THE BRITISH JOURNAL OF OPHTHALMOLOGY

DECEMBER, 1921

COMMUNICATIONS

THE FOURTH CRANIAL NERVE*

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LONDON

THE fourth cranial nerve is an unsolved riddle. It is the only nerve which has a dorsal decussation, that is to say, in the complete sense of the term. Of course, we are familiar with the fact that motor nuclei are connected with other nuclei on the opposite side of the central nervous system, e.g., the motor cells in the anterior cornua are connected with the opposite side of the spinal cord by decussating fibres. But the case of the fourth nerve is totally different, in that its fibres pass out of the central nervous system to a muscle on the opposite side of the body.

This nerve seems to be unique in the central nervous system. The other nuclei dealing with ocular muscles show variations of the ordinary type of decussation. The sixth nucleus probably has comparatively few decussating fibres; the third nucleus has a considerable number in the posterior part. But with regard to the fourth, it is probable that there are no decussating fibres within the central nervous system other than those which pass out in the trunk of the nerve. The diagram of the third and fourth nerve nuclei (Edinger,⁽¹⁾ I., Fig. 171) taken from Bernheimer, of all the varieties which Mr. Paton showed us some time ago, probably represents the condition better than any other, or most other, of

*Communicated to the Section of Ophthalmology of the Royal Society of Medicine on October 14, 1921.

the theories. Another peculiarity of the fourth nerve is, that it is essentially somatic in mammals, that is to say, it supplies purely somatic muscles; it has no visceral fibres: but this requires further consideration, as I hope to show later on.

Little assistance in solving the problem is afforded by disease in man, not only with regard to the fourth nucleus, but also other motor ocular nuclei, owing to the absence, so far as I can find in the neurological literature to which I have had access, of information of definite nuclear lesions, proved pathologically to be so. Consequently it is very difficult to get any information from pathological sources, such as one gets in regard to other lesions of the central nervous system, as to the conditions which occur as the result of purely nuclear lesions.

Another point is the absence of experimental lesions in this neighbourhood sufficiently exactly localised to produce definite results. Practically it is an inaccessible part of the central nervous system from the experimental point of view, and nothing but Clark's apparatus would succeed in producing lesions sufficiently well defined for one to obtain good results from experimental lesions, and the literature of the subject gives us but little help. Therefore the explanation must be sought in comparative anatomy and embryology.

Comparative anatomy.—With regard to comparative anatomy, it is extraordinary that the fourth nerve exists right down to the very beginnings of the vertebrates. It is present in the lowest group of fishes, the Cyclostomata, as, e.g., in the lamprey (*Petromyzon*). It is even represented in *Myxine* (the hag fish), in which the eyes are in a very degenerate condition, and the sixth nerve is absent. The fourth nerve, therefore, is represented throughout the vertebrate series, and in all it decussates dorsally, passing through the anterior medullary velum, exactly as in the highest mammals. Hence, phylogenetically it is a very primitive nerve.

Figs. 1-3 are derived from the excellent work of Davidson Black,⁽²⁾ a pupil of Ariëns Kappers, and show the position of the nuclei of the cranial nerves, and the points of exit of the nerves from the central nervous system in the various groups of vertebrates. The diagrams illustrate a transparent view of the anterior part of the central nervous system. They show the third nerve and third nerve nucleus, the relation of the fourth nerve, and so on, throughout the different species. In fishes, the fourth is close up to the third; in the Dipnoan fishes there is an approximation between the fourth and the fifth.

Many interesting points have been brought out by Davidson Black's laborious researches, but time does not permit me to enter into details. One point of interest may be mentioned, viz., the starting of Deiter's nucleus, and the extremely near relationship

there is between the sixth nerve and Deiter's nucleus. On some future occasion it would be instructive to consider the sixth nerve and its relations to Deiter's nucleus, the vestibular nerve, and the cerebellum; i.e., the relationship of the sixth nerve to the co-ordination of movement, with special reference to tonus and posture.

A point which comes out of Davidson Black's and other allied investigations is one which is not immediately related to the fourth nerve, but which throws some light on it; viz., the division of the third nerve nucleus into sub-groups of cells. We are familiar in man with the very definite sub-grouping of the nerve cells in the third nucleus. In the lowest species the third nucleus forms one scattered group of nerve cells, not gathered together into specific groups; but when we consider the species in which specific grouping occurs, we find a somewhat unexpected distribution. The differentiation of the third into sub-groups is found in ganoid and teleostean fishes, but not in selachians and dipnoans. The Dipnoi are fishes with lungs as well as gills, and they form a sort of bridge to the amphibia. The sub-grouping is found to persist in anuran amphibians, reptiles, birds and mammals. Consequently this particular grouping is of some importance, and tends to show, as Davidson Black points out, that this differentiation is a late feature, and is not explained by the straightforward trend of phylogenetic evolution. Thus, this author says: "It would thus seem probable that the factors which determine the anuran oculomotor cell arrangement must have appeared comparatively late in phylogeny. The eyes of most fishes are normally focussed for near objects when at rest, and since the eyes of most amphibians, reptiles, birds, and mammals are normally focussed for distance (Beer), it is not improbable that the chief original cause of the amphibian oculomotor nuclear specialization may be seen in the readjustment of the mechanism of accommodation which must have taken place in phylogeny during the evolution of the amphibian type." (Davidson Black⁽³⁾.)

This brings out a very important point, much emphasized by Kappers in his theory of neurobiotaxis. As his pupil, C. J. Herrick⁽⁴⁾ says, "Functional differentiation in the phylogeny, as in the ontogeny, began at the periphery; and here the elaboration of functionally specific end organs and conduction paths advances much more rapidly on the sensory side than on the motor side of the reflex circuits. At an early stage when all the sense organs and afferent nerve components are differentiated substantially as in the adult the motor mechanisms of the spinal cord and nerves may show very little evidence of capacity for diversified response, simple swimming movements toward or away from the source of the stimulus being almost the only possible reactions. In other

words, the elaborately diversified receptor mechanisms converge into a very simply organised final common path."

I lay special stress on these points, because they support Kappers' theory of neurobiotaxis. According to this theory, the migration of motor nuclei is especially associated with a chemotactic force. The nucleus is attracted to the foci of the specific afferent impulses for which the given motor nerve provides the final common path. The theory is extremely attractive, and Kappers and others have attached great importance to it; but we must be on our guard against using it as a *deus ex machinâ* in problems of difficulty. Thus, Sir Arthur Keith, in the last edition of his *Human Embryology*, "explains" the riddle of the fourth nerve by neurobiotaxis. He does not, however, venture to elaborate the steps of the explanation. The theory does seem to afford some explanation of the mesencephalic situation of the third and fourth nuclei. These nuclei are morphologically serial with spinal hind brain somatic motor nuclei, and their displacement forwards may be attributed to the increasing preponderance of the head segment as the site par excellence of the projicient sense organs, and above all, of the eyes.

Embryology.—In 1881 Milnes Marshall⁽⁵⁾ pointed out that the ocular muscles were derived in Elasmobranchs (sharks and rays) in the following way: The muscles associated with the third nerve came from the first or pre-mandibular head cavity; the fourth nerve muscles came from the mandibular head cavity; and the sixth from the hyoid. This may be the case in fishes, but it is very difficult to get definite evidence with regard to these points in higher mammals, because in the highest mammals either head cavities do not exist, or are very transient, and it is very difficult to locate the different muscles. Figs. 4-8 are diagrams of Miss Platt's work⁽⁶⁾ on the Elasmobranchs, and show how these muscles are developed in the shark (*Acanthias*). Fig. 4 represents the anterior part of an embryo, 6 mm. in length, and the anterior part of the foetus is towards the right; *a* is a cavity anterior to the premandibular cavity, which forms, then atrophies, and disappears; no satisfactory explanation of this cavity has been advanced. 1 is the first or pre-mandibular head cavity, which gives rise to all the muscles supplied by the third nerve; 2 is the second or mandibular, giving rise to those supplied by the fourth; 3 is the third or hyoid, giving rise to the muscles supplied by the sixth nerve. Note the posterior prolongation of 2, forming a large mandibular muscle; so that in addition to forming the basis of the superior oblique, which this head cavity forms, it also forms a mandibular muscle, emphasizing the association between the superior oblique and the mandibular arch.

Another point of great importance is the minute association, at

FIG. 2.—AMPHIBIA. (After Davidson Black).

an early stage, of the fourth and fifth nerves; *c.g.* is the rudimentary ciliary ganglion, formed apparently by both fourth and fifth nerves.

Fig. 5 is the next stage, 12mm.; *a* is still existent, but it entirely disappears subsequently; 2 gives signs of forming the superior oblique; the large mandibular muscle is still developing. There is very closely associated with this cavity a branch of the fifth (*V an*), with which the fourth nerve anastomoses in the shark. The very near relationship between the fourth and fifth nerves is thus further emphasized. The external rectus is being formed from 3, and the sixth nerve is seen passing into it.

Fig. 6, of a 16 mm. embryo, shows the development of the inferior oblique (*inf. obq.*). The superior oblique (*supr. obq.*) is well developed.

In Fig. 7 the inferior oblique is definitely formed, the foremost head cavity (*a*) still persists; the superior and inferior recti are becoming differentiated, and the large mandibular muscle has atrophied and disappeared.

The best confirmation of these observations on Elasmobranchs in their relation to higher vertebrates is the work of Miss E. A. Fraser⁽⁷⁾ on marsupials. This work is of great importance, as is shown by the following quotation (*loc. cit.*, p. 341):—

"The abducens complex and the *m. obq. supr.* are difficult to identify in our earliest stages, but by comparison with slightly older embryos it is possible to make out their contours in the surrounding mesenchyme from which they are not easily distinguished. In our first stages, up to 8.5 mm., the primordia of both these muscles are united with the maxillo-mandibular mesenchyme by an intermediate mass of more loosely-connected cells, the position of which is well seen in *Phascolomys* (wombat) (text fig. 21, p. 332). The *m. obq. supr.* arises from this intermediate mass as an upgrowth which extends forwards above the eye, the intermediate mass itself apparently degenerating. In the rabbit Edgeworth (1903) regards the *m. obq. supr.* and the *m. rectus ext.* as "specialised portions of the mandibular and hyoid myotomes, which separate, the former late, the latter very early in development, from the upper ends of their respective myotomes" (p. 82). In *Chelydra* (a tortoise), according to Johnson (1913), the *m. obq. supr.* (p. 159) "grows forward as a stream of cells from the dorsal portion of the mesenchymal cell-mass, which results from the second head somite," the ventral portion of the latter at the 5 mm. stage being in close contact with the mesoderm of the mandibular arch. If we compare these conditions with those in *Trichosurus*, *Phascolarctos*, and *Phascolomys*, we may conclude with some probability that the intermediate mass answers to the second somite of the head whose cavity is already obliterated, or in which the

FIG. 3.—REPTILES. (After Davidson Black).

cavity has never developed, and from whose dorsal region the m. obq. supr. takes its origin. In *Chelydra* also, at a certain stage in development, the identification of the second somite is a matter of some difficulty. In the embryo of 7 mm. Johnson says (p. 142):—"The second head somite of the 7 mm. stage is of such indistinct and indefinite form that it may easily escape notice. It reaches here the most obscure phase of its development. The more or less conspicuous cavities of earlier stages have collapsed and broken down, and with their disappearance the cells of their walls are with difficulty distinguished from the intruding and intermingling mesenchymal elements."

No cavity is seen in the abducens muscle-mass, which in our earliest embryo is quite solid and shows a temporary attachment, as above mentioned, to the intermediate mass, this connection

FIG. 4. (After Miss Platt). *aud.*, auditory vesicle; *ch.*, notochord; *c.g.*, ciliary ganglion; *opt.*, optic vesicle; *sp.* spiracular cleft.

being probably a secondary phenomenon as in *Chelydra*, where it also occurs. It is possible that the intermediate mass, i.e., the second somite, may contribute towards the formation of the m. rectus ext. as in some fishes (Dohrn, 1904, Neal, 1914), but we have no direct evidence of this in *Trichosurus*. The m. rectus ext. and m. retractor bulbi develop exactly as in *Chelydra*; the origin of the m. retractor bulbi bearing no resemblance to that of the pig, where, according to Reuter (1897), p. 376:—"Dieser Muskel entsteht aus dem inneren Mantel des Augenmuskelkelches durch Abspaltung von vorn nach hinten."

In *Chelydra*, however, the m. retractor bulbi separates off from the m. rectus ext. at an early stage, before the second somite has completely degenerated, and when the m. rectus infr. and int. first begin to differentiate from each other, whereas in *Trichosurus*

it only becomes an independent muscle at 17.5 mm., after the other muscles of the eye have assumed their final positions, and at a time when the m. rectus infr. and int. are almost completely separated. The m. retractor bulbi in both animals is the last of the eye muscles to reach its adult position.

The cranial nerves, three, four and six, arise from the brain and grow towards their respective muscles, their connection with the mesodermal somites being a secondary one, as shown by Neal (1914). No independent origins in the muscles themselves are present as described by Filatoff (1907) in *Emys lutaria* (a tortoise). The oculomotor runs at its distal end into the proliferation on the postero-lateral wall of the head cavity and breaks up into many fibres at the region where the m. obq. infr. and m. rectus infr. first grow out, these two muscles being innervated at precisely the same time; later, at the earliest indication of the m. rectus int.,

FIG. 5. (After Miss Platt). *mdb.m.*, mandibular muscle.

fibres are seen to run into the root of the latter. The abducens develops in the typical manner and runs into the posterior end of the abducens muscle-mass; when the m. retractor bulbi grows forwards and separates off from the m. rectus ext. the nerve branches into the two muscles at the point where the former crosses the medial side of the latter. The trochlear, as is usually the case, arises later than the other two nerves. In *Trichosurus* it first appears at 8.5 mm. and does not reach the m. obq. supr. until 11 mm., when it penetrates into the posterior side of the medial end of the muscle."

The chief points I want to bring out here, apart from the distribution of the eye muscles according to the branchial arches, is the near association of the fifth nerve, both in the origin of

the fourth and fifth nerves, and also in the relationship of their branches at a very early stage in development, and the relationship of these branches to the ciliary ganglion.

The ideal segmental nerve consists of a number of different parts: Motor somatic, sensory somatic, motor visceral, and sensory visceral. Both motor somatic and motor visceral fibres in the spinal region pass out of the cord by the ventral roots, being derived from cells in the anterior and lateral horns respectively. The cells of origin of both sensory somatic and sensory visceral fibres are in the dorsal root ganglia in the spinal region. In lower vertebrates the motor visceral fibres supply not only the viscera proper, but also the muscles of the branchial clefts, which are essentially respiratory, and therefore visceral in function. In

FIG. 6. (After Miss Platt).

higher vertebrates many of the branchial muscles lose their visceral character and assume all the characteristics of somatic muscles, as, e.g., the pterygoids, trapezius, sterno-mastoid, etc. Their nerve supply is the chief criterion of their visceral origin. Thus it comes about that a nerve originating in lateral horn cells or their homologues in the brain stem appears to supply ordinary somatic muscles, e.g., the motor part of the fifth nerve. It is unnecessary to consider other complications, such as the nerves associated with the lateral line organs in fishes, since these complications affect especially more posterior regions, viz., the eighth nerve system.

The observations of Froriep, Kupffer and others prove that the third, fourth, and sixth nerves are not quite so simple as we are

accustomed to regard them. In some Elasmobranchs, e.g., the electric fish *Torpedo*, the fourth nerve has a ganglion developed upon it—in fact, two ganglia, and the third nerve also has one (Cf. Edinger,⁽¹⁾ II., Fig. 9). The interesting point is the different morphology of these ganglia. The ganglion on the third nerve is due to a migration of motor nerve cells from the neighbourhood of the third nerve nucleus down the course of the nerve; and there is no doubt that these cells enter into the formation of the ciliary ganglion. They are motor cells, and they represent the motor visceral part of the third nerve. Hence the third nerve is not only motor somatic, but motor somatic *plus* visceral. On the other hand, investigation of the chief ganglion on the fourth nerve

FIG. 7. (After Miss Platt).

shows that it does not migrate from the neighbourhood of the motor nucleus, but develops from cells which originate in the neural crest, i.e., the ganglion develops exactly like the dorsal root ganglia of the spinal cord, so that there is no doubt that this ganglion on the fourth nerve is a posterior root ganglion; and therefore, at this stage, the fourth nerve has at any rate motor somatic fibres *plus* sensory somatic fibres or sensory visceral fibres as well. Possibly the second ganglion on the course of the fourth nerve in the *Torpedo* embryo represents a motor visceral part; in any case it atrophies. Therefore this nerve is not as incomplete in the early stages as in the later.

The differences between the third, fourth and sixth nerves are

interesting. The third has motor somatic and motor visceral fibres, the latter going to the ciliary ganglion; the fourth has motor somatic which persist, and sensory somatic (and (?) both motor and sensory visceral), which atrophy; and the sixth has motor somatic which persist, and motor visceral which atrophy. So that we have, in the embryological stages, some indications of the composite nature of the fourth nerve, representations of other fibres which bring it more into line with any other ordinary segmental nerve.

I wish to draw attention to the relationship of the fourth with the fifth nerve. I have pointed out, briefly, the minute relationship between them in their early origin; but there is also a near

FIG. 8. (After Miss Platt).

relationship between certain parts of the fifth and the fourth in late stages. Sections of the mesencephalon throughout the vertebrate series show a remarkably constant relationship between the nucleus of the fourth nerve and a group of smaller cells which undoubtedly belong to the fifth nerve, and are known as the mesencephalic nucleus of the fifth. The relationship of the mesencephalic root of the fifth to the fibres of the fourth is so close that some observers (e.g., Davidson Black) think that some of the fibres actually join the fourth nerve.

Much discussion has arisen with regard to the nature of the mesencephalic root of the fifth. For instance, in Schäfer's

Physiology Sherrington has depicted them as motor fibres. In Quain's Anatomy Schäfer has depicted them as sensory fibres. The position of the fourth nucleus corresponds with that of other motor somatic nuclei, homologous to the anterior horn of the spinal cord; that of the mesencephalic nucleus of the fifth, slightly lateral to the fourth, corresponds with the motor visceral nuclei, homologous to the lateral horn of the cord. The question arises, therefore, whether this part of the fifth does not represent the motor visceral part of the segmental nerve of which the fourth is the motor somatic part. The nerve of the mandibular arch would then be made up of: (1) a motor somatic part, represented by the fourth; (2) a sensory somatic part represented by the fourth, with its ganglion, which atrophies, and now possibly replaced by fibres from the sensory part of the fifth; (3) a motor visceral part, represented by the mesencephalic root of the fifth; and (4) a sensory visceral part, at present unknown. The somatic muscles of the mandibular segment are the superior oblique which persists, and the mandibular muscle which atrophies; the visceral muscles are the pterygoids and other muscles supplied by the motor branch of the fifth.

There is no satisfactory explanation of the dorsal decussation of the fourth nerves, but several ingenious suggestions have been made. Hoffman⁽⁸⁾ in 1889 suggested that the trochlear nerve was originally a sensory nerve for a protecting organ of the pineal eye, which subsequently became a motor nerve for the lateral eye as the pineal eye degenerated. Fürbringer⁽⁹⁾ in 1897 considered that the nerve was originally motor, associated with the movements of the median pineal eyes. He made the striking suggestion that the decussation is due to shifting of the muscle supplied from one side to the other. The ancestor of the superior oblique was a muscle the fibres of which were attached to the mid-dorsal line and interlaced with those of the opposite side, the two muscles thus forming an arch through which the nervous system with its central canal passed. Gaskell⁽¹⁰⁾ found such a pair of muscles in the anterior dorso-plastron muscles (Miss Beck) of the scorpion, corresponding with similar muscles in fossil arthropods, e.g., Eurypterus, and fossil fish with head shields, e.g., Cephalaspis. He held that the ancestors of the eye muscles of mammals are to be found in these dorso-ventral muscles of arthropods, which have been brought into the service of the lateral eyes as these have replaced the median eyes in the course of evolution. The ingenious working out of this theory, which fits in remarkably well with Gaskell's theory of the origin of the vertebrates from arthropod ancestors, must be sought in Gaskell's book (esp. pp. 263-279). It must be borne in mind, however, that Gaskell's theories have not found favour with zoologists.

One other point which I wish to emphasize deals with the synergic activities of these motor ocular muscles. We have seen that the third, fourth and sixth nerves are built on exactly the same plan throughout the vertebrates, down to the lowest. It is clear that the synergic activities of these muscles must vary enormously from species to species. Neurologists have made us very familiar in man with the pre-eminently synergic control of lower motor neurons by the cortex cerebri. Now, if the brains of the vertebrate species are compared with each other, we find that in all there is a palaeencephalon—the corpus striatum; but in the lowest fishes there is no neoencephalon, the roof of the fore-brain consisting simply of an epithelial membrane. Even when the pallium first appears it is in direct relationship with the olfactory system and probably has little to do with the visual apparatus. Yet in all these animals the eye movements are coordinated, and are correlated with body movements. These synergic activities must be brought about by complex decussations and interrelations between various motor nuclei, and there must be some mechanism for their co-ordination. Doubtless these phylogenetically older co-ordination mechanisms become in turn controlled by higher cortical mechanisms in higher species as these eventually appear and increase in importance—and it is with these that we are most familiar. We should not, however, forget the lower any more than we neglect the lowest and middle level mechanisms. This is not to derogate from, but merely to elaborate Hughlings Jackson's ideas. He himself would probably have been the first to admit the division of his highest level into substrata.

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