AN ANALYSIS OF FIBRE-SIZE IN THE HUMAN OPTIC NERVE*

BY

L. W. CHACKO

DEPARTMENT OF HUMAN ANATOMY,
UNIVERSITY OF OXFORD

DATA on the fibre-size " spectrum " in the optic pathways must form an essential anatomical preliminary to electro-physiological studies of the visual neural system. Extensive studies on peripheral nerves have brought to light some of the factors on which the differences of calibre of nerve fibres appear to be based. Studies of fibre-size in the central nervous system have been carried out by Häggquist (1936) on the spinal cord, and by Szentágothai-Schimert (1941) on several of the important pathways of the brain.

It has been recognised from the time of Gudden (1886) that the optic nerve contains myelinated fibres of graded size. Arey and his co-workers in their extensive investigation on the quantitative (and to a certain extent qualitative) composition of the optic nerve in a series of vertebrates, observed that in man all the fibres are myelinated and are of widely varying size. A considerable body of electro-physiological work on the optic nerve has been completed on frogs, rabbits and cats, and attempts have been made to group the fibres in this nerve on a physiological basis using conduction rate, threshold to electric stimuli, refractory period, time to maximum, etc., as criteria for grouping. In the histological study which this work entailed the authors arbitrarily distinguished certain fibre-sizes and attributed to them certain physiological properties. As yet, however, no systematic analysis of the range and frequency of the fibre-sizes in the optic nerve has been attempted. The importance of this investigation is emphasised by the findings of Granit that the electrical activity in the optic nerve (as recorded from its constituent fibres by his micro-electrode technique) indicates a specific sensitivity of the related receptors and their associated neurons in the retina to monochromatic lights. Such elements in the retina, possessing specific sensitivity to different wave-lengths of light, will give rise to impulses which are probably conducted along nerve fibres of one particular type in preference to others. The qualitative variations of nerve fibres so far recognised are the varying thickness of the axis cylinder and of the myelin sheath, and the presence or absence of the sheath of Schwann and the nodes of Ranvier. The present investigation deals with fibre-sizes, which are analysed in detail.

Material and methods

Human optic nerve sections of 5μ thickness were prepared and several standard silver and myelin stain techniques were employed.

* Received for publication, May 7, 1948.

Of these, Weigert-Pal preparations were found most suitable for measurement, while the others were used for the purpose of checking and confirmation. The particular specimen which was used for measurement was the optic nerve of a man, aged 61, in whom no defective vision or any other affection of the visual system was reported. No reduction in the size of the fibres of the central nervous system is apparent at that age according to the report of Szentágothai-Schimert (1941).

In order to measure the diameter of the fibres and to group them simultaneously, a method was devised (Allison and Chacko, 1948) in which an Abbé camera lucida was used to superimpose the image of a scale with lines of graded thickness corresponding to the range of size of the nerve-fibres in the optic nerve. The scale is so prepared and calibrated that when the width of a line coincides in its image with the diameter of a nerve fibre it indicates the actual diameter as well as the size-group to which it belongs. Thus, it is possible to arrange the fibres into groups of smaller range than those adopted by Häggquist or Szentágothai-Schimert. A square corresponding to $(60\mu)^2$ area of the microscopic field and containing 25 small squares each $(12\mu)^2$ was drawn and fixed under the mirror of the camera lucida. The nerve fibres in each small square were measured one after the other and ticked off. From the average number of fibres within the area $(60\mu)^2$ the total number of fibres in the optic nerve was also estimated in the usual way.

It was found that in a well-prepared section the myelin rings are undistorted and in fibres cut transversely appear as smooth circles. However, in their course through the optic nerve, the constituent fibres undergo a certain amount of rearrangement and in cross-sections of the nerve, many fasciculi may be seen running a more or less oblique course as they change their relative positions. Such fibres appear in sections as oval or rod-shaped, and in this case it was decided to take the short diameter as approximating to the true diameter of the fibres. The total diameter of the fibres (including the myelin sheath) was measured in each case. Measurements of about 4,000 fibres contained in fifteen fields of $(60\mu)^2$ along eight radii of the cross-sectional outline of the nerve were taken and grouped in $\frac{1}{2}\mu$ ranges. The frequency percentages of these groups were then calculated and a histogram was drawn.

Results

The human optic nerve contains fine, closely packed, myelinated fibres without Schwann sheaths; these fibres exhibit a continuity in range of size from the smallest to the largest diameter (Fig. 1). The minimum calibre measured was $0{\cdot}7\mu$ and the maximum $8{\cdot}0\mu$, and very occasionally fibres of $10{\cdot}0\mu$ sizes were also noted (Fig. 1*c*). The histogram (Fig. 2) shows that the greatest frequency of the fibres is under $1{\cdot}0\mu$ and the next greatest from $1{\cdot}0$ to $2{\cdot}0\mu$, at which

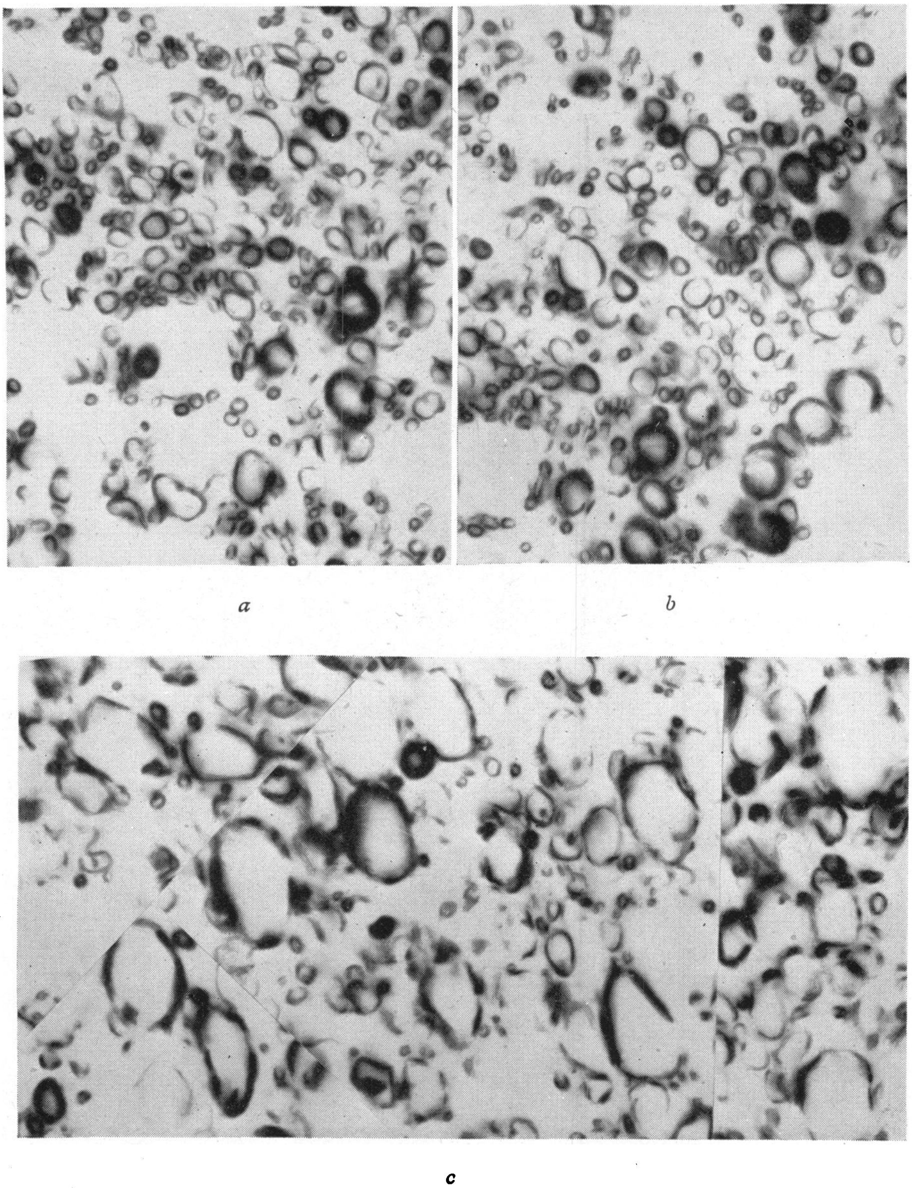

Fig. 1.

Microphotographs of Weigert-Pal preparations of the optic nerve in man. Magnification ×1000. (*a*) Note the variation in the sizes of fibres, their distribution, and the predominance of small fibres of about 1μ size. (*b*) In this particular region fibres of 4-6μ size appear in greater number. (*c*) Microphotograph of the same preparation from regions where large fibres of about 10μ form the outstanding feature.

level the frequency drops rather steeply towards the base line and then more gradually in the direction of the larger fibres with an indication of a second low rise in the region of 5·0 to 7·0μ. This last feature was more pronounced in confirmatory measurements carried out from other preparations.

Minute " dots and rods," mentioned by Brodal and Harrison (1948) as indicative of the possible existence of minute myelinated fibres in the central nervous system, were not particularly evident in any of our preparations although their presence could not be positively excluded. Moreover, the continuous range that characterises the sizes between 0·7μ and 8·0μ did not extend below 0·7 down to the sizes indicated by " dots and rods " that may be present. The total number of optic fibres in the human optic nerve was estimated to be between 815,000 and 1,000,000 fibres.

Comments

The histogram of the fibre-calibre of the optic nerve corresponds very roughly to the first of the two peaks of the fibre size histogram

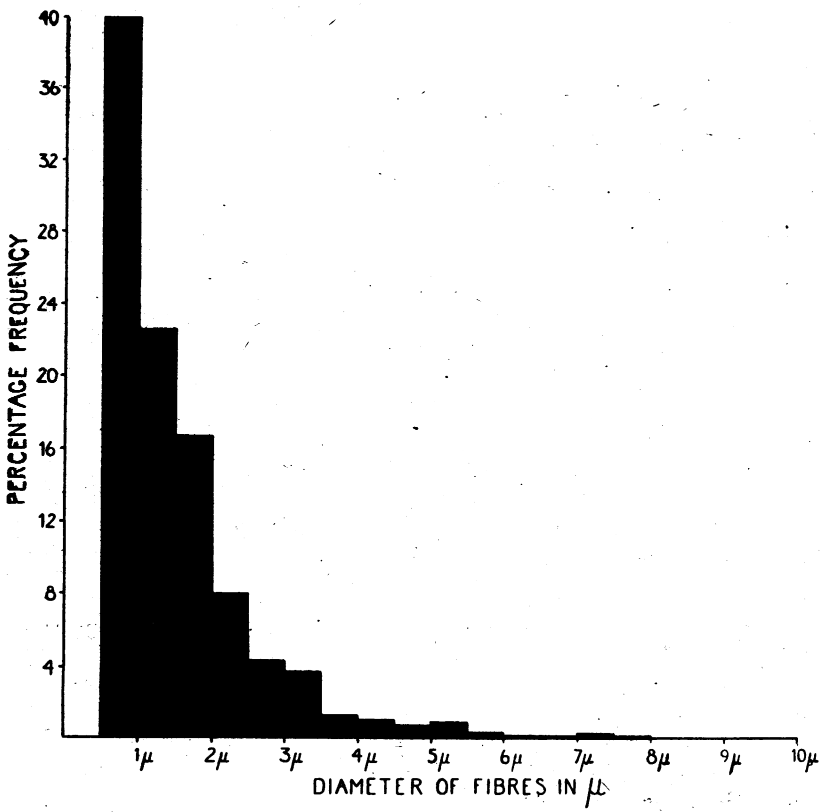

FIG. 2.

Histogram of the percentage distribution ofa bout 4000 nerve fibres of various sizes in the human optic nerve in somatic motor (Häggquist, 1937) and somatic sensory nerves (Szentágothai-Schimert, 1941), with the difference that the maximum is shifted to the left, showing a much higher frequency in the under-2μ range. It approximates more closely to the range and frequency in visceral nerves. There is a closer comparison, however, between the height and position of the maximum in the optic nerve histogram and that of the pyramidal pathway in the basis pedunculi which, as shown in the investigation of Szentágothai-Schimert, is due to the inclusion in it of cortico-pontine fibres. The picture of the ponto-cerebellar tract is also similar (Szentágothai-Schimert 1941).

The second much smaller maximum at about 5-7μ may also be significant in view of the possibility that these fibres are related to the larger cell layers of the lateral geniculate body.

Polyak (1942) has observed that the optic fibres proceeding from the periphery of the retina towards the optic disc are thicker than those from the macula. He also points out that the larger ganglion cells are more numerous towards the periphery of the retina and small ganglion cells towards the area centralis and that, generally speaking, the larger cells send out thicker axons than the smaller cells. The possibility may be conjectured, therefore, that the disproportionately large number of fine fibres in the human optic nerve (as compared with other mammals) proceed mainly from the small ganglion cells, possibly from the midget ganglion cells which are in the majority in the macula. The increase in the midget ganglion cells and their related midget bipolars and cones in the central area of the retina (Polyak 1942), the relative increase in the number of fine fibres of the optic nerve, and the remarkable increase in the number of small cells in the central vision area of the lateral geniculate body in the ascending phylogenetic series (Chacko 1948), appear to be consequent upon the differentiation of central vision. The higher frequency of fine fibres, the great number of monosynaptic connections and neurons of smaller size in contrast to thicker fibres, converging pathways and larger neurons are interesting features of the visual neural system. If the suggestion proves to be correct, that the nerve fibres forming the macular pathways from the retina to the cortex are of relatively smaller calibre, then the current idea that the relatively thicker and fast-conducting fibres convey impulses destined for the visual cortex, while the thinner slow-conducting fibres only reach the tectum, will need to be revised. However, increase of fibre diameter is only one of the factors related to a higher conduction velocity (Young 1946). An alteration of the histochemical properties of its sheath may have the same result. As is clear in Fig. 1, the fine fibres have a distinct myelin sheath, but there is a relatively greater thickness of myelin sheath in the finer fibres. The nature of the sheath in these fine fibres is well worth study with the technique of polarization optics and X-ray diffraction analysis. Histograms of the optic nerve fibre-calibre in clinical cases of toxic amblyopia where the macular bundle is mainly affected, or in experimental lesions of the macula, and also a comparative study of the normal histograms in a series of primates and sub-primates, should throw further light on the subject; work along these lines is in progress.

I wish to thank Prof. W. E. Le Gros Clark for encouragement and advice while carrying out this work.

REFERENCES

ALLISON, A.C. and CHACKO, L. W. (1948).—*Jl. Royal Microscopic. Soc.* (In the Press)
BRODAL, A. and HARRISON, R. G. (1948).—*Quart. Jl. Micr. Science*, Vol. LXXXVIII, Series 3, No. 4 (In the Press).
CHACKO, L. W. (1948).—*Jl. Neurology, Neurosurgery and Psychiatry* (In the Press).
GUDDEN, B. von (1886).—*S. B. Ges. Morphol. Physiol., Münch.*, Vol. I, p. 169. Quoted by G. H. Bishop and J. O'Leary, *Jl. Neurophys.*, Vol. III, 1940, p. 308.
HÄGGQUIST, G. (1936).—*Z. Mikrosk. Anat. Forsch.*, Vol. XXXIX, p. 1.
——— (1937).—*Ibid.*, Vol. XLII, p. 1.
POLYAK, S. L. (1942).—The Retina. The University of Chicago Press.
SZENTÁGOTHAI-SCHIMERT, J. (1941).—*Z. f. Anat. u. Entwick. Gesch.*, Vol. CXI, p. 201.
YOUNG, J. Z, (1945).—Essays on Growth and Form, Ed. by W. E. Le Gros Clark and P. B. Medawar. Oxford Univ. Press.

ACUTE RETINOPATHY WITHOUT HYPERPIESIS IN DIABETIC PREGNANCY*

BY

R. D. LAWRENCE

OF THE DIABETIC DEPARTMENT, KING'S COLLEGE HOSPITAL, LONDON

I HAVE recently seen acute haemorrhagic retinopathy in two pregnant diabetic women such as has not hitherto been described. Retinopathy is all too common in *long-standing diabetes*, but is a slow process with characteristic venous haemorrhages and exudates developing slowly over years, although a form which quickly develops into retinitis proliferans is occasionally seen. The severe *toxaemia* of *pregnancy* too produces an acute retinopathy with oedema, papillitis, severe haemorrhages, " albuminuric " in nature and appearance, always associated with hypertension, albuminuria and toxaemia. The following two cases fall into neither of the above categories, have not been described in ophthalmology or diabetic literature and presented a novel problem as to the termination of these pregnancies. The condition must be very rare and I have seen it in only 2 of some 200 diabetic pregnancies closely followed and is so striking in visual defect that I could not have missed other such cases.

* Received for publication, March 19, 1948.