THE OCULAR PARASYMPATHETIC NERVE SUPPLY AND ITS MESENCEPHALIC SOURCES

By R. WARWICK
Department of Anatomy, University of Manchester

It is usually stated that the parasympathetic innervation of the eyeball has its central origin in the Edinger-Westphal nucleus, and perhaps also in the other small-celled component of the oculomotor complex, the antero-median nucleus of Perlia (1889), and that their axons emerge from the midbrain in the third nerve, leaving it to relay in the ciliary ganglion, whence post-ganglionic fibres pass to the ciliaris and sphincter pupillae by the short ciliary nerves (Text-fig. 1). The literature concerning this pathway is vast, and only the more significant contributions can be mentioned here.

The post-ganglionic neurons were the earlier studied. Fallopius (1600) referred briefly to a plexiform junction between branches of the third and fifth nerves in the orbit. Willis (1664) first clearly described the short ciliary nerves; he wrote of a 'plexus rotundus', belonging to the oculomotor nerve, as their source. It was Schacher (1701) who recognized this as a ganglion, and its connexion with the trigeminal nerve in man was first depicted by Eustachius (1714), according to Meckel (1748). With the descriptions of Winslow (1732), and particularly Haller (1743), the arrangement of the short ciliary nerves, their ganglion, and its motor and sensory roots was clarified in man. Extensive comparative data were added by Zinn (1780), Muck (1815), Longet (1842), Budge (1855), Krause (1861), Schwalbe (1879), Jegorow (1886, 1887) and many others.

Ruysch (1722) and Winslow (1732) gave early accounts of the ramification of the ciliary nerves in the eyeball, and these have been amplified by later observers, especially Agababow (1893, 1912), Pines & Pinsky (1932), and Boeke (1933, 1936), who have reviewed the literature. Anatomical proof of innervation of the ciliaris and sphincter pupillae by these nerves was not early forthcoming, but Mayo (1823), Hall (1846), Bernard (1852) and Budge (1855) stimulated them electrically and produced meiosis; Muck (1815) and Longet (1842) cut them, and noted pupillo-dilation. Hensen & Völckers (1868) confirmed the pupillary response to stimulation and also recorded movements of the ciliary body. All these experimenters claimed that oculomotor stimulation caused meiosis, except Bernard (1852), whose disagreements focused interest on the nature of the ciliary ganglion, and of ganglia in general. Fallopius (1600), who introduced the term 'ganglion' to neurology, had regarded them as 'little brains', a view shared by Lancisi (1723), Winslow (1732), and Johnstone (1771).

The recognition, in man, of connexions between the ciliary ganglion and both the third and fifth cranial nerves intensified controversy over its function. Valentin (1839), Budge (1855), and Reichardt (1875) considered it a dependent of the third nerve, a view confirmed in all classes of vertebrates by Schneider (1879), Schwalbe (1879), Peschel (1893), Apolant (1896*a*) and Pitzorno (1913*a*, *b*). Schwalbe found no trigeminal connexion in teleosts, amphibians, or reptiles, but observed an oculomotor root in all mammals examined, as did Zeglinski (1885), d'Erchia (1894), and

Carpenter (1911) in birds. In spite of this, and of Arnold's (1831) previous suggestion that the ciliary ganglion was autonomic, most of these authorities thought it the homologue of a spinal root ganglion. Numerous and conflicting studies of its cells were reported. Reichardt (1875), Schwalbe (1879), Goldberg (1891), Peschel (1893), and Van Gehuchten (1893) considered them 'spinal', while Retzius (1881, 1884), Michel (1894), Apolant (1896*b*), von Kölliker (1896) and Onodi (1901) considered them 'sympathetic'. Holtzmann (1896) described them as sensory in amphibians but autonomic in birds and mammals. Krause (1881), Bernheimer (1897*a*), Bach (1899), Bumm (1899), Fritz (1899) and Marina (1901) found varying proportions of motor and sensory cells in the ganglion, according it a dual function.

Meanwhile, Gaskell (1885) had shown that 'Remak's' fibres in the oculomotor nerve reached the ciliary ganglion; Langley & Dickinson (1889) had introduced the nicotine block, which was soon applied to the ciliary ganglion by Langley & Anderson (1892). These classical studies clearly established the existence of an autonomic pathway to the eye by way of the third nerve and its ganglion. Anatomical experimentation confirmed Langley's work. Apolant (1896*a*), Bumm (1901) and Marina (1899) traced small degenerating fibres as far as the ciliary ganglion from the oculomotor trunk following its division. Schwalbe (1879), Bach (1896, 1899), van Biervliet (1899), and Marina (1899) also noted retrograde degeneration of most of the ganglion's cells after procedures such as ciliary neurectomy, removal of the eyeball or its contents.

Nevertheless, Marinesco, Parhon & Goldstein (1908), Müller & Dahl (1910), and Sala (1910) added to the complexity of cell types already described in the ciliary ganglion, and Pines & Friedmann (1927, 1929) claimed to recognize no less than eight categories in human and simian ganglia. Kiss (1932), Hollinshead & Clark (1935), and other workers, have subsequently differentiated less numerous types. All were agreed that small nerve cells, autonomic in character, formed the predominant type. Embryological observers, however, such as Carpenter (1906), Ganfini (1911), and Kuntz (1920), have closely associated the ciliary ganglion with the trigeminal as well as the oculomotor nerve in its development.

In contrast with these inconclusive histological investigations, animal experiments have largely corroborated the views of Gaskell (1889) and Langley & Anderson (1892). Hensen & Völckers (1868, 1878) had already produced meiosis and ciliary contraction by stimulation of the oculomotor trunk, ciliary ganglion, and short ciliary nerves in dogs, cats and monkeys. Their observations were repeated by Jegorow (1886), Spallita & Consiglio (1893), Langendorff (1894), Jendrássik (1896), Marina (1899), and François-Franck (1904), most of whom, like Angelucci (1899), Lodato (1900), and Anderson (1905), noted that stimulation failed to produce intra-ocular movements after division of the third nerve or destruction of the ganglion. Luco & Savvestrini (1942) and Kuntz, Richins & Casey (1946) have confirmed these findings.

It is apparent that much evidence, anatomical, physiological and experimental, has combined to prove that the sphincter of the iris and the ciliaris muscle are supplied by an autonomic pathway in the oculomotor and short ciliary nerves, which relays in the ciliary ganglion. On the other hand, proof of the precise source of the pre-ganglionic fibres of this pathway is much less satisfactory.

Although Spitzka (1888) claimed priority, Edinger (1885) and Westphal (1887)

are usually credited with the discovery of the paired groups of small cells, dorso-medial to the main oculomotor nucleus of man, which still bears their names. Perlia (1889) confirmed these observations, describing in addition another median mass of similar small nerve cells, the antero-median nucleus, situated at the cephalic end of the oculomotor complex. Panegrossi (1898) noted the latter in monkeys, and Siemerling (1891), Cassirer & Schiff (1894), Tsuchida (1906), Zweig (1921), Benjamin (1939) and Crosby & Woodbourne (1943), regarded these small-celled nuclei as a continuous mass, the antero-median nucleus forming a cephalic extension of the Edinger-Westphal columns.

The midbrain stimulation experiments of Hensen & Völckers (1868, 1878) and Adamük (1870) had indicated that cells near the cephalic end of the oculomotor nucleus innervated the ciliaris and sphincter, a view supported by the clinical arguments of Kahler & Pick (1881) and Starr (1888). It was therefore logical to suppose that the newly discovered Edinger-Westphal nuclei might be these centres. Clinical evidence in support of this was reported by Déjérine & Darkschewitsch (1887), Oppenheim (1888), Spitzka (1888), Knies (1891), Kostenitsch (1893), Jakob (1894), Pacetti (1894), Stuelp (1895), Pineles (1896), Ahlström (1900), Majano (1903), and Angelucci (1910). Some of these accounts were perhaps unduly dogmatic; Knies, for example, devised an elaborate scheme of oculomotor functions, on unspecified evidence, in which the Edinger-Westphal nucleus mediated accommodation, the pupillo-constrictor centre being Darkschewitsch's nucleus. Zeri (1895), von Bechterew (1897), Juliusberger & Kaplan (1899), and Bach (1906) disagreed with these views, which were indeed no more than clinical deductions from scanty pathological data. More extensive clinicopathological investigations by Siemerling (1891), Boedeker (1892), Cassirer & Schiff (1894), von Kölliker (1896), Siemerling & Boedeker (1897), Panegrossi (1898), von Monakow (1895, 1905), and Tsuchida (1906), produced no positive findings, although Brouwer (1918), Frank (1921), Grünstein & Georgieff (1925), and Lenz (1928, 1929) have more recently found pathological reasons to favour the Edinger-Westphal nuclei as the source of the ocular parasympathetic. Levinsohn (1917), Brouwer (1918), and Latumeten (1924) have reviewed *in extenso* this aspect of the literature.

Meanwhile, anatomical experimenters were likewise reporting contradictory results. Midbrain retrograde changes due to third nerve interruption and ciliary ganglionectomy were studied by Bernheimer (1897*a*, *b*), Bach (1899, 1900), van Biervliet (1899), Marina (1899), and Levinsohn (1904), of whom only Bernheimer and Levinsohn reported implication of the Edinger-Westphal nucleus, destruction of which, according to the former (1901), paralysed the sphincter pupillae. Van Gehuchten & van Biervliet (1901) merely admitted that the parasympathetic centre was probably cephalic in position in the oculomotor complex. Latumeten (1924) emphatically denied that Edinger-Westphal axons entered the third nerve, a view based on late midbrain changes in four cats on which Magnus had carried out two oculomotor divisions and two ciliary ganglionectomies. Crouch (1936), in a more extensive series of cats, found no clear response to ganglionectomy, but the results of third nerve injury were clear enough to lead him to conclude that some of the Edinger-Westphal fibres crossed before entering it. Kuré, Susuki, Kaneko & Okinaka (1933) found ganglionectomy regularly effective in dogs.

Comparative methods have also led to conflicting conclusions. Panegrossi (1904), Tsuchida (1906), Ramon y Cajal (1911), and Neiding & Frankfurther (1911) discounted the Edinger-Westphal column as a radicular oculomotor nucleus, but Brouwer (1918) claimed that it mediated accommodation; he compared its progressive differentiation in mammals with the development of Perlia's nucleus (convergence), regarding both as closely associated with the evolution of binocular vision. Zweig (1921), on morphological grounds alone, was prepared to assign the functions of pupillary constriction and accommodation to the Edinger-Westphal and antero-median nuclei respectively. Le Gros Clark (1926) concluded that comparative data merely suggested the inclusion of these nuclei in the oculomotor complex, and subsequent topographers of these centres, such as Crosby & Woodburne (1943), have likewise expressed reserved opinions.

Little pertinent embryological information exists. Cramer (1894) and Tsuchida (1906) could not distinguish the Edinger-Westphal nucleus before the 7th month. Magitot (1921) has observed an active light reflex early in the 6th month; but this is not a serious discrepancy, since Hertel (1907) has shown that the human iris may respond directly to light. Moreover, Paton & Mann (1925) and Mann (1927) identified the nucleus in 48 mm. embryos, and Pearson (1944) at the 5th month, at which stage its cells are already distinguishable from somatic oculomotor neurones, according to Malone (1913). Cooper (1946) identified the nucleus even earlier, at the 40 mm. stage.

Recent experimenters have returned to stimulation methods, with the modern advantages of sterotaxic instruments. Ranson & Magoun (1933) found that stimulation in or near the Edinger-Westphal nucleus caused ipsilateral meiosis. Benjamin (1939) agreed with this but included the antero-median nucleus, whereas Szentágothai (1943) thought the Edinger-Westphal alone was concerned. All these workers used cats. In monkeys Bender & Weinstein (1943) could not accurately locate centres for meiosis or accommodation.

From this review it is apparent that the origin of the ocular post-ganglionic fibres from the ciliary ganglion has been established. That the pre-ganglionic fibres issue in the oculomotor nerve to relay in the ganglion is not so well authenticated. The precise central source of these fibres remains in doubt. All methods of study have led to disagreements. It was therefore decided to re-examine the problem, with special regard to the location of the pre-ganglionic nerve cells.

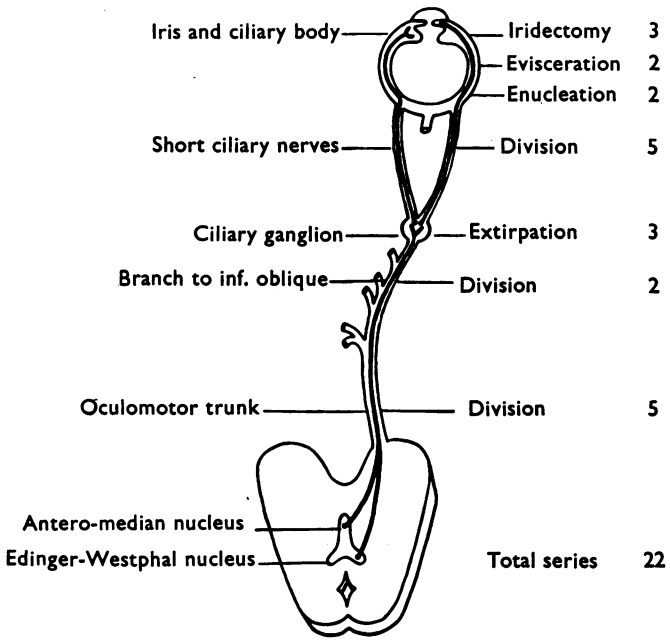
MATERIALS AND METHODS

The observations of this research were made upon the midbrains and ciliary ganglia of twenty-three monkeys (*Macaca mulatta*) and five cats. The monkeys were submitted to the following operative lesions (Text-fig. 1):

(1) Iridectomy	3
(2) Exenteration of the eyeball	2
(3) Removal of the eyeball	2
(4) Division of the short ciliary nerves	5
(5) Extirpation of the ciliary ganglion	3
(6) Division of the nerve to the obliquus inferior	2
(7) Division of the inferior oculomotor ramus	1
(8) Division of the oculomotor trunk	5

The cats were all subjected to procedure 4. In addition to this material, serial sections prepared from the midbrains of a large number of monkeys were also available for examination of topographical details.

All the operations were unilateral and were performed under intravenous or intraperitoneal anaesthesia (Kemithal, Nembutal, or Pentothal). The ocular operations were carried out in the usual manner and presented no special difficulties. Interruption of the short ciliary nerves was effected through a wide incision in the



Text-fig. 1. This diagram illustrates (with the exception of the inclusion of the antero-median nucleus) the anatomical pathway from the midbrain to the eyeball as usually described in text-books. On the right of the diagram are listed the procedures carried out in this research. The figure indicate the number of monkeys used in each kind of experiment.

upper lid; careful dissection within the muscle cone led to identification of the optic nerve, around which the short ciliary branches were isolated and divided. The ciliary ganglion was usually approached through the lower lid. This route permitted early recognition of the inferior oblique and its nerve supply. The nerve was followed back under the eye towards the apex of the orbit by gentle dissection, chiefly carried out by means of pledgets of cotton-wool soaked in 1/1000 adrenalin hydrochloride solution. This method kept the operation field dry, an important point in searching for such small structures in so restricted a working space. It was usually possible to find the ganglion, but to isolate it clearly enough to sever its connexions under direct vision was difficult and sometimes impossible. In the latter eventuality the short ciliary nerves were divided instead, since blind cutting under such conditions may easily divide other structures than those intended. The short ciliary nerves were always cut well anterior to the ganglion, because of the danger of interfering

inadvertently with its blood supply, which is said to reach it by branches from the muscular and posterior ciliary branches of the ophthalmic artery. It was clear, however, that the effects produced in the ciliary ganglion by this procedure were not an artefact due to devascularization, since precisely the same results followed removal of the ocular contents.

Exposure of the ganglion by removal of the lateral orbital wall was also tried, but this afforded even less space. To ensure that ganglionectomy had been accomplished, the excised nervous tissue was always sectioned; post-mortem dissection of both orbits was also always carried out, not only as a further check upon the effectiveness of the operation, but also to secure the normal ganglion from the undisturbed orbit for comparison. Although these procedures were sometimes lengthy, all animals made rapid and uneventful recoveries. No post-operative infections occurred.

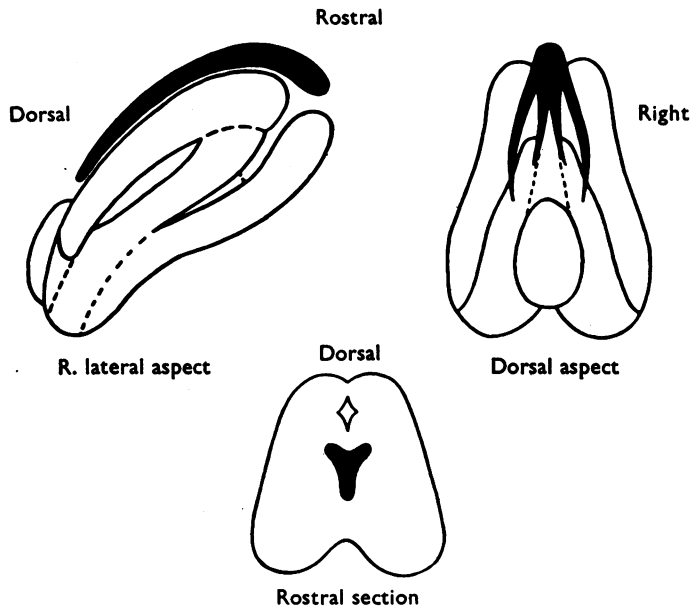
At periods varying from 8 to 16 days after operation each animal was anaesthetized as above, bled, and perfused with 10% formol saline solution at a pressure maintained at 120 mm. of mercury by a small pump. The midbrains and ganglia were carried through to paraffin wax embedding in the usual manner. All were sectioned serially at 10μ thickness. Sections were stained by Bielschowsky's dilute cresyl fast violet technique in most cases, some by Einarson's gallocyanin method.

RESULTS

Topography

A detailed description of the topography of the oculomotor complex, including its parasympathetic nuclei, will form part of a later communication, but a brief note of the arrangement of these centres is necessary as a preface to the experimental results which follow.

The Edinger-Westphal nucleus of each side consists of a slender column of small multipolar cells scattered irregularly and in small numbers in sections through the cephalic three-fifths of the main third nerve nucleus, to which they are dorsal at caudal levels, becoming dorso-medial in position at more cephalic levels (Text-fig. 2). Thus the right and left columns approach each other, fusing across the midline raphé at the cephalic extremity of the oculomotor complex (Pl. 1, fig. 2). A ventral extension of this conjoined mass, of similar nerve cells, arches over the cephalic aspect of the main oculomotor mass in the midline, forming the so-called antero-median nucleus (nucleus medianus anterior of Perlia) (Pl. 1, fig. 1). Dorso-lateral to the cephalic half of the Edinger-Westphal columns an ill-defined group of like cells can sometimes be made out in the monkey; this, the lateral Edinger-Westphal nucleus of human topography, merges with the main or medial Edinger-Westphal nucleus caudal to the fusion of the latter with its fellow. Although regional names were applied to parts of this mass of small motor neurones before their confluence was clearly recognized, it is important to note that their continuity is complete in the monkey (Text-fig. 2). Throughout this account, however, the established usage of the terms 'Edinger-Westphal' and 'antero-median' nuclei has been followed, although it is apparent that the latter is a cephalic prolongation of the Edinger-Westphal columns.



Text-fig. 2. These diagrams represent the topographical structure of the oculomotor complex in the rhesus monkey. The parasympathetic nuclei (in black) are the Edinger-Westphal columns, dorsal to the somatic nuclei, and the midline antero-median nucleus, formed by the coalescence of these columns at the cephalic or rostral extremity of the complex.

EXPERIMENTAL RESULTS

(*a*) *Division of the short ciliary nerves*

The bundles of short ciliary nerves were completely severed in one orbit of five monkeys and five cats. Serial sections of the right and left ciliary ganglia, and of the midbrain, were examined in each experiment. No changes were observed in the oculomotor or other mesencephalic nuclei of these animals, but in the ganglion from the side of operation extensive and unmistakable retrograde degeneration was always evident. The ganglion of the opposite side, which was never affected, provided a group of normal cells for comparison. The normal ciliary ganglion neurones, both in the monkey and the cat, possess cytons averaging respectively 45 (30–63)μ and 35 (15–30)μ in size. In preparations stained for chromatin material they appear multipolar and contain uniformly distributed Nissl granules, which are numerous, fine and sometimes elongated (Pl. 2, fig. 4). In the series inspected, most of the cells were alike, and no elaborate range of types could be identified. There was some variation in size, and in the amount of visible chromatin substance, but the only other distinct type of cell encountered was extremely infrequent; it was much smaller, containing a few large granules around a relatively large nucleus (Pl. 2, fig. 5). This type of cell averaged 23 (15–30)μ in size in the monkey; it was not satisfactorily identified in the cat's ganglion. Normal cells exhibiting chromophily were seen occasionally in some series, but were absent from most. Their significance, which has been discussed elsewhere (Warwick, 1951, 1953*b*), was clearly unrelated to the retrograde changes studied.

In the ganglion from the side of operation the classical phenomena of the retrograde reaction, chromatolysis and nuclear eccentricity, were clear in every series (Pl. 2, fig. 6). Extrusion of nuclei was seen less often, and the swelling characteristic of acute retrograde degeneration in some kinds of nerve cells was not evident in ganglia from monkeys, a slight degree of shrinkage being more usual (Pl. 2, figs. 6, 7). Swelling was present but never marked in the cats' ganglia; in both animals chromatolytic cells were sometimes rounded and sometimes misshapen. A chromophil stage in the reaction was occasionally encountered, and the peripheral clumping of chromatin material typical of the earlier phases of chromatolysis was seen in some cells (Pl. 2, fig. 7). As reported previously (Warwick, 1951, 1953*b*), in connexion with retrograde changes in somatic oculomotor neurones, the most striking and reliable feature was found to be chromatolysis. This was apparent to a marked degree in almost all the cells in each series, and in many all visible chromatin material had disappeared (Pl. 2, figs. 6, 7). Counts of normal and degenerating cells were made in numerous sample fields in four ganglia from the side of operation. These figures are tabulated herewith:

Animal	Sections examined	Total cells	Normal cells	Percentage chromatolytic
Cat no. 5	20	2690	104	96·1
Cat no. 6	20	2480	75	97·1
Monkey no. 87	20	2595	71	97·2
Monkey no. 88	23	3102	84	96·8

These counts show that an almost universal degeneration of the ciliary ganglion's cells followed division of its short ciliary branches. The widespread and unequivocal nature of the reaction was so evident that the normal and affected ganglia could be distinguished easily under magnification low enough to include them in the same field (Pl. 1, fig. 3).

(*b*) *Exenteration of the eyeball and iridectomy*

Evacuation of all tissues within the scleral tunic was carried out in two monkeys. In both the ipsilateral ciliary ganglion showed retrograde changes as marked and widespread as were those resulting from ciliary neurectomy. Normal cells were extremely few. This manoeuvre naturally interrupted all nerve fibres entering the eyeball, including those from the ciliary ganglion. To estimate the proportion of the cells in the ganglion whose fibres enter the iris, a unilateral iridectomy was performed in three other monkeys. In each case most of the cells in the ipsilateral ganglion were normal; but occasional neurones, scattered singly or in small groups, were plainly degenerating (Pl. 2, fig. 7). Counts of normal and chromatolytic cells were made in numerous sample fields in two of the affected ganglia; the results were as follows:

Series	Sections examined	Total cells	Chromatolytic cells	Percentage
83	20	3027	95	3
85	20	3687	135	3·5

Equal numbers of serial sections of the ganglia of the opposite side were also examined in all three animals; the cells in these were all normal.

(*c*) *Ciliary ganglionectomy*

Removal of the ciliary ganglion on one side was accomplished in three monkeys. Following this procedure clear retrograde changes were evident in the cells of the Edinger-Westphal and antero-median nuclei ipsilateral with respect to the orbital lesion. The normal cells of these groups were seen to be small and usually multipolar, ranging from 15 to 25μ. By their size, their relatively large nuclei, and the paucity of their Nissl granules, they were easy to distinguish from the neighbouring somatic oculomotor nerve cells, and the comparatively undifferentiated cells of the surrounding central grey matter (Pl. 3, fig. 8). The cells of the antero-median nucleus appeared to be little different from those in the Edinger-Westphal columns, being merely somewhat elongated in the sagittal plane (Pl. 3, figs. 9, 11). The usual features of retrograde degeneration were visible in the cells of both nuclei, except for swelling, which was not always seen and rarely marked, although the cells were usually rounded (Pl. 3, fig. 10). On the other hand, a chromophil stage in chromatolysis was often observed (Pl. 3, fig. 12).

Degenerating cells were confined to the ipsilateral Edinger-Westphal nucleus and the ipsilateral half of the antero-median nucleus (Pl. 3, figs. 8, 9). In the latter the contrast between normal and affected neurones lying on opposite sides of the mid-sagittal plane was especially noticeable (Pl. 3, fig. 9). Inspection of serial sections through the whole length of the Edinger-Westphal columns showed that the proportion of cells affected was less here than in the antero-median nucleus, where chromatolysis was almost universal in the cells on the side of operation. Nevertheless, retrograde changes were seen in cells at all levels of the ipsilateral Edinger-Westphal group. No unequivocal degeneration was noted in any of the cells of the contralateral nuclei.

In one series some of the cells in the ipsilateral somatic oculomotor nucleus also showed chromatolysis. These were grouped in a manner corresponding to the results of resection of the obliquus inferior, as reported elsewhere (Warwick, 1953*b*). Post-mortem dissection of the orbit of this monkey showed that this muscle's nerve supply had been divided during ganglionectomy, thus accounting for these additional effects.

(*d*) *Orbital interruption of the oculomotor nerve*

Serial sections were examined from the midbrains of two monkeys submitted to deliberate division of the nerve to the obliquus inferior and one in which the inferior oculomotor ramus had been cut. In all three preparations the lesion, checked by post-mortem dissection, was proximal to the origin of the motor radix of the ciliary ganglion. In each series ipsilateral retrograde changes were observed in the Edinger-Westphal and antero-median nuclei. The results were in every way identical with those caused by ciliary ganglionectomy.

(*e*) *Intracranial division of the oculomotor nerve*

The oculomotor complex was inspected serially in the midbrain of five monkeys which had been subjected to unilateral division of the oculomotor trunk close to its superficial origin from the cerebral peduncle. In addition to changes in the main third nerve nuclei, which have already been described (Warwick, 1951, 1953*a*, *b*),

retrograde degeneration was marked in the ipsilateral Edinger-Westphal and antero-median nuclei. The cells of these were never affected by divisions of the branches of the third nerve, except when the nerve to the obliquus inferior was cut proximal to its ciliary branch. By exclusion, therefore, these small-celled nuclei of the oculomotor complex cannot be concerned with the innervation of the extra-ocular muscles, but must supply the fibres which relay in the ciliary ganglion to supply the eyeball.

DISCUSSION

Concerning the post-ganglionic neurones of the ocular parasympathetic supply agreement may be said to have been reached, except for minor details; the voluminous literature about them therefore requires no protracted discussion. Bernheimer (1897*b*, 1898), Fritz (1899), Marina (1899, 1901), and Marinesco, Parhon & Goldstein (1908) claimed that some of the cells of the ciliary ganglion innervate the cornea. Although most workers who have examined these cells have deemed them motor in function, the occurrence of sensory cells in this ganglion is a possibility which cannot be entirely refuted. The almost uniform nature of the cell population in all the ganglia examined in this investigation makes it unlikely that any are sensory. It is more probable that all the cytons of corneal afferents lie in the trigeminal ganglion, changes in some of the cells of which follow corneal injury, as Marina (1899) has shown.

Langendorff (1894), Moeli (1897), and François-Franck (1904) suggested that the ciliary ganglion might be a peripheral reflex centre, and Clark (1937) thought that it contained internuncial neurones, despite his own observation that total degeneration of its cells followed division of the short ciliary nerves. It could be supposed that such internuncial cells, if they existed, might exhibit transneuronal degeneration, but in view of our ignorance of the connexions they might effect, such considerations are purely hypothetical. All such views of the existence of different functional types of neurone in this ganglion are seriously weakened by electrophysiological studies of its cells by Whitteridge (1937). He found that in the monkey they all behaved alike, and he could not support concepts of the ganglion as a co-ordinating centre.

Kuré, Susuki, Kaneko & Okinaka (1933) stated that dystrophic changes occurred in the extra-ocular muscles after destruction of the ciliary ganglion. It is not clear how the axons of such cells were thought to reach the muscles. This view has received no corroboration, and the present findings contradict it, since almost all the ganglion's cells reacted to exenteration of the eyeball, a procedure which could not disturb such supposed arrangements.

The association of the ciliary ganglia with the third nerve is no longer in doubt, and the fact that the nerve contains motor fibres for the sphincter pupillae and ciliaris is attested by an imposing accumulation of evidence. Numerous workers, over a period of almost a century, have cut and stimulated the oculomotor nerve, noting, with few exceptions, some sort of pupillary response. It is true that some disagreement has arisen over the precise mechanisms of pupil movements. Von Bechterew (1883) first suggested that dilatation in response to pain was due to central parasympathetic inhibition rather than to sympathetic activation of the dilator muscle. Braunstein (1894) confirmed this idea, while Karplus & Kreidl (1912, 1918) admitted that reflex mydriasis was not wholly effected by sympathetic

activity in the iris. The participation of parasympathetic inhibition in reflex pupil dilatation resulting from other stimuli, including light withdrawal, has been confirmed by McDowall (1925), Byrne (1933), Bain, Irving & McSwiney (1935), Gullberg, Olmsted & Wagman (1938), Urey & Gellhorn (1939), Hodes (1940), and others. Kuntz & Richins (1946), like some previous workers, found that division of the third nerve abolished reflex pupil dilatation, as did also ciliary ganglionectomy in their experiments. These views are in accord with the results of cortical stimulation. Pupillary dilatation in response to this was first noted by Bochfontaine (1875), and Parsons (1901) reviewed the early literature, noting that the dilatation was abolished in dogs and cats by oculomotor division. Karplus & Kreidl (1910), Ingram, Ranson & Hannett (1931), Harrison, Magoun & Ranson (1938), Urey & Oldberg (1940), Hodes & Magoun (1942*a*, *b*), and Ward & Reed (1946) adduced evidence that an inhibitor pathway, of extra-pyramidal nature, descends from the vicinity of the frontal and occipital eye-fields via the hypothalamus to the tegmentum. They considered that excitation of this produced pupil dilatation by inhibition of oculomotor nerve cells. Keller (1946) has claimed that the cells of the Edinger-Westphal nuclei continue to discharge after isolation of the oculomotor centres by brainstem transections, an activity which, as Adler (1950) has suggested, would support the concept of central parasympathetic inhibition in dilatation of the pupil. Whether such interpretations prove correct or not, the experiments which formed their basis have uniformly confirmed the innervation of the sphincter pupillae by way of oculomotor fibres.

In a similar manner more complex ideas of the nervous control of accommodation have been advanced. Helmholtz (1855) first suggested a duality of function in the ciliaris, a concept also sponsored by Henke (1860). Morat & Doyon (1891) thought that the ciliaris received sympathetic and parasympathetic nerve supplies, mediating respectively distant and proximate accommodation. Jessop (1886) produced flattening of the lens by stimulation of the cervical sympathetic, and a controversial literature, reviewed by Cogan (1937), has since accumulated. Latterly, Jessop's claims have received fresh support from the experiments of Morgan, Olmsted & Watrous (1940), Olmsted & Morgan (1941), Mohoney, Olmsted, Morgan & Wagman (1942), and Olmsted (1944). Clark (1937) and Kuntz & Richins (1946) did not favour these views, and Stotler (1937) reported complete denervation of the ciliaris by ciliary ganglionectomy in the cat, an animal in which, according to Jegorow (1886), Anderson (1905), and Christensen (1934, 1936), no sympathetic fibres traverse the ganglia. Although a dual innervation of the ciliaris thus remains uncertain, it is noteworthy that none of these workers found reasons to doubt that it is supplied by oculomotor axons.

Certain observations concerning regeneration of the human third nerve after peripheral injury may be alluded to here. Bender & Alpert (1937), Ford, Walsh & King (1941), Bender (1945), Cristini (1947), and Russell & Wright (1948) have described the abnormal synkineses which characterize recovery of ocular movement in such cases. Bender & Fulton (1939) have noted like phenomena in the chimpanzee and monkey. It was commonly found by these authorities that abnormal nerve supplies were established. They ascribed this to mis-shunting, and it is of interest here to note that the sphincter pupillae, and sometimes the ciliaris,

were involved in these effects, a further indication of the innervation of these muscles by way of the third nerve.

In contrast to this mass of evidence, confirming the existence of an ocular parasympathetic element in the third nerve, uncertainty persists with respect to the precise central origin of these autonomic pre-ganglionic fibres. Clinico-pathological deductions, prominent in the earlier literature, produced contradictory views. It is well recognized that chronic morbid changes in brain stem nuclei are not easy to assess, and the more so in the case of small-celled and inconspicuous nuclei, such as these under discussion. The negative findings of even the more extensive investigations regarding the Edinger-Westphal nucleus are therefore unconvincing.

Most evidence obtained by experimental anatomy has been against the Edinger-Westphal nuclei as oculomotor parasympathetic components. Bernheimer (1897*b*) was almost unique among contemporary experimenters in stating that they were the source of the ocular parasympathetic. He regarded these nuclei as pupillo-constrictor centres and Perlia's nucleus (despite its somatic type of nerve cells) as the centre for the ciliaris. His conceptions of general oculomotor function have been shown to be largely inaccurate (Warwick, 1953*b*). His claims that enucleation and other lesions distal to the ciliary ganglion produced retrograde changes in the midbrain provoked criticism by his contemporaries, such as Bach (1899), who were aware of the convincing proof of a relay in the ganglion reported by Langley & Anderson (1892). These errors detract from the credibility of Bernheimer's results, which nevertheless were accepted almost in their entirety by Brouwer (1918). If the axons of nerve cells in the Edinger-Westphal group do indeed issue in the third nerve, cutting it should cause changes in these cells. The evidence of this research was entirely positive on this point and to this extent confirmed the findings of Bernheimer (1897*a*), Levinsohn (1904), and Crouch (1936). Latumeten (1924), whose opinions have attracted perhaps disproportionate interest, reached a negative conclusion, based upon experiments on two cats. (It is noteworthy that Crouch's work involved nine.) For technical reasons, detailed elsewhere (Warwick, 1951, 1953*b*), little weight can be attached to Latumeten's emphatic denial that Edinger-Westphal fibres enter the third nerve.

Physiological evidence, on the contrary, has clearly and almost uniformly indicated a pupillo-constrictor and accommodation pathway, of autonomic type, in the oculomotor nerve. Midbrain stimulation experiments, from the classical studies of Hensen & Völckers (1868, 1878) to those of Ranson & Magoun (1933) and Szentágothai (1943), have provided less agreement concerning the nuclei of origin of these fibres; but most of those who have used such methods have found indications of a centre for the sphincter, and sometimes one for the ciliaris, both near, if not identical with, the Edinger-Westphal nuclei. It has been objected that such methods, even with modern refinements, are not exact enough to identify such small cell masses, even if supplemented, as in Szentágothai's work, by tracing degenerating fibres into peripheral nerves from central destructive lesions. Nevertheless, the existence of a pupillo-constrictor centre, at the cephalic end of the oculomotor nucleus, appears to have been amply established by such means.

Although the histological effects of oculomotor division have demonstrated more certainly than physiological methods that some of the oculomotor axons come from

the Edinger-Westphal nuclei, their function can only be deduced from such findings. If all other radicular neurons of the third nerve can be made to show retrograde changes by division of its muscular branches, it is justifiable to presume that these small-celled nuclei are the source of the fibres which relay in the ciliary ganglion. Such was Bernheimer's view (1897*a*). Studies reported previously (Warwick, 1951, 1953*b*) have demonstrated that only the antero-median and Edinger-Westphal nuclei, among all the nerve cells affected by oculomotor trunk division, remain unaltered by lesions of the branches of the third nerve, provided that the injury is distal to the motor root of the ciliary ganglion in the case of the nerve of the obliquus inferior. This permits a strong presumption that the axons which issue from these nuclei pass from the third nerve into the ciliary ganglion, as commonly accepted. As stated above, the retrograde effects of short ciliary nerve injury have often been demonstrated, and this was confirmed in both the cat and the monkey in this research. Ciliary ganglionectomy is therefore the crucial anatomical experiment in linking up the ocular post-ganglionic fibres with the midbrain source of the pre-ganglionic axons of this pathway. Levinsohn (1904), from such procedures in nine cats, concluded that these fibres originate in the Edinger-Westphal nuclei; Bach (1906) decided that in rabbits they do not. Both authors inspected each other's preparations and disagreed with their respective interpretations: (Bach used the Weigert technique, unsuitable for observations on chromatin granules). Latumeten (1924) and Crouch (1936) also recorded negative findings, in two and nine cats respectively, but Kuré, Susuki, Kaneko & Okinaka (1933) described retrograde changes as constant in the Edinger-Westphal nuclei after ciliary ganglionectomy. No previous workers appear to have described such experiments in monkeys. My results in this animal were unequivocal; in each experiment both the Edinger-Westphal and antero-median nuclei were the seat of widespread chromatolysis. Only Levinsohn (1904) has also included the antero-median nucleus in the changes produced by ganglionectomy. This nucleus has rarely been mentioned by experimental anatomists, although the changes noted in it in this investigation were particularly striking.

Certain other views may be conveniently considered here. Von Bechterew (1883) and Mendel (1887) suggested the habenula nucleus (ganglion habenulae) as the pupillo-constrictor centre, but this view has not been corroborated by others. Darkschewitsch (1889) thought that his nucleus might perform this role; evidence excluding this nucleus from the oculomotor complex has been recorded by Ingram & Ranson (1935) and Warwick (1953*a*). Von Bechterew (1897), von Monakow (1895, 1905), Tsuchida (1906), and Mingazzini (1913, 1928) believed that the sphincter was controlled by cells scattered in the central grey matter near the floor of the third ventricle and aqueduct. These views, and Frank's conception of the Edinger-Westphal nucleus as a convergence centre, are contradicted by the present findings. Bernheimer's opinion that the central nucleus of Perlia innervated the intrinsic ocular muscles, ousted by Brouwer's ideas, was revived by Foerster, Gagel & Mahoney (1936); but, while Bernheimer had included the Edinger-Westphal nucleus as a part of this centre, they could find no changes in it after oculomotor divisions in ten monkeys and one chimpanzee. (They claimed that ciliary ganglionectomy confirmed this result, but gave no details of this aspect of their work.) Evidence that Perlia's nucleus, which is rarely a distinguishable entity in monkeys,

consists of nerve cells supplying extrinsic rather than intrinsic musculature, has been reported (Warwick, 1951, 1953*b*). It is improbable that the large motor cells, forming the central nucleus pictured by these authors, could be the cytons of autonomic neurones, although accommodation is a function which, by virtue of its close association with the conscious use of the eyes, might be regarded as voluntary in nature. It is perhaps curious that such an activity appears to be carried into effect by an autonomic pathway, which is also the efferent limb of the light reflex arc. This nervous pathway is itself unusual in the myelination of its post-ganglionic axons, a peculiarity indicated by Gaskell (1885) and coupled by him with the striated condition of the avian ciliaris. Lenhossék (1911) has drawn attention to the large size of these axons and of the ciliary ganglion cells in birds. Nevertheless, the ciliaris is non-striated in lower vertebrates and remains so in mammals, a condition consonant with its type of innervation. It may be suggested that as the mesencephalic reflex mechanisms of the visual function have become progressively replaced by an increasing degree of cortical control, this process of encephalization has affected not only the control of accommodation but also of the pupil in the reaction of convergence. This might explain not only the preservation of an autonomic pattern of innervation for the ciliaris and sphincter pupillae, but also the continued close anatomical association of the neurones supplying them.

Separate midbrain centres have sometimes been ascribed to these two muscles, but the uncertain pathological evidence upon which such hypotheses have been built makes their validity highly dubious. Stimulation experiments have failed to reveal such separate centres, and since trans-neuronal degeneration does not occur at the ciliary ganglion, it seems improbable that anatomical methods could do so. A comparison of the results of iridectomy and exenteration of the eyeball has shown that most of the ciliary ganglion's cells innervate the ciliaris and that few of their axons enter the iris. The bulk of the ciliaris relative to the sphincter leads one to expect that this would be so. It is logical to assume that the greater number of the fibres of the conjoined mass of the antero-median and Edinger-Westphal nuclei therefore innervate the ciliaris. Although the cells of the Edinger-Westphal columns appear in sections through more than the cephalic half of the oculomotor complex, they are more numerous at cephalic levels, where the columns coalesce to become continuous with the antero-median nucleus. The parasympathetic component of the oculomotor centres thus occupies a predominantly cephalic position, a finding which accords with the results of most stimulation studies and with the views of many clinical observers.

The antero-median nucleus, the most cephalic portion of the parasympathetic group of the third nerve complex, has attracted little attention, even as a topographical entity. Its continuity with the Edinger-Westphal nuclei, although not yet a feature of text-book accounts, has been confirmed in this research, the experimental results of which have also shown that both groups of cells have the same autonomic function. Szentágothai (1943), from an extensive stimulation study in cats, discounted the antero-median nucleus as a source of ocular parasympathetic fibres, a conclusion refuted by the present results, which confirm in this regard the experiments of Levinsohn (1904) and Benjamin (1939). Neither used monkeys. Crouch (1936) considered that some of the Edinger-Westphal axons decussated

before entering the third nerve; as in Benjamin's stimulation experiments, my experience was that they do not. Similarly, the fibres derived from the antero-median nucleus, a midline structure, were observed to issue in the oculomotor nerve on the side of their own half of the nucleus.

It must be concluded that the usually accepted conception of the ocular parasympathetic pathway is correct, both as regards its peripheral route and central origin. It may be added that the pre-ganglionic fibres do not decussate in monkeys, and are derived not only from the Edinger-Westphal columns, as usually described, but also from their infrequently included cephalic extension, the antero-median nucleus.

SUMMARY

The extensive literature concerning the ocular parasympathetic nerve supply is reviewed. Although convincing evidence exists that this pathway issues in the oculomotor nerve and relays in the ciliary ganglion, its mesencephalic sources, reputedly the Edinger-Westphal nuclei, are less satisfactorily substantiated.

The retrograde response to interruption at numerous points in this pathway was therefore studied in cats and particularly in monkeys; the latter have seldom been used in investigating this problem.

All lesions affecting the short ciliary nerves (e.g. enucleation, exenteration, ciliary neurectomy) produced chromatolysis in about 97 % of the cells of the ciliary ganglion. After iridectomy about 3 % only of these cells showed such changes.

These results confirmed that practically all the cells in the ciliary ganglion innervate intrinsic ocular musculature; they also showed that a small fraction only of their axons supply the sphincter pupillae.

Ciliary ganglionectomy and division of the third nerve (in monkeys) regularly caused a retrograde reaction of striking degree in most of the cells of the ipsilateral Edinger-Westphal nucleus and in the ipsilateral half of the antero-median nucleus. Topographical observation showed that these nuclei form a continuous small-celled mass in the macaque.

It must be concluded that the usual account of the Edinger-Westphal nucleus as the parasympathetic component of the oculomotor complex is correct, and that the antero-median nucleus is an integral part of this centre.

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REFERENCES

ADAMÜK, F. (1870). Über die Innervation der Augenbewegungen. *Zbl. med. Wiss.* 8, 65–67.

ADAMÜK, F. (1870). Zur Physiologie des Nervus Oculomotorius. *Zbl. med. Wiss.* 8, 177–180.

ADLER, F. H. (1950). *Physiology of the Eye.* London: Kimpton.

AGABABOW, A. (1893). Die Innervation des Ciliarkörpers. *Anat. Anz.* 8, 558–561.

AGABABOW, A. (1912). Über die Nerven in den Augenhäuten. *v. Graefes Arch. Ophthal.* **83**, 318–380.

AHLSTRÖM, G. (1900). Bidrag till kännedomen om lokalisationen inom oculomotorius-kärnan hos människan. *Nord. med. Ark.* **16**, 1–11.

ANDERSON, H. K. (1905). The paralysis of involuntary muscle. Pt. II. On paralysis of the sphincter of the pupil. *J. Physiol.* **33**, 156–174.

ANGELUCCI, A. (1899). Ricerche sul mecanismo del movimento pupillare. *Arch. Ottal.* **7**, 6, 8, 226–283.

ANGELUCCI, A. (1910). Sulle flogosi oculari post-operative. *Arch. Ottal.* **17**, 453–458.

APOLANT, H. (1896*a*). Über die Beziehung des Nervus oculomotorius zum Ganglion ciliare. *Arch. mikr. Anat.* **47**, 655–668.

APOLANT, H. (1896*b*). Über das Ganglion ciliare. *Arch. Anat. Physiol., Physiol. Abt.* pp. 344–345.

ARNOLD, F. (1831). *Die Kopftheil des vegetativen Nervensystems beim Menschen*, p. 173. Heidelberg: Karl Groos.

BACH, L. (1896). Über die Localisation der Oculomotoriuskerne. *Neurol. Zbl.* **15**, 997.

BACH, L. (1899). Zur Lehre von den Augenmuskellähmungen und den Störungen der Pupillenbewegung. *v. Graefes Arch. Ophthal.* **47**, 339–386, 551–630.

BACH, L. (1900). Die Localisation des Musculus sphincter pupillae und des Musculus ciliaris im Oculomotoriuskernegebiet. *v. Graefes Arch. Ophthal.* **49**, 519–532.

BACH, L. (1906). Über das Verhalten der motorischen Kernegebiete nach Läsion der peripheren Nerven und über die physiologische Bedeutung der Edinger-Westphalschen Kerne. *Zbl. Nervenheilk.* **29**, 140.

BAIN, W. A., IRVING, J. T. & MCSWINEY, B. A. (1935). The afferent fibres from the abdomen in the splanchnic nerves. *J. Physiol.* **84**, 323–333.

VON BECHTEREW, A. (1883). Über den Verlauf der die Pupille Verengernden Nervenfasern im Gehirn und über die Localisation eines Zentrums für die Iris und Contraction der Augenmuskeln. *Pflüg. Arch. ges. Physiol.* **31**, 60–87.

VON BECHTEREW, A. (1897). Über die Kerne der mit den Augenbewegungen in Beziehung stehenden Nerven (des Oculomotorius, Abducens, und Trochlearis) und über die Verbindung derselben unter einander. *Arch. Anat. Physiol., Anat. Abt.*, pp. 307–315.

BENDER, M. B. (1945). Synkinetic pupillary phenomena and the Argyll Robertson pupil. *Arch. Neurol. Psychiat., Lond.*, **53**, 418–422.

BENDER, M. B. & ALPERT, S. (1937). Abnormal ocular and pupillary movements following oculomotor paralysis. *Arch. Ophthal., N.Y.*, **18**, 411–414.

BENDER, M. B. & FULTON, J. F. (1939). Factors in functional recovery of the oculomotor nerve in monkeys. *J. Neurol. Psychiat.* **2**, 285–292.

BENDER, M. B. & WEINSTEIN, E. A. (1943). Functional representation in the oculomotor and trochlear nuclei. *Arch. Neurol. Psychiat., Chicago*, **49**, 98–106.

BENJAMIN, J. W. (1939). The nucleus of the oculomotor nerve with special reference to innervation of the pupil and fibers from the pretectal region. *J. nerv. ment. Dis.* **89**, 294–310.

BERNARD, C. (1852). Expériences sur les fonctions de la portion céphalique du grand sympathique. *C.R. Soc. Biol., Paris*, **3**, 163–165.

BERNHEIMER, S. (1897*a*). Experimentelle Studien zur Kenntniss der Innervation des inneren und äusseren von Oculomotorius versorgten Muskeln des Auges. *v. Graefes Arch. Ophthal.* **44**, 481–525.

BERNHEIMER, S. (1897*b*). Ein Beitrag zur Kenntniss der Beziehungen zwischen den ganglion ciliare und der Pupillarreaction. *v. Graefes Arch. Ophthal.* **44**, 526–538.

BERNHEIMER, S. (1898). Die Reflexbahn der Pupillarreaction. *v. Graefes Arch. Ophthal.* **47**, 1–49.

BERNHEIMER, S. (1901). Die Lage des Sphinktercentrums. *v. Graefes Arch. Ophthal.* **52**, 302–316.

VAN BIERVLIET, J. (1899). Noyau d'origine du nerf oculo-moteur commun du lapin. *Cellule*, **16**, 7–29.

BOCHFONTAINE, L. T. (1875). Contributions à l'étude des phénomènes produits par la faradisation de l'écorce grise du cerveau. *C.R. Soc. Biol., Paris*, 6 sér. **2**, 387–392.

BOEDEKER, J. (1892). Über einen Fall von chronischer progressiver Augenmuskellähmung. *Arch. Psychiat. Nervenkr.* **23**, 313–338.

BOEKE, J. (1933). Innervationsstudien. III. Die Nervenversorgung des M. ciliaris und des M. sphincter iridis bei Saügern und Vögeln. *Z. mikr.-anat. Forsch.* **33**, 233–275.

BOEKE, J. (1936). Innervations Studien. IX. Zur Nervensorgung der Augenhäute. *Z. mikr.-anat. Forsch.* **39**, 477–520.

BRAUNSTEIN, P. C. (1894). *Zur Lehre von der Innervation der Pupillenbewegung.* Wiesbaden: J. F. Bergmann.

BROUWER, B. (1918). Klinisch-anatomische Untersuchung über den Oculomotoriuskern. *Z. ges. Neurol. Psychiat.* **40**, 152–193.

BUDGE, J. (1855). *Über die Bewegung der Iris.* Braunschweig: F. Vieweg und Sohn.

BUMM, A. (1899). Experimentelle Untersuchungen über das Ganglion ciliare der Katze. *Neurol. Zbl.* **18**, 957–958.

BUMM, A. (1901). Experimentelle Untersuchungen über das Ganglion ciliare der Katze. *Allg. Z. Psychiat.* **59**, 5–14.

BYRNE, J. G. (1933). *Studies on the Physiology of the Eye*, pp. 360 *et seq.* London: H. K. Lewis.

CARPENTER, F. W. (1906). The development of the oculomotor nerve, the ciliary ganglion, and the abducent nerve in the chick. *Bull. Mus. comp. Zool. Harv.* **48**, 141–228.

CARPENTER, F. W. (1911). The ciliary ganglion of birds. *Folia. neuro-biol., Lpz.*, **5**, 738–784.

CASSIRER, R. & SCHIFF, A. (1894). Beiträge zur Pathologie der chronischen Bulbärerkrankungen. *Arb. neurol. Inst. (Inst. Anat. Physiol. ZentNerv.) Univ. Wien*, **2**, 110–252.

CHRISTENSEN, K. (1934). Sympathetic and parasympathetic nerves in the orbit. *Anat. Rec.* **58**, Supplement 8–9.

CHRISTENSEN, K. (1936). Sympathetic and parasympathetic nerves in the orbit of the cat. *J. Anat., Lond.*, **70**, 225–232.

CLARK, S. L. (1937). Innervation of the intrinsic muscles of the eye of the cat. *J. comp. Neurol.* **66**, 307–325.

CLARK, W. E. LE GROS (1926). The mammalian oculomotor nucleus. *J. Anat., Lond.*, **60**, 426–448.

COGAN, D. G. (1937). Accommodation and the autonomic nervous system. *Arch. Ophthal., N.Y.*, **18**, 739–766.

COOPER, E. R. A. (1946). Development of the nuclei of the oculomotor and trochlear nerves (somatic efferent column). *Brain*, **69**, 50–57.

CRAMER, J. B. (1894). *Beiträge zur feineren Anatomie der Medulla oblongata und der Brücke.* Jena: G. Fischer.

CRISTINI, G. (1947). Movimenti associati palpebrali e pupillari anomali da rigenerazione errata delle fibre nervose dell' oculomotore commune. *Riv. oto-neuro-oftalm.* **22**, 323–334.

CROSBY, E. C. & WOODBURNE, R. T. (1943). The nuclear pattern of the non-tectal portions of the midbrain and isthmus in primates. *J. comp. Neurol.* **78**, 441–482.

CROUCH, R. L. (1936). The efferent fibres of the Edinger-Westphal nucleus. *J. comp. Neurol.* **64**, 365–373.

DARKSCHEWITSCH, L. (1889). Über die oberen Kern des N. oculomotorius. *Arch. Anat. Physiol., Anat. Abt.*, pp. 107–116.

DÉJÉRINE, J. & DARKSCHEWITSCH, L. (1887). Sur l'existence d'altérations nucléaires dans certaines paralysies des muscles de l'œil chez les tabétiques. *C.R. Soc. Biol., Paris*, **8**, sér. **4**, 70–76.

EDINGER, L. (1885). Über den Verlauf der centralen Hirnnervenbahnen mit Demonstrationen von Präparaten. *Arch. Psychiat. Nervenkr.* **16**, 858–859.

D'ERCHIA, F. (1894). Contributo allo studio della struttura e delle connessioni del ganglio ciliare. I. Sulla struttura del ganglio ciliare. *Monit. zool. ital.* **5**, 235–238.

D'ERCHIA, F. (1894). Contributo allo studio della struttura e delle connessioni del ganglio ciliare. II. Connessioni del ganglio ciliare. *Monit. zool. ital.* **6**, 157–164.

EUSTACHIUS, B. (1714). *Tabulae Anatomicae.* Romae: F. Gonzagae. Tab. XVIII.

FALLOPIUS, G. (1600). *Opera-Omnia.* Frankfurti: apud. haer. A. Welcheli. Tom. Sec. 293–294.

FOERSTER, O., GAGEL, O. & MAHONEY, W. (1936). Über die Anatomie, Physiologie, und Pathologie der Pupillarinnervation. *Verh. dtsch. Ges. inn. Med.* **48**, 386–398.

FORD, F. R., WALSH, F. B. & KING, A. (1941). Clinical observations on the pupillary phenomena resulting from regeneration of the third nerve with special reference to the Argyll-Robertson pupil. *Johns Hopk. Hosp. Bull.* **68**, 309–318.

FRANÇOIS-FRANCK, C. A. (1904). *Cours du Collège de France*, p. 257. Paris: O. Doin.

FRANK, C. (1921). Über die Lokalisation in den Augenmuskelnervenkernen und zwei noch unbekannte Kerne in Mittelhirn des Menschen. *J. Psychol. Neurol., Lpz.*, **26**, 200–227.

FRITZ, K. W. (1899). *Untersuchungen über des Ganglion ciliare.* Marburg: Köster und Schell.

GANFINI, C. (1911). Lo sviluppo del sistema nervoso simpatico in alcuni pesci. *Arch. ital. Anat. Embriol.* **10**, 574–645.

GASKELL, W. H. (1885). On the structure, distribution, and function of the nerves which innervate the visceral and vascular system. *J. Physiol.* **7**, 1–80.

GASKELL, W. H. (1889). On the relation between the structure, function, distribution and origin of the cranial nerves. *J. Physiol.* **10**, 153–211.

VAN GEHUCHTEN, A. (1893). *La Système Nerveux de l'Homme*, pp. 399 *et seq.* Lierre: J. van In et Cie.

VAN GEHUCHTEN, A. & VAN BIERVLEIT, J. (1901). Le noyau de l'oculo-moteur commun, 16, 19, et 21 mois après le résection du nerf. *Cellule*, **2**, 207–213.

GOLDBERG, M. (1891). Über die Entwickelung der Ganglien beim Hühnchen. *Arch. mikr. Anat.* **37**, 587–602.

GRÜNSTEIN, A. & GEORGIEFF, O. (1925). Zur Frage der Pupilleninnervation. *Z. ges. Neurol. Psychiat.* **94**, 438–486.

GULLBERG, J. E., OLMSTED, J. M. D. & WAGMAN, I. H. (1938). Reciprocal innervation of the sphincter and dilator pupillae. *Amer. J. Physiol.* **122**, 160–166*a*.

HALL, C. R. (1846). An experimental inquiry into the functions of the ophthalmic ganglion. *Edinb. med. surg. J.* **65**, 355–383; **66**, 84–108 and 312–353.

HALLER, A. (1743). *Iconum Anatomicarum Corporis Humani.* Gottingae: A. Vanderhoeck. Fig. VI and p. 46, n. 50.

HARRISON, F., MAGOUN, H. W. & RANSON, S. W. (1938). Some determinations of thresholds to stimulation with faradic and direct current in the brain stem. *Amer. J. Physiol.* **121**, 708–718.

HELMHOLTZ, H. L. F. (1855). Über die Accommodation des Auges. *v. Graefes Arch. Ophthal.* **1** (ii), 1–74.

HENKE, W. (1860). Der Mechanismus der Accommodation für Nähe und Ferne. *Arch. Ophthal.* **6**, 53–72.

HENSEN, V. & VÖLCKERS, C. (1868). *Experimentaluntersuchung über den Mechanismus der Accommodation.* Kiel: Schwers.

HENSEN, V. & VÖLCKERS, C. (1878). Über den Ursprung der Accommodationsnerven. *v. Graefes Arch. Ophthal.* **24**, 1–26.

HERTEL, E. (1907). Experimenteller Beitrag zur Kenntnis der Pupillenverengerung auf Lichtreize. *v. Graefes Arch. Ophthal.* **65**, 106–134.

HODES, R. (1940). The efferent pathway for reflex pupillomotor activity. *Amer. J. Physiol.* **131**, 144–155.

HODES, R. & MAGOUN, H. W. (1942*a*). Autonomic responses to electrical stimulation of the forebrain and midbrain with special reference to the pupil. *J. comp. Neurol.* **76**, 169–190.

HODES, R. & MAGOUN, H. W. (1942*b*). Pupillary and other responses from stimulation of the frontal cortex and basal telencephalon of the cat. *J. comp. Neurol.* **76**, 461–473.

HOLLINSHEAD, W. H. & CLARK, S. L. (1935). The Nissl granules of autonomic neurons. *J. comp. Neurol.* **62**, 155–169.

HOLTZMANN, H. (1896). Untersuchungen über Ciliarganglion und Ciliarnerven. *Morph. Arb.* **6** (i), 114–142.

INGRAM, W. R. & RANSON, S. W. (1935). Nucleus of Darkschewitsch and nucleus interstitialis in the brain of man. *J. nerv. ment. Dis.* **81**, 125–137.

INGRAM, W. R., RANSON, S. W. & HANNETT, F. I. (1931). Pupillary dilatation produced by direct stimulation of the tegmentum of the brain stem. *Amer. J. Physiol.* **98**, 687–691.

JAKOB, C. (1894). Über einen Fall von Hemiplegie und Hemianästhesie mit gekreuzter Oculomotoriuslähmung. *Dtsch. Z. Nervenheilk.* **5**, 188–223.

JEGOROW, J. (1886). Recherches anatomo-physiologiques sur le ganglion ophtalmique. *Arch. slav. Biol.* **2**, 376–399.

JEGOROW, J. (1887). Recherches anatomo-physiologiques sur le ganglion ophtalmique. *Arch. slav. Biol.* **3**, 50–129 and 322–345.

JENDRÁSSIK, E. (1896). Allgemeine Betrachtungen über das Wesen und die Functionen des vegetativen Nervensystems. *v. Graefes Arch. Ophthal.* (*Separatabr.*), **145**, 427–457.

JESSOP, W. H. (1886). On the anatomy, histology and physiology of the intraocular muscles of mammals. *Proc. roy. Soc. Lond.* **60**, 478–484.

JOHNSTONE, J. (1771). *An Essay on the Use of the Ganglions of the Nerves*, pp. 14–23. Shrewsbury: J. Edowes.

JULIUSBERGER, O. & KAPLAN, L. (1899). Anatomischer Befund bei einseitiger Oculomotoriuslähmung im Verlaufe von progressiver Paralyse. *Neurol. Zbl.* **18**, 486–495.

KAHLER, O. & PICK, A. (1881). Zur Localisation partieller Oculomotoriuslähmungen. *Prag. Z. Heilk.* **2**, 301–312.

KARPLUS, J. P. & KREIDL, A. (1910). Gehirn und Sympathicus. II. Sympathicuszentrum im Zwischenhirn. *Pflüg. Arch. ges. Physiol.* **135**, 401–416.

KARPLUS, J. P. & KREIDL, A. (1912). Über die Pupillarreflexbahn. *Klin. Mbl. Augenheilk.* **1** (i), 586–588.

KARPLUS, J. P. & KREIDL, A. (1918). Gehirn und Sympathicus. IV. Mitteilung. *Pflüg. Arch. ges. Physiol.* **171**, 192–200.

KELLER, A. D. (1946). The striking inherent tonus of the deafferentated central pupillo-constrictor neurons. *Fed. Proc.* **5**, 55.

KISS, F. (1932). Sympathetic elements in the cranial and spinal ganglia. *J. Anat., Lond.*, **66**, 488–498.

KNIES, M. (1891). Über die centralen Störungen der willkürlichen Augenmuskeln. *Arch. Augenheilk.* **23**, 19–51.

VON KÖLLIKER, A. (1896). *Handbuch der Gewelbehedre des Menschen*, **6**, Aufl., Bd. 2, 293–300. Leipzig: W. Englemann.

KOSTENITSCH, J. (1893). Über einen Fall von motorischer Aphasie, zugleich ein Beitrag zur Frage nach der anatomischen Grundlage der Pupillenstarre. *Dtsch. Z. Nervenheilk.* **4**, 367–376.

KRAUSE, W. (1861). *Anatomische Untersuchungen.* Hannover: Hahn.

KRAUSE, W. (1881). Über die Doppelnatur des Ganglion ciliare. *Morph. Jb.* **7**, 43–56.

KUNTZ, A. (1920). The development of the sympathetic nervous system in man. *J. comp. Neurol.* **32**, 173–214.

KUNTZ, A. & RICHINS, C. A. (1946). Reflex pupillodilator mechanisms. An experimental analysis. *J. Neurophysiol.* **9**, 1–7.

KUNTZ, A., RICHINS, C. A. & CASEY, E. J. (1946). Reflex control of the ciliary muscle. *J. Neurophysiol.* **9**, 445–451.

KURÉ, K., SUSUKI, T., KANEKO, Y. & OKINAKA, S. (1933). Die Kerne der extrapyramidalen Fasern für die Augenmuskeln. *Z. Zellforsch.* **17**, 453–466.

LANCISI, J. M. (1723). *Altera de Gangliis Nervorum.* In J. B. Morgagni's *Adversaria Anatomica Quinta*, pp. 101–119. Lugduni: apud J. A. Langerak.

LANGENDORFF, O. (1894). Ciliarganglion und Oculomotorius. *Pflüg. Arch. ges. Physiol.* **56**, 522–527.

LANGENDORFF, O. (1900). Zur Verständigung über die Natur des Ciliarganglions. *Klin. Mbl. Augenheilk.* **38**, 307–314.

LANGLEY, J. N. & ANDERSON, H. K. (1892). The action of nicotine on the ciliary ganglion and the endings of the third cranial nerve. *J. Physiol.* **13**, 460–468.

LANGLEY, J. N. & DICKINSON, W. L. (1889). On the local paralysis of peripheral ganglia, and on the connexion of different classes of nerve fibres with them. *Proc. roy. Soc., Lond.*, **46**, 423–431.

LATUMETEN, J. A. (1924). *Over de Kernen van den Nervus Oculomotorius.* Utrecht: P. den Boer.

VON LENHOSSÉK, M. (1911). Das Ganglion ciliare der Vögel. *Arch. mikr. Anat.* **76**, 745–769.

LENZ, G. (1928). Untersuchungen über die anatomische Grundlage von Pupillenstörungen. *Ber. dtsch. ophthal. Ges.* **47**, 234–246.

LENZ, G. (1929). Über die anatomische Grundlage der Ophthalmoplegia interna. *Z. Augenheilk.* **69**, 102–113.

LEVINSOHN, G. (1904). Beitrag zur Physiologie des Pupillenreflexes. *v. Graefes Arch. Ophthal.* **59**, 191–220 and 436–458.

LEVINSOHN, G. (1917). Zur Kenntnis der Physiologie und Pathologie der Pupillenbahnen. *Dtsch. Z. Nervenheilk.* **56**, 300–319.

LODATO, G. (1910). Sulle alterazioni del ganglio ciliare in sequito al taglio delle sue radici. *Arch. Ottalmol., Palermo*, **8**, 165–215.

LONGET, F. A. (1842). *Anatomie et Physiologie du Système Nerveux*, T. **2**, 377–390. Paris: Fortin, Masson et Cie.

LUCO, J. V. & SAVVESTRINI, H. (1942). Responses of the iris to prolonged stimulation of its nerve supply. *J. Neurophysiol.* **5**, 27–31.

MCDOWALL, R. J. S. (1925). The reactions of the pupil in the chloralosed animal. *Quart. J. exp. Physiol.* **15**, 177–180.

MAGITOT, A. (1909). L'apparition précoce du réflexe photo-moteur au cours du développement. *Ann. Ocul., Paris*, **141**, 161–181.

MAGITOT, A. (1921). *L'Iris.* Paris: O. Doin.

MAJANO, N. (1903). Über Ursprung und Verlauf des Nervus oculomotorius im Mittelhirn. *Mschr. Psychiat. Neurol.* **13**, 1, 139, 229 and 291.

MALONE, E. F. (1913). Recognition of the somatic motor chain of nerve cells by means of fundamental type of cell structure. *Anat. Rec.* **7**, 67–82.

MANN, I. C. (1927). The developing third nerve in human embryos. *J. Anat., Lond.*, **61**, 424–438.

MARINA, A. (1899). Das Neuron des Ganglion ciliare und die Centra der Pupillenbewegungen. *Dtsch. Z. Nervenheilk.* **14**, 356–412.

MARINA, A. (1901). Studien über die Pathologie des Ciliarganglions bei Menschen. *Dtsch. Z. Nervenheilk.* **20**, 369–396.

MARINESCO, G., PARHON, C. & GOLDSTEIN, M. A. (1908). Sur la nature du ganglion ciliare. *C.R. Soc. Biol., Paris*, **64**, 88–89.

MAYO, H. (1823). *Anatomical and Physiological Commentaries*, No. II, p. 5. London: T. and G. Underwood.

MECKEL, J. F. (1748). *De Quinto Pare Nervorum Cerebri*, pp. 29–30.

MENDEL, E. (1887). Über den Kernsprung des Augen-Facialis. *Neurol. Zbl.*, **6**, 537–542.

MICHEL, J. (1894). Über die feinere Anatomie des Ganglion ciliare. *Trans. 8th Int. Ophthal. Congr., Edinb.*, pp. 195–197.

MINGAZZINI, G. (1913). *Anatomia Clinica dei Centri Nervosi*, 2nd ed., pp. 412 *et seq.* Torino: Unione Tipografico.

MINGAZZINI, G. (1928). *Medulla Oblongata und Brücke.* In G. von Möllendorf's *Handbuch der Microskopische Anatomie des Menschen*, Bd. 4, pp. 966 *et seq.* Berlin: Julius Springer.

MOELI, C. F. (1897). Weitere Mittheilungen über die Pupillenreaction. *Berl. Klin. Wschr.* **34**, 373–401.

MOHONEY, J. B., OLMSTED, J. M. D., MORGAN, M. W. & WAGMAN, I. H. (1942). The pathway of sympathetic nerves to the ciliary ganglion. *Amer. J. Physiol.* **135**, 759–762.

VON MONAKOW, C. (1895). Experimentelle und pathologische anatomische Untersuchungen über die Haubenregion. *Arch. Psychiat.* **27**, 286–478.

VON MONAKOW, C. (1905). *Gehirnpathologie*, pp. 1040 *et seq.* Wien: G. Hölder.

MORAT, J. P. & DOYON, M. (1891). Le grand sympathique nerf accommadateur. *Arch. Physiol. norm. path., Paris*, 5 sér., **3**, 507–521.

MORGAN, M. W., OLMSTED, J. M. D. & WATROUS, W. G. (1940). Sympathetic action in accommodation for near vision. *Amer. J. Physiol.* **128**, 588–591.

MUCK, F. (1815). *Dissertatio Anatomica de Ganglio Ophthalmico et Nervis Ciliaribus Animalium*, p. 67. Landshuti: Typis Josephi Thoman.

MÜLLER, L. R. & DAHL, W. (1910). Die Beteiligung des sympathischen Nervensystems an der Kopfinnervation. *Dtsch. Arch. klin. Med.* **99**, 48–107.

MÜLLER, L. R. & DAHL, W. (1912). Die Innervierung der männlichen Geschlechtsorgane. *Dtsch. Arch. klin. Med.* **107**, 113–159.

NEIDING, M. & FRANKFURTHER, W. (1911). Über das Vorkommen des Edinger-Westphalschen Kerns bei einigen Säugetieren und seine Bedeutung. *Neurol. Zbl.* **30**, 1282–1293.

OLMSTED, J. M. D. (1944). The role of the autonomic nervous system in accommodation for far and near vision. *J. nerv. ment. Dis.* **99**, 794–798.

OLMSTED, J. M. D. & MORGAN, M. W. (1941). The influence of the cervical sympathetic nerve on the lens of the eye. *Amer. J. Physiol.* **133**, 720–723.

ONODI, A. D. (1901). Das Ganglion ciliare. *Anat. Anz.* **19**, 118–124.

OPPENHEIM, H. (1888). Über einen durch Störungen im Bereich der Augenmuskeln und der Kehlmuskulaturmerkwürdigen Fall von juveniler progressiver Muskelatrophie. *Char.-Ann.* **13**, 384–391.

PACETTI, G. (1894). Sulla lesione del tronco dell' encephala nella tabe. *Riv. sper. freniat.* **20**, 518–558.

PANEGROSSI, G. (1898). Contributo allo studio anatomo-fisiologico dei centri dei nerve oculomotorii dell' uomo. *Ric. morf., Roma*, **6**, 103–155.

PANEGROSSI, G. (1904). Weiterer Beitrag zum Studium der Augenmuskelnervenkerne. *Mschr. Psychiat. Neurol.* **10**, 268–281 and 344–376.

PARSONS, J. H. (1901). On dilatation of the pupil from stimulation of the cortex cerebri. *J. Physiol.* **26**, 366–379.

PATON, L. & MANN, I. C. (1925). The development of the third nerve nucleus and its bearing on the Argyll-Robertson pupil. *Trans. ophthal. Soc. U.K.* **45** (2), 610–633.

PEARSON, A. A. (1944). The oculomotor nucleus in the human foetus. *J. comp. Neurol.* **80**, 47–63.

PERLIA, R. (1889). Die Anatomie des Oculomotoriuscentrums beim Menschen. *v. Graefes Arch. Ophthal.* **35**, 287–304.

PESCHEL, M. (1893). Über das Orbital-Nervensystem des Kaninchens mit specieller Berücksichtigung der Ciliarnerven. *v. Graefes Arch. Ophthal.* **39** (2), 1–44.

PINELES, F. (1896). Zur pathologischen Anatomie der reflectorischen Pupillenstarre. *Arb. neurol. Inst.* (*Inst. Anat. Physiol. ZentNerv.*) *Univ. Wien*, **4**, 101–109.

PINES, J. L. (1927). Zur Morphologie des Ganglion ciliare beim Menschen. *Z. mikr.-anat. Forsch.* **10**, 313–380.

PINES, J. L. & FRIEDMAN, E. (1929). Zur vergleichenden Histologie des Ganglion ciliare bei Säugetieren. *Z. mikr.-anat. Forsch.* **16**, 259–294.

PINES, J. L. & PINSKY, J. (1932). Über die Nervenapparate des Corpus ciliare bei Säugetieren. *Anat. Anz.* **75**, 160–168.

PITZORNO, M. (1913*a*). Il ganglio ciliare dei selacei. *Arch. ital. Anat. Embriol.* **11**, 527–535.

PITZORNO, M. (1913*b*). Contributo allo conoscenza della struttura del ganglio ciliare dei cheloni. *Arch. ital. Anat. Embriol.* **12**, 367–379.

RAMON Y CAJAL, S. (1911). *Histologie du Système Nerveux.* T. ii, pp. 235 *et seq.* Trad. par L. Azoulay. Paris: A. Maloine.

RANSON, S. W. & MAGOUN, H. W. (1933). The central path of the pupillo-constrictor response to light. *Arch. Neurol. Psychiat.* **30**, 1193–1204.

REICHARDT, M. (1875). Beitrag zur Anatomie des Ganglion ophthalmicum, pp. 1–28. München: E. Stahl.

VON RETZIUS, G. (1881). Untersuchungen über die Nervenzellen der cerebrospinalen Ganglien und der übrigen peripherischen Kopfganglien. *Arch. Anat. Physiol., Anat. Abt.*, pp. 369–402.

RETZIUS, G. (1894). Über das Ganglion ciliare. *Anat. Anz.* **9**, 633–637.

RUSSELL, W. R. & WRIGHT, M. H. (1948). Case Report: abnormal innervation of the sphincter pupillae and ciliary muscle following third nerve regeneration. *J. Neurol. Neurosurg. Psychiat.* **11**, 288–290.

RUYSCH, F. (1722). Thesaurus Anatomicus, II, p. 4. Amstelaedami: apud Jansonio-Waesbergio.

SALA, L. (1910). Sulla fina struttura del ganglio ciliare. *Mem. Inst. Lombardo sci. lett.* **21**, 133–139.

SCHACHER, P. C. (1701). *De Cataracta*, p. 9. Lipsiae: typ. J. C. Brandenburgeri.

SCHNEIDER, A. (1879). *Beitrage zur vergleichenden Anatomie und Entwicklungsgeschichte der Wirbelthiere.* Berlin.

SCHWALBE, G. (1879). Das Ganglion oculomotorii. *Jena. Z. Naturwiss.* **13**, 173–268.

SIEMERLING, E. (1891). Über die chronische progressive Lähmung der Augenmuskeln. *Arch. Psychiat. Nervenheilk.* **22** (Supplementheft), 1–206.

SIEMERLING, E. & BOEDEKER, J. (1897). Chronische fortschreitende Augenmuskellähmung und progressive Paralyse. *Arch. Psychiat. Nervenheilk.* **29**, 421–473 and 716–767.

SPALLITA, F. & CONSIGLIO, M. (1893). Richerche sopra i nervi costrittori della pupilla. *Arch. ottal. Palermo*, **1**, 18–35.

SPITZKA, E. C. (1888). The oculomotor centres and their co-ordinators. *J. nerv. ment. Dis.* **13**, 413–432.

STARR, M. A. (1888). Ophthalmoplegia externa partialis. *J. nerv. ment. Dis.* **13**, 300–316.

STOTLER, W. A. (1937). The innervation of the intrinsic muscles of the eye; an experimental study. *Proc. Soc. exp. Biol., N.Y.*, **36**, 576–577.

STUELP, O. (1895). Zur Lehre von der Lage und die Function der einzelnen Zellgruppen des Oculomotoriuskernes. *v. Graefes Arch. Ophthal.* **41**, 1–29.

SZENTÁGOTHAI, J. (1943). Die zentrale Leitungsbahn des Lichtreflexes der Pupillen. *Arch. Psychiat. Nervenheilk.* **115**, 136–156.

TSUCHIDA, U. (1906). Über die Ursprungskerne der Augenbewegungsnerven. *Arb. hirnanat. Inst. Zürich*, pp. 1–205.

UREY, B. & GELLHORN, E. (1939). Role of the sympathetic system in reflex dilatation of the pupil. *J. Neurophysiol.* **2**, 268–275.

UREY, B. & OLDBERG, E. (1940). Effect of cortical lesions on affective pupillary reactions. *J. Neurophysiol.* **3**, 201–213.

VALENTIN, G. (1839). *De Functionibus Nervorum Cerebralium et Nervi Sympathici.* p. 19. Bernae: sumpt. Huber et Socii.

WARD, A. A. & REED, H. L. (1946). Mechanism of pupillary dilatation elicited by cortical stimulation. *J. Neurophysiol.* **9**, 329–335.

WARWICK, R. (1951). A study of retrograde degeneration in the oculomotor nucleus of the rhesus monkey. *Brain*, **73**, 532–543.

WARWICK, R. (1953*a*). Observations upon certain reputed accessory nuclei of the oculomotor complex. *J. Anat., Lond.*, **87**, 46–53.

WARWICK, R. (1953*b*). Representation of the extra-ocular muscles in the oculomotor nuclei of the monkey. *J. comp. Neurol.* **98**, 449–504.

WESTPHAL, C. (1887). Über einen Fall von chronischer progressiver Lähmung das Augenmuskeln (Ophthalmoplegia externa) nebst Beschreibung von Ganglienzellengruppen im Bereiche des Oculomotoriuskerns. *Arch. Psychiat. Nervenheilk.* **98**, 846–871.

WHITTERIDGE, D. (1937). The transmission of impulses through the ciliary ganglion. *J. Physiol.* **89**, 99–111.

WILLIS, T. (1664). *Cerebri Anatome*, p. 172. Amstelodami: apud Casparum Commelinum.

WINSLOW, J. B. (1732). *Exposition Anatomique de la Structure du Corps Humain*, T. III. Paris: Desprez et Desessartz.

ZEGLINSKI, A. (1885). Experimentelle Untersuchungen über die Irisbewegung. *Arch. Anat. Physiol., Physiol. Abt.*, pp. 1–14.

ZERI, A. (1895). Sulla alterazione dei centri nervosi nella tabe. *Riv. sper. freniat.* **21**, 586–641.

ZINN, J. G. (1780). *Descriptio Anatomica Oculi Humani*, p. 167. Goettingae: apud Abrami Vanderhoeck.

ZWEIG, H. (1921). Studien zur vergleichenden Anatomie des zentralen Hohlengraus bei den Wirbeltheiren. *Jb. Psychiat. Neurol.* **41**, 18–38.

EXPLANATION OF PLATES

PLATE 1

Fig. 1. A transverse section just rostral to the main oculomotor nuclei. The Edinger-Westphal columns have fused caudal to this and are extended ventro-dorsally in the midline as the antero-median nucleus. Cresyl fast violet. ×32.

Fig. 2. This field shows the various cell groups visible in transverse sections through the rostral third of the oculomotor complex. Note the Edinger-Westphal columns (*E.W.*), which lie dorsal to the main third nerve nuclei (III) and are approaching close to each other at this level. The interstitial nucleus (I) and the nucleus of Darkschewitsch (*D*) are also shown. Cresyl fast violet. ×32.

Fig. 3. Sections through the left and right ciliary ganglion of a monkey subjected, 11 days before death, to removal of the contents of the right eye. Even at this low magnification it is obvious that most of the cells in the right ganglion (on the right in the photograph) are paler than those in the normal left ganglion of this animal (on the left). The pallor is due to chromatolysis. Cresyl fast violet. ×50.

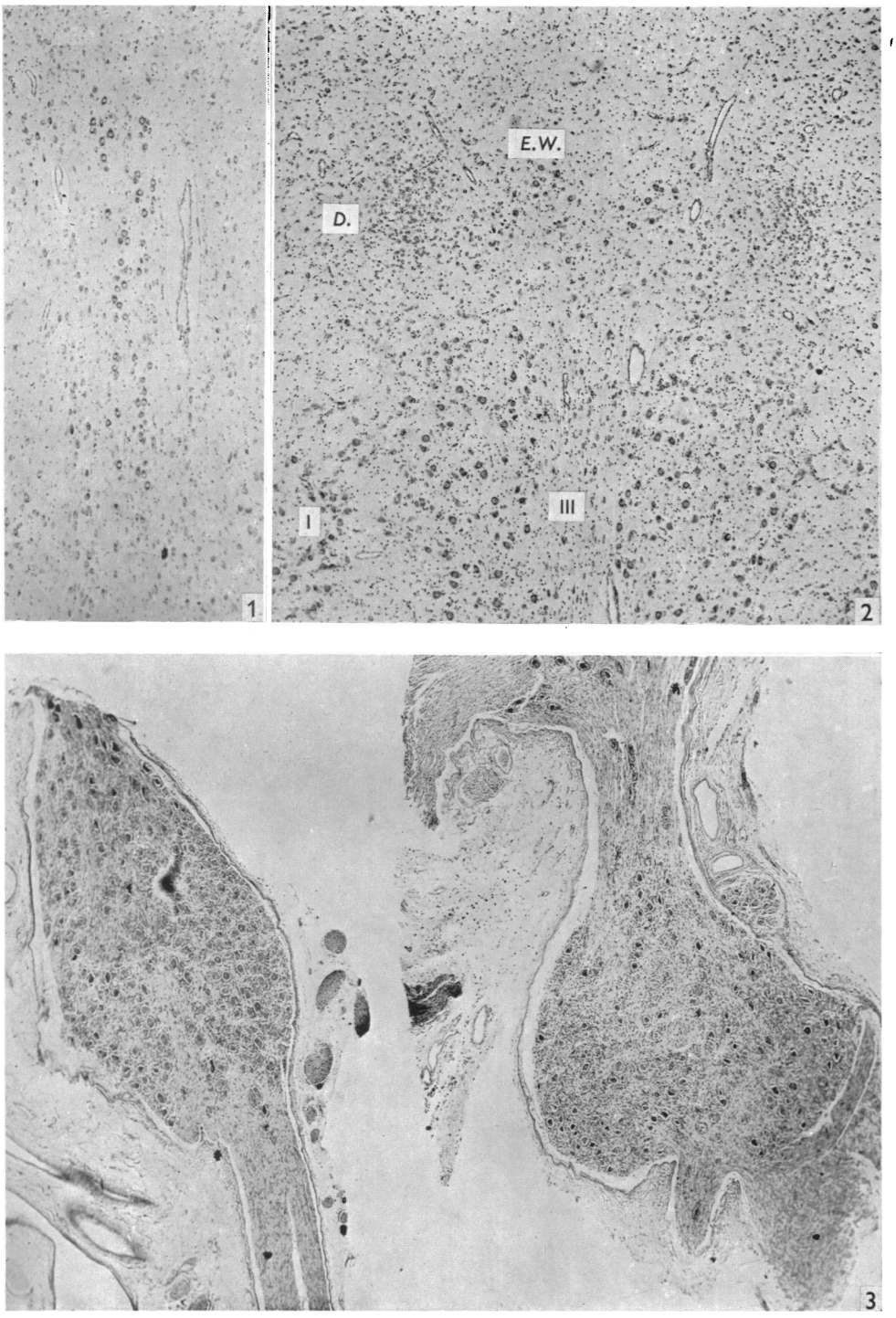
PLATE 2

Fig. 4. Nerve cells in a normal ciliary ganglion from a rhesus monkey. Note the prominent and evenly distributed chromatin granules and central nuclei of these neurones. Cresyl fast violet. ×176.

Fig. 5. Another field in a normal ciliary ganglion to show the only other type of cell encountered in this ganglion in the present research. Two such cells appear amongst the usual type; note their small size and peripheral disposition of chromatin granules. Cresyl fast violet. ×176.

Fig. 6. Degenerating nerve cells in the right ciliary ganglion of a monkey killed 10 days after division of the short ciliary nerves in the right orbit. All the cells show pronounced retrograde reaction, in their loss of Nissl granules and nuclear eccentricity. The dense appearance of one cell exemplifies the chromophil phase of chromatolysis seen in many types of neurone during retrograde degeneration. Contrast these cells with those in the left ciliary ganglion of the same animal (fig. 4). Cresyl fast violet. ×176.

Fig. 7. Field in ciliary ganglion showing chromatolysis in a small group at its nerve cells following iridectomy on the same side. Many of the cells contain obvious Nissl granules and are normal. Contrast this limited distribution of retrograde changes with the almost universal effects after evacuation of the eyeball (fig. 6). Cresyl fast violet. ×176.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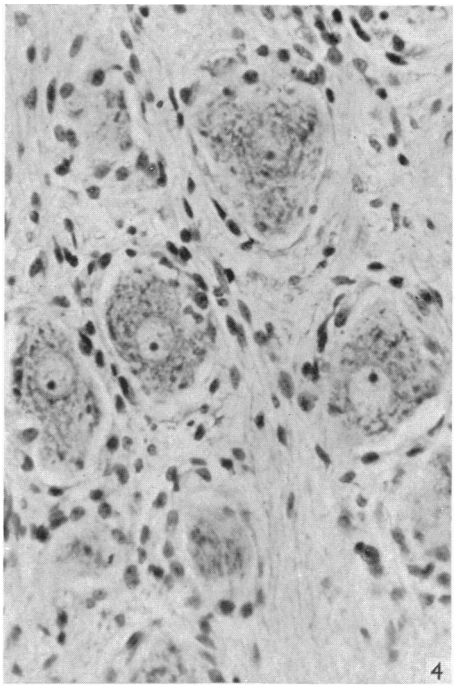
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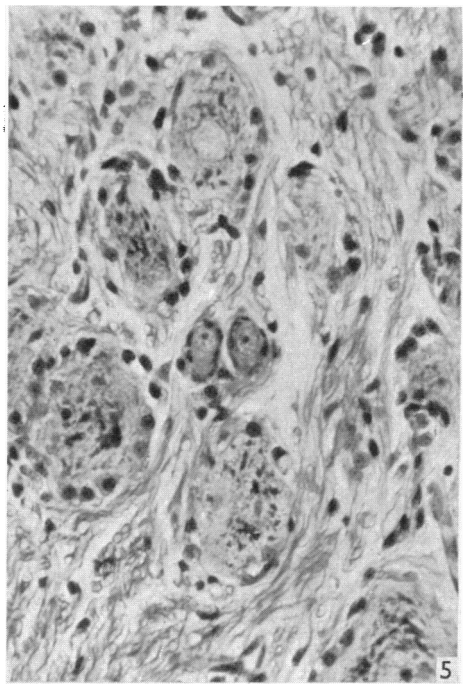
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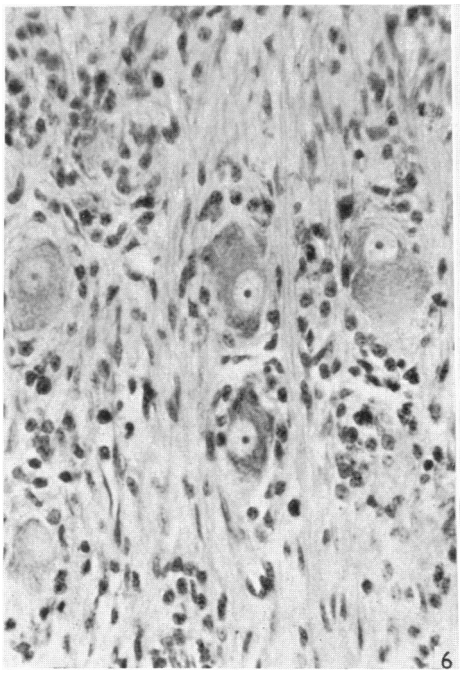
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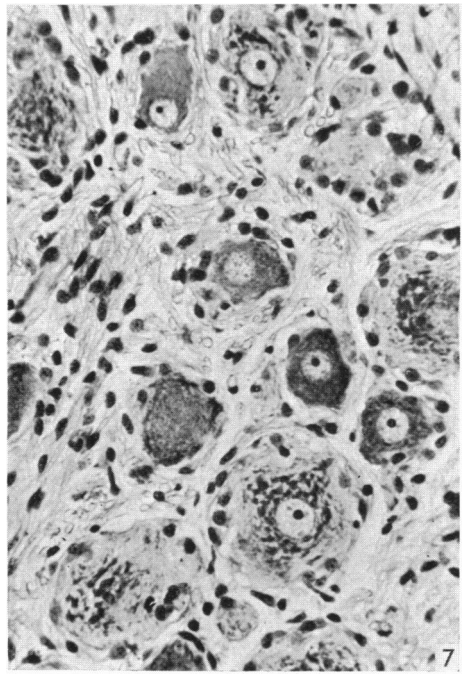
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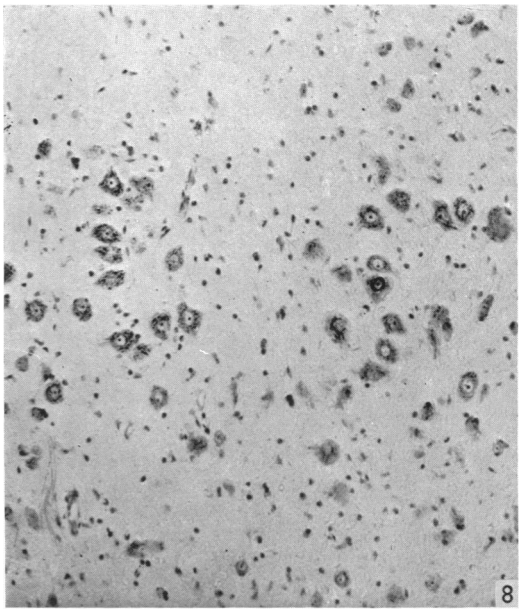
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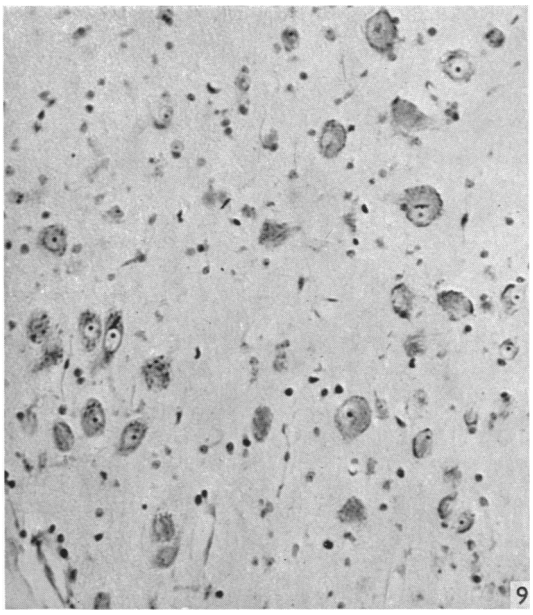
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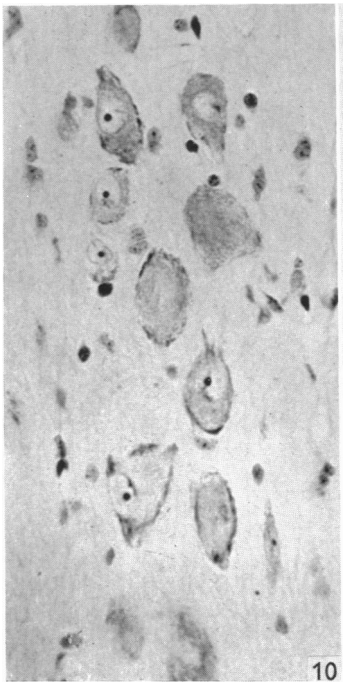
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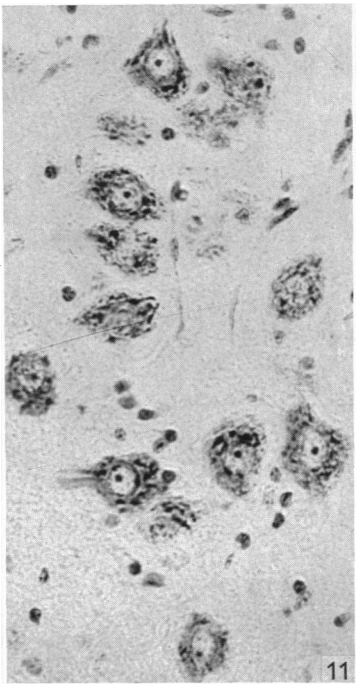
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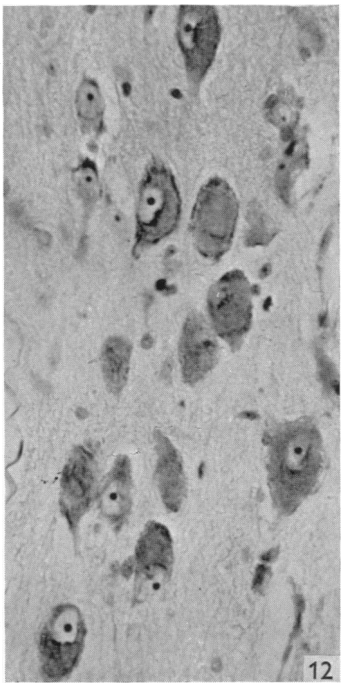
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PLATE 3

Fig. 8. This field show the right and left Edinger-Westphal columns in the midbrain of a monkey subjected to right ciliary ganglionectomy. Even at this magnification some of the cells in the right nucleus display a loss of Nissl granules. Cresyl fast violet. ×80.

Fig. 9. A field from the same animal as in the preceding figure, but at a more rostral level. Cells in the right and left halves of the antero-median nucleus can be compared. Those on the left contain Nissl granules, whereas almost all the cells on the right display marked retrograde degeneration (chromatolysis, swelling, and nuclear eccentricity). Cresyl fast violet. ×80.

Fig. 10. Chromatolysis in the nerve cells of the antero-median nucleus of another monkey, 11 days following ciliary ganglionectomy. All the cells in the ipsilateral half of the nucleus showed such changes. Cresyl fast violet. ×176.

Fig. 11. Normal nerve cells of the monkey's antero-median nucleus. Compare with the adjacent figures and note the contrast. Cresyl fast violet. ×220.

Fig. 12. Chromophil stage of retrograde degeneration in nerve cells of the antero-median nucleus of a third monkey which had been subjected to ciliary ganglionectomy. Compare these cells with the normal neurones of this nucleus, shown in fig. 11. Cresyl fast violet. ×176.