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THE SIZE AND GROWTH OF THE HUMAN OPTIC NERVE

BY

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Marked agenesis or atrophy of the intracranial portion of the optic nerve is easily detected but, when these abnormalities are moderate or slight, their detection is often difficult and often creates a need to assess the size of the nerve during pathological examination of the nervous system. However, lack of measurements at different ages from birth to maturity have made this task hard to achieve and so it was decided to measure the diameters of the intracranial portion of a number of optic nerves. This paper reports the findings.

Published figures for the diameter of the nerve have been expressed in one dimension only as though the nerve had a circular cross-section. This is correct for the intraorbital part but, in the intracranial section, the more accessible part and the site of measurement in this study, is more often elliptical. Scammon and Armstrong (1925) measured the optic nerve just before the constriction at the bulbus oculi and reported the diameter to be 2·8 mm. at birth. Vierordt (1906) found the diameter of the adult optic nerve to be 3·2 mm. at a point 2 mm. behind the lamina cribrosa. The site of measurement reported by other workers is not clear. Keeney (1951) found the diameter to be 2·7 mm. at birth and 3 to 4 mm. at puberty. Hervouët (1958), without giving the number of cases observed, reported the diameter to be 2 to 4 mm. at 3 months and 3 to 4 mm. at puberty.

The square area of the cross section of the optic nerve was estimated in its intraorbital part in three cases by Salzer (1880) and found to be 7·03, 8·13, and 8·76 sq. mm. Donaldson and Bolton (1891) measured the square area of both nerves in 10 adults. Seven of them were males who had a mean cross-sectional area of 12·79 sq. mm. (9·07-17·37 sq. mm.); three females had a mean area of 10·46 sq. mm. (8·74-11·61).

Materials and Methods

Optic nerves of 210 patients came from various sources. Some were obtained from 12 premature infants whose mean birth weight was 2,023 g. (4 lb. 6 oz.), S.D. = ± 410 g. (14 oz.), of whom 10 were born alive and two were stillborn. Others were available from 18 mature infants whose mean birth weight was 3,398 g. (7 lb. 6 oz.), S.D. = ± 496 g. (1 lb. 1 oz.), of whom eight were born alive and 10 were stillborn. The brain of one premature infant of birth weight 910 g. (2 lb.), who lived 25 hours, had incomplete formation of gyri, otherwise all the infants' brains were well formed. The brains of the remaining 180 patients, mostly low-grade mental defectives from whom nerves were acquired, had been collected in the Neuropathology Department at the Fountain Hospital over a period of nine years. Many of the brains were light in weight and had pathological changes found in this field of study such as gliotic encephalopathy, lipidosis, and microgyria. A number had mongolism.

However, included in the total of 180 there were 26 brains which were of normal weight and showed no naked-eye abnormality. They were either of high-grade mental defectives or of mentally normal patients whose tissues were used for control purposes. Wherever possible, both optic nerves were measured but in many cases, because the brain had been dissected, it was only possible to measure one nerve. The material had been fixed in neutralized 10% formaldehyde B.P. in normal saline.

Measurements were made in a gauge specially designed for this survey. The gauge (Fig. 1) was made of two pieces of transparent acrylic sheet (perspex) 3 mm. (2/16 in.) thick measuring 30 × 6 cm. Adjacent edges of each piece had been accurately cut so that, when they were placed together, they formed a slender V, the sides of which opened to 1·0 cm. at a distance of 20 cm. from the angle, which was indicated as zero. One side of the V was calibrated in 10 divisions, each of which represented the distance in millimetres between the sides of the V. It was possible to subdivide the space between each division by 10 and measure to 0·1 mm. The two pieces of perspex were fixed rigidly by four screws to a brass plate at either end, the whole gauge being mounted on a stand.

The fixed nerves were removed from the brain, stripped of any extraneous tissue and inserted into the V of the gauge by being held at one end in forceps. Each nerve was measured at a point 3-7 mm. from the centre of the chiasma and was held vertically and moved down the gauge until its progress was gently impeded. Force was avoided. At this point the nerve is elliptical and so the major and minor axes of the nerves were presented to the gauge and adjustments made until constant readings were

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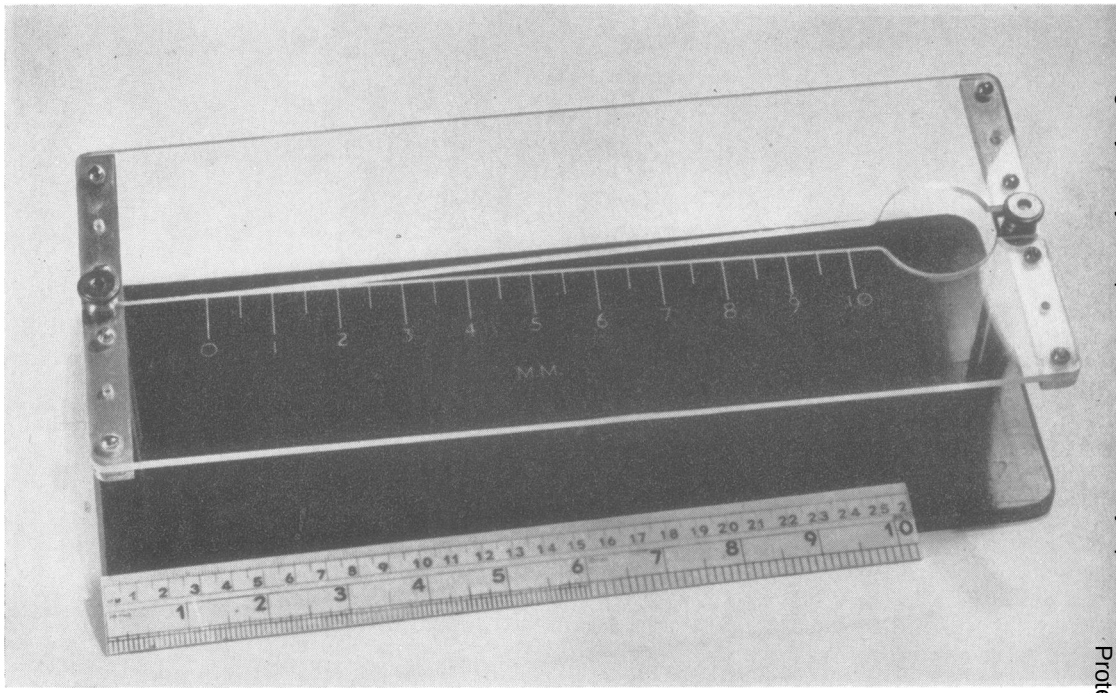

FIG. 1.—The gauge used for the measurements.

achieved in each diameter. Some of the infants' nerves were less firm than those of older children and could not be inserted into the gauge satisfactorily. They were measured by means of small geometrical dividers which were not found to be so convenient or accurate as the gauge. The measurements were grouped, according to the age of the patient. from birth to adult. (This group included patients of 12 years and older since the brain is often considered to attain adult size at about 12.) The area of the cut surface of each nerve was calculated from the formula π ab where a = half the major axis and b = half the minor axis.

Nerves were also measured from brains of 26 children who had optic atrophy.

Results and Discussion

The range, means, and standard deviation of the two axes and the area of the cross section of the optic nerves are presented in Table I; from these figures a graph (Fig. 2) was constructed. It will be seen that the curves, particularly that of the square area, indicate an increase in size from birth to the age of 4 years, after which the curve straightens. A possibility that the cases did not have a curve of normal distribution and hence could not belong to the same sample was tested. In the age groups 1 to 2 years, 2 to 3 years, and adult, it was possible

TABLE I

RANGE, MEAN, AND STANDARD DEVIATIONS OF MAJOR AND MINOR AXES AND CROSS-SECTIONAL SQUARE AREA OF INTRACRANIAL PART OF OPTIC NERVES DERIVED FROM 210 PATIENTS

	No.	Major Axis			Minor Axis			Area		
		Range	Mean	S.D.	Range	Mean	S.D.	Range	Mean	S.D.
Premature infants	12	1·5-3·0	2·50	±0·60	1·0-2·0	1·69	±0·47	1·18-4·71	3·41	±1·05
Infants newborn S.B.	18	2·4-3·5	2·82	±0·38	1·5-2·7	1·90	±0·18	2·36-7·43	4·27	±1·12
Infants 0-6 months	6	2·2-3·2	2·7	±0·36	1·7-2·2	2·05	±0·17	3·21-5·53	4·44	±0·86
Infants 6-12 months	6	2·3-3·3	3·03	±0·37	2·1-2·6	2·25	±0·17	3·8-6·74	5·39	±0·89
1-2 years	33	3·1-4·5	3·58	±0·336	1·8-3·1	2·43	±0·27	4·53-10·84	7·19	±1·56
2-3 years	25	3·0-4·5	3·81	±0·35	1·9-3·2	2·76	±0·356	5·42-10·60	8·34	±1·53
3-4 years	19	3·5-4·5	3·93	±0·31	2·6-3·4	2·86	±0·29	6·79-12·02	8·90	±1·47
4-5 years	18	3·5-4·4	3·96	±0·26	2·2-3·4	2·89	±0·363	6·88-11·75	9·12	±1·56
5-6 years	11	3·7-4·5	4·15	±0·17	2·6-3·5	3·01	±0·281	7·76-12·37	9·84	±1·48
7-10 years	16	3·0-4·6	4·03	±0·47	2·1-3·6	3·04	±0·431	4·95-12·37	9·76	±2·18
Adults	16	3·7-4·8	4·22	±0·26	2·6-3·3	2·99	±0·225	5·51-11·92	9·93	±0·33
Adults diseased	30	3·5-4·7	4·02	±0·39	2·1-3·9	2·80	±0·37	5·75-13·01	8·95	±1·99

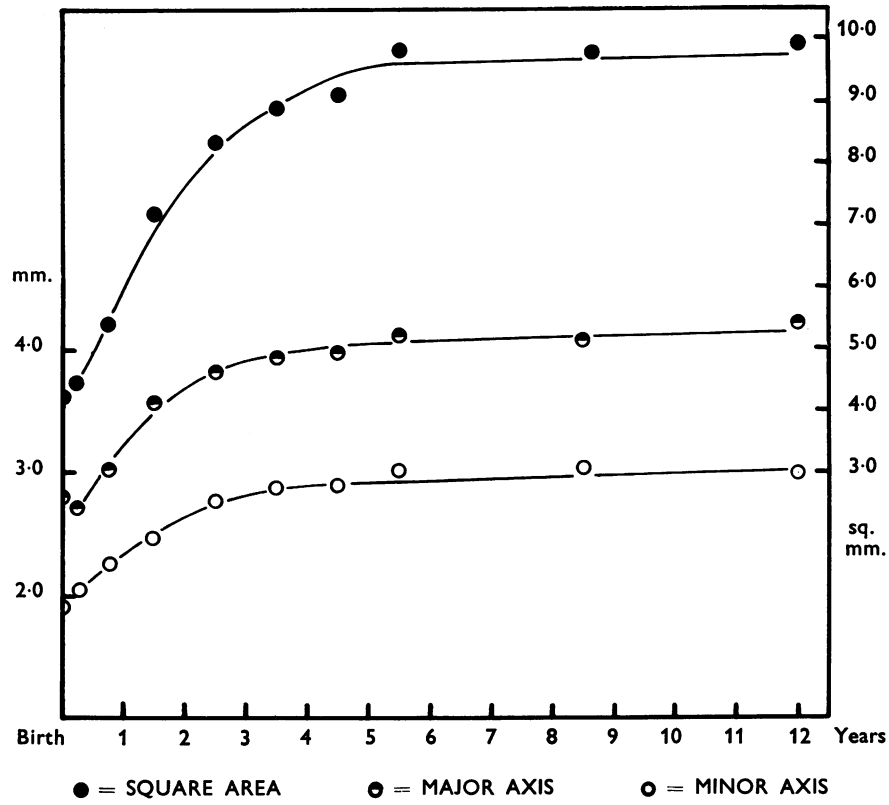

FIG. 2.—The cross-sectional area in square mm. (upper curve), the major axis (middle curve), and the minor axis in mm. (lower curve) of the optic nerve at ages from newborn to adult life, charted from measurements made on 210 patients.

to split each group into two subgroups. One of these contained the brains with known pathological changes, such as gliotic encephalopathy and lipidosis. The other group used as a control consisted of cases in which the brain appeared normal to the naked eye, control specimens from patients who had healthy nervous systems during life and had died from other causes, and mongol brains which had well-formed optic nerves. Student's t test and the F test were applied to these two subgroups. It was found that, in the age groups 1 to 2 years and 2 to 3 years, there was no significant difference between the control and pathological groups, so they were combined into one larger sample. However, in the case of the adults, the differences were on the borderland of significance, therefore only the control half of the sample was used in charting the graph. Differences due to sex were not significant.

Table II presents the measurements of the 26 brains of patients who had optic atrophy. The range and standard deviations of any particular age in the main sample seem to be large, which would make impossible the detection of moderate or slight abnormalities. Comparison with Table II suggests that severer abnormalities can be detected with certainty from 3 to 4 years since, at that time and beyond, the ranges of the comparative groups differ appreciably.

Alterations in the size of the nerves due to fixation were estimated by measuring 20 pairs of optic nerves in the fresh state and one month after fixation in similar formaldehyde solution to that used for the other optic nerves. Cross-sectional areas were calculated as in the main sample. These results are given in Table III. Nerves were not suspended during fixation and many of them became flattened and more oval so comparison of the changes before and after fixation were made on the cross-sectional areas. Thirty-four nerves shrank in the fixative and there was a wide range in the extent to which this varied, for instance 52·1% (in one nerve of Case 5) to 2·0% (in Case 12); three nerves showed no change and three nerves appeared to swell. The mean effect was that of shrinkage to the extent of 12·3%. Since the soft consistency of the unfixed nerves made handling, and thus measurements, difficult, there was a significant difference ($P<0·05$)

TABLE II

RANGE, MEAN, AND STANDARD DEVIATIONS (WHERE APPLICABLE) OF MAJOR AND MINOR AXES AND CROSS-SECTIONAL SQUARE AREA OF INTRACRANIAL PART OF OPTIC NERVES DERIVED FROM 26 PATIENTS WITH OPTIC ATROPHY

	No.	Major Axis			Minor Axis			Area		
		Range	Mean	S.D.	Range	Mean	S.D.	Range	Mean	S.D.
Infants 0-6 months	2	1·8-2·5	2·2	—	1·5-2·1	1·8	—	2·26-4·49	3·38	—
1-2 years	11	1·5-2·9	2·65	±0·36	1·1-2·4	1·80	±0·33	1·51-5·66	3·97	±1·10
2-3 years	3	2·6-2·9	2·7	—	1·6-2·8	2·1	—	3·27-6·60	4·76	—
3-4 years	2	2·6-3·0	2·8	—	1·8-1·9	1·9	—	3·68-4·71	4·20	—
4-5 years	3	3·2-3·5	3·3	—	2·2-2·7	2·5	—	5·53-7·92	6·66	—
5-6 years	2	2·9-3·2	3·1	—	2·0-2·3	2·2	—	4·71-6·03	5·37	—
7-9 years	1	—	2·5	—	—	1·5	—	3·27	3·27	—
Adults	2	3·0-3·4	3·2	—	1·7-2·2	2·0	—	4·18-5·18	5·0	—

TABLE III

MEASUREMENTS ON 20 PAIRS OF OPTIC NERVES IN THEIR INTRACRANIAL PORTIONS BEFORE, AND ONE MONTH AFTER, FIXATION IN 10% FORMOL-SALINE

Case	Sex	Age	Naked-eye State of Brain	Before Fixation				After Fixation			
				Diameters (mm.)		Square Areas (sq. mm.)		Diameters (mm.)		Square Areas (sq. mm.)	
				I	II	I	II	I	II	I	II
1	F	1 year, 2 months	Normal	4·5×3·2	4·0×3·2	11·56	10·05	4·4×2·4	4·0×2·5	8·30	8·17
2	M	2 years	Mongolism	4·0×3·4	4·7×3·5	10·68	12·07	4·5×2·9	4·5×3·1	10·84	11·56
3	F	3 years, 11 months	Multiple congenital malformations	3·6×2·8	3·5×2·8	7·92	7·92	3·8×2·5	3·6×2·5	7·76	7·35
4	M	4 years, 1 month	Mongolism	3·6×2·8	3·4×2·4	7·92	6·41	3·7×2·7	3·4×2·5	8·36	6·99
5	M	4 years, 4 months	Micrencephaly	3·0×2·5	2·9×2·4	6·13	5·66	2·8×2·0	2·7×2·1	4·40	4·84
6	F	4 years, 4 months	Normal	4·0×3·2	4·2×3·2	10·05	10·56	4·1×3·1	4·0×2·9	10·56	9·43
7	F	10 years, 6 months	Ulegyria	4·2×3·2	3·8×3·3	10·56	10·15	4·0×3·2	3·8×3·0	10·05	8·98
8	M	11 years	Inclusion body encephalitis	4·7×3·2	4·5×3·7	12·07	13·73	4·1×3·2	4·0×3·5	10·56	11·31
9	M	48 years	Normal	5·2×3·6	5·3×3·6	14·71	15·27	5·6×2·7	5·1×3·2	12·32	13·07
10	F	55 years	Cerebral glioma	5·4×3·2	5·5×3·4	13·57	14·96	6·0×2·8	5·5×2·9	13·20	13·20
11	M	55 years	Normal	4·4×3·0	5·2×3·0	10·37	12·25	4·5×2·5	5·0×2·6	9·40	10·21
12	M	55 years	Normal	4·6×3·2	4·6×2·9	11·56	10·84	4·8×2·5	4·9×2·5	9·80	10·21
13	F	57 years	Subarachnoid haemorrhage	4·8×2·8	5·2×3·3	10·56	13·89	4·2×2·5	4·4×2·4	8·58	8·30
14	M	60 years	Normal	5·1×3·2	5·6×3·2	13·07	14·08	5·2×3·1	5·5×3·2	13·07	14·08
15	M	61 years	Subarachnoid haemorrhage	5·6×3·2	5·3×3·2	14·08	13·57	5·7×2·5	5·7×2·6	11·85	11·85
16	F	62 years	Cerebral haemorrhage	5·0×3·1	5·0×3·5	12·56	14·14	4·9×2·7	5·0×3·0	11·00	11·73
17	M	63 years	Subarachnoid haemorrhage	5·3×3·8	5·3×3·8	16·12	16·12	5·3×2·6	5·5×2·5	11·03	11·44
18	M	64 years	Lobectomy of brain	5·6×3·3	5·5×2·9	14·96	13·20	5·6×2·7	5·3×2·4	12·32	10·18
19	F	72 years	Subarachnoid haemorrhage	5·5×3·0	5·5×3·0	13·20	13·20	6·2×2·4	6·2×2·4	11·69	11·69
20	M	89 years	Normal	5·3×2·8	5·6×2·6	11·88	11·44	5·5×2·5	5·3×2·6	11·44	10·41

between the experimental error of the unfixed nerves and that of the fixed nerves. It was conceivable that local conditions affecting the chemical and physical state of a nerve, for instance, oedema, amplified the differences between the fresh and fixed states. The age of the subject had no effect on the extent of the shrinkage. However, the fixed nerves being firm and easier to manipulate and revealing a smaller experimental error, suggested that the fixed nerves were a better medium on which to conduct a study of this sort. Nevertheless, it is conceivable that the variable effects produced by formalin fixation may give a misleading idea of the size of the nerve in the living condition.

The gradual increase in girth from birth till the age of 4 years is at variance with the view of Keeney (1951), who stated that the optic nerve was fully medullated at 3 months, by which time it had reached full size. Further statistical analysis of the sample signified that the sample was not homogeneous; for instance, there was a highly significant difference between the newborn period to the ages 1-2 years, a significant difference between age groups 1-2 years and 2-3 years, and an insignificant difference between age groups 3-4 years and 4-5 years. Thus the growth curve was a real and correct estimation of the facts, namely, that growth in thickness of the optic nerve continues from birth till the age of 4 years.

Since a post-natal growth curve of the optic nerve had not so far been reported in the literature, confirmation of the findings was sought amongst anatomical and physiological studies on other tissues. Todd, Beecher, Williams, and Todd (1940) compiled a growth curve of the weights of 69 pairs of eyeballs between birth and 21 years. They found considerable growth during the first year, continuing with diminished velocity to the third birthday. Eyeball growth, in general, followed brain growth. Their curve coincides closely with that of the optic nerve in this study. Rexed (1944) observed and confirmed that myelin sheaths and axis cylinders of

peripheral nerves increase in diameter during the first four years of life. Physiological development of the visual pathway continues for the first few years of life; for instance, Keeney (1951) reported that vision does not reach 6/6, or nearly so, until the fourth year. If these points are considered, it is reasonable to suppose that the optic nerve would continue to increase in size for the first four years of life, thus supporting the findings in this study.

Summary

Measurements of the major and minor axes were made on fixed tissues of the intracranial section of the optic nerves from 210 patients. The cross-sectional square areas were calculated. Brains of subjects from whom the nerves were obtained ranged from the newly born to adults, and thus it was possible to chart a growth curve. It was found that there was an increase in thickness of the nerve from birth till the age of 4 years, up to which time major growth occurs, and after which possible minor changes in growth continue up to the age 6-8 years. Twenty pairs of optic nerves were measured in the fresh state and after fixation for one month. A wide range of effects was revealed. The overall mean effect was shrinkage in fixative to the extent of 12·3%.

Optic nerves from brains of 26 patients who had optic atrophy were similarly measured and the findings given for comparison.

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