THE NERVE SUPPLY TO THE PITUITARY BODY

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THREE FIGURES

It is but natural that neglect of an organ itself should yield a proportional lack of interest in its more detailed structure and even more so, in its less important adjuncts—the blood and nerve supply. Such has been true of the pituitary body.

The recent tremendous stimulus produced by Paulesco's (1) sudden transformation of the hypophysis from a structure of vestigial curiosity to a vitally essential organ, has borne its fruit in the rapid accumulation of co-working histological, (2) experimental (3) (4) (5) (6) and clinical (7) (8) observations. Though still very meager our information is now sufficient to have established a hypophyseal clinical entity, amenable in many cases to medical and surgical treatment.

Forming as it does a link in the chain of internal secreting glands, the hypophysis, essentially of hormone action, must be regulated as other glands in this system, by an autonomic nervous mechanism.

Recent studies from the Hunterian Laboratory (5) by Goetsch, Cushing and Jacobson gave evidences of hypophyseal influence over carbohydrate metabolism. It has been shown that sugar tolerance is dependent upon the functional activity of the posterior lobe of the pituitary body. It was later shown by Dandy and Fitz Simmons (observations unpublished) that a piqûre of the hypophyseal region in rabbits produced a heavy glycosuria, therefore giving results similar to a piqûre of the so-called Bernard's sugar center in the floor of the fourth ventricle. These results have been amplified by Weed, Cushing and Jacobson (6).

The combination of glandular or hormone activity and the results of mechanical stimuli (presumably of nervous origin) has suggested the possibility of a neuro-hypophyseal sugar center.

The rational interpretation of this and other physiological data has been handicapped by the uncertainty and meager evidence of the regulatory autonomic nervous mechanism. Accordingly at the suggestion of Dr. Cushing under whose direction the experimental hypophyseal investigations have been conducted, the determination of the source and distribution of the nerve supply was undertaken.

Lying as does the hypophysis in such close proximity to the carotid arteries with their abundant superimposed plexus of sympathetic nerve fibers, it is but natural to assume that this is the source of the hypophyseal nerve supply. Indeed evidence of this is found in the infrequent passing reference to a nerve filament which could be traced from this plexus to the hypophysis.

EARLY REFERENCE TO THE NERVE SUPPLY

Probably the earliest reference to a hypophyseal nerve supply is the casual mention by Bourgery ('45) that he observed sympathetic nerve fibers passing to the pituitary body. Further substantiation is subsequently given in similar casual mention by Fontona, Cloquet, Bock, Ribbes, (9) and possibly others.

In his Anatomie des Menschen ('79) Henle (9) devotes a paragraph to the hypophyseal nerve supply and supplements this description by a drawing of the carotid sympathetic system, which includes a cluster of two or three twigs running from each plexus to the pituitary body. This is the most extensive description of the hypophyseal nerve supply extant. He casts doubt upon the previous discovery of nerve fibers to this gland and concludes that on account of the inherent difficulties they have mistaken fibrous filaments of connective tissue for nerve filaments, saying, "Ohne Zweifel beruhen diese und manche ältere Angaben auf Verwechselung fibröser Bälkchen mit Nervenfasern, doch zeigte mir das Mikroskop in dem Netzförmigen zwischen Carotis und Hypophyse ausgespannten Gewebe feine Nerven-

faserbündelchen dieselben, von denen Luschka sagt, dass sie zwei bis drei jederseits, in den vorderen Lappen der Hypophyse sich einsenken." It is based upon this paragraph and drawing by Henle that an occasional brief mention of hypophyseal nerve supply is found in the more detailed and comprehensive anatomies, the majority, however, passing over the matter in silence.

The internal distribution of the hypophyseal nerves was studied by Berkley ('94) (10) in a series of Golgi stained sections. He observed numerous varicose nerve filaments in the interior of the gland, the lobus anterior and pars intermedia in particular, but some also in the posterior lobe. The external connections of the nerves were not studied. On account of his inability to observe nerve cells in the gland, he presumed they were of extraneous origin and thought they probably come from the sympathetic system.

MATERIAL AND METHODS

The purpose of this paper is to consider only the relatively grosser aspects, i.e., the origin, course and distribution of the hypophyseal nerve supply. The histological distribution and relation of the ultimate filaments to the gland cells have not been considered. It is analogous in character to a recent publication (11) dealing with the blood supply of this organ.

The difficulties of deductions and the impossibility of an accurate conception of the nerve supply based upon gross human dissection have been shown (Henle) (9) by the supposedly erroneous observations of early investigators in mistaking connective tissue trabeculae for the very delicate nerve filaments, which are almost beyond the range of naked vision. These observations are based upon the canine and feline gland, the animals used in the experimental investigations in the Hunterian Laboratory. The anatomical environment of the pituitary body in these forms is such that the difficulties of a tightly enclosed, deeply imbedded and adherent gland encountered in man and the ape are obviated. The hypophysis dangles from the brain and is readily removed with the brain after liberation of its single point of dural

attachment posteriorly, so that the entering nerves may be studied in their true relations, without tearing or distortion.

We have used almost exclusively the specific methylene blue intra vitam method of staining the nerves. For the details of this technique we are greatly indebted to the excellent contribution by J. Gordon Wilson (12). Three essentials are necessary for the successful use of this stain: the exsanguination of the tissues must be thorough in order to get a sharply defined picture of the nerves, since the combination of the methylene blue with blood presents a diffuse, indistinct picture with poorly stained nerves; the nerves must be superficial or covered only by a thin layer of tissue; the air must come in contact with the nerves, otherwise no differentiation takes place.

During the final stages of bleeding the anaesthetized animal from the femoral arteries, a $\frac{1}{20}$ per cent isotonic solution of methylene blue "nach Ehrlich" at body temperature was injected into both carotid arteries and continued until the injecting fluid emanated perfectly clear from the femorals. A tourniquet was then applied around the neck below the point of injection under a pressure sufficiently low to insure filling of the cephalic vessels without danger of diffusion or rupture.

On account of the capricious character of this stain, litters of very young puppies or kittens were injected at the same sitting, so that the defects of some might be supplemented by better staining of others. The total nerve supply then is a summation of results, a reconstruction as it were.

After a few minutes to allow penetration of the stain, the skull was opened and a block of tissue, including the hypophysis with its vessels and nerves in their normal relations, was removed from the base of the brain. The hypophysis was gently retracted so as to allow full exposure of one side to the air. The nerves then assume their differential blue. These specimens were immediately studied under the binocular microscope. The study of fixed specimens with post mortem staining was far less satisfactory, because of the collapse of blood vessels, with which the nerves are intimately associated, the more stiffened picture, and the deficient maintenance of the blue in the nerve fibers.

NERVES TO THE ANTERIOR LOBE

The key to the nerve supply of the pituitary body is the arterial supply to this organ. In a recent publication from this laboratory, it was shown (11) that the anterior lobe received an extensive blood supply from a large number of minute vessels, most of which, even when injected, were beyond the range of naked vision. These vessels radiate from the Willisian circle to the hypophyseal stalk like spokes to the hub of a wheel. The majority of these branches are from the anterior and posterior communicating arteries. The network of sympathetic nerves comprising the carotid plexus is continuous along the three main branches which result from its trifurcation. The distribution, however, is very uneven. A few fibers continue along the anterior and middle cerebral arteries for a short distance but the great majority are found on the two communicating arteries which supply the hypophysis; the posterior communicating artery is particulary well supplied. From these extensions of the carotid plexus numerous filaments are given off and pass along the blood vessels to the stalk of the hypophysis, from which they delve into the substance of the anterior lobe and are lost to view. Some arterial branches have as many as three or even four small filaments, the majority, however, only one or two. The course of the fibers is fairly direct and very few branches are given off. These filaments frequently entwine the vessels but no minute plexuses or anastomoses are visible after leaving the plexus on the main trunks. No nerves have been observed on the external surface of the anterior lobe. All nerves going to the hypophysis are in contact with the sheaths of minute blood vessels. On reaching the stalk it is of course impossible to trace this relation further. Their distribution in the gland has not been observed.

NERVES OF THE PARS INTERMEDIA

Only by dissection of the hypophysis can the nerve supply of the pars intermedia be traced. By gently separating and retracting the posterior lobe from the clasping mitten-like anterior lobe, it is often possible to trace a single nerve fiber with its branches passing down the stalk and spreading out over the pars intermedia which envelops the posterior lobe (fig. 3).

NERVES OF THE POSTERIOR LOBE

It has been shown that the posterior lobe is supplied by a median artery which is formed by the confluence of two branches, one from each carotid artery immediately after its entrance into the cavernous sinus. In the canine this vessel enters the posterior lobe at the only point of dural attachment. Vital nerve staining is somewhat more difficult in this region on account of the relatively thicker dural covering which excludes the action of the air and necessitates a delicate dissection of this vessel. For a long time we were unable to find any trace of a nerve entering the posterior lobe. Several branches were always visible at the origin of the vessels from the carotid but the fibers were lost in the dura before the posterior lobe was reached.

However, it was finally possible to demonstrate nerve fibers actually entering the posterior lobe along the artery. Certainly the disparity between the nerve supply to the posterior and anterior lobes is most striking—in the anterior lobe almost superabundant, in the posterior lobe very few. This contrast may in some measure be due to the difficulties mentioned above; we are however disinclined to lay much emphasis on them.

A most striking color contrast is demonstrated upon removing the hypophysis after vital staining. The anterior lobe is a yellowish white, the posterior a deep indigo blue, possibly due to the (autogenic?) nervous character of the posterior lobe. The blue is of a homogeneous character, no nerve fibers being differentiable under the higher magnifications of the binocular microscope. The intensity of the blue is even much more marked than that of the adjacent, deeply staining oculomotor nerve.

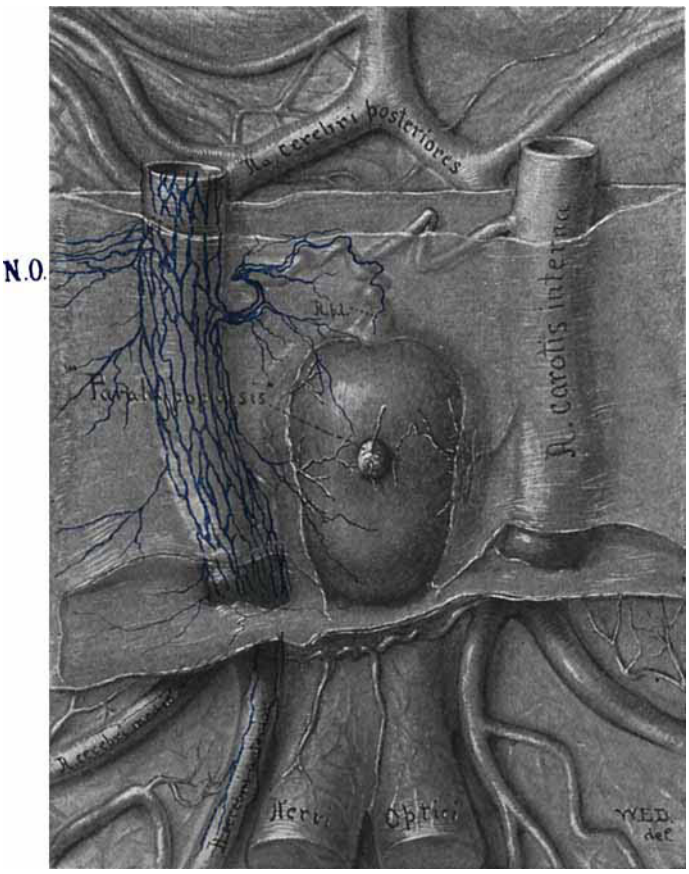

Fig. 1 Semi-diagrammatic representation of one side of the cavernous sympathetic system of a canine, showing the nerves passing to the posterior lobe along its artery. Other branches to the dura and a cluster (No) to the N. oculomotorius. The hypophyseal region is viewed from below with dura intact.

NERVES OF THE PARAHYPOPHYSIS

This little 'nubbin' resting in a small depression in the floor of the sella, usually enclosed in dura, is present in over 80 per cent of canines, and is evidently a remnant of the embryonic Rathke's pouch. In some adults it may be traced to the pars

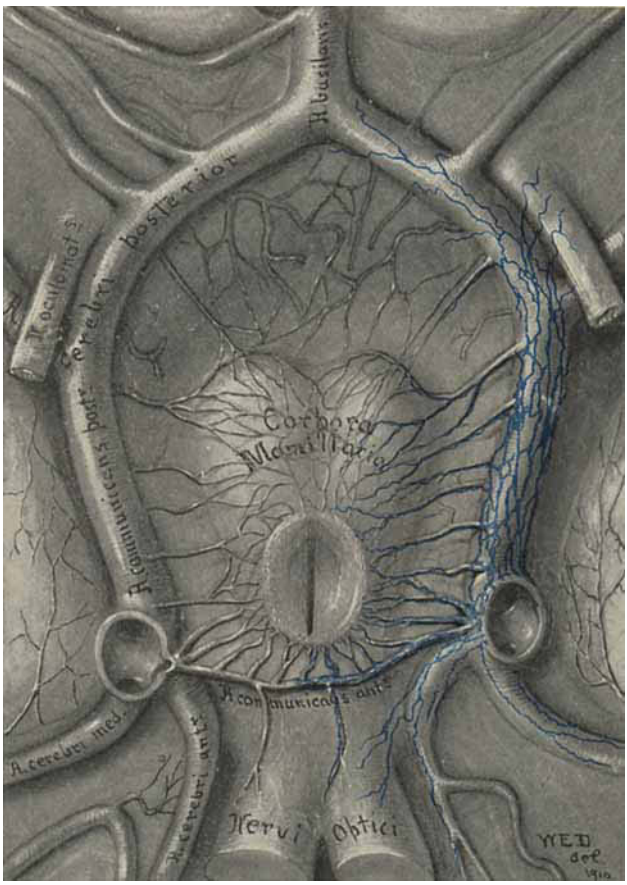

Fig. 2 Semi-diagrammatic reconstruction of sympathetic nerves passing along the arterioles to the stalk of the hypophysis to supply the anterior lobe and pars intermedia. Note relative dwindling of nerves away from the hypophyseal region. The view is from below with dura, hypophysis and carotid artery removed.

intermedia; it varies greatly in size and histological character. It has an individual blood supply, a small artery given off by each posterior lobe artery. Frequently it has been possible to trace a nerve some distance along this vessel toward this "body" but never have we been able to observe a definite nerve connection.

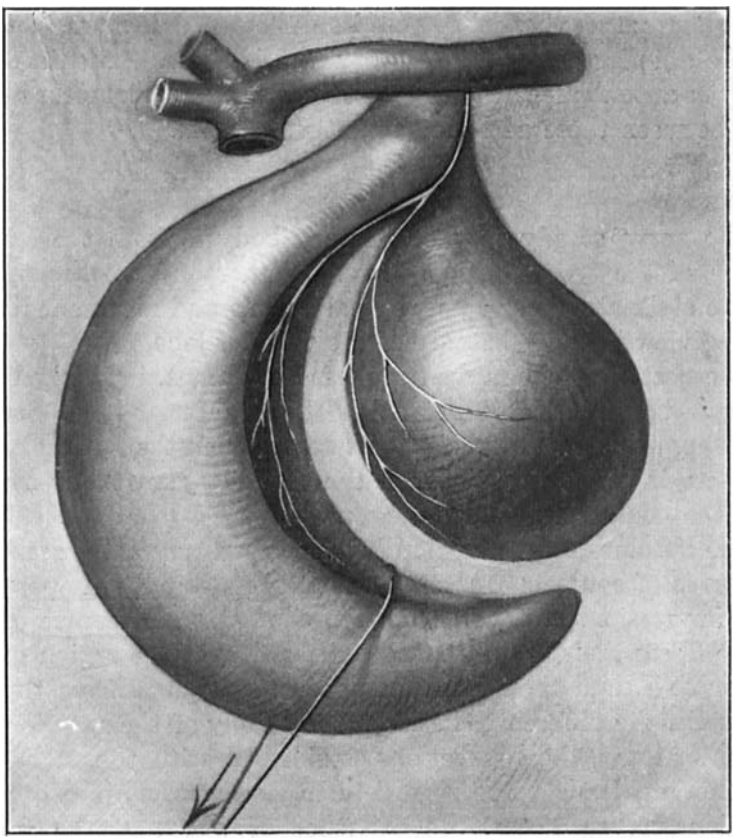

Fig. 3 Drawing to show the nerve passing from the plexus surrounding the posterior communicating artery, down the stalk of the hypophysis to the anterior lobe and the pars intermedia which covers the posterior lobe. The anterior lobe has been dissected from the posterior lobe and gently retracted to permit this view.

OTHER BRANCHES OF THE CAROTID PLEXUS

During observations on the hypophyseal nerve supply naturally the distribution of the sympathetic filaments were noted in the immediate vicinity. The dura of the sella region is exceptionally well supplied with filaments from the carotid plexus. Several branches run from the carotid plexus direct to the oculomotor nerve. A couple of twigs were also observed entering the

optic nerve; these branches were from the nerves in the adventitia of the anterior cerebral artery. There is thus afforded a direct nervous autonomic path between the optic and oculomotor nerves and between these and the sympathetic trunk.

SUMMARY

The nerve supply to the pituitary body is from the carotid plexus of the sympathetic system. Numerous branches radiate to the stalk along the hypophyseal vessels and are immediately lost to view in the substance of the anterior lobe.

The posterior lobe nerve supply is very scant, in marked contrast to the extensive innervation of the anterior lobe.

The pars intermedia receives its nerves from the stalk.

There is connection between the carotid sympathetic system and the oculomotor and optic nerves.

The absolute differentiation between secretory and vasomotor nerves is of course a matter of much dispute and is impossible. The impression, however, from the character and course of the nerve fibers their greatly increased number in the region of the hypophysis, and their disappearance at a distance from the hypophysis, the differences between the supply of the anterior and posterior lobes, the connections established with the other cranial nerves, leads us to regard them as secretory, in contradistinction to vasomotor, the existence of which in the cranial chamber has not been observed.

It is a pleasure to express my gratitude to Dr. Harvey Cushing for his suggestions during the progress of this problem.

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