Anatomy. — "*On the Nervus Terminalis from man to Amphioxus.*" By Prof. J. W. VAN WIJHE. [1])

(Communicated in the meeting of April 26, 1918).

Although hardly credible, it is a fact that a good three years ago — in 1914 — a new nerve, arising independently in the brain, was discovered in man. This is the Nervus Terminalis. Naturally it is not visible to the naked eye, but can be seen through the magnifying glass, especially through the dissecting microscope, with the aid of which its discoverer, the American BROOKOVER found it. (Journ. of Comp. Neurology. Vol. 24.)

It has its course through the pia mater, parallel and mesial to the olfactory bulb and tract, running over the middle of the gyrus rectus (vide fig. 1.) When a rectangular piece of the pia mater in this region is taken up and placed under the microscope, the fine fibres of this nerve can be seen. Here and there the fibres are retracted from each other to come together again later on.

The nerve is independent of the olfactory tract and bulb, and in the opinion of BROOKOVER enters the brain at the mesial root of the tract. A number of ganglionic cells, BROOKOVER taxes their number at about 50, lie spread in the nerve in its course along the olfactory tract.

The nerve can be followed not only along the tract but also somewhat further distally along the olfactory bulb, but in this vicinity it is embedded in the dura mater, while it has here also partially pierced the former and lies on the lamina cribrosa.

In the vicinity of the bulb the number of its ganglionic cells is considerably larger than is the case along the tract. It was estimated by BROOKOVER at about 100 to 200 cells. Undoubtedly its branches pass through the mesial row of openings in the lamina cribrosa to the mucous membrane of the nasal septum, but the research did not extend as far as this.

In adult man the course of the new nerve is as yet known in the brain-case only, not on its outside. [2])

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[1]) Lecture delivered before the meeting of the Neth. Zoological Society, Jan. 26, 1918.

[2]) Vide, however, the postscript at the end of this article.

As was to be expected, in the adults of the mammals the nerve was not first found in man. The dog and the cat (Mc. COTTER. 1913.) and the rabbit (HUBER & GUILD. 1913.) were the first, but it is remarkable, that in the embryonic stages of the mammals the human embryo was the first in which, although incompletely, the nerve was discovered. This was done by our countryman ERNST DE VRIES, who also observed it in the embryos of the guinea-pig. He described his research (published in the Proceedings of the Royal Academy of Sciences of April the 22nd 1905), which also drew much attention abroad, in an article of four pages, which proves that it is not necessary or even desirable to be loquacious when one has found something of importance.

DE VRIES found ganglionic cells spread in the course of the nerve which supplies the organon vomeronasale, (the organ of JACOBSON, or better the organ of RUYSCH) [1]) near the base of the nasal septum. He moreover found that the so-called olfactory ganglion, by him called the ganglion vomeronasale, does not belong to the fila olfactoria, which are taken collectively as the true olfactory nerve. In his opinion it belongs to the N. Vomeronasalis, which supplies RUYSCH's organ, lined by a layer divided off from the nasal mucous membrane. As the vomeronasal nerve also enters the central nervous system at a different place — the area vomeronasalis — than do the fila olfactoria, DE VRIES drew the conclusion that the N. Vomeronasalis is not, as was the general opinion, a component part of the olfactory nerve, but an independent nerve, homologous to the N. Terminalis in the fish.

A serious difficulty to this explanation however is that, according to the illustrations of DE VRIES, the N. Vomeronasalis issues from the olfactory bulb, while the N. Terminalis of the Dipnoi and the Selachii issues out of the true hemisphere and not out of the bulb. [2])

This difficulty seems to have escaped DE VRIES's notice. On the first page of his publication he rightly distinguishes between the olfactory lobe and the hemisphere, which are separated from each other laterally by the fissura rhinica, and mesially by the fissura prima. On pages 3 and 4 he states that the area vomeronasalis, where the nerve of this name enters the brain, belongs to the hemisphere. According to his own communication and illustration, however, this area lies at the sulcus circularis bulbi, hence *not* on

[1]) Concerning RUYSCH's organ see postscript at the end of this paper.

[2]) Entering and issuing out of a nerve are used in this address, indiscriminate of the direction in which the impulse moves.

the hemisphere, but on the olfactory lobe. In young embryos the tract is thicker than the bulb, later on this relation is reversed.

It was therefore very desirable that more light were thrown on the question whether the vomeronasal nerve should be considered as the homologue of the N. Terminalis of the fishes.

This happened in 1913 in America, more especially through two publications viz. of JOHNSTON in the Journ. of Comp. Neur. Vol. 23. and of HUBER & GUILD in the Anatomical Record Vol. 7. [1])

JOHNSTON examined embryos of the pig, the sheep, and of man. Besides mammals he also examined embryos of tortoises and a larva of Amblystoma.

The elucidation which JOHNSTON brought, consists herein that (as he found) the ganglion and the ganglionic cells do not belong to the N. Vomeronasalis, but to another nerve, which does not enter the brain in the olfactory bulb, but in the true hemisphere, near or in the lamina terminalis, as is the case in the Selachii.

What DE VRIES had considered as one nerve, was in reality two nerves which for the greater part cover each other; one is the N. Terminalis, the other is the true N. Vomeronasalis.

The vomeronasal nerve has no ganglionic cells and arises out of the cells of a part of the nasal mucous membrane which had been split off (Organon Vomeronasale). In structure and development it is exactly similar to the bundles of the olfactory nerve. It also enters the brain in the olfactory bulb, just as the fila olfactoria, which collectively form the olfactory nerve. It is true that it enters the bulb at a special place, on its mesial plane rising high up caudally, but then it is a *specialised* bundle of the olfactory nerve. The peripheral ganglionic cells and the true ganglion belong to the N. Terminalis.

DE VRIES' mistake is easily comprehensible; he used no special methods to make the nerves visible, could not expose his material of human embryos to this risk and was thus compelled to consider the proximal end of the N. Vomeronasalis (split into four bundles according to him) as a root of the Ganglion Terminale, by him incorrectly called the Ganglion Vomeronasale, which is as it were pasted up against it, while the true roots of this ganglion escape observation in cross section through their fineness. That it is possible to make mistakes even when using nerve-staining methods is proved by the work of DÖLLKEN (1909). He examined embryos of mice, rabbits, guinea-pigs and man. Following in the footsteps of DE VRIES

[1]) Further literature is found mentioned in these publications.

he also took the roots of the N. Vomeronasalis to be those of the N. Terminalis.

Regarding the mouse he says "Die sog. mediale Riechwurzel von der bereits CAJAL, KAPPERS u. A. behauptet haben, sie sei nicht als eigentliche Riechwurzel zu bezeichnen, ist eine Wurzel des N. Terminalis". No wonder that he continues "Sie hat bedeutende Beziehungen zum Olfactorius".

The second important elucidation appeared, as has already been said, in a communication, also in 1913, of HUBER and GUILD, who had come on this subject á propos of the work of JOHNSTON, which had partly been done in HUBER's laboratory.

These writers examined rabbit embryos by the silver-pyridine method. They could fully confirm JOHNSTON's results that the N. Terminalis and the N. Vomeronasalis were two different nerves, and that the ganglion and the disseminated ganglionic cells belong, not to the N. Vomeronasalis, which is evidently a specialised bundle of the olfactory nerve, but indeed to the N. Terminalis.

While JOHNSTON however was still of opinion that the peripheral termination of the N. Terminalis was limited, principally in any case, to the region of the N. Vomeronasalis, these investigators discovered that this ending is to be found in the foremost part of the nasal septum, reaching caudally to the rear border of the Organon Vomeronasale. It is only a small part of the peripheral branches that reaches this organ and the true olfactory mucous membrane, the region of the fila olfactoria, was free from branches of the N. Terminalis.

Through difference in tint the branches of the Terminalis could well be distinguished from those of the Trigeminal nerve (Nasociliary and Nasopalatine), which are also found in the mucous membrane of the nasal septum.

As will presently become clear, it is of importance in following the nerve to Amphioxus, that the N. Terminalis does not branch in the olfactory mucous membrane.

In 1912 and 1913 Mc. COTTER published his investigations on the N. Vomeronasalis and the N. Terminalis. By means of the dissecting microscope, thus as it were at magnifying glass magnification, he found the latter in the adult dog and cat, but not in the rat, the rabbit, the sheep, the guinea-pig or the oppossum. That he did not find it is not to be wondered at considering his method. His opinion that the N. Terminalis ends peripherally at or near the vomeronasal organ is also comprehensible because the bundles here are thicker, the fibres of the N. Terminalis being strengthened by those of the vomeronasal nerve.

This much as regards the *mammals*, which I have considered somewhat more extensively as most, and to my mind the most accurate, investigations have been done on them.

I can be brief about the birds, reptiles, and amphibians.

There does not seem to be much known about the N. Terminalis in the *birds*.

In the *frog* it was found in 1909 by C. JUDSON HERRICK, who also described its central termination more especially; its peripheral branches could not be traced accurately. This was also the case in the *Urodela*, where the nerve was observed by MC. KIBBEN (1914), who could not however find any ganglionic cells in it. Some time later JOHNSTON succeeded in this. He says "In Amblystoma the nervus terminalis is ganglionated and supplies the vomeronasal organ, as in reptiles and mammals". Concerning the reptiles he says that the peripheral termination takes place "in the turtle to a medial diverticulum of the nasal sac, which presumably corresponds to the vomeronasal organ or a part of it".

We now come to the *fishes* wherein, setting aside an isolated observation by G. FRITSCH about one of the Selachii, the nerve was first found by PINKUS in Protopterus. His preliminary communication appeared in 1894 in the "Anatomischer Anzeiger" and was followed in 1895 by his elaborate treatise "Die Hirnnerven des Protopterus annectens" in the "Morphologische Arbeiten". PINKUS found that his new nerve originates in the brain, places itself rostrally against the most mesial bundle of the olfactory nerve, takes its course over the nasal mucous membrane and is to be followed to the roof of the anterior nasal opening. The nerve consists of nonmedullated fibres and has in its course a cellular swelling, which is undoubtedly the Ganglion Terminale of later writers, although PINKUS could not convince himself of the ganglionic nature of the cells.

SEWERTZOFF (1902) found the nerve in embryos of Ceratodus. He mentions the fact, of importance for the homologisation, that the nerve does not branch in the olfactory mucous membrane and that it terminates in the skin at the external nasal opening. Soon (1904—1905) BING and BURCKHARDT described the nerve in the adult Ceratodus also.

Concerning the *Selachii* the treatise of LOCY, which appeared in the "Anatomischer Anzeiger" after several smaller publications, is well known. In this treatise, which is accompanied by a large number of handsome illustrations, he described the structure and development of the nerve in Acanthias as seen in series of sections, as well as its course as this is to be seen, by means of the dissecting microscope.

in 20 genera of sharks and rays. At first he held the nerve to be a part of the olfactory nerve, but later on he recognised its homology to the new nerve of PINKUS, and called it the N. Terminalis.

In the Selachii the distance between the nasal sac and the olfactory bulb is small, hence the olfactory nerve is short. Immediately on its appearance out of the nasal sac it is separated into a lateral and a mesial bundle by a small groove into which the distal termination of the N. Terminalis enters.

Scoliodon terrae novae alone has something peculiar. Here the two bundles are not only completely separated from each other, but the division also continues on to the bulb, and even to the distal (foremost) end of the tract, which usually is long in the Selachii. After the N. Terminalis of the Selachii has made its appearance out of the hemisphere, it takes its course along the mesial border of the tract, and when it has reached the bulb it forms a ganglion. In some species two ganglia were observed in the course of the nerve.

LOCY assures that the nerve in its distal ramifications is principally limited to the olfactory mucous membrane, but to my mind he has not proved this. His method was not sufficient to do this, and considering the results of other investigators in other classes of animals this assertion needs corroboration by preparations treated with silver compounds.

In the *Ganoids* the N. Terminalis was first found and clearly represented by PHELPS ALLIS (1897, fig. 64) in Amia calva. He could follow it caudally up to the fore-brain. In the larvae he also found its ganglion.

In 1910 BROOKOVER described its development in these fishes. His investigation contains many new finds and interesting communications, but his conclusion that the nerve is a branch of the olfactory nerve cannot in my opinion be correct. In his work in 1914 on the nerve in Lepidosteus he also came to this conclusion.

In the *Teleostei* SHELDON and BROOKOVER (1909) found the nerve in the carp and in Amiurus. According to them the roots of the ganglion enter the olfactory bulb to reach the hemisphere, contained in the tract. Here however the question arises whether they have not made a mistake analogous to that of DE VRIES in the embryos of man, as this is not the condition in the Dipnoi, in the Selachii, in the amphibians or in the mammals, nor either in man according to what BROOKOVER himself (1914) found in the last-named.

Concerning the lungfishes I can here demonstrate to you two fine models of the fore-end of the brains, with the nerves arising therefrom, of Ceratodus and Protopterus, both constructed by Dr. VAN DER

HORST in the Institute for Brain Research of Dr. ARIËNS KAPPERS, who was so kind as to lend them for this evening. One sees the N. Terminalis arising out of the hemisphere, and running rostrally quite independent of the olfactory lobe, as is also the case in man according to BROOKOVER (c.f. fig. 1).

Finally I come to *Amphioxus*, on whose cerebral nerves I published a communication in the meeting of the Royal Academy of October the 27th. 1894. As is known the trigeminal nerve of the craniata forms a complex of two dorsal segmental nerves, the components being the N. Ophthalmicus profundus (N. Nasociliaris) and the rest of the N. Trigeminus. I found both these components in the two nerves, of which the one appears before and the other behind the first well developed myotome (which has morphologically to be considered as the second). Before the homologue of the profound ophthalmicus, however, there is in Amphioxus still another nerve which supplies the utmost point of the snout. On account of this and because it arises from the morphological fore-end of the cerebral ventricle I called it the N. Apicis.

At first I thought that the N. Apicis would be aborted in the higher chordata, but shortly before the publication of my article the preliminary communication of PINKUS appeared (Anat. Anz. 1894), in which he reported the discovery of a new nerve in Protopterus, later named the N. Terminalis by LOCY.

This had to be considered the homologue of the N. Apicis considering its course, ramification and origin, not from the infundibulum as I concluded out of the preliminary communication, but near the Lamina Terminalis as became clear when the more extensive treatise appeared the next year.

I must acknowledge that I have later on sometimes doubted whether this homologisation were correct, when I read the investigations of LOCY in the Selachii, of BROOKOVER and SHELDON in the Ganoids and Teleostei, and of ERNST DE VRIES and DÖLLKEN in the mammals, because all these writers assert that the peripheral termination of the N. Terminalis is wholly or principally limited to the olfactory mucous membrane (or in mammals to the vomeronasal organ, which is covered by a split-off part of the olfactory mucous membrane). In Amphioxus on the other hand the N. Apicis stands in no relation whatever to the covering of the olfactory groove.

After however reading the research of HUBER and GUILD (1913) this doubt was dispelled.

Their illustration (c. f. fig. 2) shows the N. Apicis of Amphioxus in the rabbit — I could almost say "in optima forma", even to the

disseminated ganglionic cells, which have already been long known in the N. Apicis.

As the N. Apicis is an ordinary cutaneous nerve [1]), the relation in which the N. Terminalis stands to the olfactory epithelium in some of the higher animals must be of a secondary nature. It is even possible that the terminal ramification of the nerve has become principally limited to the olfactory mucous membrane, as appears to be the case in many fishes.

Thus has the N. Terminalis completed its course through science in 20 years (1894—1914) beginning in the lung-fishes, I may as well add in Amphioxus, and ending in man. It can no longer be doubted that we have here to do with an independent cerebral nerve and not with a bundle of the olfactory nerve. In most or all of the craniata however branches of both nerves run close alongside of each other, and on account of this it is difficult to distinguish their peripheral distribution.

From Amphioxus to man the N. Terminalis is provided with disseminated ganglionic cells, which can partly be gathered together to one or more ganglia. On the other hand the olfactory nerve (including its specialised bundle, the N. Vomeronasalis of the Amniota) is distinguished by the complete absence of ganglionic cells.

At the end of this summary I want here to express my thanks to Dr. ARIËNS KAPPERS, who was so kind as to send me for perusal a dozen treatises on the N. Terminalis, nearly all of American investigators, which have become the occasion of this address.

POST SCRIPTUM.

Early in March Dr. KAPPERS sent me for perusal a copy of a new work by BROOKOVER, which he had received a few days earlier: "The Peripheral Distribution of the Nervus Terminalis in an Infant" (Journal of Comp. Neurology Vol. 28 N°. 2).

BROOKOVER found the branching of the N. Terminalis in the nasal septum of the child analogous to that in the rabbit, according to HUBER and GUILD, only much more strongly developed. In it he could count about 1500 ganglionic cells, not considering the Ganglion

[1]) It is a well known fact that ganglionic cells are found not only in the first but also in the second cutaneous nerve (N. Ophthalmicus prof.) of Amphioxus. DE QUATREFAGES discovered them here in 1845 already, but held them for mucous cryptes, "cryptes mucipares". Incorrectly it is assumed that peripheral ganglionic cells are not present in the other nerves. I found multitudes of them in the nerves running under the atrial epithelium which covers the intestine and the liver.

Terminale. This ganglion was a compound of 6 to 8 ganglia, combined by a net of nervous fibres.

He mentions nothing about a N. Vomeronasalis, but found a stout nerve without ganglionic cells, which, with a branch of the N. Terminalis, passes through one of the hindmost openings of the Lamina Cribrosa to the nasal septum and anastomoses peripherally with the N. Nasopalatinus.

BROOKOVER considers the above-named stout nerve as a sympathetic anastomosis between the Ganglion Sphenopalatinum and the Ganglion Terminale. To my mind this nerve is the N. Vomeronasalis, which has then not been aborted after birth, in man, as was hitherto the general opinion. In case this conjecture is correct, it must arise behind in the olfactory bulb and supply the vomeronasal organ.

This organ is generally present in the vertebrates higher than the fishes [1]), and seems to be a product of adaptation to terrestrial life. It first appears in the amphibians, and has been lost or is present only in the early stages of development in the higher forms which have secondarily become aquatic again (crocodiles, partly also the Chelonia, the Cetacea, and the Pinnipedia).

Flying also seems to be unfavourable for the development of the organ (birds and some — not all — of the bats).

The organ is usually named after JACOBSON, who found it independently in a large number of mammals, and who also discovered the N. Vomeronasalis. His work became known through the report CUVIER made on it [2]).

After the considerable praise which CUVIER bestows on the work, for a part done in his laboratory, one would expect at the end of his report to the "Institut" the advice to have the treatise of JACOBSON, "pensionnaire et chirurgien-major dans les armées de Roi de Danemark", printed. The end of the report, however, reads as follows: "Nous croyons que le Mémoire de M. JACOBSON mérite l'approbation de la classe [de l'Institut] et que cet anatomiste doit être invité à continuer des recherches, qui ont déjà fourni un résultat aussi curieux".

This encouragement does not, however, seem to have had the desired result. At least it is not known that JACOBSON has published his treatise, enlarged or not.

For the rest CUVIER makes a mistake in believing that nobody had observed the organ before JACOBSON, and that it is not present

[1]) C.f. R. WIEDERSHEIM, Vergleichende Anatomie der Wirbeltiere, Jena, 1909.

[2]) G. CUVIER, Rapport fait à l'Institut, sur un Mémoire de M. JACOBSON intitulé: Description anatomique d'un Organe observé dans les Mammifères. Annales du Muséum d'Histoire naturelle, Tome 18, 1811.

in man. It has escaped his attention that RUYSCH, who is cited by him à propos of the Meatus Nasopalatinus, (l.c. p. 414. He writes: RUISCH) is the discoverer of the organ, and just in man in whom it is normally present as was corroborated later on.

KÖLLIKER[1]) and HERZFELD[2]) found it regularly in children while it is seldom wanting in adults. When this was the case it had probably to be ascribed to former diseases of the nasal septum.

The description of RUYSCH[3]), who also gives a clear representation of the orifice of the organ, with a sound brought into it, on the nasal septum of a child, reads as follows: "In anteriore et inferiore parte septi juxta palatum in utroque latere foramen apparet, seu osculum cujusdam ductus de cujus usu et existentia nil apud authores legi; inservire muco excernendo existimo".

JACOBSON also, not knowing RUYSCH's work, is inclined to consider the organ as being secretory, although the powerful innervation pleads for a sensory function, but (l.c. p. 422): "quel agent extérieur pourroit aller se faire percevoir dans un réceptacle si caché, si profond, si peu accessible?"

CUVIER himself still thinks — under reserve — he has to accept a kind of olfactory perception and the later writers do this too. It is usually assumed that the organ serves to smell the food which has already been taken into the mouth; in mammals the odour would then rise up through the Meatus Nasopalatinus. This can however not be the case in the horse or the donkey (nor in the camel or giraffe), because here the Meatus is no longer opened to the buccal cavity, while their Organon Vomeronasale cannot be held to be rudimentary as is the case in man.

The secretory function is evident on account of the numerous glands (KÖLLIKER, l. c. p. 11) which fill the organ with mucus, which streams out through ciliary motion, but the difficulties against accepting

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[1]) A. KÖLLIKER, Ueber die Jacobsonschen Organe des. Menschen. Reprinted from the Festschrift für RINECKER, Leipzig 1877.

[2]) P. HERZFELD, Ueber das Jacobsonsche Organ des Menschen und der Säugethiere, Zoologische Jahrbücher, Abth. für Anat. und Ontogenie der Thiere Bd. 3, 1889.

HERZFELD gives a summary of the mammals in which the organ had been found by him and others up to 1889, also in connection with the meatus nasopalatinus. He might have added that JACOBSON had also already observed it in the marsupials (kangaroo). Later on it was also found in the Monotremata and Edentata.

[3]) F. RUYSCH, Thesaurus anatomicus III, Amstelodami, 1724, p. 26, N°. LXI, 5. Illustration: Tab. IV, fig. 5.

KÖLLIKER (1877) cited the description, mentioned above, from an edition of 1703 p. 49; hence more than 100 years before CUVIER's report.

an olfactory function, already hinted at by JACOBSON, and which KÖLLIKER tries to evade in a peculiar manner, are not to be got out of the way.

In this regard an observation of HERZFELD in connection with the venous sinus, with a strong circular layer of nonstriated muscular fibres, which is found in the wall of the organ of the rat on the inner side of the bony capsule, — cartilaginous in the majority of the mammals — seems to me worthy of attention. He assumes that the air will be sucked into the organ through contraction of the sinus and the lessening of the volume of the wall, inside the rigid capsule, caused by this.

If this appears to be the case in other animals also — the opportunity for research will probably present itself in a veterinary college — then a sort of olfactory function would become comprehensible. It would then also become clearer why the Cetacea and Pinnipedia are nearly the only [1]) mammals in which the search for the organ [2]) of RUYSCH has been in vain.

It is comprehensible that the Cetacea and Pinnipedia have lost the true olfactory organ, adapted to aquatic life in earlier fishlike ancestors, it became adapted to smelling in the air in later ancestors, which lived on land as mammals, When these, in a still later period, again went back to aquatic life, as Protocetacea and Protopinnipedia, the true olfactory organ could not undergo this change and became rudimentary or disappeared altogether. If the organ of RUYSCH in terrestrial mammals is always filled with liquid (mucus), and does not need to adapt itself to smelling in the air, then there is not the same reason for its disappearance in the Cetacea and Pinnipedia as there is for the degeneration of the true olfactory organ of the Cetacea.

[1]) One would expect the Sirenia here also. It is remarkable however that Manatus, according to STANNIUS (Lehrbuch 1846, p. 399) possesses an exceptionally well developed Organon Vomeronasale. In some bats and catarrhine apes the organ has disappeared through some cause or other, as in the Cetacea and Pinnipedia.

[2]) The numerous morphological investigations on this organ have taught us very little about its function. On histological grounds a sort of olfactory function is not to be doubted, (c.f. amongst others M. VON LENHOSSEK, Die Nervenursprünge und Endigungen in Jacobsonschen Organ des Kaninchens. Anat. Anzeiger. 1892). This is about the only result, concerning the function which we can, after about 200 years, add to the words of the discoverer: "Inservire muco excernendo existimo."

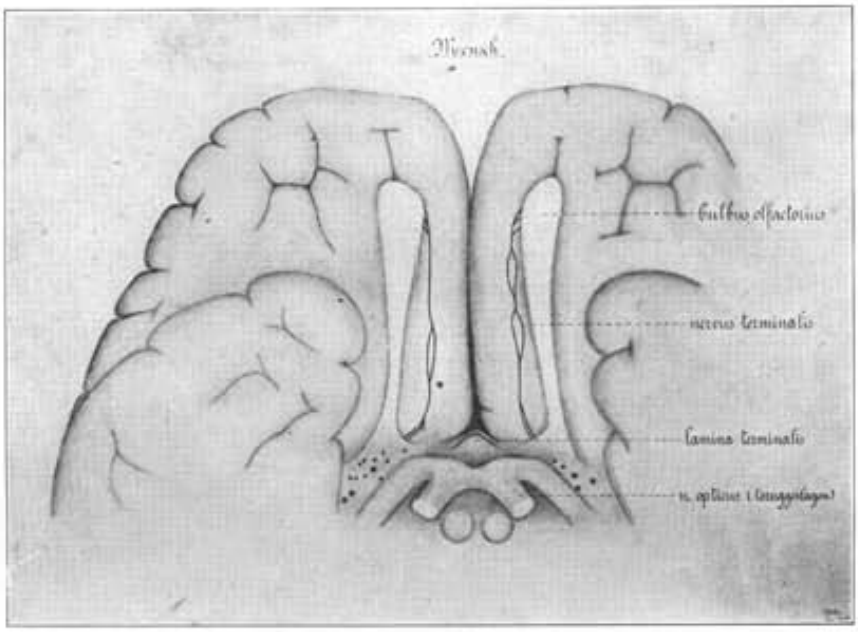

Fig. 1. Shows the lower surface of the foremost part of the brain of man and the intracranial part of the N. terminalis. (According to a figure of BROOKOVER, slightly modified).

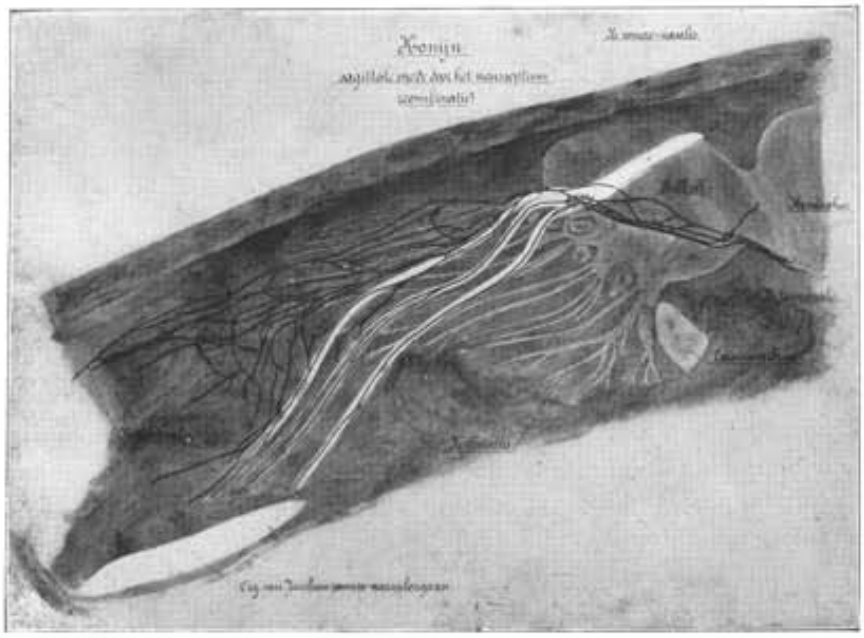

Fig. 2. Shows the mesial surface of the right olfactory lobe and of the contiguous part of the hemisphere with the nerves which radiate from this into the septum, after a combination of sagittal sections in the rabbit. (After a fig. of HUBER and GUILD, slightly modified).