Citation:

On the delvelopment of the cerebellum in man (first part), in:
KNAW, Proceedings, 8 I, 1905, Amsterdam, 1905, pp. 1-7

KONINKLIJKE AKADEMIE VAN WETENSCHAPPEN TE AMSTERDAM.

PROCEEDINGS OF THE MEETING

of Saturday May 27, 1905.

(Translated from: Verslag van de gewone vergadering der Wis- en Natuurkundige Afdeeling van Zaterdag 27 Mei 1905, Dl. XIV).

CONTENTS.

The following papers were read:

Anatomy. — "*On the development of the cerebellum in man.*" (First part). By Prof. L. Bolk.

(Communicated in the meeting of March 25, 1905.)

On account of the fact that the lobulisation of the adult cerebellum of Primates generally and of man in particular, deviates in various respects from that of the remaining mammals, so that a homologisation of the lobes of the cerebellum of Primates occasionally presents difficulties, I undertook an investigation concerning the development of the grooves and lobes of the cerebellum in man, in order to try to elucidate certain obscure points in the anatomy of the Primate-cerebellum in this way. This investigation comprises some forty cerebella of human embryos, varying in length from crown to sole from 5 to 30 cm.

All the objects had been hardened in formol *in situ*; alcoholic material cannot be used for the study of this developmental process.

A complete systematic investigation of the formation of the lobes in the cerebellum of man has until now not been carried out. RETZIUS gives in his well-known standard work — Das Menschenhirn — a great number of pictures of developmental stages, also of the cerebellum, but a reasoned explanation to them is lacking. Of an earlier period we moreover mention the communications of KÖLLIKER and SCHWALBE, of more recent date those of KUITHAN, ELLIOT SMITH and CHARNOCK BRADLEY. In general, however, these investigations have been made with material which for this purpose was insufficient and as a consequence of this, opinions have become current which I have found to be wrong. This is more especially the case with the view concerning the way in which the sulcus horizontalis develops. Particularly with a view to the individual variations which arise especially in the later period of the lobulisation, it is essential to carry out the investigation with an extensive material, if we want to form a clear and continuous idea of the process and if we desire to distinguish well what is norm here and what exception.

In the morphogenetic process of the human cerebellum three periods may be distinguished, the first period is that of the development of the "cerebellar lamella" until the appearance of the first cortical groove; the second and third periods are those of the formation of grooves and lobes, during which, in the second period, those grooves appear which are generally characteristic for the cerebellum of mammals, in the third, the specific grooves and lobes of the Primate cerebellum. In this first communication only the first and second periods will be described.

Fig. 1, 2, 3 and 4 are sufficient to give an idea of the development of the "cerebellar lamella" until the time of appearance of the first groove. Fig. 1 has been taken from a foetus of 5 cm. length from crown to sole. The curvatures of the pons and neck have reached their maximum. The cerebellum appears as the already fairly thickened "cerebellar lamella" of MIHALCOVICS. It is remarkable that the thickening is turned intraventricularly in man whereas in the rabbit and pig (CHARNOCK BRADLEY) and the sheep (KUITHAN) it is exactly the extraventricular face which is most prominent.

From figs. 2*a* and 3*a* it appears that the convexity of the intraventricular plane becomes greater and greater, while the outer plane is only slightly vaulted. As a consequence of this, the cerebellum has in Fig. 3 acquired a triangular shape in the section with one extra- and two intraventricular planes; of these latter one faces

basalwards, the other caudalwards. The original caudal edge of the "Lamina cerebellaris" has consequently been shoved upward together with the insertion of the epithelial ventricular roof. Since in the mean time the plica-chorioidea has been formed, the peculiar condition has arisen, described by His for the human cerebellum, of which KUITHAN, however, denies the existence, since he could discover no trace of it in the sheep, although a complete developmental series was at his disposal. The anterior plait of the plica chorioidea, the so-called lamina chorioidea, is now stretched parallel to the intraventricular plane of the cerebellum which is turned backwards and this gives origin to a slit-shaped space between this plane and the lamella mentioned. His described this in this way that the lamina chorioidea partially encloses the cerebellum like a sac and how far this is the case appears from fig. 3*b* where the cerebellum is seen laterally. Now in fig. 4 nothing is found any longer of this condition, the plica chorioidea is now inserted at the edge of the cerebellum which now is turned to the back. Also in this respect I can confirm the observations of His against those of KUITHAN, that namely the lamina chorioidea lays itself upon the intraventricular plane and coalesces with this. Through this the latter has become an extraventricular plane and the plica chorioidea has obtained a new secondary line of insertion with the cerebellum. At the same time the outer plane has in this way become convex, the inner plane shows as a first indication of the "tent" in its posterior part a shallow groove which is to be distinguished as Incisura fastigii. The primitive line of insertion of the lamina chorioidea has to be sought in fig. 4 at the top of the extraventricular plane, laterally it lies more caudally, as follows from fig. 3*b*. This developmental stage of the cerebellum in man seems, by the peculiar way in which it thickens, to differ fundamentally from that of other mammals, where the cerebellar lamella retains in the section a more flattened lenticular shape.

At first the thickened lamina cerebellaris has the shape of a semiring, standing vertically on the anterior part of the longitudinal axis of the rhombencephalon and laterally passing into the still smooth regio pontis without a sharp border (fig. 2*b*). Soon the lateral parts of the lamina cerebellaris show a fairly strong clublike swelling (fig. 3*b*) by which a clear demarcation between cerebral base and cerebellum is formed. These lateral swellings remind us of the bilateral origin of the cerebellum in lower vertebrates (observed e.g. by SCHAPER in Teleosteans). Yet this lateral demarcation is only temporary; as soon as the pons begins to differentiate, it disappears again and arises

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anew only at a much later stage when the cortex has already become amply lamellised.

In the mean time, during the thickening of the lamina cerebellaris, developmental phenomena have taken place in the bordering region between Mesencephalon and Rhombencephalon, giving rise to the formation of Plica encephali dorsalis (KUPFER), Isthmus rhombencephali and Velum medullare anterius. In the youngest stage represented (fig. 1) the anterior edge of the Lamina cerebellaris passes directly into the mesencephalic roof, only the posterior edge of this latter is a little inwardly invaginated. An Isthmus rhombencephali or Plica encephali dorsalis do not yet exist. In the next stage of development (fig. 2*a*) the mesencephalon has obtained a clearly defined posterior wall, vertical to the roof; the inward invagination of the posterior edge of the roof is still in existence and is partly visible in fig. 3, but has disappeared in fig. 4 on account of the thickening of the posterior wall of the mesencephalon. In fig. 2 the plica encephali dorsalis has developed, bordered in front by the posterior wall of the mesencephalon, at the back by the lamina cerebellaris. The formation of the Plica is accompanied by a rotation of the Lamina cerebellaris, the anterior edge of which is now no longer situated at the front but below and as a consequence of this the Isthmus rhombencephali is now also indicated in principle. Next the bottom of the plica encephali dorsalis becomes broader, there arises between the thickened lamina cerebellaris and the mesencephalon a thin middle plate (figs. 3*a* and 4), the first origin of the velum medullare anterius. The further details of this stage and the following stages will be extensively described elsewhere.

The lobulisation of the cerebellum in the second stage is characterised by the fact that the grooves which divide the surface of the cerebellum into several regions originate with a single exception in the median plane and from there extend laterally. These interlobular grooves are consequently unpaired with one exception and divide the foetal cerebellum of man into a number of lobes, which can be homologised without difficulty with those which I learnt to be typical for the adult mammalian cerebellum.

The median section of a cerebellum with indications of the grooves that appear first, is given in fig. 5. The incisura fastigii has been shifted more to the front compared with fig. 4. On the extraventricular plane two grooves can be clearly distinguished, one, a little rostrally from the top of the cerebellum, another at a short distance from the margo myelencephalicus. Which of these two arises first I have not been able to make out, evidently they both arise about simultaneously,

since in three cerebella of this stage I found both of them already present in each (total length of the foetus 8 to 10 cm.). The anterior groove is the sulcus primarius (1), the typical principal groove, easily recognised in every mammalian cerebellum, separating the two lobes of the cerebellum, the lobus anterior and lobus posterior. The posterior groove is the sulcus uvulo-nodularis (*mihi*) (sulcus postnodularis of ELLIOTT SMITH, sulcus praeuvularis of ZIEHEN, Fissure IV of CHARNOCK BRADLEY). It borders the nodulus in front, i. e. in the direction of the mesencephalon. Between these grooves a still shallow depression is visible on the upper part of the posterior plane, the first indication of the fissura secunda (ELLIOTT SMITH, *mihi*, sulcus inferior anterior of ZIEHEN, fissure *d* of CHARNOCK BRADLEY). The cerebellum, seen at this stage from behind, is somewhat biscuitshaped (fig. 6) and lies with the front planes of its lateral parts against the occipital poles of the hemispherical vesicles. Besides the two mentioned grooves, proceeding from the median line, the cerebellum possesses at this stage already a sulcus which is bilaterally symmetrical and lies at a short distance of the margo myelencephalicus. This groove (*p*), which develops in a latero-medial direction is the homologon of the groove which I have distinguished in the mammalian cerebellum as fissura paraflocccularis. It borders in front the already slightly prominent so-called recessus lateralis. The anterior wall of this recessus lateralis has been distinguished by KÖLLIKER as gyrus chorioideus. It seems to me that the name "Gyrus floccularis" is more characteristic, since from this narrow cerebellar seam which is already marked out at so early a stage, the flocculi are later formed.

In a successive stage (Figs. 7 and 8) the sulcus primarius (1) has become deeper and the fissura secunda (2) has become a distinct groove; moreover a first secondary groove has arisen in the lobus anterior. Later this lobus is separated into four small lobes by three grooves; I have not been able, however, to make out which of these three is the first to appear. That the sulcus in the lobus anterior, seen in figs. 6 and 7, which is first in appearing, is really the groove, distinguished by ELLIOT SMITH as sulcus praeculminatus, I have not been able to confirm, while also from a comparison of my human cerebella of this stage with corresponding figures given by CHARNOCK BRADLEY for the rabbit and pig, it appears that this first groove lies in the lobus anterior of man farther away from the sulcus primarius than with the two animals mentioned. So I cannot decide whether this first groove in the lobus anterior in man is homologous with the "Fissure 1" of CHARNOCK BRADLEY. Also in the lobus posterior a new groove has appeared in the median line, between

the sulcus primarius (1) and the fissura secunda (2). This groove, indicated in the following figures by 4, is the sulcus praepyramidalis (mihi) (sulcus inferior posterior of ZIEHEN, fissure suprapyramidalis of ELLIOT SMITH, fissure III of CHARNOCK BRADLEY). This fissura praepyramidalis borders in front the pyramis and soon reaches the length of the fissura secunda. This latter can in its further development lengthen itself regularly in a lateral direction, or otherwise there independently arises (fig. 8*b* 2') in the hemisphere at a short distance above the fissura parafloccularis (*p*) a groove which soon becomes confluent with the fissura secunda. While at the same time the recessus laterales bend out further, the fissura parafloccularis (fig. 7*b*, 8*b*, *p*) becomes confluent with the sulcus uvulo-nodularis, by which the gyri flocculares form with the nodulus a part which is marked off from the remainig cerebellum. ELLIOTT SMITH mentions that the fissura parafloccularis can also flow together with the fissura secunda (2). This observation I can confirm for other mammals on account of the structure of the adult cerebellum; with the embryonic material of man I have not observed such a case. At a later stage the fissura secunda does terminate, above in the fissura parafloccularis.

In the cerebellum of a foetus of 13 cm. the hemispheres are no longer swollen balloonlike, but have, when seen from behind, obtained the more angular form which now is characteristic for them during a longer period of development (fig. 9*a*). The median zone is still a little depressed, even in the posterior part of the lobus anterior. The sulcus primarius (1) lies still relatively far at the back, the sulcus praepyramidalis (4) has already pretty far advanced into the hemispheres, but in such a way that the lateral parts with the transversally proceeding middle part form an obtuse angle, with the opening downwards. This peculiar shape forms during the successive stages of development, in which the interpretation of the grooves is not always easy, an excellent diagnostic for the sulcus praepyramidalis. The fissura secunda (2) has advanced as far as the lateral wall of the cerebellum so that the regio tonsillaris (fig. 9*a t*) is now bordered on all sides. This region is always more or less swollen in the shape of an egg. The gyrus floccularis is divided by a longitudinal groove into two small lobes. At this stage consequently the uvula with the appertaining lateral parts and so also the nodulus with its lateral regions are already differentiated in principle. This rapid developmental process contrasts strongly with the still very simple condition found in the remaining part of the lobus posterior and supports to some extent the opinion of ELLIOTT SMITH who looks upon the complex of uvula with tonsils, nodulus with flocculi, as a more independent

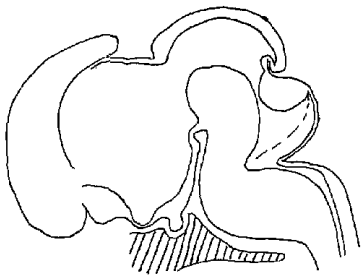

Fig. 1.

Fig. 2*a*.

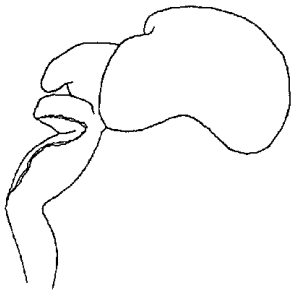

Fig. 2*b*

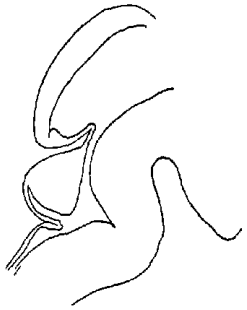

Fig. 3*a*.

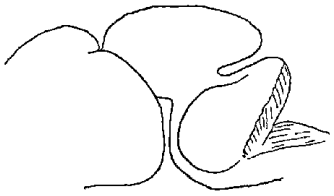

Fig 3*b*.

Fig. 4

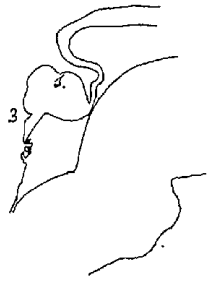

Fig. 5.

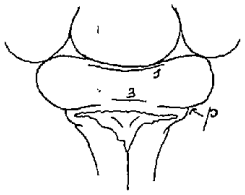

Fig. 6.

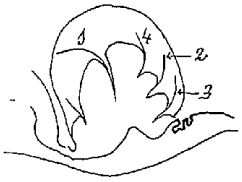

Fig 7*a*.

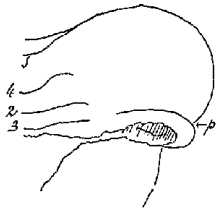

Fig 7*b*

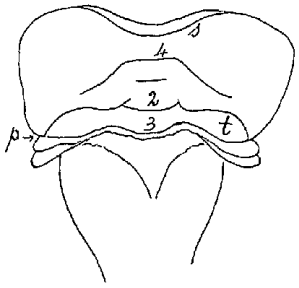

Fig. 9*a*.

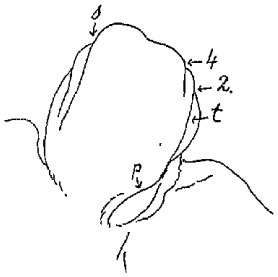

Fig. 9*b*.

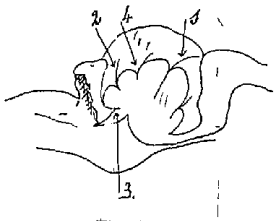

Fig. 8*a*.

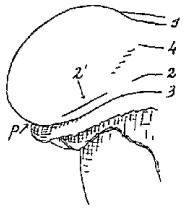

Fig. 8*b*.

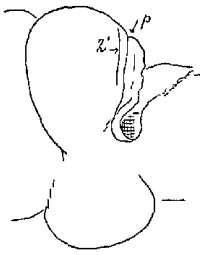

Fig. 8*c*.

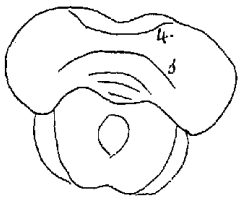

Fig. 10*a*

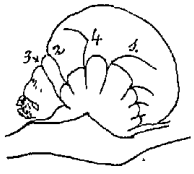

Fig. 10*b*.

lobe of the cerebellum. Then the peculiar surface division in the median line between sulcus primarius (1) and fissura secunda (2) deserves notice. The sulcus praepyramidalis (4), namely, at first always divides this region into two unequal parts; the lower half, the greater, situated between sulcus praepyramidalis (4) and fissura secunda is the origin of the pyramis, while from the very narrow upper half, situated between sulcus primarius (1) and sulcus praepyramidalis, must originate: declive, folium vermis and tuber vermis. In this respect a parallelism can be noticed between the phylogenetic and ontogenetic development of the cerebellum. For the narrow region between sulcus primarius and sulcus praepyramidalis is homologous with that lobulus which in the median section of the mammalian cerebellum I have distinguished as lobulus C_2 and which only in the Primates attains a very strong development.

The frontal plane and median section of the cerebellum of a foetus of 15 cm. are given in fig. 10. This stage of development is important because now the foetal human cerebellum shows the same lobulisation which I learnt to be the fundamental type of the mammalian cerebellum generally, a stage which only lasts a short time, since now soon the grooves appear that characterise the Primates generally or the Anthropoids and man more particularly and the homologa of which are missed with other mammals. For as will be seen from fig. 10*b*, now in the median section, as well the lobus anterior as the lobus posterior, is divided by three grooves into four lobuli. With the mammalian cerebellum I have distinguished the four lobuli of the lobulus anterior as lobulus 1, 2, 3 and 4, the latter being situated immediately before the sulcus primarius, the four lobuli of the lobus posterior I distinguished as lobulus *a* (homologous with the nodulus), lobulus *b* (homologous with the uvula), lobulus C_1 (homologous with the pyramis) and lobulus C_2 (homologous with the complex of declive, folium vermis and tuber vermis). It will be seen by a comparison with the investigations of CHARNOCK BRADLEY, that the stage with man, sketched in figs. 9 and 10, has a strong resemblance with a developmental stage which the cerebellum of other mammals (pig and rabbit) traverse before the final lobulisation of the cerebellum. However much the Primate cerebellum may in its final form differ from that of other mammals the groundplan of its lobulisation is, as is evident from the now sketched period of development, not different from that of other mammals. In the next following stage, however, it follows a development of its own, grooves occur, introductory to the lamellisation of the cortex, which are specific for the Primates and which will be described in the second communication.