

The Ohio Journal of Science

Vol. XX

JUNE, 1920

No. 8

THE ORIGIN OF CEREBRAL GANGLIA.*

F. L. LANDACRE.

The problem of the origin of the cerebral ganglia presents many difficult, as well as many interesting phases. An attempt to form some conception of the present status of the problem by an examination of text books and monographs leaves one suspended between the explanations that are so simple that they will apply to no particular case, and observations and descriptions that are so complicated that one can form no general conclusion from them.

Possibly it is too early yet to form broad generalizations on this subject, and it is further possible that the generalizations may not seem what they claim to be on account of the number of exceptions cited, but since we cannot avoid generalization, and since even an incomplete generalization, provided it directs our efforts, has its value, I have ventured to attempt to reduce our present knowledge of this question to some simple statements or formula which will, at least, clear the way for investigation.

The problem has its historical background, of course, but much of this we must ignore for the present, unless it bears directly on the point of view which seems to be the most tenable at the present time. There is probably no more confused or hopeless mass of literature in Biology than that dealing with the cerebral nerves, especially the earlier literature dealing with their relation to the problem of the vertebrate head. Most of this we shall ignore, because the origin of the cerebral ganglia present a distinct problem, whose solution will undoubtedly throw much light on the larger problem. The head problem is so huge that it can not be reduced to a simple generalization at present.

*Presidential address given before the Ohio Academy of Science at its annual meeting in 1918.

One of the earliest advances that we need to note was the definite determination that all ganglia are derived from ectoderm rather than from mesoderm. This is significant, because it determined once for all the course of progress in this line.

Second, and of more significance to us today, is the fact that nearly all of the early work on ganglia was done on the spinal ganglia, and from this fact arose a very definite attitude toward the whole problem. Anyone at all familiar with this problem knows how easy it is to secure a series of stages in the development of the spinal ganglia. Since these structures are arranged segmentally, one embryo properly chosen furnishes a whole series of ganglia in the various stages of development, from very early to fairly late stages, so that the question of securing material for investigation is relatively simple. Most of the problems concerning the spinal ganglia were settled satisfactorily, and there has been no marked modification of these early views in recent years. Authors agreed on most points, as to the mode of origin, and also as to the final fate of the ganglia. The definiteness of these results, however, gave a very decided bias to the conclusions drawn in regard to the cerebral ganglia. The ease with which the origin of spinal ganglia was determined and the uniformity with which they arise from the neural crest, and the simplicity of the neural crest in this region, influenced, unquestionably, the conception of the position and the behavior of the neural crest in the head. It is undoubtedly true that too much emphasis was given at first to the role played by the neural crest in the head. As a result, other ganglion forming structures were either overlooked or underestimated at first. For some years the tendency was very marked to attribute to the neural crest in the head too much importance in the formation of cerebral ganglia. It was not fully realized that in addition to the neural crest there were other ganglion forming structures, and, further, that the neural crest itself might behave differently in different types in the head region. It is just this fact that has obscured many of the descriptions of the formation of the cerebral ganglia. The neural crest is not at all uniform in its behavior in different types. This bias was not corrected until a different point of view had become established as a result of the nerve component work.

The next fact historically that is of great significance to this discussion is the development of the doctrine of nerve components. The first effect of this doctrine on our problem was the establishment of the conception that there were more ganglia in the head than had been suspected, since a given ganglion such as the vagus may contain a number of components, and, further, to emphasize the importance, not of the individual nerves and ganglia, but of the component parts of which they are composed. The significance of this is apparent when your attention is called to the fact that seven out of twelve cerebral nerves, exclusive of the nervus terminalis, possess ganglia; when, however, you enumerate the components of these ganglia, there are found about twenty different ganglionic masses, the origin of which must be accounted for and these are distributed among only four components. Evidently, the mode of attack must be changed from that of individual nerves and ganglia to that of their components. Fortunately, there are not twenty different modes of origin for these components. There are about five, at the most; but the point to be emphasized is that these five are distributed among components rather than among ganglia.

The general tendency of the nerve component work has been to emphasize the analysis of nerves rather than of ganglia. This was perfectly natural and inevitable. There is always, in adult types, more or less combination of these various ganglionic components, which renders the identification of the individual ganglionic masses somewhat difficult. By the study of embryos in favorable stages it has been possible to isolate and describe in detail these ganglionic masses and to plot them. This analysis was evidently the second step in the effort to determine the mode of origin of these ganglia. It would have been utterly impossible to write an accurate description of the origin of these ganglia without knowing how many there were and how they were distributed in the various cerebral nerves. The complications that have arisen from ignoring this difficulty are almost innumerable.

The next step, evidently, was to determine the origin of the ganglia whose number, position and morphological relations are known. The diversity in modes of origin is not nearly so great (as mentioned above) as are the number of ganglia, and, in fact, barring the first and second nerves, not so numerous as the number of sensory components.

The simplest way to approach this problem is to return to the neural crest as we find it in the trunk, and then call attention to the variations in its mode of behavior in the head. The classical description of the mode of origin of the neural crest in the trunk is as follows: A mass of cells derived from the ectoderm and lying in the re-entering angle between ectoderm and neural tube becomes detached, migrates ventrally, and assumes the position of the adult spinal ganglia. This conception was established early and has never been materially modified for spinal ganglia. The spinal ganglia send fibers to two general regions, first to the skin forming the somatic group of fibers and second to visceral structures directly from the spinal ganglion or from its derivative the afferent sympathetic ganglia forming the visceral afferent system.

In the head region, however, two other types of behavior of the neural crest are present. It should be emphasized in passing that the neural crest in the head gives rise to exactly the same elements, viz., the general somatic or tactile, and the general visceral ganglia, as does that in the spinal cord region. This is a generalization of the first importance in our effort to establish general principles. We need not enter into the old discussion of the derivation of the head from the body or the reverse. The homology of ganglia derived from the neural crest in the head and in the body is well established, regardless of one's conception of this disputed question. Nor, need we raise the question of the segmental value or position of the cerebral ganglia. That is another problem that is frequently dragged into the discussion of the origin of the cerebral ganglia, to the confusion of the student. Leaving aside the disputed question of cephalization, including the segmentation of the head, we can examine the behavior of the neural crest in the head region as a distinct problem.

The neural crest behaves then in three different ways in the head region. It may behave just as it does in the spinal cord region, that is, become located in the re-entering angle between the ectoderm and the brain tube and, later becoming detached, move ventrally to a position lateral to the brain tube. This whole process is identical in type with the behavior of the spinal cord neural crest, and, as mentioned above, gives rise to the same components. If we accept the current descriptions, this is probably the most common type of behavior among vertebrates.

In the second mode of behavior as seen in *Ameiurus*, the homologue of the neural crest remains in the lateral ectoderm, and is not located in the re-entering angle. From its position in the lateral ectoderm, it becomes detached finally and migrates to the usual position of neural crest ganglia, after which time there is nothing to indicate that its early behavior was different from the neural crest in the spinal cord region. Since, however, there are other ganglion forming structures in the lateral ectoderm, this mode of behavior raises difficulties not experienced in the study of the first type.

A third type of behavior is illustrated by the Urodeles, and, according to Tilney, by certain of the cerebral ganglia in the cat. In this mode of behavior, the neural crest is incorporated in the neural tube and completely detached from surface ectoderm. It is later erupted from the dorsal surface of the neural canal, and assumes the usual position of neural crest ganglia, after which there is nothing to indicate that its mode of origin is different from that of the neural crest in the cord.

These three types of neural crest behavior can be reduced to one type, theoretically, at least. An extremely broad neural plate would, before invaginating to form the neural canal, reach so far laterally as to incorporate the neural crest in the neural tube from which, later, it is erupted (type III). At the other extreme would be the very narrow neural plate, which would leave the neural crest completely stranded in the ectoderm, as in *Ameiurus* (type II). The intermediate stage would have a moderately broad neural plate, which would carry the neural crest as far mesially as the re-entering angle (type I).

The ganglia derived exclusively from the neural crest in the head are, Gasserian of V, the jugular or root ganglion of IX when present, and the jugular or root ganglion of X. All of these belong to the general somatic or tactile ganglia. The neural crest further furnishes the general visceral ganglia supplying apparently free nerve endings in the mucosa. These are found in the geniculate, nodosal and petrosal ganglia, but do not form all of these ganglia, since they contain special visceral or gustatory ganglia derived from the epibranchial placodes.

The only ganglion of the general somatic or general visceral series that deviates from this description in any noticeable degree is the profundus ganglion. This ganglion always

becomes more or less closely associated with the Gasserian, but it always arises from the lateral ectoderm and, curiously, sometimes so far ventrally on the side of the head that its thickening, or placode, has been taken frequently for a dorso-lateral placode, and consequently the 5th nerve has been sometimes described as having a vestigial dorso-lateral placode, or lateral line organ. This is, of course, incorrect.

The profundus ganglion and nerve have none of the characteristics of lateral line nerves, but do have the characteristics of general somatic or tactile nerves. The mode of origin of the profundus ganglion seems to be constant, regardless of the way in which the neural crest behaves throughout the remainder of the head; that is, whichever of the three modes of behavior the neural crest follows, the profundus ganglion always arises from the lateral ectoderm, somewhat dorsal in position, however, to the dorso-lateral placode to be described later. It is best, in my opinion, to consider the source of the profundus ganglion as the most marked and constant displacement of the neural crest in the head region. This will lead to fewer complications than any other conception.

In addition to the neural crest in the head, there are two other general sources of cerebral ganglia, namely, the dorso-lateral placodes, giving rise to the acoustico-lateral, or special somatic ganglia and nerves, and the epibranchial placodes, giving rise to the gustatory, or special visceral ganglia and nerves.

Before taking these up in detail, however, it is advisable to call attention to the behavior of the ectoderm in forming the olfactory and optic placodes, so-called. Nothing is to be gained, in the present state of our knowledge, by attempting to place the placodes of these two organs in the neural crest, or dorsolateral or epibranchial series. The olfactory placodes remain in the ectoderm at the ventrolateral portion of the neural tube primitively, and are unique among the vertebrates in retaining their position in the ectoderm. They certainly have no resemblance to a lateral line placode or ganglion, and their detachment from the gill slit, at least in existing vertebrates, prevents us from homologizing them with the epibranchial series. Their origin is as unique as their anatomical structure in that they remain in the ectoderm and as compared with other nerves they are usually considered the most primitive

type of receptive and conductive apparatus in the vertebrate body.

The so-called optic ganglion and placode are still more unique, in that their cells are invaginated into the neural tube and, later, evaginated to form the optic cup, thus undergoing two displacements, whereas the olfactory placode undergoes none.

There is not much satisfaction, while attempting to reduce these phenomena to a system, to have two such striking exceptions as these organs present. Still, it is better, for the present, in my opinion, to so treat them than to attempt, as is often done, to reduce all sense organs and other thickenings, even the lens, to the three ganglion forming series, and thus weaken the principle involved by doubtful homologies in the attempt to explain every detail. By admitting that we do not see the homology of these placodes with the three ganglion forming series, we at least leave something interesting to be done in the future. Aside from the fact that these placodes come from the ectoderm, they show so little resemblance to each other, or to the three fundamental series, that we cannot combine them or place them in any of our three series. It would be more logical to have five classes: *a*, neural crest, *b*, dorso-lateral, *c*, epibranchial, *d*, olfactory, or permanent skin placode, and *e*, optic, or brain placode. This increases the number of classes, but does not establish any uncertain homologies. If the area that forms the eye had remained in the lateral ectoderm and had formed the eye in that position as it does in some invertebrates, the process would have been homologous to the formation of the olfactory vesicle. It could not even then have been placed in any of the three ganglia forming series, since they form only ganglia which serve as intermediaries between sense organs and brain, while both the optic and olfactory organs contain both receptors and conductors.

Let us return now to the second of our ganglion forming series, viz., the dorso-lateral placodes. These placodes give rise to the acoustico-lateral ganglia and nerves, and are always situated at or about the level of the auditory vesicle. This series must be sharply distinguished from (1) the profundus thickening or placode, which lies at a somewhat higher level on the side of the body and appears earlier; (2) from the primordia of the lateral line organs, which usually arise much

later, and give rise, not to ganglia, but to specific lateral line organs. If, as in the urodele, the lateral line primordia arise early, the relations are not so easy to understand as in *Lepidosteus*, where there is a considerable time interval separating the appearances of the two structures.

From this series of placodes we get the lateral line ganglia of the VIIth, VIIIth, IXth and Xth nerves, and, with the exception of the VIIIth, the behavior shows a fair degree of uniformity. The following variations should be noted:

(a) If the neural crest remains in the lateral ectoderm, as described in the second type of behavior, illustrated by *Ameiurus*, a large lateral mass is formed containing both the neural crest and the dorso-lateral placode combined in such a manner that it is very difficult at first to differentiate the two components. This condition in *Ameiurus*, however, is to be interpreted in the light of those forms which present a distinct neural crest and distinct dorso-lateral placode.

(b) Sometimes, as indicated above, it may be difficult to differentiate a dorso-lateral placode which forms ganglia from lateral line placodes which form lateral line organs, but I believe these structures to be morphologically distinct, and if any given case they are not well separated by a time interval in appearance, they should still be interpreted in the light of those forms in which there is a well defined time interval between the two sets of thickenings.

(c) Next, attention should be called to the mode of origin of the auditory ganglion. Authorities are almost equally divided as to whether it rises, on the one hand, from the auditory vesicle, or on the other, from the neural crest. If it rises from the neural crest, and is not included in (a) above as illustrated by *Ameiurus*, it is an exception to the behavior of the lateral line ganglia, and I have no suggestion to make as to the interpretation of this condition. However, in the types I have studied it seems to come from the auditory vesicle. The precocious appearance of the auditory vesicle seems to have incorporated the dorso-lateral placode at this level and forced it to appear, not from the smooth ectoderm, but from the infolded vesicle. The last word, however, has not been said concerning the origin of the auditory ganglia, by any means. Streeter has shown that in mammals it is distinctly double in form, and there are indications, both in *Ameiurus* and in the urodeles, that this

double condition appears very early, and there may be two sources for this ganglion instead of one. The one source is unquestionably the auditory vesicle, and the other is somewhat in doubt. Whether this double condition corresponds to the vestibular and cochlear divisions cannot be stated.

(d) A fourth source of confusion arises in following the dorso-lateral series of placodes. Where the auditory vesicle begins to form, the thickening in the ectoderm and sometimes even the invaginations is much longer than the vesicle itself. The greater portion of the anterior and posterior extensions of the vesicle disintegrate or are incorporated in the vesicle and are concerned in the formation of neither ganglia nor lateral line organs, but their position makes it difficult to distinguish them from ganglion forming dorso-lateral placodes, and sometimes from lateral line organ placodes and even from epibranchial placodes when these form early and the anterior extension of the auditory vesicle extends ventrally in the region of the VII ganglion.

It must be evident from these facts, that the generalization that acoustico-lateral ganglia come from the dorso-lateral placodes, must be made with the clear understanding of the several modifying factors that obscure, or, possibly, alter the generalization. The dorso-lateral placodes have been studied more extensively than any other series, except the neural crest, but much of the work was done without a clear conception of the components involved, and was frequently confused by the failure to distinguish between the origin of lateral line ganglia and the origin of lateral line organs, as well as the failure to distinguish the placodes from other thickenings lying adjacent to them in the ectoderm.

The third of the sources of origin of the cerebral ganglia is the epibranchial placodes. These are much more uniform in their behavior than the dorso-lateral series, and less disturbed by adjacent structures, although sometimes closely related in position to structures resembling placodes, and concerned in gill slit formation, and of a transient nature. It must be admitted that less work has been done and less positive evidence collected as to the ganglion forming activity of the epibranchial placodes than on either of the other two ganglion forming series. This is due to several causes. First, the evidence for this conception is not so easily observed, although convincing enough when

once understood. Second, until the nerve component work on the analysis of the cerebral nerves was well under way, there was no particular reason for suspecting separate gustatory or special visceral ganglia, and certainly no reason for suspecting a separate source. Third, there very early became established, on the basis of the work of Froriep and van Wijhe, the idea that the neural crest ganglia grow ventrally and form a contact with the vestigial sense organs in the position of the epibranchial placodes. This tended toward the conception that the neural crest ganglia grew into contact with the ectoderm, rather than that the ectoderm proliferates cells mesially that form a contact with the neural crest portion of the ganglion, and later became detached and added to it.

There are serious theoretical objections to this earlier view, in addition to the fact that it is not true. 1st, the neural crest proper forms, so far as we know, only general visceral and general somatic ganglia; 2nd, contact with sense organs in the vertebrate is always formed by the nerve growing out from the ganglion and not by the ganglion itself; 3rd, the epibranchial placode, with which the neural crest ganglion is supposed to form a contact, has absolutely no resemblance to a sense organ, gustatory or any other type. In addition to these three considerations, there is the well established fact that the epibranchial placodes do form typical ganglion cells, which are added to the neural crest portions of ganglia VII, IX and X.

While we are on this topic of the possible significance of the epibranchial placode, I should like to call attention to the conception that occurs in most of our standard text books on neurology, viz., that the epibranchial placodes represent phylogenetic sense organs, which may move out of the ectoderm and become buried in mesenchyme to form ganglia. This conception, in my opinion, is entirely erroneous, if we are to depend on histological and embryological evidence at hand. The conception has secured a hold on the minds of neurologists, apparently because it helps to fill in a series in the origin of ganglia, in which the olfactory cell, acting both as a receptor and as a conductor, is the simplest form. The epibranchial placode, if conceived phylogenetically as a sense organ, is thought of as moving out of the ectoderm and thus forming a ganglion. This connects the olfactory with other ganglia more detached from the ectoderm. Now, exactly the same line of

reasoning could be applied to the dorso-lateral placodes, and yet, to my knowledge, this has not been done. It becomes still more unsatisfactory if applied to the neural crest. The idea is attractive, however, but certainly receives no confirmation from evidence furnished by either the structure or the mode of development of the epibranchial placodes. They are simply ganglion forming structures, as are the dorso-lateral placodes and the neural crest. In all cases the specific sense organs arise entirely separate in position, and usually later, and very frequently without any close connection with epibranchial or dorso-lateral placodes. The attractive conception should, in my opinion, be entirely disregarded for the more accurate idea that these are simply ganglion forming structures.

The evidence that epibranchial placodes form gustatory ganglia rests upon the facts, (1) that in some types a ganglion such as the visceral portion of the IXth is almost, if not entirely, placodal in origin, and in this case the visceral IXth nerve is almost exclusively gustatory in function. (2) In other types, every step in the contribution of placodal cells to the ganglion can be clearly traced. (3) Every nerve, in all forms studied that possess gustatory fibers, has epibranchial placodes proportionate in size to the gustatory component. (4) No nerve not having gustatory components has an epibranchial placode. The ganglia showing these characteristics are the genticulate, nodosal and petrosal in all forms. The Vth ganglion and nerve gives rise to no gustatory fibers, and never has an epibranchial placode.

To summarize these generalizations, it seems to me fairly safe to make the following statements:

1. That all spinal ganglia arise from neural crest cells detached from the re-entering angle between the ectoderm and the neural canal. These cells, of course, give rise to general somatic and general visceral fibers.

2. In the head region the same general condition exists, namely, that the neural crest and its homologue give rise to all general somatic and general visceral ganglia, but the neural crest in the head shows three rather distinct modes of behavior: First, that which is identical with the behavior in the spinal cord region; second, that in which the neural crest remains in the ectoderm, and later becomes detached from this position; third, that in which the neural crest is incorporated in the neural

tube and later erupted. Whichever of these three modes is followed, the end result anatomically is the same. The exceptional behavior of the profundus ganglion must, of course, be kept in mind.

3. The acoustico-lateral system of ganglia and nerves arises from the dorso-lateral placodes, which, however, are subject to certain marked variations in time and in relation to other placode like thickenings that make this generalization somewhat less valuable than it seems.

4. The gustatory ganglia arise from the third series of placodes, the epibranchial. These are not to be considered as old sense organs phylogenetically, but simply as ganglion forming structures.

5. The two special senses, the olfactory and the optic, are such striking variations from the three ganglion forming series mentioned that it does not seem best for the present to attempt to incorporate these with the three series. They are best treated separately, in which case we must establish five types of behavior which the ectoderm undergoes in forming sensory conductors between the periphery and the central nervous system. (a) The neural crest ganglia furnishing general somatic and general visceral nerves, (b) the dorso-lateral placodes furnishing acoustico-lateral fibers, (c) the epibranchial placodes furnishing gustatory fibers, (d) the olfactory or permanent skin placode furnishing olfactory fibers, (e) the optic or brain placode furnishing optic fibers.