PATHWAY OF CENTRIFUGAL FIBRES IN THE HUMAN OPTIC NERVE, CHIASM, AND TRACT*†

BY

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THE pathway of the centrifugal (efferent, antidromic) nerves has been studied histologically in the optic nerves, chiasm, and optic tracts of a patient who had both eyes enucleated 50 years before.

Centrifugal fibres in the optic nerve of animals have been known to exist for a long time (Cajal, 1894; Dogiel, 1895), and this fact is supported by recent physiological observations (Granit, 1955; Dodt, 1956). There can no longer be much doubt that a great number of centrifugal nerves also exists in the human optic nerve. Numerous remaining nerve fibres in two atrophic nerve stumps eleven and sixteen years after enucleation were the first evidence (Wolter and Liss, 1956). Subsequently, the terminal branches of centrifugal nerves were demonstrated in the normal human retina and optic nerve (Liss and Wolter, 1956; Wolter, 1957a) and it was concluded that at least some of the centrifugal nerves supply blood vessels. The observation of interrupted neurites in the human nerve fibre layer with terminal swellings pointing away from the optic disc was further evidence of the presence of centrifugal fibres (Wolter, 1956). Attempts at regeneration of centrifugal fibres were observed in a child's optic nerve stump eleven days after enucleation (Wolter, 1960) and later the reactions of these fibres could be studied four days after enucleation (Pfister and Wolter, 1963) in another case. A peculiar proliferation (hyper-regeneration) of centrifugal nerves was observed around blood vessels and micro-aneurysms in advanced diabetic retinopathy (Wolter, 1961). Very recently the remaining centrifugal nerves in the human optic disc were examined histologically ten days after complete occlusion of the central retinal artery that caused necrosis of the ganglion cells and all centripetal (afferent) retinal nerves (Wolter, n.d.). This latter study allowed for the conclusions that there are several morphologically different types of centrifugal nerves and that about 10 per cent. of the nerves in the normal human optic disc are centrifugal in nature.

Case Report

A 79-year-old Negro male died on December 12, 1963, at Hurley Hospital in Flint, Michigan, of cachexia and liver cirrhosis with ascites and hydrothorax. Surgical absence of both eyes was observed at necropsy—along with much other pathology that is of no interest in this study. The history revealed that in 1913 the patient injured his right eye with a branch while hunting.

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FIG. 1.—Gross view of the chiasm with the atrophic optic nerves (n), the pituitary stalk (p), and the internal carotid artery (i). $\times 3$.

FIG. 3.—Nerve fibres with pearl-string-like myelin swellings on a parallel course in the right optic nerve stump. Frozen section, Hortega stain, photomicrograph $\times 450$.

FIG. 2.—One of the serial frozen sections through the chiasm (ch), with end of the optic nerves (n), and the optic tracts (t). Frozen section, Hortega stain, photomicrograph $\times 10$.

FIG. 4.—Nerve fibres with myelin swellings on an irregular course in the right optic nerve next to the chiasm. Frozen section, Hortega stain, photomicrograph $\times 450$.

Removal of this eye was advised, but the patient refused. Sympathetic ophthalmitis developed and involved the other eye. Finally, both eyes had to be removed.

Fifty years after the bilateral enucleation the brain with the atrophic chiasm and optic nerve stumps (Fig. 1) was obtained for this study.

Pathological Findings.—The brain was fixed in formalin. Frozen sections were cut of the optic nerve stumps, the chiasm (Fig. 2), and the optic tracts. The Hortega silver carbonate technique for staining nerves (Scharenberg and Zeman, 1952) was used.

Both optic nerve stumps still contained many nerve fibres (Figs 2 and 3). The axons of these nerves were continuous and stained well. Their myelin sheath, however, was of irregular distribution with nodular swellings and areas of attenuation alternating. In the areas of the nodular myelin swellings the axon usually also exhibited some swelling and an irregular course (Figs 4, 8,

FIG. 5.—Thin "unmyelinated" nerves criss-crossing between chiasm and pituitary stalk. Frozen section, Hortega stain, photomicrograph $\times 400$.

FIG. 6.—Terminal bulb of interrupted thin nerve (t) in the chiasm pointing towards the optic nerve stump. Frozen section, Hortega stain, photomicrograph $\times 400$.

FIG. 7.—Two thin "unmyelinated" nerves (arrows) joining the other fibres of the left optic nerve stump. Frozen section, Hortega stain, photomicrograph $\times 400$.

FIG. 8.—Nerves with nodular myelin swellings in right optic tract. Frozen section, Hortega stain, photomicrograph $\times 500$.

FIG. 9.—More distinct stain of axons showing irregularities within the areas of nodular swellings of nerves in the left optic tract next to lateral geniculate body. Two hyaline bodies (arrows) are also seen. Frozen section, Hortega stain, photomicrograph $\times 500$.

and 9). This degenerative change of optic nerve fibres with nodular myelin swellings has been recognized before and has been called "pearl-string-like nerve degeneration" (Wolter, 1957b). Other nerves—fibre tracts next to the optic tract, for example—did not show this pearl-string-like change. There were also numerous hyaline bodies of nerve fibre origin (Wolter and Liss, 1959) all through optic nerves, chiasm, and optic tracts of this case. Mixed with the majority of nerve fibres with pearl-string-like degeneration were fewer neurites that had virtually no myelin sheath. These "unmyelinated" neurites seemed to increase in number as one progressed from the distal ends of the optic nerve stumps towards the chiasm. All nerves of the optic nerve stumps were arranged in the regular pattern of fibres on a parallel course (Fig. 3).

The pattern of the nerve fibres with nodular myelin swellings became more irregular next to the chiasm (Fig. 4). At the chiasm about half of these neurites were seen to cross from the optic tract of the other side. The other half was seen to come more or less directly from the optic tract of the same side.

At the back of the chiasm there were some thin "unmyelinated" nerve fibres criss-crossing and extending into the chiasm from a posterior direction (Fig. 5). A reconstruction showed that these nerves came from the pituitary stalk. We could not be certain from what direction these thin fibres came in the pituitary stalk, but our impression was that they were ascending. A few of the thin fibres which were seen to come from the pituitary stalk and to join the chiasm were interrupted and showed rather large terminal swellings (Fig. 6). All these terminal swellings pointed towards the optic nerve stumps. In the optic nerve stumps the same thin "unmyelinated" nerves could be recognized (Fig. 7).

Most of the nerves of the optic nerve stumps—and all fibres with the pearl-string-like myelin swellings—could be traced into the optic tracts. They were still present in the optic tracts in a region immediately adjacent to the lateral geniculate bodies (Figs 8 and 9). The drawing (Fig. 10) is to explain the course of the centrifugal nerves found in this case.

FIG. 10.—Drawing to give impression of the course of the two types of centrifugal nerves. One type (with myelin nodules) goes from optic tracts (T) by way of chiasm (CH) to the optic nerves (N). The other thin nerve type comes into the chiasm from pituitary stalk (P). The location of numerous degeneration bulbs of interrupted thin nerves is indicated.

Discussion

The centrifugal (efferent) and centripetal (afferent) fibres of the normal human optic nerve, chiasm, and tract look alike in a histological section. Therefore, it is impossible with present-day techniques to find the pathway of the centrifugal nerves in a normal human brain. The period of 50 years after bilateral enucleation in the present case must have caused complete atrophy of all centripetal nerves. All remaining nerves in the optic nerves, chiasm, and tracts must, therefore, be centrifugal in nature. It is already known that the centrifugal nerves show only partial or no retrograde degeneration (Wolter and Liss, 1956). Thus, this case represents a unique opportunity to study the pathway of the centrifugal fibres of the human optic nerve.

At first, this study revealed that continuous centrifugal nerve fibres survived in the optic nerve stumps 50 years after bilateral enucleation. Most of the remaining fibres in the optic nerve stumps of the present case showed a peculiar pearl-string-like

degenerative change of their myelin sheath that also involved the axon. This change is well known to us from atrophic optic nerves due to other causes (Wolter, 1957b; Wolter and Liss, 1959) and it serves very well in this study for an easy recognition of the remaining optic nerve fibres all the way up to the lateral geniculate body.

All fibres with the pearl-string-like myelin change could be traced to the optic tracts next to the lateral geniculate bodies. It cannot be said as yet whether the fibres originate there or whether they just pass through the lateral geniculate body and really have another origin. About half of the fibres with the pearl-string-like change were seen to cross in the chiasm while the other half remained uncrossed. In the optic nerve these fibres formed no distinct bundle, but were distributed about evenly.

Additional thin fibres virtually without a myelin sheath were found in both optic nerve stumps. These fibres could be traced into the chiasm. All these "unmyelinated" fibres, however, were seen to come into the chiasm from a posterior direction—from the region of the pituitary stalk—and not from the optic tracts. No fibres of this type were found in the optic tracts. In this case it has not been possible to trace the thin centrifugal nerves which come from the pituitary stalk to their origin. These nerves are of the greatest interest, of course. Extensive hyper-regeneration of terminal centrifugal nerves around blood vessels and micro-aneurysms was demonstrated several years ago as "the only specific pathologic change of diabetic retinopathy" (Wolter, 1961). The presence of such fibres connecting pituitary stalk and eye could perhaps also be important in relation to the fact that removal of the pituitary gland or pituitary stalk section has both been found to improve advanced diabetic retinopathy.

Summary

Nerve fibres were still present in the optic nerve stumps 50 years after bilateral enucleation and represent new evidence for the existence of centrifugal fibres in the human eye. These nerves were traced back through the chiasm into the optic tracts. About half of them were seen to cross at the chiasm while the other half was observed to come from the same side. Additional "unmyelinated" fibres found in the optic nerve stumps were seen to come from the pituitary stalk.

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