

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SUMMARY A directional Doppler ultrasound cerebrovascular examination was compared with angiographical findings of 152 internal carotid arteries. The Doppler examination was abnormal in 36 of 38 (95%) arteries with occlusion or stenosis greater than 75%. Of 63 arteries with lesser degrees of stenosis, the Doppler examination identified only four. There were no false-positive Doppler examinations. If the decision to perform angiography had been predicated exclusively on the presence of abnormal Doppler findings, 61 of 101 (60%) carotid lesions of potential clinical significance would have been overlooked. While the Doppler ultrasound cerebrovascular examination is the most useful noninvasive technique available for the evaluation of certain specific categories of patients with cerebrovascular disease, the technique is based on hemodynamic alterations of pressure and flow, and cannot be expected to identify the relatively large number of non-hemodynamically significant carotid lesions that are still clinically significant as sources of emboli. This paper illustrates that in the routine evaluation of patients with symptomatic cerebrovascular disease, the Doppler examination should not play a part in the decision to proceed with angiography.

cerebral thromboemboli may originate from plaques which do not significantly narrow the carotid lumen, the clinician must be mindful that some patients with non-stenotic but nonetheless clinically significant lesions will perforce be found to have a normal Doppler examination.

The clinical implications of the Doppler cerebrovascular examination findings in 76 patients referred with suspected cerebrovascular disease, who also had conventional contrast angiography, constitute the basis of this report.

Methods

Patients

The clinical records, Doppler findings, and available angiograms of 227 consecutive patients with symptoms of cerebrovascular disease who were evaluated between January, 1974, and July, 1975, were reviewed for this study. Of this group, both angiograms and Doppler examinations of 76 patients (152 carotid arteries) were available for comparative analysis. There were 75 men and one woman; the average age was 59 years with a range of 43 to 82 years.

Doppler Examination Technique

Our modification of Brockenbrough's original technique of Doppler ultrasound assessment of ophthalmic artery directional flow has been the subject of a prior report. In brief, this examination was based upon the fact that the ophthalmic artery served as a major conduit of collateral...
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Stroke. 1976;7:270-271
doi: 10.1161/01.STR.7.3.270

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