THE SEGMENTATION OF THE PRIMITIVE VERTEBRATE BRAIN.

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PART I.

THE primitive segmentation of the vertebrate brain is a problem which has probably attracted as much of the attention of morphologists as any one of the great, unsettled questions of the day, and many views have been advanced which have, it is true, reached one important point of agreement; namely, that the primitive brain was undoubtedly a segmented structure. But beyond this, in regard to the character of these segments and the number of segments of which the brain originally consisted, I think it can be said with perfect freedom that nothing whatever has been definitely proved. It is the purpose of this paper to add a few more links to the chain of evidence necessary for the elucidation of this important question.

The majority of investigators on this subject have made use of the cranial nerves as a means of determining the number of segments of the primitive brain. Investigations in this line are good as far as they go, but as far as the determination of the original number of segments and the character of these segments by this method is concerned, it is largely conjectural for the following reasons:

I. We have positive proof that the degeneration of certain branches has taken place.¹ This being the case, we have every reason to assume that whole segmental nerves may have once existed, which have completely degenerated, leaving no trace whatever of their previous existence. If such be the case, the segments originally connected with these degenerated nerves must necessarily be overlooked, if the existing nerves are made

¹ Marshall states that the IV nerve possesses a sensory branch in Selachians and Amphibians. Gegenbaur notes the same for Selachians.

use of as a means of determining the original number of segments.

2. Furthermore, the vagrant changes in the position of some of the cranial nerves must necessarily cause confusion. For example, take the VI nerve which in the frog and tadpole stages is situated between the first and second roots of the IX. nerve,¹ a position somewhat posterior to its place of origin. This remarkable shifting clearly shows not only what great changes in position the cranial nerves are capable of undergoing, but it also goes to prove that we can find no reliable means of determining the primitive segments by means of their connection with the exit of the existing cranial nerves. Beard in taking up this problem made use of an important series of sense organs for which he has proposed the name of "Branchial Sense Organs," from their development from thickenings of the epiblast over each branchial cleft. The dorsal branches of certain cranial nerves fuse with these epiblastic thickenings; the superficial part of the thickening giving rise to a branchial sense organ, while the deeper portion becomes the ganglion of the dorsal root of the cranial nerve. This close relation which exists between the dorsal branches of the cranial nerves and their corresponding sense organs is undoubtedly of segmental character. But this line of research is beset by a great difficulty, namely, that the degeneration of certain branchial sense organs would, in time, involve the degeneration of their corresponding cranial nerves, and such degeneration has certainly taken place, in part or in whole, leaving in doubt the primitive segments with which they were connected. As far as I have been able to compare Beard's investigations with my own, I think they are correct when he considers the I., III., V., VII., VIII., IX., and X nerves in connection with their corresponding branchial sense organs, as representing respectively the remains of primitive segments. In fact, my own observations lead me to the same conclusions, but in addition to these I find intermediate encephalic segments between I. and VIII. nerves which Beard's method has led him to pass over entirely.

These investigations were carried on in the Morphological Laboratory of Princeton, under the direction of Dr. Henry F.

¹ I am indebted to Mr. Strong of Princeton for this point.

Osborn, to whom I feel greatly indebted for his kindness in furnishing me with everything necessary for the accomplishment of this work, as well as for valuable advice in connection with it. I also wish to express my thanks to Dr. Henry Orr for the use of his sections of the Lizard. Also to Professor Ryder for some fish embryos which he kindly sent me.

The following types were studied in connection with this subject, which, though not the most desirable, were the only ones obtainable at the season :—

Amphibia, *Amblystoma punctatum*.

Reptilia, *Anolis sagroei*.

Aves, chick embryos.

The general object of this paper is to show that the symmetrical constrictions or folds found in the lateral walls of the embryonic brain are remains of the primitive segmentation of the neural tube, in part atavistic, extending into the primary fore-brain.

Literature.—The folds in the side walls of the medulla or hind-brain have been frequently noticed and commented upon, but only recently has their importance as segmental structures been recognized. Remak in 1850 observed these folds in the medulla, and rightly considered them as structures formed in connection with the “Anlagen” of the cranial nerves. They were observed by Von Baer in 1828 and Dursy in 1869: the latter counted six folds in the hind-brain. In 1875, Dohrn pointed out the segmental significance of these folds with relation to the mesoblastic somites, and in the joint resemblance to the segmentation of an insect embryo. In 1876, Foster and Balfour, and in 1877, Mihalkovics, inclined to give a mechanical explanation to these medullary folds. Béraneck quite recently observed five folds in the medulla of the lizard, and described and figured their connection with the origin of some of the cranial nerves. Kupffer finds in the mid and hind-brains of the trout and salamander at least eight segments, and, if I understand him correctly, says these segments not only correspond to the lateral somites (p. 476), but that there is something similar to these brain segments to be observed in the spinal cord. He concludes, however, by expressing the opinion (p. 477) that the fore-brain is not to be reckoned in the

segmented region. He does not, in his brief paper, give any of the histological characteristics of the segments. I am also indebted to this paper for many bibliographical references.

Gegenbaur has recently expressed the following opinion : "So interessant und so vielversprechend diese Thatsachen sind, so wenig scheinen sie mir gegenwärtig geeignet, zur Beurtheilung der Metamerie des Kopfes selbst als Faktoren in Geltung gebracht zu werden. Das wird erst eintreten können, wenn ihre Beziehung zu anderen, den Kopf aufbauenden Organen erkannt ist."

In 1887, Orr described six folds in the hind-brain of the lizard, five of which are of equal size, and the 6th, from which the 10th nerve originates, somewhat longer than the others. He described the mid-brain as consisting of one fold, and in addition to this described two folds in the primitive fore-brain. He gave the name "neuromeres" to these folds, — a name previously used by Ahlborn with a somewhat different significance. Orr found that the V., VII., VIII., IX., and X. nerves each originated in connection with a neuromere which degenerated after the nerve was formed. He fully described the typical structure of a "neuromere," which I quote, as it bears directly on my own work :

1. "Each neuromere is separated from its neighbors by an external dorso-ventral constriction, and opposite this an internal sharp dorso-ventral ridge, — so that each neuromere (*i.e.* one lateral half of each) appears as a small arc of a circle."

"The constrictions are exactly alike on each side of the brain."

2. "The elongated cells are placed radially to the inner curved surface of the neuromere."

3. "The nuclei are generally nearer the outer surface, and approach the inner surface only towards the apex of the ridge."

4. "On the line between the apex of the internal ridge and the pit of the external depression, the cells of adjoining neuromeres are crowded together, though the cells of one neuromere do not extend into another neuromere."

"This definition of adjacent neuromeres presents, in some sections, the appearance of a septum extending from the pit of the external depression to the summit of the internal ridge (*Spt.*)"

Dr. Hoffmann, of Leiden, published in the *Zoologischer Anzeiger*, June 24, 1889, an article on the segmentation of the hind-brain in the reptiles, which appeared after my abstract of June 14th had been sent to the same journal. (See Bibliography.) He refers to his previous article in Bronn's "Reptilien" (published in 1888), p. 1967, where he considered the hind-brain as consisting of seven metameres or segments, each of which is connected with a nerve in substantially the same manner as described by Orr in his "Embryology of the Lizard," 1887. In his more recent article, as I understand him, he considered the IV. nerve to originate from the first segment of the hind-brain, and to gradually shift its position forward into the mid-brain. I will show that Dr. Hoffmann is probably wrong in considering the hind-brain as consisting of seven segments, and that the segment considered by him as the first segment of the hind-brain is rather the posterior segment of the mid-brain; in other words, it is the second neuromere of the mid-brain (my neuromere Trochlear, Nm. IV.).

In addition to the above statement, Dr. Hoffmann gives the following important evidence in connection with the Trochlear nerve, which I quote in full. "Aus alledem scheint also mit Bestimmtheit hervorzugehen, dass der N. trochlearis einen dorsalen Kopfnerven bildet, denn er besitzt bei Embryonen von *Lacerta* in jungen Entwicklungsstadien ein ziemlich mächtiges Ganglion, welches einen bis unmittelbar an die Epidermis tretenden Fortsatz abgibt, der aber, wie das Ganglion, bald wieder vollständig abortirt, ja es fragt sich selbst. Ob der Nervus trochlearis vielleicht nicht als der vorderste, segmentale Kopfnerv zu betrachten ist, der dem 1, vordersten Segment zuge hört: für diese Meinung spricht auch die Thatsache, dass Ganglion, sobald es sichtbar zu werden anfängt, fast vollständig allein dem 1. Segment aufsitzt, und später auch auf das Mittelhirn übergreift."

From an examination of longitudinal horizontal sections of *Amblystoma*, *Anolis*, and chick embryos, the latter ranging from 30 hours to five days old, I find that the lateral walls of the Myelion and Encephalon (hind, mid, and primitive fore-brain) consist of a series of constrictions which are exactly alike on each side of

the brain; and that the constrictions of the Myelon gradually pass or merge into those of the Encephalon, thereby forming a continuous series of constrictions throughout the entire length of the neuron, which increase in size anteriorly.

For sake of clearness I have classified the constrictions of the neuron as follows:

Constrictions of the Myelon = Myelomeres } Neuromeres.
Constrictions of the Encephalon = Encephalomeres }

The number of encephalomeres¹ actually observed in the types examined is as follows:

	HB	MB	FB
Amblystoma	5		2
Anolis and Chick	6		2

I do not, with Orr, consider the mid-brain as equivalent to a single encephalomere,² but rather relying upon the observations of Kupffer, as equivalent to two (or even three) which have degenerated in the above-mentioned forms, but persist in the Teleosts, and probably in other fishes. The total number of encephalomeres was thus probably ten, divided as follows:

Fore-brain, 2 and possibly a portion of a third.

Mid-brain, 2 or 3.

Hind-brain, 6 or 5.

In order to avoid confusion when speaking of the encephalomeres individually, I have given them names which I think for the present will answer the purpose.

<p>I. <i>Olfactory Neuromere.</i>
The most anterior neuromere of the primitive fore-brain.</p> <p>II. <i>Optic Neuromere.</i>
The second neuromere of the primitive fore-brain.</p> | <p>III. <i>Oculomotor Neuromere.</i>
Mid-brain neuromere.</p> <p>IV. <i>Trochlear Neuromere.</i>
Second neuromere of the mid-brain (demonstrated in <i>Petromyzon</i>).</p> |
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¹ Term proposed by Wilder for the large encephalic vesicles which we cannot now consider in any proper sense segmental. See article "Brain" by Wilder in Reference Handbook of the Medical Sciences, Vol. VIII 8., § 23, prop. X., p. 113.

² For mid-brain neuromeres, see Appendix.

V. <i>Trigeminal Neuromere.</i> The first and most anterior neuromere of the hind-brain.	VIII. <i>Auditory Neuromere.</i> The fourth neuromere of the hind-brain.
VI. <i>Abducens Neuromere.</i> The second neuromere of the hind-brain, absent in the Newt.	IX. <i>Glossopharyngeal Neuromere.</i> The fifth neuromere of the hind-brain.
VII. <i>Facial Neuromere.</i> The third neuromere of the hind-brain.	X. <i>Vagus Neuromere.</i> The sixth neuromere of the hind-brain.

Comparative Structure of the Myelomeres.

The spinal cord is of clearly segmental character, and at a certain period of its embryonic development, at the time of formation of the mesoblastic somites, we see that its lateral walls are constricted in a manner similar to those of the encephalon, and that the transition from the former to the latter is a gradual one.

Gross mounts of chick embryos ranging between 35 and 46 hours old clearly show this structure; also Figs. 4, 4a, which are longitudinal horizontal sections of *Amblystoma*.

I find that the structure of the Myelomeres in the NEWT, LIZARD and CHICK, conforms in every respect to the four characteristics which Orr gives as found by him in the neuromeres of the hind-brain of the Lizard. These four characteristics are quoted in full on a previous page.

An examination of Figs. 1, 2, 3, all of which are camera drawings of neuromeres of the spinal cord, shows—

1. "That the neuromeres have the appearance of small arcs of circles, *i.e.* one lateral half of each (*Nm*). And that the constrictions are exactly alike on each side of the brain."

2. "That the cells are elongated and are placed radially to the inner curved surface of the neuromere" (*in*).

3. "The nuclei are generally nearer the outer surface (*out*), and approach the inner surface (*in*) only towards the apex of the ridge" (*ap*).

4. "On the line between the apex of the internal ridge (*ap*) and the pit of the external depression (*ex*) the cells of adjoining neuromeres are crowded together, though the cells of one neuromere do not extend into another neuromere."

The Relation of the Myelomeres to the Mesoblastic Somites.

The Myelomeres are intersomitic; that is, the centre of each Myelomere is opposite the space between two somites (Figs. 1, 2 and 3). The dorsal branches of the spinal nerves pass from the external surface of the Myelomeres to the space between two somites, which is opposite their point of origin, and fuse with the epiblastic thickenings to form the spinal Ganglia.

Comparative Structure of the Neuromeres.

In the hind-brain of the lizard and chick six neuromeres are distinctly seen. Figs. 5, 5a, 6, and 6a, which in each case are of exactly the same size with the exception of the Vagus Neuromere (*Nm X.*) which is slightly longer than the others. In *Amblystoma*, Figs. 4, 4a, only five neuromeres are found in the hind-brain. The Abducens Neuromere (*Nm VI.*) is not present. The remaining neuromeres are of equal length except the Vagus Neuromere (*Nm X.*) and the Trigeminal Neuromere (*Nm V.*), which are somewhat longer than the others. We have already seen that the Vagus Neuromere in the lizard and chick is somewhat longer than the others, but that the Trigeminal Neuromere does not vary. In *Amblystoma*, the Trigeminal Neuromere is equal in length to about two of the three remaining neuromeres of the average dimensions. (Figs. 4, 4a.)

This variation in size of the Trigeminal Neuromere is due in all probability to the coalescing of the Abducens Neuromere with the Trigeminal Neuromere to form one neuromere. The fact that the recent Amphibia are somewhat removed from the main vertebrate line, and that their development has been influenced by the great quantities of food yolk present, may account in some degree for the varying structure of the Trigeminal Neuromere in *Amblystoma*.

So much for the similarity and points of difference which exist between the neuromeres of the medulla of *Anolis*, *Amblystoma* and the chick, so far as their relations of size are concerned. Now in regard to their histological structure, I find that the four characteristics given by Orr for the neuromeres of the medulla of *Anolis* are represented in every respect in the structure of the neuromeres of the medulla of *Amblystoma* and the chick; that is, the cell arrangement of

the neuromeres in the medulla of all three classes is the same. It has already been shown that the structure of the Myelomeres, in all three of the types studied, conforms in every respect to the typical neuromere of the hind-brain. Thus we see that a conformity of structure exists between the neuromeres of the spinal cord and those of the hind-brain in the three forms studied.

By applying the description given for the structure of the neuromeres in the spinal cord to Figs. 4*b*, 4*c*, 5*b*, and 6*b*, which are camera drawings of the neuromeres in the medulla of *Amblystoma*, *Anolis*, and the chick, it will be seen that the structure of the neuromeres of the medulla and spinal cord in the Amphibia, Reptilia and Aves is identically the same.

Comparative Structure of the Neuromeres of the Primitive Fore-brain.

So far as known to myself, Orr was the first to notice the presence of two neuromeres in the primitive fore-brain of the Lizard, but he did not compare their cell-structure with that of the neuromeres of the hind-brain. In addition to confirming the presence of two neuromeres in the primitive fore-brain of the Lizard, I have also found that the primitive fore-brain of the Newt and Chick consists of two neuromeres. Also between the mid-brain and optic neuromere (*Nm II.*) of the Lizard, Fig. 8*a*, there is a structure (*Nm II.'*) which resembles a portion of a neuromere. Its form is that of an arc of a circle, but the radius of its arc is less than that of either of the two remaining neuromeres of the primitive fore-brain, which I have already said resemble arcs of circles. I make merely a passing mention of this, for the reason that from the existing data nothing but conjecture can result as to its neuromeric value; while on the other hand if it is a neuromere, it ought to be present in toto in some of the lower vertebrates. (See Appendix.)

The fore-brain neuromeres of the Lizard and Chick, so far as their external character and histology is concerned, are true neuromeres. By external character I mean their form and position with respect to each other. Figs. 8*a*, 9, illustrate the following description of the neuromeres in the primitive fore-brain of the Lizard and Chick.

1. One lateral half of each neuromere is an arc of a circle.
2. The elongated cells are placed radially to the inner curved surface of the neuromeres (*in*).
3. The nuclei are generally nearer the outer surface (*out*), and approach the inner surface (*in*) only towards the apex of the ridge (*ap*).

The arrangement of nuclei in the neuromeres of the primary fore-brain does not always conform to the typical structure.

4. On the line between the apex of the internal ridge (*in*) and the pit of the external depression (*ex*) the cells of the adjoining neuromeres are crowded together, though the cells of one neuromere do not extend into another.

The fore-brain neuromeres of the Lizard and Chick persist up to a certain stage in the embryo and finally disappear.

The stage in which the fore-brain neuromeres of the Lizard are fully developed is represented by Fig. 8*a*. In the Chick these neuromeres are prominent in embryos from 36 to 96 hours old. The external character of the neuromeres in the primitive fore-brain of the Newt is not found to be as perfectly developed as those in the Lizard and Chick; that is, each lateral half of a neuromere does not form as perfect an arc of a circle as in the latter, (Fig. 7). I am, however, in doubt whether this variation from the general form is due to the fact that I did not study the stages in which the neuromeres were most fully developed, but rather those in which degeneration had already begun but not been completed. In any case this was unavoidable, as the stages of this species which I possessed were limited to a few. Possibly their development may have been arrested by external means, due to the presence of yolk spherules, which were found present in such great quantities, mixed in among the cells, that it was a difficult task to make out the structure of the neuromeres. It seems probable that one of the above-mentioned reasons may explain this variation of form in the fore-brain neuromeres of the Newt. But that these structures are neuromeres or remains of neuromeres I think there can be no doubt whatever, since their structure in most respects conforms to the typical structure. The cells have a radial arrangement (Fig. 7), and between the neuromeres they are crowded together, but the cells of one neuromere do not enter into another neuromere. The arrangement of the nuclei is variable and does not always conform to the typical one.

The fore-brain neuromeres of the Newt persist up to a certain period and finally disappear, leaving no trace whatever. This we have already found to be the case in the Lizard and Chick.

Up to this point we have seen that the structure of the folds in the lateral walls of the myelon (myelomeres) conforms in every respect to the four characteristics which are found in the hind-brain and primitive fore-brain folds of all three forms studied (with one exception in the Newt), which goes to prove that the encephalomeres are not only remnants of neural segments similar to the myelomeres, but that they were originally continuous.

The mid-brain has been purposely omitted up to this point, but will be considered further on.

Relation of the Auditory Vesicles to the Neuromeres of the Hind-brain.

The importance of this relationship will be seen further on in connection with the nerves of the hind-brain. The auditory vesicle (*aud ves*) in the Newt and Lizard is opposite, in a transverse line, to the auditory neuromere (*Nm VIII.*; Figs. 4, 4a, 5, and 5a). In the embryo Chick it holds the same position as in the Newt and Lizard up to the 96th hour, or slightly later; after this its position is shifted backwards to a point between the auditory and glossopharyngeal neuromeres (Figs. 6, 6a, *Nm VIII.* and *Nm IX*).

Relation of the Myelomeres and Encephalomeres to their Respective Nerves.

All the neuromeres of the spinal cord give off (on each side) from their dorsal half a mass of ganglion cells, which constitute the dorsal or sensory roots of the spinal nerve (*SpN*), Figs. 1, 2, and 3. In a like manner I find that four neuromeres in the hind-brain and one in the primary fore-brain give rise to dorsal or sensory roots of cranial nerves.

The myelomeres on giving rise to the spinal nerves, in the manner stated above, degenerate soon after the nerves are

formed. The encephalomeres, after giving rise to their respective nerves, likewise degenerate.¹

All nerves mentioned as originating from the centre of a neuromere have reference to the dorsal or sensory root, unless otherwise specified. Orr states that the 1st, 3d, 5th and 6th neuromeres in the hind-brain of the Lizard (neuromeres, *trigeminal*, *facial*, *glossopharyngeal* and *vagus*) give off (on each side) from their dorsal half a mass of ganglion cells which constitute the roots of the V. (VII., VIII.), IX. and X. nerves respectively, and that the 4th neuromere (auditory neuromere) gives off no nerve, but the space opposite to it is occupied by the auditory vesicle. He also states that the VI. nerve arises, though at a much later period than the others, from the ventral portion of the 2nd neuromere (abducens neuromere). Béraneck previously to Orr mentioned the fact that certain of the hind-brain neuromeres of the Lizard held a definite relation to the origin of the V., VII., VIII., and IXth nerves.

My own observations upon the Lizard confirm the above statements of Béraneck and those of Orr in every instance but one; that is, in regard to the origin of the VI. nerve² from the ventral portion of the 2nd neuromere of the hind-brain (abducens neuromere). That it originates ventral to the origin of the other nerves, somewhere *between* the origin of the V. and VII. and VIII. nerves, there is no doubt, but I cannot definitely confirm its point of origin as stated by Orr from the ventral portion of the 2nd neuromere. (See Fig. 5a, which is a camera drawing of the hind-brain neuromeres of the Lizard.) From an examination of this figure it will be seen that the V. nerve arises from the trigeminal neuromere (*Nm I.*); that the abducens neuromere (*Nm VI.*) gives rise to no dorsal root; that the facial neuromere (*Nm VII.*) is connected with the origin of the VII. and VIII. nerves; that the auditory neuromere (*Nm VIII.*) gives off no nerve, but the space lateral to it is

¹ Orr states that the degeneration of the encephalomeres takes place in the hind-brain of the Lizard as soon as the nerve fibres begin to develop. This point I did not satisfactorily make out, either for the neuromeres of the spinal cord or those of the medulla, but I am inclined to think that Orr's statement is correct.

² The preliminary announcement of this paper, which appeared in the *Zoologischer Anzeiger*, No. 314, 1889, states incorrectly on Orr's authority, that the VI. nerve originates in connection with the most anterior neuromere of the hind-brain. It should read that it arises from the ventral portion of the 2nd neuromere.

occupied by the auditory vesicle; that the glossopharyngeal neuromere (*Nm IX.*) gives rise to the IX. nerve; and that the vagus neuromere (*Nm X.*) gives rise to the X. nerve. I find in the hind-brain of the Chick an exact correspondence in structure to that of the Lizard; that is, in the hind-brain of the Chick the auditory vesicles and nerves hold exactly the same relation to their respective neuromeres as the corresponding auditory vesicles and nerves in the hind-brain of the Lizard do to their respective neuromeres. I think this relationship of neuromeres to nerves has been fully described for the Lizard, and I refer the reader to Fig. 6*a*, which is a camera drawing of the hind-brain of the Chick, that comparisons may be made. We have already seen that the abducens neuromere (*Nm VI.*) is absent in the Newt. I find also, with this one exception, that the remaining neuromeres in the hind-brain of the Newt hold exactly the same relation to the auditory vesicles and nerves as do their corresponding neuromeres in the hind-brains of the Lizard and Chick.

(See Fig. 4, which is a camera drawing of the hind-brain of the Newt, for comparison with the above-mentioned figures of the Lizard and Chick.)

It has been shown in the preceding pages that there are two neuromeres in the hind-brain of the Lizard and Chick, which do not give rise to dorsal or sensory roots (abducens neuromere) (*Nm VI.*) and auditory neuromere (*Nm VIII.*; Figs. 5*a*, 6*a*). It seems probable that these two neuromeres must have once been connected with sensory roots when we consider similar structures in the spinal cord and hind-brain and their systematic connection with dorsal roots. The fact that the abducens neuromere is absent in the Newt may be accounted for in the following manner: namely, that the degeneration of the sensory nerve of this neuromere has resulted in the consequent degeneration of the neuromere itself. But this is pure conjecture, and then the fact still remains, that these two neuromeres have not degenerated in the Lizard and Chick, both of which are representatives of much higher forms than the Newt. Again, the VI. nerve may be the motor element of the primitive segmental nerve of this neuromere (abducens neuromere), its sensory branch having become degenerate. The position of its origin, somewhere between the neuromeres, trigeminal and

facial, may give credence to this view. It is also possible that the VI. nerve is a motor branch of the V. or VII. nerves: the persistence of the VI. nerve and the absence of the abducens neuromere in the *Newt* certainly imply as much.

Most of the early investigators are agreed concerning the origin of the VII. and VIII. nerves from a primitively single trunk, based on the relations of the VII. and VIII. in Mammals. The opposed view of their separate nature has been steadily gaining ground, and I think at present the latter theory has the greater number of supporters. The double nature of these nerves certainly suggests the probability that they were primitively of separate origin, and the following theoretical evidence may throw some light on this theory. The auditory neuromere (*Nm VIII.*) has no nerve connected with it, and it is situated posterior and adjacent to the facial neuromere (*Nm VII.*), which gives rise to the VII. and VIII. nerves. (*Nm VII.*, *Nm VIII.*; Figs. 4, 5a, 6a.)

The auditory vesicle (on each side of the brain) is situated in the space lateral to the auditory neuromere, (*aud*; Figs. 4, 5a, 6a), but the dimensions of the vesicle occupy so much of this lateral space, that the space left between the neuromere and the vesicle is very narrow; so narrow, in fact, that a nerve arising from the neuromere could not possibly obtain a growth in it sufficient to perform the functions required of the auditory nerve. Thus it is possible that the VIII. nerve may have been primitively connected with the auditory neuromere before the auditory vesicle became so prominent, and that the gradual growth of the vesicle has pushed it from its original position anteriorly into the facial neuromere, where the fusion of its root with that of the VII. nerve has taken place.

Mid-brain Neuromeres (Nm III. and Nm IV.).

In the *Newt*, *Lizard*, and *Chick* the mid-brain has the appearance of being an enlarged neuromere, larger than any one of the remaining neuromeres of the brain, but equal in size to about three or four of the first five neuromeres in the hind-brain, and not quite as large as the three neuromeres in the primitive fore-brain. Its cell structure is radial, but its nuclear arrangement does not conform to that of a typical neuromere, except that at

its anterior and posterior limits the cells are crowded together and do not enter the adjoining structures. Two nerves are connected with this neuromere of the mid-brain, — the *Oculomotor*, and *Trochlear*, — each of which, according to the recent investigations of Gaskell, conforms to the type of a complete segmental nerve, in that each contains remnants of the primitive sensory elements; that is, they possess “nerve fibres and groups of ganglion cells corresponding in position, and doubtless also in function, with the nerve fibres and nerve cells of the stationary ganglia on the afferent root of a spinal nerve.” Gaskell suggests that both of these nerves (III. and IV.) are probably complete segmental nerves of the type which Balfour supposes to have been the original type, when mixed motor and sensory roots were the only roots present. I do not consider Gaskell’s investigations with respect to the III. and IV. nerves as conclusive without further evidence on the subject, but I agree with him, and on entirely different grounds, that the III. and IV. nerves represent two separate segmental nerves. Taking into consideration the size of the mid-brain neuromere in comparison with the remaining neuromeres of the brain as well as its “neuromeric” characteristics, also the fact that two nerves arise from it, which are probably either two segmental nerves or parts of the same, also the investigations of Kupffer, previously mentioned, in which he states that he found at least eight segments in the hind and mid-brains of the Trout and Salamander, there can be little doubt left but that the mid-brain originally consisted of at least two neuromeres, and that in all probability the III. and IV. nerves were the segmental nerves of these neuromeres respectively. (See Appendix.)

The Primitive Fore-brain Neuromeres and their Nerves.

The optic neuromere (Figs. 7, 8a, 9; *Nm II.*) has no connection whatever with any segmental nerve. The optic nerve is undoubtedly secondary in its nature, and is, I believe, considered by all as outside the series of segmental nerves. It seems probable that the primitive segmental nerve of this neuromere degenerated as soon as the vertebrate eye came into existence, the latter requiring a nerve better suited to perform its functions than the nerve which primitively belonged to the neuromere.

The olfactory neuromere (Figs. 7, 8a, 9; *Nm I.*) is connected with the olfactory nerves, which arise from the neural crest, according to Marshall, in exactly the same manner as the sensory roots of segmental nerves. He also states that the olfactory nerves arise before the cerebral hemispheres, and in the Dog-fish, Trout, Salmon, Axolotl, Frog, Lizard, Turtle, and Chick their development is fundamentally the same.

Orr states that in the Lizard the olfactory nerves spring laterally from the anterior dorsal (nasal) tip of the primary fore-brain, and run a very short distance direct to the nasal thickenings of the epiblast, in which they end. In the Chick it is fundamentally the same. In addition to confirming Orr's statement in regard to the origin and course of the olfactory nerve in the Lizard, I find an exact correspondence in the Newt (Figs. 7a, 7b, 7c). Thus it is seen that in the Lizard, Newt, and Chick the olfactory neuromere (anterior dorsal tip of primary fore-brain) gives off (on each side) a mass of ganglion cells which constitute the roots of the olfactory nerves. This mode of origin, as we have already seen, is exactly the same as that described for the sensory roots in the segmental nerves of the spinal cord and hind-brain. Therefore I think it is safe to say that the olfactory nerve is the sensory division of the segmental nerve which belonged to the olfactory neuromere, which accords with Marshall and Beard, who upon entirely different grounds consider this a true segmental nerve.

General Summary.

It has been my endeavor in the preceding pages to show that a continuous and symmetrical series of folds (neuromeres), increasing in size anteriorly, extend from the lateral walls of the embryonic brain, throughout the entire length of the neuron, and that these neuromeres are the remains of the primitive segmentation of the neural tube.

1. By proving that a conformity exists in the structure of these neuromeres throughout the entire length of the neuron. (See typical structure of neuromeres.)

2. That all of the neuromeres in the spinal cord, four in the hind-brain, and one in the primitive fore-brain, give rise to dorsal or sensory roots.

(a) That the relation of the neuromeres to the origin of their respective dorsal or sensory roots is fundamentally the same in all three regions of the brain in which neuromeres give rise to sensory roots.

(b) That all the neuromeres of the brain, whether giving rise to sensory roots or not, degenerate before the adult stage of the animal is reached.

It has also been shown (see Appendix).

3. That in all probability the mid-brain originally consisted of two neuromeres, and that the III. and IV. nerves were the segmental nerves of these segments.

4. That the number of primitive Encephalic segments was probably ten (six in the hind-brain, two in the mid-brain, and two in the primary fore-brain).

5. That the neuromeres of the spinal cord, opposite the mesoblastic somites, are "intersomitic"; that is, the centre of each neuromere is opposite the space between two somites, or *vice versa*; hence it is seen that nine mesoblastic somites exactly correspond to the nine spaces between ten neuromeres.

It is now a well-known fact that the segmented mesoblast of the trunk extends into the head region, and according to the investigations of Van Wijhe it is there divided into nine mesoblastic head segments, or "Myotomes," as he calls them, which theoretically correspond to the nine spaces between the ten Encephalomereres.

Conclusions.

I consider that the primitive vertebrate brain consisted of a series of segments similiar to those found in the embryonic spinal cord, and that the encephalomereres probably held the same relation to the mesoblastic head segments as the myelomereres do to their respective mesomereres; that is, they were intersomitic, the centre of each neuromere being opposite the space between two somites and giving off a mixed nerve from the apex.

The region known as the Encephalon is the result of a great differentiation and specialization of the anterior segments of this primitive structure. That differentiation first began and has been the greatest in the most anterior segments, which may account for the greater size of the folds in this region than in

the hind-brain, which, less differentiation and specialization having taken place, naturally conforms more to the primitive vertebrate type. I am aware that the forms examined are insufficient to enable us to reach any positive conclusion in regard to the exact number of segments, but I feel confident that the method which I have adopted is the one by which this vexed question of the primitive segmentation of the head region, both of the neural tube and indirectly of the surrounding mesoblast, will eventually be decided.

In conclusion, I may say that I feel confident that the full number of primitive encephalomeres will be found in Elasmobranch, Ganoid, or Teleost embryos, the investigation of which will form the second part of this paper.

APPENDIX.

The Mid-brain Neuromeres.

Just before sending this paper to the press my attention was called by Dr. Osborn to an article published in the *Journal of Morphology* by Dr. W. B. Scott, on the Embryology of *Petromyzon*, in which two distinct neuromeres are figured in the mid-brain (Figs. 10, 11). Dr. Scott makes no mention of these structures as having any segmental value, and in Fig. 11 the cell structure shown is evidently purely schematic. My Figs. 10 and 11 are taken from Dr. Scott's plates. The gradual transition of the hind-brain neuromeres into those of the mid-brain is clearly shown in Fig. 10. The gradual transition of the myelomere into the neuromere of the hind-brain in the Newt, Lizard, and Chick has already been mentioned. Thus I think that an examination of various stages of *Petromyzon* embryos will show a continuous series of neuromeres throughout the entire length of the neuron.

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EXPLANATION OF PLATES.

INDEX LETTERS.

- In, IIn, IIIIn, IVn.* First, second, third, fourth, etc., cranial nerves.
Ant. Anterior.
Ap. Apex of internal ridge of neuromere.
Aud. Ves. Auditory vesicle.
Ep. Epiblast.
Ex. Pit of external depression of neuromere.
FB. Rudiment of secondary fore-brain.
HB. Hind-brain.
in. Inner surface of neuromere, or that surface of the neuromere which lines the neural canal.
MB. Mid-brain.
Mes. Som. Mesoblastic somite.
Myl. Myelomere.
Na. Nasal thickening of epiblast.
Nm I. Olfactory neuromere. First neuromere of the primitive fore-brain.
Nm II. Optic neuromere. Second neuromere of the primitive fore-brain.
Nm II'. Possibly a portion of a third neuromere of the primitive fore-brain.
Nm V. Trigeminal neuromere. First and most anterior neuromere of the hind-brain.
Nm VI. Abducens neuromere. Second neuromere of the hind-brain.
Nm VII. Facial neuromere. The third neuromere of the hind-brain.
Nm VIII. Auditory neuromere. Fourth neuromere of the hind-brain.
Nm IX. Glossopharyngeal neuromere. Fifth neuromere of the hind-brain.
Nm X. Vagus neuromere. Sixth neuromere of the hind-brain.
Nu. Nuclei.
Out. Outer surface of neuromere.
Op. Ves. Optic vesicles.
Spn. Spinal nerve.
Spt. Neural septa.
Thal. Thalamencephalon.

All figures of sections have been drawn with the Abbey camera lucida and a Zeiss microscope. Z. 2 A means Zeiss ocular 2, and objective A, etc.

FIG. 1. Longitudinal horizontal section of spinal cord of *Amblystoma*, showing the neuromeres of the spinal cord and their relation to the mesoblastic somites. Also the typical nuclear and cell arrangement. Z. 4 D.

FIG. 1a. Longitudinal horizontal section of spinal cord of *Triton*, showing the same features as in Fig. 1. Z. 4 D.

FIG. 2. Longitudinal horizontal section of spinal cord of *Anolis sagrei*, showing same features as in Fig. 1. Z. 4 D.

FIG. 3. Spinal cord of Chick. Longitudinal horizontal section, showing same features as in Fig. 1. Z. 2 D.

FIG. 4. Longitudinal horizontal section of hind-brain of *Amblystoma punctatum*, showing the five neuromeres in the hind-brain. Also the gradual transition of the neuromeres of the spinal cord into those of the hind-brain; the relation of the auditory neuromere (*Nm VIII.*) to the auditory vesicle (*aud ves*), and the intersomitic relation of the myelomeres to the mesoblastic somites (*mes som*). Also the relation of the neuromeres to the origin of the V., VII., VIII., IX., and Xth nerves. Z. 2 A.

FIG. 4a. Longitudinal horizontal section of a slightly later stage than Fig. 4, in which the neuromeres have begun to degenerate. Z. 2 A.

FIG. 4b. Longitudinal horizontal section of the hind-brain of *Amblystoma punctatum*, in the region of the glossopharyngeal neuromere (*Nm IX.*), showing the typical cell and nuclear arrangement. Z. 2 E.

FIG. 4c. Longitudinal horizontal section of the hind-brain of *Amblystoma punctatum*, between the glossopharyngeal (*Nm IX.*) and vagus (*Nm X.*) neuromeres, showing the cell and nuclear arrangement between two neuromeres (*Spt*). Z. 2 E.

FIG. 5. Horizontal longitudinal section of the hind- and mid-brain of *Anolis sagrei*, showing the six neuromeres in the hind-brain and the relation of the auditory neuromere (*Nm VIII.*) to the auditory vesicle (*aud ves*). Z. 2 A.

FIG. 5a. Longitudinal horizontal section of *Anolis sagrei*, showing the six neuromeres in the hind-brain and their relation to the origin of the V., VII., VIII., IX., and Xth nerves.

FIG. 5b. Longitudinal horizontal section of the hind-brain of *Anolis sagrei*, in the region of trigeminus (*Nm V.*), abducens (*Nm VI.*), and facial (*Nm VII.*) neuromeres, showing the typical nuclear and cell arrangement. Z. 2 D.

FIG. 6. Longitudinal horizontal section of the hind-brain of a five-day Chick embryo, showing the six neuromeres in the hind-brain and the position of the auditory neuromere with respect to the auditory vesicle (*aud ves*). Z. 2 A.

FIG. 6a. Longitudinal horizontal section of a four-day Chick embryo, showing the relation of the six neuromeres in the hind-brain to the V., VII., VIII., IX., and Xth nerves. This section is not cut exactly in a longitudinal horizontal plane. Z. 2 A.

FIG. 6b. Longitudinal horizontal section of the hind-brain of a four-day Chick embryo in the region of the neuromeres, abducens (*Nm VI.*), facial (*Nm VII.*), and auditory (*Nm VIII.*), showing the typical cell and nuclear arrangement of the neuromere facial and the septum (*Spt*) between the adjoining neuromeres. Z. 2 D.

FIG. 7. Longitudinal horizontal section of the primitive fore-brain of *Amblystoma punctatum*, showing the two neuromeres, — olfactory (*Nm I.*) and optic (*Nm II.*). Also the typical cell and nuclear arrangement of the neuromeres. Z. 4 A.

FIGS. 7a, 7b, 7c. Longitudinal horizontal sections through the primitive fore-brain of *Amblystoma punctatum*, showing the origin of the olfactory nerve from the olfactory neuromere (*Nm I.*) and its final fusion with the nasal thickening of the epiblast. These sections are two or three apart. Z. 4 A.

FIG. 8a. Horizontal section of *Anolis sagrei*, dorsal, and parallel to the axis of the primary fore-brain, showing the neuromeres of the thalamencephalon (*Nm I.* and *Nm II.*). Also *Nm II.*, which has the appearance of a portion of a neuromere.

FIG. 9. Horizontal section of a four-day Chick, dorsal, and parallel to the axis of the primary fore-brain, showing the neuromeres of the thalamencephalon. Z. 2 A.

FIG. 10. Horizontal section through the superior portion of the brain of *Petromyzon*, 22 mm. larva. Taken from Dr. Scott's plates on "The Embryology of *Petromyzon*."

FIG. 11. Horizontal section through the anterior portion of the head of a *Petromyzon* embryo just before hatching. After Scott. This section does not show the primitive fore-brain, as it lies at an angle to the mid-brain, due to cranial flexure. The oculomotor and trochlear neuromeres (*Nm III.* and *Nm IV.*) lie anterior to the trigeminal neuromere (*Nm V.*), between it and the primitive fore-brain.