OBSERVATIONS ON THE PERIPHERAL DISTRIBUTION OF THE NERVUS TERMINALIS IN MAMMALIA

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THREE FIGURES

The occurrence and relations of the nervus terminalis in various types of vertebrates has in recent years been the subject of a relatively large number of contributions, appearing in the main from American laboratories. Johnston in a recent communication summarized this literature in tabular form, and to this the reader is referred for a general consideration. From a study of this literature and from his own contributions, Johnston concludes that, "In all the forms in which the nerve enters the olfactory bulb it as been shown that its fibers pierce the formatio olfactoria to pass on to their proper endings in some part of the forebrain," and further, that the facts appear to show "that the nervus terminalis in most fishes and amphibians is a ganglionated nerve whose root enters the forebrain caudal to the olfactory bulb, usually near the site of the embryonic neuropore, and whose fibers are distributed to the wall of the nasal sac." In this paper Johnston notes the presence, and gives a general description of the nervus terminalis as observed in reptilian and mammalian embryos, his study including among the latter, pig, sheep and human embryos. His investigation show that in reptilian and mammalian embryos this nerve, "enters the brain at a point somewhat removed from the median plane but otherwise holding the same relation to the primordium hippocampi, precommisural body and neuroporic recess which the root holds in selachians." The fibers are said to arise from bipolar ganglion cells, collected into a compact ganglion terminale in the pig and human embryos

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and into several clumps in the course of the nerve and its branches in turtle embryos. So far as concerns the peripheral distribution of the nervus terminalis in mammalia he notes that, "In the pig the nervus terminalis is clearly distributed to the vomeronasal organ," and, "In man the fibers mingle with the olfactory strands of the nasal septum." McCotter has called attention to the presence of a nervus terminalis and a ganglion terminale in adult dogs and cats. These results were obtained in the main by gross dissection, controlled by sections and tissue membranes, spread and stained to admit of study under the microscope. The nervus terminalis was traced to its entrance to the forebrain in both the dog and the cat, ganglion cells were noted in its intracranial course as also small collections of ganglion cells in the septal portion of the vomeronasal nerve just dorsal to the vomeronasal organ. McCotter concludes, "that there is normally present in the adult dog and cat a ganglionated nerve connected with the vomeronasal nerves on the one hand and apparently with the forebrain on the other, having thereby the same morphological relations in these mammals as is described for the nervus terminalis in the lower forms."

Johnston's recent studies, above referred to, and as noted in his communication, were made in part on series of embryos in this laboratory. Our interest in the presence of the nervus terminalis in mammalian embryos having thus been stimulated we were pleased to note a differential staining of this nerve in a series of sagittal sections of the heads of two rabbit embryos, which from size and general development were estimated as having been removed about a week before birth. These heads had been stained after the pyridine-silver method as used by Ranson, with certain modifications to be noted. Our observations on the peripheral distribution of the nervus terminalis in mammalia pertain, therefore, to the rabbit.

Method. The essential steps in the Ranson pyridine-silver technic are as follows: Fixation in ammoniated absolute alcohol; thorough pyridine penetration; thorough washing in distilled water; impregnation with a 2 per cent silver nitrate solution; reduction of the silver by means of a formalin-pyrogallic acid solution. Early in our use of this method we became aware of very evident shrinkage of the nerve cells, probably

due to the ammoniated alcohol fixation. This was largely obviated by the injection of the ammoniated alcohol solution into the fresh tissues. The investigations undertaken demanded that the method be made applicable to decalcified tissues. It was found that this could be done by using nitric acid as a decalcifier.

The method as now used in this laboratory is as follows: The animal is prepared by chloroform anesthesia and the heart incised before it ceases to beat. This to obtain as complete drainage of the vascular system as is possible. A cannula is then inserted into the main artery supplying the area containing the nervous tissues to be subjected to silver staining and the cannula filled with normal salt solution. By clamping branches the area to be injected can be restricted. A solution consisting of 95 per cent alcohol and a 1 per cent concentrated ammonia is then rapidly injected under a pressure of from 5 to 10 pounds, this being continued until the parts seem well injected. The ganglia, nerve trunks, pieces of the central nervous system, as desired, are then removed and placed in a similar ammoniated alcohol solution, in which they remain for from two to three days. The further treatment is as is given by Ranson for the pyridine-silver method. This method of fixation by a preliminary injection of the ammoniated alcohol solution seems to us to present distinct advantages, especially when used in the study of ganglia and peripheral nerves. For instance, the shrinkage and distortion of the peripheral layers of cells of sensory ganglia is largely obviated. The elements are well fixed and are slightly separated so that much thicker sections may be cut and studied to advantage. The impregnation and reduction of the silver seems more uniform and more certain.

The pyridine-silver method as adapted so as to include decalcification of the tissues is as follows:

1. Adult or young animals and embryos of sufficient size to admit of injection are injected with ammoniated alcohol solution, as above described, and the tissues placed in the ammoniated alcohol for from two to four days, depending on the size of the tissue mass to be fixed.
2. Transfer to distilled water, in which the pieces remain until they sink.
3. The pieces are then transferred to a 7 per cent solution of nitric acid, made with distilled water, in which they remain until the decalcification is complete; which varies with the age and size of the tissue block.
4. Wash in distilled water for about one-half hour, the water being changed frequently.
5. The pieces are then transferred to alcohols of 80, 90 and 95 per cent, to each of which is added 1 per cent of concentrated ammonia. A thorough treatment with ammoniated alcohol at this step seems to us essential; three to eight days, depending on the size of the pieces.
6. Rinse in distilled water and place for twenty-four hours in pyridine.

7. Wash thoroughly in distilled water for twenty-four hours, the water being frequently changed. As the immediate transference of the tissues from the pyridine to the distilled water is liable to result in a swelling of the tissues, which may lead to a bursting of the hemispheres, a gradual transference from the pyridine to the distilled water is recommended.

8. Transfer to a 2 per cent solution of silver nitrate in distilled water, in which the tissues remain for from three to five days, in the dark and at a temperature of about 35°C.

9. Rinse in distilled water and place for from one to two days in a 4 per cent solution of pyrogallic acid in 5 per cent formalin.

10. Dehydrate thoroughly, beginning with 80 per cent alcohol. Aceton may be used to hasten the dehydration, but should be preceded and followed by alcohol. Clear in xylol and embed in paraffin. A necessary stay in the warm oven, even to forty-eight hours, to insure thorough paraffin penetration, does not seem to affect the stain.

The possibility of decalcification combined with preliminary ammoniated alcohol injection greatly extends the applicability of the pyridine-silver method. We have found it possible to stain half of the head of a six day rabbit, head and neck of a medium sized frog, head of a small turtle, and so forth. After the injection with the ammoniated alcohol we have removed the skin and exposed the brain. Further cutting of the pieces was delayed until after the decalcification and second ammoniated alcohol treatment. The paraffin sections may be cut serially, and fixed to the slide by the water albumen method in the usual way.

We are able to confirm Ranson's statement, and find it applicable to the method as here modified, namely, "With fresh pure chemicals, absolutely clean utensils, and a reasonably constant temperature this method can be relied upon to give uniform results."

Material. The material on which our observations on the peripheral distribution of the nervus terminalis in mammalia is based, consists of series of sections of heads of rabbit embryos and young rabbits, cut in the sagittal plane, as follows: *a*, rabbit embryos, 3 cm. head-breech length; *b*, rabbit embryos removed about one week before birth; *c*, young rabbits one day old; *d*, young rabbit six days old. For the two younger stages the entire head was cut, for the older stages a little over one-half of the head, the series beginning about 2 mm. to the left of the mid sagittal plane, thus including the nasal septum and the entire left half of the brain and head. Two complete sagittal series of each of the three younger stages are at our disposal and one complete sagittal series of the oldest stage. In each of these series the fibers of the nervus terminalis, throughout their entire course, are stained deeply brown or black and are of relatively fine caliber, while the olfactory formation, and the olfactory nerves including the vomeronasal portion, are colored a light brown and are traced as large compact bundles with sheath cells rather than separate fibers. The differential staining is so distinct and characteristic that the two types of fibers can not well be confused.

Graphic reconstruction of the oral part of the forebrain, the olfactory bulb and nerves, the vomeronasal nerves and the nervus terminalis of the right side have been made for the three younger stages. Of the two younger stages by Guild, of the one day stage by the senior author, as well as a partial reconstruction of the six day stage. The resultant figures of the three stages completely reconstructed are so similar that a publication of all seemed unnecessary. The one day stage was chosen for the reason that the parts sketched were less compactly grouped and can thus be followed in the figure with greater ease. The graphic reconstructions were made with the aid of a camera lucida at a magnification of 75 diameters for the one day stage and 85 diameters for the two younger stages. Doubtful points were controlled under higher powers. By the use of orienting points selected in the sections, field after field was adjusted and the pertinent parts traced in pencil. In the final figure only nerve segments clearly joined were sketched in ink. The right side was chosen for the graphic reconstructions by reason of the fact that the final figures were somewhat easier to make in that in tracing the series, beginning with the nasal septum and proceeding lateralwards, the nervus terminalis was superimposed on the olfactory bulb and nerves. The distribution of this nerve on the left side is, it may be anticipated, the same as that on the right side. As concerns the graphic reconstruction reproduced, we desire to state that while the distribution of the nervus terminalis is, as we believe, correctly given, with the magnification used it was not possible to show in detail the size and number of the component nerve fibers of the several branches of the nerve. In order to make the figure intelligible we found it necessary to emphasize the branches of the nervus terminalis and sketch them as solid black lines and thus bring out disproportionately large certain of the finer branches and connections. The distribution of the ganglion cells as given is based on camera lucida projections. In the final drawing the ganglion cells, for the sake of clearness, are sketched disproportionately large. As stated above in all of our series the nervus terminalis was found differentially

stained so that under the magnification used it was possible to distinguish between its branches and those of the olfactory and vomeronasal nerves.

Our observations on the superficial origin of the nervus terminalis in mammalia are in harmony with those of other authors who have dealt with this subject. In the rabbit the main portion of the nervus terminalis arises from the ventro-mesial surface of the forebrain; caudal to the olfactory bulb and stalk and oral to the lamina terminalis. Its origin is not by a single compact bundle and from a limited area, but rather by several smaller bundles or roots which pierce the brain substance rather gradually, in smaller subdivisions. In the two younger stages a smaller root was traced to its entrance in the forebrain, at a region more dorsally placed on the medial surface. In the one day stage this root could not be clearly traced to its entrance in the forebrain. The nervus terminalis passes forward along the ventro-mesial aspect of the olfactory bulb, in the form of a loose plexus consisting of three or four strands joined by anastomoses, to a position mesial to the region where the branches of the vomeronasal nerve unite to form a main strand, just above the cribriform area. In this intracranial portion of the nervus terminalis there are found here and there small groups of ganglion cells, either at nodal points of the plexus or as single cells or clusters of two or three ganglion cells along the course of the nerve filaments, and in all of our series there was observed a relatively larger mass of ganglion cells in the region where the nervus terminalis crosses the vomeronasal nerves. This latter mass we regard as the 'ganglion terminale' of authors. The origin, general course and relations to the olfactory bulb and vomeronasal nerves of the nervus terminalis of the rabbit may be seen in figure 1, which figure duplicates in all essentials the figures obtained by graphic reconstruction of this region for the two younger stages studied and for the six day stage. In its passage through the cribriform area the nervus terminalis accompanies in the main the vomeronasal branches, lying on their mesial aspect. If in our sagittal series of heads of embryos and young rabbits the study is begun with the nasal septum and carried from here to the right, it may

be seen that the branches of the nervus terminalis are in the deeper portion of the septal mucosa and are first met with on the mesial surfaces of the vomeronasal branches, which pass mesially to the filaments of the olfactory nerves as they radiate to the different parts of the septum, thus in a deeper plane of

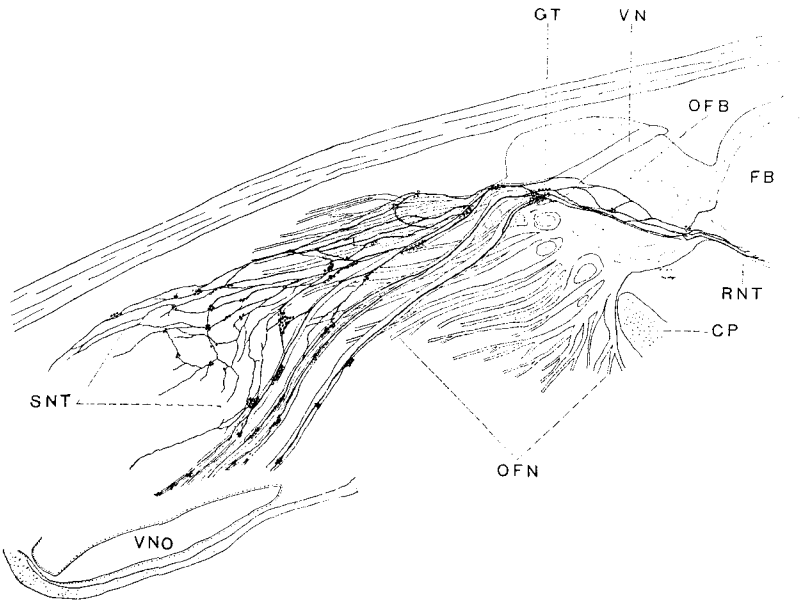

Fig. 1 Graphic reconstruction of right side of olfactory bulb and stalk, olfactory and vomeronasal nerve, and nervus terminalis, based on a sagittal series of sections of head of a one-day-old rabbit, stained after the pyridine-silver method, and showing differential staining of the nervus terminalis. The nervus terminalis is given throughout its course in jet black; the olfactory and vomeronasal nerves are given in outline; *fb*, forebrain; *ofb*, olfactory bulb; *vn*, vomeronasal nerve; *rnt*, roots of nervus terminalis; *gt*, ganglion terminale; *snt*, septal distribution of nervus terminalis; *cp*, cribriform plate; *vmo*, vomeronasal organ, given in outline. × 10.

the septal mucosa. In all of our series, terminalis branches are associated with each of the three main branches of the vomeronasal nerve and may be traced with them to their termination in the vomeronasal organ. Scattered along the course of the terminalis branches there are found smaller and larger groups

of ganglion cells, even in connection with the end branches of the nervus terminalis found in the mucosa of the vomeronasal organ. Here and there there may be observed anastomosis between terminalis branches accompanying the vomeronasal branches with ganglion cells at nodal points. In all of our series certain of the most dorsally placed filaments of the plexus on the mesial surface of the olfactory bulb leave the fibers accompanying the vomeronasal branches as they pass through the cribriform area and course orally toward the upper and anterior part of the nasal septum, to participate in the formation of a plexus found in the deeper portion of the septal mucosa of this region. In the deeper portion of the septal mucosa anterior or oral to the region crossed by the vomeronasal nerves there is found a distinct plexus of terminalis fibers, associated with numerous small groups of ganglion cells, a plexus which reminds one of the enteric plexus, although the groups of ganglion cells are much smaller and the uniting nerve filaments much finer. That this anterior septal plexus is a part of the nervus terminalis distribution is shown on the one hand by the differential staining as found in our series, on the other hand by the fact that the more dorsally placed filaments of the nervus terminalis may be traced into this plexus as well as branches from the terminalis filaments which accompany the vomeronasal nerves. Numerous small groups of ganglion cells are found at the nodal points of this plexus, the number of ganglion cells constituting such a group varying greatly, varying from one cell to perhaps 10 or 15 cells. We have not observed branches of the nervus terminalis nor ganglion cells in the septal mucosa caudal to the region crossed by the vomeronasal nerves. The general peripheral distribution of the nervus terminalis of the rabbit, as also the disposition of the associated ganglia, is so clearly shown in figure 1, that further and fuller description seems to us unnecessary.

In our series it is possible to trace the branches of the trigeminal distribution to the nasal septum. In the main the nerve fibers of trigeminal origin appear to us as somewhat coarser, as stained more intensely black, and as presenting other characteristics, less distinct and more difficult to formulate, but evident

to one who has studied the series carefully. The trigeminal branches to the nasal septum were confirmed as such in graphic reconstructions of the two younger stages, and in an incomplete reconstruction of the six day stage. It was found inadvisable to attempt to reproduce trigeminal distribution to the nasal septum in figure 1, since added to the structures already shown, the figure presented too complex a network of fibers to admit of following even the main nerve bundles in the reduced reproduction with any degree of certainty.

Two rather large branches of the trigeminal nerve enter this region; *a*, the rami mediales of the n. nasociliaris and *b*, the n. nasopalatinus. The former is from the first division of the trigeminal nerve and was traced from the Gasserian ganglion into the orbit, where it passes over the optic nerve and forward to enter the cranial cavity through the anterior ethmoidal foramen. Here it passes laterally about the base of the olfactory bulb and enters the nasal cavity through the anterior part of the cribriform plate. The larger rami mediales course along the anterior nasal wall to reach the septum about one third of the way down. Branches from these are distributed over the rostral and anterior part of the septum. The n. nasopalatinus was traced from the sphenopalatine ganglion, and at least a part of its fibers appear to have origin in the Gasserian ganglion, passing through the sphenopalatine ganglion. This nerve courses along the posterior part of the nasal septum as it leaves the sphenopalatine ganlion, toward the caudal end of the vomeronasal organ where it divides in two branches; one going to the palate, the other passing along the ventro-lateral border of the vomeronasal organ, giving off numerous branches which course upward and forward to reach the ventral and posterior or caudal portion of the nasal septum. Branches of this nerve are also distributed to the nasal septum caudal to the path of the vomeronasal nerve. Some of the smaller branches of the trigeminal nerve, especially those coming from the nasopalatine branch appear to join the plexus formed on the nasal septum by the nervus terminalis, others remain separate to their terminal twigs. This anastomosis of nerve filaments of Terminalis and Trigeminal origin renders it more

difficult to determine the ultimate distribution of each. However, in no case was a ganglion cell or groups of such found on a nerve trunk clearly composed entirely of trigeminal fibers. A part of the nerve fibers leading from a group of ganglion cells could always be traced to nervus terminalis branches and in most cases all of the nerve fibers associated with a group of ganglion cells could be traced to nervus terminalis origin.

It seemed to us desirable to determine even approximately the number and distribution of the ganglion cells associated with

TABLE 1

RABBIT	SERIES	SIDE	INTRACRANIAL PORTION	ALONG COURSE OF THE VOMERONASAL NERVE[1]	ON THE DISTRIBUTION OF THE NERVES ABOUT THE VOMERONASAL ORGAN[2]	NASAL SEPTUM ANTERIOR TO THE PATH OF VOMERONASAL NERVES	TOTALS
3 cm. embryo	A	R	163	181	409	120	873
	B	R	283	266	379	151	1079
Embryo about one week before birth	H	R	148	137	500	202	987
	Ha	R	158	127	455	174	914
1 day after birth	A	L	130	220	153	173	676
	B	R	120	205	132	166	624
6 days after birth	A	L	166	144	86	161	557
	A	R	93	139	117	119	468

[1] The vomeronasal cartilage was taken as the line of division between course and distribution of the vomeronasal nerve.

[2] The first four numbers of this column no doubt include sheath cells in the count.

the nervus terminalis. The results obtained are collated in the accompanying table. For the two older stages the number of ganglion cells as given appears to us to present the facts fairly accurately, in that it was possible to differentiate between ganglion cells and sheath cells with relative certainty. In the counts attention was paid largely to the nuclei, and only cells in which the nuclei were evident in a given section were counted for that section. For the two younger stages the count is, we believe, relatively high, since in the compact masses, especially in ganglia

found in the region of the vomeronasal organ, in which the cytomorphosis seems less complete, it was difficult to determine clearly between the nuclei of ganglion cells and the sheath cells.

A certain degree of uniformity will be noted in the figures presented for the two older stages. The figures given for the two younger stages for corresponding regions are throughout somewhat higher than for the two older stages. Especially is this noticeable in the column headed, "On the distribution of the nerves about the vomeronasal organ." In the two younger stages, as was noted, it was difficult in this region to differentiate clearly between sheath cells and ganglion cells, while in the other regions this differentiation was more readily made.

In the material at our disposal it is not possible to determine definitely and finally the character of the neurones composing the numerous small ganglia associated with the nervus terminalis. The evidence at hand is negative rather than positive. Throughout the several series the peripheral nerves are well stained. The cell bodies of the neurones are stained various shades of brown, the nuclei appearing as lighter or again as darker areas in the cytoplasm, often distinctly circumscribed. Many of the nerve cells present distinct evidence of a neurofibrillar network in the cytoplasm. The cell outline, however, is not always as distinctly and definitely brought to view as could be desired. The neurones of the sensory ganglia of the cranial nerves are throughout our series differentiated with distinct outline and sharply demarked processes. A want of distinct differentiation is on the whole also noted for the cranial autonomic ganglia. In the sphenopalatine ganglion of our series, the neurones are not distinctly outlined and their processes are not clearly brought to view. In figure 2, we have presented, for comparison, a group of detail figures comprising clusters of ganglion cells associated with a septal branch of the nervus terminalis, situated anterior to the path of the vomeronasal nerves, and small but characteristic areas taken from the Gasserian ganglia of the corresponding series. The nervus terminalis ganglia, one for each stage of our series, are arranged in vertical column to the left of the figure, placed chronologically, *A* to *D*, and designated by lower case '*a*'. The areas taken from

the Gasserian ganglion of each of the respective stages of our series are chronologically arranged in vertical column to the right of the figure, and designated by a lower case '*b*.' A glance at

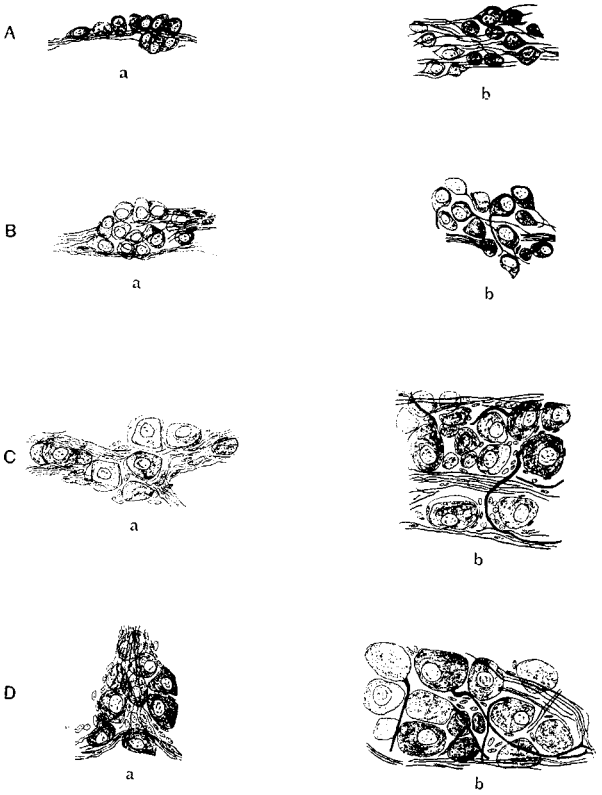

Fig. 2 Groups of ganglion cells of nervus terminalis and portions of the Gasserian ganglion from each of the stages of rabbit embryos and young rabbits used in this study. *A*, rabbit embryo, 3 cm. crown-breech length; *B*, rabbit embryo about one week before birth; *C*, young rabbit one day old; *D*, young rabbit six days old; *a*, ganglion cell groups taken from septal distribution of nervus terminalis, anterior to the path of the vomeronasal nerves; *b*, portions of the Gasserian ganglion. Pyridine-silver stain. × 200.

the figure will show the distinct difference in the form and grouping of the nerve cells shown in the figures comprising the two columns. In column *a*, there are no distinct processes to the

nerve cells and these are grouped around relatively fine nerve fibers. In column *b*, a progressive metamorphosis, characteristic for developing peripheral sensory or afferent neurones is noted. In *A*, *b*, from the Gasserian ganglion of a 3 cm. rabbit embryo the nerve cells are distinctly bipolar; in *B*, *b*, certain of the cells are unipolar with a short single process, presenting Y-shaped or T-shaped divisions; in *C* and *D*, *b*, neurones with long single processes dividing into central and peripheral branches as characteristic of afferent or sensory neurones, are evident. The series of figures *A* to *D*, *a*, present a structure which is very similar to that shown by the sphenopalatine and ciliary ganglia of the corresponding stages, as shown in our series. Even in the two older stages of our series, fixed by means of preliminary ammoniated acohol injection, the processes of the neurones of the autonomic cranial ganglia are not clearly brought to view. The statements here made relative to the ganglion cell groups found in connection with the septal portion of the nervus terminalis are equally pertinent when applied to the ganglion cell groups of its intracranial portion. In not one instance were we able to observe nerve cells, found in relation with the intracranial portion of the nervus terminalis of the rabbit, even in the 'ganglion terminale,' which presented clearly the characteristics of peripheral sensory or afferent neurones; and this in material in which the neurones of the sensory cranial ganglia were well characterized.

In figure 3, we present the very few instances in which neurones found in connection with the terminalis were distinctly stained, not the jet black of the ordinary chrom-silver preparations, as the figure would lead one to assume, but of a dark brown color with processes clearly brought to view. Cells *a*, *b*, and *c* of figure 3, are from the intracranial portion of the terminalis of a one-day-old rabbit. Cell *d*, of this figure is taken from a small group of ganglion cells found in connection with the septal portion of the terminalis of a rabbit, six days old. The nerve cells here shown present the morphologic characteristics of sympathetic neurones and are regarded as such. In *e*, of figure 3, is shown the

one instance observed of a structure resembling a pericellular ending of a white ramus or preganglionic fiber in a sympathetic ganglion. This was observed at one edge of a small group of ganglion cells in the immediate vicinity of the 'ganglion terminale' of a one-day-old rabbit. It is sketched at a much higher magnification than are the nerve cells of the same figure. The coil complex appears too small to enclose the cell body of a sympathetic neurone, judging from adjacent nerve cells. We may dismiss this structure with the statement that its appearance suggests a pericellular ending of a white ramus or preganglionic fiber characteristic for sympathetic ganglia.

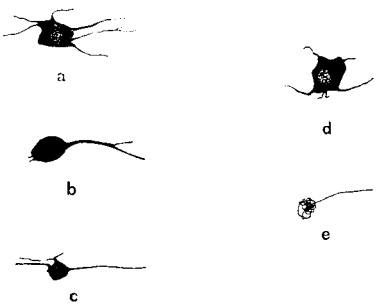

Fig. 3 Types of ganglion cells found in the course of the nervus terminalis, pyridine-silver staining; *a*, *b*, *c*, cells taken from the intracranial portion of a rabbit one day old; *d*, from septal portion of a rabbit six days old. × 200. *e*, a structure resembling a pericellular basket, the ending of a preganglionic nerve fiber, from the ganglion cell group of the intracranial portion of the nervus terminalis of a rabbit one day old. × 300.

As concerns the ultimate terminations of the nervus terminalis, our material is not wholly adequate to enable us to draw definite conclusions. We have been able to trace terminalis branches to certain blood vessels of the septal mucosa, but their ultimate endings have not been clearly determined. We are, therefore, not in a position to state whether such endings are to be regarded as of the type of free sensory endings distributed to the adventitial coat or motor endings distributed to the muscular coat. Terminalis branches in the older stages, especially in the six-day stage, have been traced to the ducts of septal glands, less clearly to

the gland alveoli. Here also the ultimate endings have not been clearly defined. Ultimate terminalis branches have not been traced with certainty to the epithelium of the olfactory mucosa, although fine terminal nerve branches which are independent of the special sense cells, such as are described by authors, have been observed in the olfactory epithelium, especially that of the vomeronasal organ. As previously noted, terminal nerve filaments which were traced to trigeminal branches commingle here and there with the end filaments of the terminalis and this renders it difficult to speak with certainty concerning the ultimate distribution of the nervus terminalis.

A brief review of the literature dealing with the nervus terminalis of mammalia, and considered in the light of our investigations, may here be permitted. We have previously noted the work of Johnston and McCotter. To the references made the following may be added: Johnston's observations were made largely on sections of mammalian embryos, not stained with differential nerve stains. The Golgi method was used on pig embryos and an impregnation of the peripheral fibers obtained and the distribution of the terminalis to the vomeronasal organ verified. Whether a differential staining of the terminalis fibers was obtained is not stated. A few bipolar cells connected with its fibers were stained by the Golgi method. Extracranial ganglion cells were apparently not observed In the human embryos studied, a distinct ganglion terminale was noted and it is stated, "that the nervus terminalis joins with numerous strands of the olfactory nerve to make up the network of nerve bundles in the septum nasale." In the rabbit, as noted, the main septal branches of the terminalis are situated in a deeper plane in the mucosa than are the olfactory strands, and except for branches following the vomeronasal nerves, cannot be regarded as accompanying the olfactory nerves. We have not observed bipolar ganglion cells in the ganglion terminale nor in the more peripherally placed ganglia, and in our preparations these ganglion cells do not resemble peripheral sensory cerebro-spinal cells. McCotter has observed the intracranial portion of the nervus terminalis in adult dogs and cats with a ganglion terminale, and has traced it to its connection with the forebrain and the vomeronasal nerve. The methods used do not seem to admit of differentiation of terminalis and vomeronasal fiber, after these have joined. The fact that ganglion cells were found attached to the vomeronasal nerve just dorsal to the vomeronasal organ leads him to conclude that filaments of the terminalis "extend into the nasal cavity along with several filaments of the vomeronasal nerves and apparently terminate within or very close to the vomeronasal organ." This our preparations demonstrate conclusively for the rabbit.

Two other observers have dealt with the nervus terminalis of mammalia, namely DeVries and Döllken. The observations of DeVries extend to human and Guinea pig embryos. His results require but brief consideration, since, as agreed by authors who have reviewed his work, DeVries regards the nervus terminalis and the vomeronasal nerve as equivalent to the nervus terminalis of fishes, and believes that a similar structure is to be found in the whole vertebrate series. He recognized the vomeronasal nerve and the ganglion terminale or the vomeronasal ganglion, with a root entering the rhinencephalon on the mesial side of the olfactory lobe caudal to the olfactory bulb. Döllken had at his disposal an abundant material, consisting of mouse, rabbit, Guinea pig, pig an human embryos. His investigation is concerned largely with the central connections of the nervus terminalis. So far as concerns his observations on the peripheral distribution of this nerve we are convinced that he is dealing not only with the nervus terminalis but has included also the vomeronasal nerve. This Johnston has recognized. Döllken uses as synonyms the words 'ganglion terminale,' 'ganglion nasale,' 'ganglion vomeronasale' and 'Nebenbulbus,' and his statements concerning the peripheral branches of the terminalis, in all of the forms studied, lead us to believe that he has not differentiated between vomeronasal nerve and terminalis, regarding the latter as a special nerve to the vomeronasal organ. His text figures, 4, 5, and 6, given to illustrate the peripheral distribution of the terminalis and its relation to the vomeronasal organ and the ganglion terminale, as observed in rabbit embryos, which we are able to compare directly to our own, made this very clear to us. A comparison of text figure 6, rabbit embryo of 28 mm. with our youngest stage, rabbit embryo 3 cm. in which the nervus terminalis is differentially stained and can thus be clearly separated from the vomeronasal nerves, makes this confusion very evident. This observer describes for mouse embryos, numerous cells which he regards as nerve cells, in connection with the peripheral distribution of the terminals. I older stages in the course of the nerve only relatively few ganglion cells were observed. He states that the appearances presented seem to indicate that these cells are only necessary to further the growth of the nerve. One may presume, he adds, that the ganglion cells are nutritive organs, subserving the growth of the fibers to the sense cells and the centrally placed nerve cells, the nerve cells after completion of their function undergoing regression, their fibrillae forming other relations in the course of the nerves. In the rabbit also, the ganglion cells found in the course of the nervus terminalis are said to show regression as development proceeds. Our observations on the rabbit, and especially such as pertain to older stages than those studied by Döllken, warrant the statement, that there is no material reduction in the number of ganglion cells found in connection with the terminalis as development proceeds. In a human embryo of 21 mm. crown-breech length and in an older stage, presumably 35 mm. crown-breech length, Döllken observed numerous cells in the ganglion termina'e which, after silver impregnation, showed great resemblance to

the cells of the intervertebral and head ganglia, and which were apparently further developed than were the cells of the Gasserian ganglion. As stated by Johnston, Döllken "has failed to recognize the clear distinction which exists between ganglion terminale and the cells lying along the olfactory nerve fibers ('olfactory ganglion') which later produce neurilemma cells," and with this we agree. In all of our preparations of rabbit material there is evident a distinct difference in the form and the relations of the ganglion cells of the nervus terminalis and of those of the Gasserian ganglion. Since Döllken has not differentiated between the fibers of the nervus terminalis and vomeronasal nerve fibers his statements concerning the ultimate distribution of the terminalis fibers must be interpreted with this fact in view. We have not in our preparations, with differentially stained terminalis fibers, been able to trace with certainty ending of these fibers into the epithelium of the vomeronasal organ, and are thus disposed to regard the fine nerve fibers found in the olfactory epithelium and not connected with the special sense cells as very probably, in part at least, of trigeminal origin. As concerns Döllken's observations on the central origin of the nervus terminalis we may state that we have not observed the four roots of entrance as described by him. His root 'c' corresponds closely with the main terminalis root as observed by us, in this we agree with Johnston. The small root entering more dorsally, as noted by us, may correspond with Döllken's root 'a'. The other roots we have not observed.

The literature dealing with the nervus terminalis of vertebrates other than mammalia requires but brief consideration, since it has been dealt with in several of the recent contributions and since in the majority of the studies stress is laid on the central connections rather than on the peripheral distribution, which was not always clearly followed. For reptilian embryos Johnston has described groups of ganglon cells found at intervals along the dorsal division of the olfactory nerve, which he attributes to nervus terminalis. An instance in which ganglion cells are found on the peripheral portion of this nerve. It is a question in our minds as to whether the olfactory ganglion, a part of the trigeminal complex as described by Rubaschkin for chick embryos, is to be considered as related to the terminalis. This olfactory ganglion is described as lying under the dorsal and caudal portion of the olfactory mucous membrane and contains in the main bipolar cells, with peripheral processes traced into fine filaments which end in the olfactory epithelium and central processes traced to the Gasserian ganglion. Further observations made in the light of more recent investigations, seem necessary before the relations of the 'olfactory ganglion' to the ganglion terminale can be determined.

Of the more recent contributions dealing with the nervus terminalis in amphibia and fishes, the following may be mentioned briefly. Herrick, in the frog, was unable to trace terminalis fibers further than "1 mm. beyond olfactory bulbs." Accordingly he does not assign a distribution although he assumes that it accompanies olfactory strands, since ganglion cells are found scattered along the course of some of the

latter. McKibben, in urodele amphibia, was able to follow the nervus terminalis only some 2 mm. distal to its superficial origin, and thus does not give its distribution. Sheldon, in the carp, states that terminalis fibers "are distributed to the epithelium with olfactory fibers." Brookover, for Amia and Brookover and Jackson, for Amieurus, give the peripheral distribution as associated with the olfactory strands. Sewertzoff reports that in Ceratodus forsteri, the distribution is to the anterior part of the nasal cavity and to the ordinary, not olfactory epithelium, and is decidedly of the opinion that it "does not serve an olfactory function." In this he is quite at variance with the conclusions of Brookover who regards the nervus terminalis as a component of the olfactory nerves. Brookover and Jackson reach the same conclusion regarding the nerve in Amieurus, basing their opinion on embryologic evidence. The majority of authors dealing with the nervus terminalis appear to have regarded it as an afferent nerve, homologous with the cutaneous sensory nerves of other regions. Brookover suggests that it may be of vasomotor function, and Brookover and Jackson express the same opinion, although in both articles it is admitted that there is no definite evidence. The evidence given by Brookover for connecting the nervus terminalis to the post optic sympathetic system by way of the intracranial sympathetic system, which he described, seems insufficient to us to establish this connection. We quote his summary of the evidence: "The nature of the Golgi impregnation on which I have had to depend to a large extent for tracing these intracranial fibers does not permit of demonstrating the connections between the nervus terminalis and the posterior portion of the sympathetic as clearly as would be the case with medullated fibers by the Weigert method, but the slightly diminished bundle of fibers of fig. 22 (intracranial sympathetic, our insertion) certainly continues rostral along the carotid artery beneath the olfactory nerve, while the fibers of the nervus terminalis just as certainly become more or less distinctly separated from the olfactory nerve, after it enters the cranial cavity, and run near the same artery." In certain of our series we find small bundles of nerve fibers, such as he describes accompanying the various intracranial blood vessels situated under the anterior part of the brain and olfactory bulbs, and passing in very close proximity to nervus terminalis strands without observing any anastomosis of nerve fiber bundles of the respective systems. We consider, therefore, that in order to establish a connection in this region it is necessary to show an actual fiber continuity, not a mere proximity.

After thus considering briefly the literature, we may proceed to our own conclusions.

CONCLUSIONS

Our observations on the nervus terminalis of the rabbit warrant, we believe, the following statements:

By reason of the differential staining of the nervus terminalis, in all of the stages of our series, we conclude that this nerve is not a component part of the olfactory and vomeronasal complex, but an independent nerve, with central connections by means of several small roots to the ventro-mesial and mesial portion of the forebrain, caudal and independent of the olfactory stalk, and courses in the form of a loose plexus along the ventro-mesial surface of the olfactory bulb, reaching the nasal septum on the mesial surface of the vomeronasal nerve, which nerve it follows to the mucosa of the vomeronasal organ, and is further distributed to the septal mucosa anterior to the path of the vomeronasal nerve, in which region especially it is joined by terminal branches of the trigeminus, mainly from the nasopalatine branches.

In the course of this nerve, even in connection with its more peripheral branches and beginning with its intracranial portion, there are found numerous smaller and larger groups of ganglion cells. One of these groups, of relatively larger size than the other, is situated on its intracranial portion in the region where the terminalis approaches the vomeronasal nerve. This larger group is regarded by us as the ganglion terminale of authors.

The groups of ganglion cells found in the course of the nervus terminalis of the rabbit present the appearance of small sympathetic ganglia, similar in general structure and appearances to cranial autonomic or sympathetic ganglia found in our series, and differing in form and arrangement of neurones from those of the intervertebral and cranial afferent sensory ganglia of the respective series. The nerve fibers of the terminalis have more the appearance of sympathetic and preganglionic fibers than of neuraxes or dendrites of sensory neurones.

Distribution of ultimate terminalis branches to blood vessels and glands of the septal mucosa seems probable, though this we cannot assert positively since the commingling of trigeminus and terminalis terminal filaments has been observed.

For the present we reserve definite statement as to the probable function of the nervus terminalis of the rabbit, realizing fully that further work with the introduction of other methods is necessary. If we consider only the peripheral distribution of the nerve, the size of its component fibers, its arrangement in loose plexus, character, number and disposition of associated ganglion cell groups, we should favor ascribing to it an autonomic function. Its central connection, however, both in character and place of origin, does not wholly conform with our conception of deep and superficial origin of the preganglionic nerve fibers of a sympathetic path.

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