Citation:

Winkler, C., On the brains of cyclops and monstra related to them, in:
KNAW, Proceedings, 18 II, 1916, Amsterdam, 1916, pp. 1399-1410

Anatomy. — *"On the brains of cyclops and monstra related to them"*. By Prof. C. WINKLER.

(Communicated in the meeting of February 26, 1916).

In the Folia neurobiologica the detailed description of the brains of a human Cyclops, which I wrote the year before, will soon appear. After having finished this description I was enabled to study still a few suchlike monstra. At present I possess, thanks to Dr. VERMEULEN, two rather well-preserved brains of cyclopian calves; thanks to Dr. BARENTSEN from Bergeyk, the brains of a cebocephalic human monstrum with microphtalmia and palatum fissum, and thanks to Prof. KOUWER a second cyclopian human misbuilding with microphtalmia.

The analogy in structure of the brains and the base of the skull in monstra, which belong to the long range of mutual related miscreations gathered by GEOFFROY ST. HILAIRE and VROLIK, have brought all independent investigators to a similar conclusion on this problem.

All of them are convinced that an earnest effort to explain those anomalies in development can only be made after an exact description of a large number of the brains of these beings.

It must be mentioned beforehand, that in the classification of GEOFFROY ST. HILAIRE and VROLIK (forming the foundation for every later arrangement of such monstra) the cyclopia is the representation of a more or less expansive medio-ventral defect in the frontal part of brain and skull.

When the ventral mid-part of the skull is lost, then the ethmoidal bone is totally missing together with the medial wall of separation in the nasal cavity. Then the orbits come close together or unite to a single orbit. When, as often happens, the most proximal part of the frontal bone develops in such cases then a part of the nose grows out, and is seen as the snout or the proboscis of the cyclops monstrum.

If there exist two separate orbits, placed side by side, the proboscis is located either above them (cebocephalia with arhinencephalia) or between them (etmocephalia with arhinencephalia).

If the orbits are fused and consequently one single orbit exists, the proboscis, when it is present, is necessarily placed above the single orbit (monorbitary misbuildings). In some cases it can be missing, when the germinative matter producing the ventral part of the frontal bone is destroyed by the defect.

The contents of that single orbit differs. In it can be found:

1. Two eyes, well developed or badly (microphthalmic or anophthalmic cyclopia).

2. One eye, surely resulting from the fusion of two eyes, because its structure (8 shaped cornea, double lens, iris, chorioidea or retina, finally two separate optic nerves) betrays it immediately (incomplete cyclopia).

3. One eye with one optic nerve, in which the insertion of a double set of eye-muscles points to the possibility that it yet can be formed by the fusion of two eye-vesicles (complete cyclopia).

A sample of complete cyclopia has been described in our country by Miss Dr. METMAN from the laboratory of Prof. W. M. DE VRIES.

The greater majority however of the described cyclopian misbuildings possesses in the single orbit one eye with two optic nerves, with the proboscis located above it.

I bring this to the foreground in order to point out the meaning of the word cyclopia, as a *circle*-eye. The four eye-lids compose around the orbit the circle, in which the two eyes, the double eye or the single eye, are lying. The cyclops can be one-eyed, but need not be so. However the cebocephalic, and ethmocephalic monstra, being arhinencephalic, are related to the incomplete and complete cyclopia, which also demonstrate arhinencephalia. Together they form the gradually proceeding range of related anomalities, described by Sr. HILAIRE and VROLIK.

Apart from the medio-ventral defect at the frontal part of the brain and skull, there is however still a second important deformation of the brain, appearing in all the monstra belonging to this range.

On examining the dorsal face of their brains one always finds a thinwalled sac, filled with fluid, which is in some cases larger, in other smaller, which covers in some cases totally, in others partially the brain matter, which does not seem to be divided by a sagittal fissure in two hemispheres and is lying at the base of the skull.

This sac has given rise to much error. Generally the wall of this sac is adhaerent to the dura mater and is torn when one is not careful in removing the latter, for if the thin membrane, forming the wall of the sac, is lost it is only with difficulty found back.

For certain however it can be stated that if the sac is not found, a technical fault is made during the dissecting.

In all the cases which I examined, it can be pointed out, that this sac is the roof of the III^{d} ventricle, pushed dorsalwards by the fluid, and prominating between the two hemispheres, which are bent lateralwards.

I cannot approve of the quotation of SCHWALBE and JOSEPHY: (Die Morphologie der Missbildungen etc. Teil III, IX^{te} Lief. S. 211. "Das "Vorderhirn ist bei den Cyclopen nie in Hemisphaeren geteilt. Es

"besteht vielmehr aus einer einheitlichen Massa, die oft die Form "eines nach hinten offenen Hufeisens hat".

Indeed the massive brain matter often has the form of a horse-shoe, but it results from two hemispheres, altered in their natural direction and united at the frontal pole. In all cases which I examined there existed two hemispheres.

On the other hand I can agree with another quotation of the previously mentioned investigators: 'dass die Blase tatsächlich der "Zwischen-hirndecke entspricht, geht aus ihren Anheftungspunkten "hervor. Es sind dies Randbogen, Taenia Thalami und Commissura "posterior".

With this thesis, also defended by KUNDRAT, I concur in so far, that the dorsally prominating sac is not always formed by the roof of the III^{d} ventricle in its total extent. It not seldom occurs that only the frontal part of this roof forms the prominating sac.

In the brain, described in details in the Folia neurobiologica, the insertion of the sac however could be followed from the lamina terminalis, along the foramen MONROI on the taenia thalami to the posterior commissure. In the case described by DAVIDSON BLACK and in the brain of the cyclopian calves the insertion of the sac begins on the lamina terminalis, bending with the latter round the very wide foramen MONROI to continue afterwards on the taenia thalami. Then however the distal part of the roof of the mesencephalon rests unaltered and does not partake of the promination.

In the case of Dr. METMAN too the sac is present and although the insertion is not described, the excellent photos which are added to the paper, prove that there too the sac is protuded between the two hemispheres, deviating widely and united together at the frontal part.

Not in accordance therefore is the supposition that the ring- or horse-shoelike cyclopian brain is formed by an undivided vesicle of the hemispheres. Both the halves of the hemispheric vesicles are present, but they are placed obliquely or even transversally to each other and they are united to each other in an undivided pole.

At the frontal pole the bulbus and olfactory tract are missing, and certainly frontal arhinencephalia exists. Moreover the anterior horns of the lateral ventricles have joined each other, but distally from the foramen MONROI there appear in all my cases two totally separated hemispheres with more or less well-developed walls, in which can be distinguished a lateral ventricle with an inferior and a posterior horn, a hippocampal fissure and a calcarine fissure.

I insist upon these facts, because they force me to join the effort

to explain this range of malformations, in the same way as KUNDRAT did.

Different efforts have been made to explain the designed monstra, and they can be divided into two groups.

In the first group those belong try to interpret the monstrum, by accepting a minus of germ material causing it.

If there was a developing embryo with insufficient germ material at the medio-ventral end of the frontal pole, then the medio-ventral end of the brain (arhinencephalia) and skull would not or only insufficiently be developed. Then the laterally placed eye vesicles will approach each other; eventually they will even confluate (their medial parts being undeveloped).

This conception accounts for the frontal arhinencephalia and the missing of the sagittal separation at the frontal pole of the hemisphere. It also accounts for the possibility of a gradual range of the monstra, from the cebocephalia to the complete cyclopia.

The most difficult part in such hypothesis, is to give a plausible interpretation of the dorsal sac. For if it may be granted, that a secondary hydrocephalus often accompanies different anomalies of the brain, the hydrocephalus localised at the roof of the III^{d} ventricle, and always there, is indeed extraordinary.

It is necessary to desire an explanation, why in cyclopian monstra the hydrocephalus always prominates the roof of the III^{d} ventricle, and is often found only there Such a conception of the cyclopia does not need a fixation in time for its commencement. There is no germ-material, therefore the tendencies for development are missing to form the medio-ventral part of the frontal pole of the embryo. This attempt of interpretation is mostly accepted by investigators, hoping, that the study of monstra may throw some light upon the history of developments of partly insufficient brains. They are not inclined to make use of pathologic influences in teratologic problems and avoid as long as possible to accept that such influences may play a role in their formation.

The second group of attempts to interpret cyclopian monstra grants an influence to pathologic instances. Their defenders however differ in many ways.

The developing embryo may lose in an early stage — e.g., when the eye-vesicles begin their differentiation, the original prosencephalon being not yet divided by a sagittal fissure — the medio-ventral part of the frontal pole. By many experiments, e. g. by cutting away precisely medially a small piece out of the embryonal shield in fundulus, LEWIS succeeded in transforming the development of this little fish into a cyclops monstrum; also STOCKARD reached the same

effect in this fish, by cultivating the larvae in a solution of sulfas magnesiae and SPEMAN caused cyclopian *larvae of triton* through putting a ligature around their "Urmund".

This interpretation however has the same difficulty as the former. It does not account for the internal hydrocephalus. Moreover STOCKARD declares that the brains of these cyclopian buildings were normal. Therefore the experimental cyclopia cannot be compared, without restriction, with that made by nature.

This interpretation points to a certain period in the development, to the so-called period of termination, of cyclopia. Its development commenced, at a time in which the eye-vesicles were differentiated, the telephalon is not yet divided and perhaps even in an earlier stage. In this interpretation the sagittal separation of the telencephalon is not formed because its ventro-medial end is ruined by the defect. The totally missing sagittal fissure in the telencephalon would be in direct opposition to the facts. It is only missing in the frontal pole.

In all the cyclopian brains of men and calves, examined by me, the hemispheres are distinctly divided at the distal end, only at the frontal pole they are united.

Another interpretation, suggested long ago by KUNDRAT, also appeals to pathologic influences. It may be supposed that a primary lesion in a localised spot in the brain can account as well for the medio-ventral defect at the embryonal frontal pole, as for the origin of the sac.

I want to insist upon the possibility of this interpretation, because I think it agrees better with some facts than the two other above-mentioned ways of interpretation do.

Suppose a pathologic process altering the proximal part of the thin roof of the III^{d} ventricle at an early period of the embryonal life, but not so early that the termination-period falls before the sagittal division of the telencephalon. On the contrary, the termination-period now asks, that the medial fissure, dividing the telencephalon into hemispheres, has already begun its formation.

The great amount of fluid, result of the pathologic process, dilates in dorsal direction the roof of the III^{d} ventricle. It prominates in the fissure between the two hemispheres, pushing the occipital poles of the hemispheres far aside, and pressing on the other hand the frontal poles against each other. As soon as the pressure in the ventricle becomes too intense, the brain vesicle will burst and probably the burst will take place there, where its resistence is small, i.e. through the lamina terminalis, in the direction of the prechordal part of the base of the ventricle.

The medio-ventral part of the frontal brain-pole is destroyed, the wounded medial faces of the frontal brain matter pressed against each other grow together, and in a later period of development, there is found no trace of their union, as is also the case in the embryo of fundulus, operated by LEWIS. The germ-material destroyed by the burst is the cause of a brain-defect. Its result is a brain, arhinencephalic in its frontal part.

The germ material lying beneath it, the future praechordal elements for the skull, is also destroyed. Their loss appears as a defect between the frontal and the sphenoid bone, which can always be demonstrated (if the skull must be spared, the X-ray foto of the skull may be necessary in men, in animals it is often directly seen).

To illustrate this view of the origin of the cyclopian brain it is not necessary to go back to the early period, in which the cyclopia probably begins.

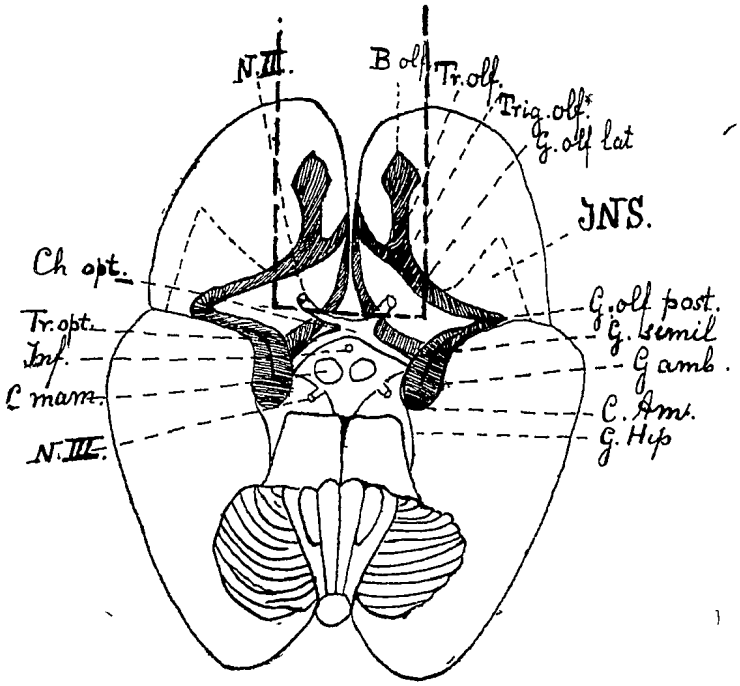

Fig. 1. Scheme of the brain of a human foetus of 5—6 months old. The rhinencephalon is striped. The thick dotted lines roughly form the border of the baso medial brain matter, which is lost by the embryonal defect.

It may be supposed e.g. that there was cut out of the brain a part of the frontal base and in the midline, which is bordered distally by the chiasma, laterally by the limen insulae (the thick lines in fig. 1).

The defect limited in this way may be removed, the wounded medial walls may be placed against each other and after uniting them, one obtains fig. 2 which represents the scheme of the brain of the cyclopian monstrum, as it was found in the case published in the Folia neurobiologica.

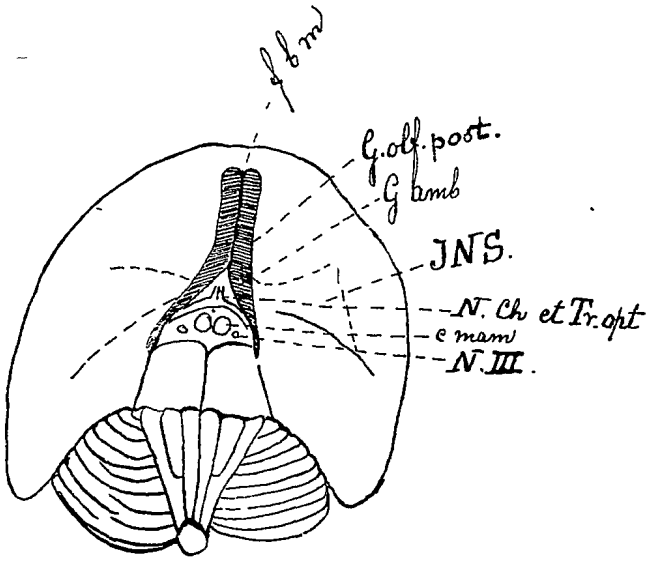

Fig. 2. Scheme of the remaining part of the telencephalon. Bulb, tractus and trigonum olfactorii are missing. The gyri olfactorii posteriores lie side by side, alongside the fissura baso-medialis (f. b. m.). Laterally from it the Insula is found.

The scheme in fig. 2 demonstrates that in the midline, frontally from the nervi optici, placed against each other, a baso-medial fissure or aperture appears, which is bordered on both sides by the posterior end of the gyri olfactorii posteriores (g. olf. post.) which have approached each other as soon as the base of the brain between the two insulae is lost. The gyrus olfactorius posterior helps to form the limen insulae and therefore it is found laterally bordered on both sides by the Insula (INS). Most distinctly these relations are seen on the left hemisphere (cf. fig. 4).

In fig. 3 and in fig. 4 a drawing is made after a photograph of the dorsal and of the ventral face of the brain of a human cyclops.

The cytologic research of the pallium of this brain demonstrated that on both sides along the fissura baso-medialis, in reality corresponded with the structure of the gyrus olfactorius posterior. In the convolution laterally from it the cortical structure of the insula was seen, with a claustrum bordering it.

This cyclopian brain therefore is arhinencephalic only in its frontal part, not in its temporal part. The necessity of the frontal arhinencephalia is sufficiently illustrated by the scheme in fig. 1 and fig. 2.

It also illustrates, that the eyestalks and eyevesicles lying much more laterally remain uninjured by the defect or if they are touched

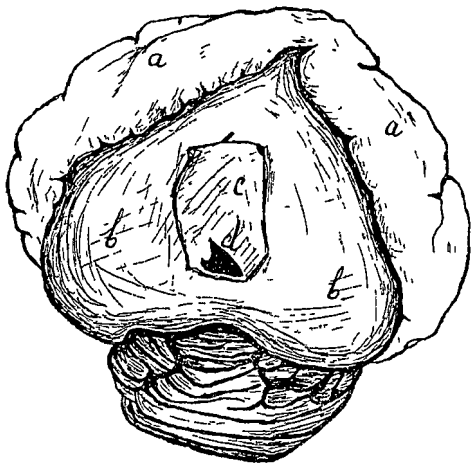

Fig. 3. The dorsal face of a human cyclopian brain (diophthalmos monorbitaris).

a. Brain-matter. *b.* roof of the 3rd ventricle. *c.* adhaesion to the dura mater. *d.* entrance to the cavity of the sac.

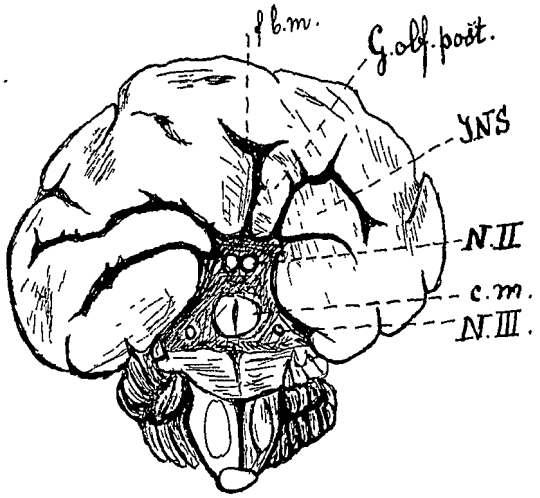

Fig. 4. Ventral face of the brain of the same cyclopian being.

f.b.m. = fissura baso-medialis. *G. olf. post.* = gyrus olfactorius posterior. *INS* = Insula Reilii. *N. II.* = Nervus opticus. *N. III.* = Nervus oculomotorius. *c. m.* = corpus mammillare.

by it, are only destroyed in the midline, in their mesial parts. The eyes are placed close together or eventually unite.

The praechordal layers, lying ventrally from the brain vesicle, do not develop. Consequently the matter, destroyed by the burst which in a later stage is going to form the tissue, found between the os sphenoïdale and the os frontale, will be missing and the orbits will appear close together or united into one. In this way the total range from the arhinencephalic cebocephalia to the complete cyclopia is also understood.

However it is obvious, that the extension as well as the place of the medio-basal frontal burst and probably also the period in which it occurs, can vary between certain limits.

First its extension. A very small, strictly medially lying bursts will always cause frontal arhinencephalia, but the loss in the midline of the future praechordal basal skull-elements are more or less independent of the extension of the brain defect. It may be

insignificant or large. On its extension, it will depend what place the future monstrum occupies in the range between arhinencephalia and cyclopia.

Still of greater importance is the location of the burst, and still more, the line of direction, in which the brain-vesicle bursts. There exist some details in different cyclopian monstra, which are not so well understood in accepting the other above mentioned interpretations, as they are by accepting that a primary lesion at the mesencephalic roof causes the burst in the base of brain.

It makes some difference for the future morphologic development of the embryo whether the burst goes through the medio-ventral vesicle-wall a little farther or a little less far frontalwards, whether it lies precisely in the midline or somewhat laterally from it. It is not even unlikely, that place and direction of the burst are connected to a certain point with the time of termination.

It is not *necessary* that the burst forces the medio-ventral wall of the vesicle exactly frontally from the place, where the chiasma is going to develop, even although the most frequently occurring form of cyclopia is represented by the cyclopia incompleta, in which, except the lamina terminalis, also the medial half of the eye vesicle is destroyed, so that afterwards the eyestalks are found as two optic nerves on one fully developed eye, composed by two half eye-vesicles.

If the burst is supposed to begin more distally, e.g. even forcing the place where afterwards the chiasma will appear and destroying at the same time the proximal part of the medial walls of one or both eyestalks; then there is no reason why — given the tendency of development of isolated parts (the independent developed eyes of the anencephalus) — the two united eye-vesicles should not develop into one eye.

In such cases the optic nerves mostly united into one nerve, ends blind, whereas there is not found a chiasma, nor even a mamillary body (e.g. in the case described by DAVIDSON BLACK).

Probably it is also of great importance, how the relations of development are between the ventral wall of the brain vesicle and the layers located ventrally from it, which will produce the middle parts of the skull.

From this point of view the brains of the two cyclopian calves seemed important to me.

They principally did not differ from those of the cyclopian human beings, which I examined. But important is the difference of the details.

In one, reproduced in fig. 5 and fig. 6 the sac (*b*) again is found

on the dorsal face (fig. 5). The vesicle is opened (*d*) and partially turned back. It is adherent to the dura mater (in *c*), and this also is turned back, but over the cerebellum. Here too two hemispheres are found, united in their undivided frontal part.

Two small optic nerves close to each other (N. II) form the

Fig. 5. Dorsal face of the brain of a cyclopian calve (cyclopia incompleta).
a. brain matter, *b*. roof of the IIId ventricle, turned over to the front and to the back. *c*. adherence to the dura mater also turned back. *d*. entrance to the IIId ventricle.

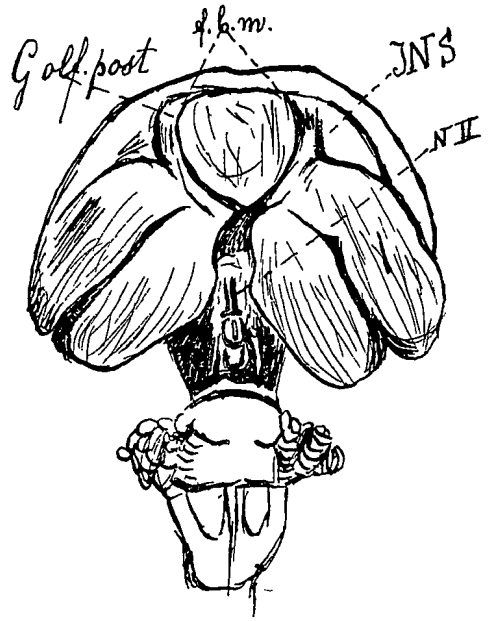

Fig. 6. Ventral face of this brain (Letters as in fig. 4).

chiasma and the occipital parts of the two hemispheres are, notwithstanding the complication of hydropically extended lateral ventricles, relatively well developed.

The defect in the bone, often only small in cyclopian human beings, is in calves very important. In the proboscis of them is seen a fully developed nose, divided into two halves, with a septum, conchae etc., fastened to a bony piece, proximally from the os frontale, as the X photo shows.

Closer research will still have to prove whether this piece of bone represents the remaining part of the ethmoidal. One thing however is certain: a large part of the praechordal tissue, out of which the middle-part of the nose will develop is not only present, it has reached a full-grown development.

In the second cyclopian calf still more interesting details appear.

There too the proboscis is a totally developed nose, with a septum, conchae, and two halves, as it was in the former case.

The figures 7 and 8 give the reproductions of the brain of this monstrum.

Dorsally the sac (*b*) appears, adherent to the dura mater (*c*) and opened in *d*. Ventrally (fig. 8) the fissure in located more distally than in the former case, although it is placed frontally from the chiasma, and, what is of more importance the burst is not located precisely in the midline, but it is deviating and has also ruptured the base of the left hemisphere.

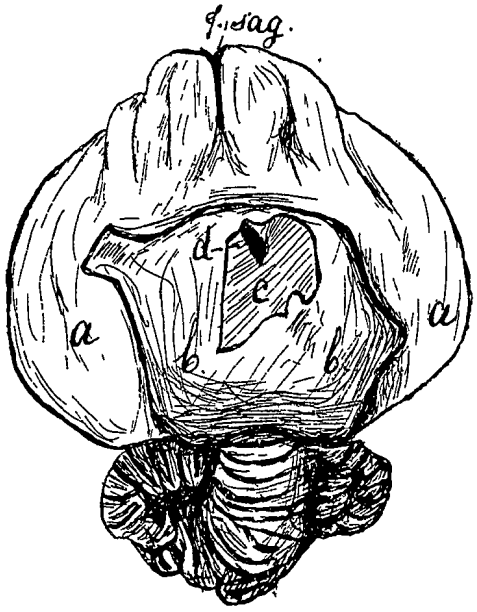

Fig. 7. Dorsal face of the brain of a cyclopian calve.
Letters as in fig. 3 and fig. 5.

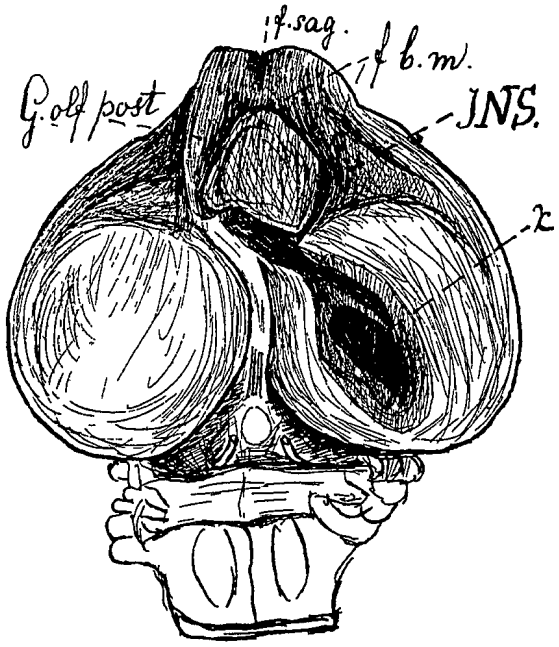

Fig. 8. Ventral face of this brain.
f. sag. = fissura sagittalis cerebri.
x = rupture in the basal face of the left hemisphere.
For the rest same letters as in fig. 4.

The frontal brainpole has not remained undivided here. If the burst does not keep strictly to the midline and is passing through a more distal plan of the brain-base, as may be supposed in this case, then there is no reason why the eye-origin on that side should not be totally destroyed and a real monorbitary clycopian being will develop, in which the eye is not composed by two eyes, but results from the one remaining eye-vesicle. Then too it is not necessary that the frontal pole has to remain undivided, for a part of the burst passes laterally from the midline. In this case the sagittal fissure becomes

visible at the frontal pole, although it does not reach the basal lamina terminalis and the brain shows frontal arhinencephaly on both sides.

Those who accept as essential in cyclopia the loss of germ-material at the frontal pole, caused (either by a primary defective germ, or by a pathologic moment acting on it directly), must not only account for the difficulty, which gives the interpretation of the dorsal sac, the hydropic protruding roof of the III^{d} ventricle. They too have to make acceptable:

a. why often a total development an internal nose appears in the proboscis;

b. why under certain circumstances, the sagittal fissure in the telencephalon, notwithstanding the arhinencephalia, still develops;

c. why there is, under circumstances, a burst at the distal base of one of the hemispheres. The result of the rupture through the frontal poles, which being pressed together, unite again, is obvious. But sometimes in one of the hemispheres also a rupture in the base of the temporal and occipital parts is demonstrable.

In short, by the examination of different cyclopian brains particularities appear, which agree with the old conception of KUNDRAT.

SCHWALBE's verdict: "Mit dem Zeitpunkt der Bildung der Grosshirn-hemisphären ist die teratogenetische Terminationsperiode der Miszbildungen gegeben, die *ein einfaches Vorderhirn* haben" — cannot concern the cyclopian brain. Cyclopian brains always possess two distinct hemispheres, they are only united to one undivided mass at their frontal poles.