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THE NUCLEUS ISTHMI OF THE FROG

O. LARSELL

Anatomical Laboratory of the University of Oregon Medical School, Portland, Oregon

NINE FIGURES

INTRODUCTION

The nucleus or ganglion isthmi is a subject of much confusion in the literature of comparative neurology. It has been described in all groups of vertebrates except cyclostomes and mammals. According to Kappers ('21, p. 789) it first appears in the Plagiostomi. There is formed in this group a new differentiation in the dorsal part of the isthmus, lateral to the anterior medullary velum, which Kappers regards as the nucleus isthmi. Franz ('12) describes it in bony fishes, and it has long been recognized in the anuran amphibia. Joustra ('18) has studied its connections in the chameleon, in which form it is very large, and in the crocodile. He concludes that in these reptiles the nucleus isthmi is homologous with the medial geniculate body of mammals. Edinger ('11) describes a nucleus of this name in various vertebrate groups, but does not always apply the term to structures having the same connections, as Johnston ('05) has pointed out. According to Kappers ('21, p. 867) the nucleus is present in birds. Regarding its presence in the mammalian brain the statement of Kappers (p. 894) is pertinent when he remarks "doch musste es jeden vergleichenden Neurologen auffallen, dass ein so konstanter Kern wie das Ganglion isthmi, welches namentlich bei den Reptilien bereits eine so mächtige Entwicklung erreicht, bei den Säugern fehlen sollte."

Johnston ('05) considers the nucleus isthmi to correspond with his secondary visceral nucleus of fishes (Rindenknoten of Mayser, '82). In another place Johnston ('06) states that the nucleus isthmi of birds and of amphibia, as Edinger applied the name, have quite different connections, and thus clearly differentiated between the midbrain structure to which the term has most commonly been applied, and the subcerebellar nucleus with which the visceral tracts of the medulla oblongata are connected. Johnston used the name nucleus isthmi, however, as equivalent to his secondary visceral nucleus. The cell mass described by Franz ('12), already noted, in teleosts and designated by him the nucleus isthmi, is very different from the secondary visceral nucleus, and corresponds in its connections with the nucleus isthmi of higher forms.

In the fishes the large size of the secondary gustatory nucleus, together with the great reduction of the nucleus isthmi in many representatives of this group, as compared with its size in anurans and many reptiles particularly, probably has caused much of the difficulty in establishing the homology of the latter nucleus. The apparent absence, or at least, great reduction, of the secondary visceral nucleus in higher forms, has accentuated the confusion.

The recent monograph of Kappers ('21) has brought the whole subject in review in the various classes of vertebrates. Kappers describes both nucleus isthmi and secondary visceral (gustatory) nucleus in fishes. He believes that the nucleus isthmi of amphibia, as described by Gaupp in the frog, corresponds with that of reptiles and birds, and with the nucleus in the bony fishes to which Franz applied the same name. He holds that in all forms where present it is homologous with the medial geniculate body of mammals.

If we examine the literature on the amphibian brain, we find the secondary visceral nucleus recognized in Urodela (Herrick, '14 and '17) and the nucleus isthmi in the Anura. The large nucleus in the frog's brain which Gaupp ('99) describes as the ganglion isthmi, and which, as he notes, corresponds to the nucleus magnus of Stieda and of Reissner, and to the corpus posterior of Bellonci, is a very different structure from the secondary visceral nucleus of urodele amphibians. However, as Kappers states, its connections in the frog are not sufficiently described. On the other hand, the only suggestion, so far as I am aware, to be found in the literature on the frog's brain, of a secondary visceral nucleus is the following quotation from Kappers ('21, vol. 2, p. 296) "Als aufsteigende sekundäre, sensible Bahn sind bei den geschwanzten Amphibien Fasern zu bezeichnen welche aus den Zellen hervorgehen, die den Fasciculus solitarius in der Oblongata begleiten (Herrick).

"Diese Fasern, die ich beim Ochsenfrosche nicht fand, steigen an derselben Seite auf und enden—wie bei den Fischen—in dem Gebiete des Isthmus in einem Kern, welcher dem Rindenknoten der Teleostier (dem vordern sekundären Geschmackskern) homolog sein muss (umsomehr, weil er auch tertiäre Neuronen in den Hypothalamus sendet)."

The present writer ('23) has recently described the secondary visceral nucleus in the frog, together with its connections. The nucleus abuts against the caudo-lateral and ventral part of the nucleus isthmi, as shown in figure 1, but the fiber tract connections are very different from those to be described below for the latter nucleus. Furthermore, our Golgi preparations do not show any fiber connections between the secondary visceral nucleus and the nucleus isthmi. We must therefore regard them as two distinct and unrelated nuclei, which topographically are closely crowded together.

The large size of the nucleus isthmi in the frog, and the relatively simple structure of the amphibian brain, make the frog's brain favorable material for a detailed study of this nucleus and its connections, the results of which are here presented.

MATERIAL AND METHODS

The study has been based on larval material of Hyla regilla, from 23 mm. to 42 mm. in length, and on adult brains of Rana pipiens and Acris gryllus, comprising some sixty series in all. These were stained by the methods of Ramón y Cajal, Weigert, vom Rath, and Golgi. One series from an adult frog which had been subjected to enucleation of the right eye, thus producing degeneration of the optic nerve, was prepared by the Marchi method.

A number of the Golgi and Weigert series had been prepared by Dr. Paul S. McKibben, and were kindly placed at my disposal by Dr. C. Judson Herrick. I wish to express my sincere thanks to Doctor McKibben and Doctor Herrick for the privilege of using this valuable material.

DESCRIPTIVE

In the species of larval frog studied the nucleus isthmi may first be seen at stages of 28 mm. to 30 mm. in length, as a structure which may be differentiated from the surrounding portions of the midbrain and isthmus. Its appearance is nearly coincident with the emergence externally of the hind leg buds, although in some of my series the nucleus isthmi is differentiated when no external limb buds are visible. In other series in which the limb buds were visible, the nucleus isthmi is present, but only poorly marked. In stages beyond 33 mm. limb buds and nucleus isthmi are both invariably well developed.

In the adult frog the nucleus forms a pyriform body, the smaller end of which is directed medially and somewhat dorsally. The larger end is rounded and extends caudally and laterally. In transverse section the nucleus appears roughly comma-shaped, as it does also at the more dorsal levels in horizontal series. The caudal portion of the nucleus crowds the subcerebellar region. It is however in no sense a part of this region, but belongs to the midbrain, as its connections and development demonstrate.

ABBREVIATIONS

ac. S., aqueductus Sylvii
br. conj., brachium conjunctivum
cb., cerebellum
ceph., cephalad
com. cb., commissura cerebelli
c. q. p., corpus quadrigeminum posterior
dec. v., decussatio veli
dors., dorsal
lat., laterad
lem. lat., lemniscus lateralis
lem. sp., lemniscus spinalis
med. obl., medulla oblongata
mes., mesencephalon
n. IV., nervus trochlearis
nu. isth., nucleus isthmi
nu. vis. sec., nucleus visceralis secundus
Pur. c., Purkinje cells
str. gr., stratum granulare
str. mol., stratum moleculare
tr. com. tr., tractus commissura transversa
tr. isth. t., tractus isthmio-tectalis
tr. isth. th., tractus isthmio-thalamicus
tr. q. isth., tractus quadrigemino-isthmi
tr. sp. cb., tractus spino-cerebellaris
tr. sp. t., tractus spino-tectalis
tr. t. isth., tractus tecto-isthmi
tr. v. cb., tractus vestibulo-cerebellaris
v. m. a., velum medullare anterior
vent., ventral
vent. IV., ventriculus quartus
vent. lat., ventriculus lateralis

The nucleus is made up of a cortical mass of closely packed cells, two or three deep, and a medulla which contains scattered nerve cells and numerous fibers. It is within the medulla that the entering fibers terminate.

Externally to the closely packed cortical cells and surrounding the nucleus except at its ventro-lateral extremity and the dorso-medial tip, is a well defined zone in which cells are entirely lacking. It is made up of fine fibers radiating from the cortical cells of the

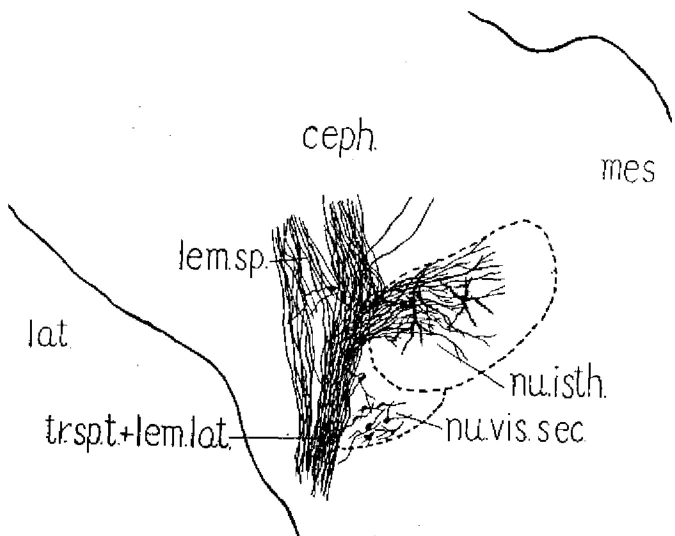


Fig. 1 Section through the nucleus isthmi and the secondary visceral nucleus of Rana pipiens. Horizontal Golgi series. Edinger-Leitz projection apparatus. × 36.

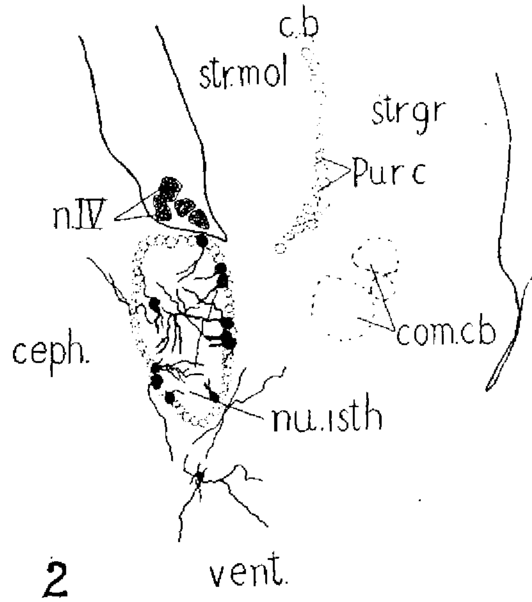
nucleus. This zone sharply marks off the nucleus isthmi from the surrounding portions of the midbrain, making it one of the most conspicuous features of the frog's brain, as seen in sections. At the ventro-lateral extremity numerous large nerve fibers enter the nucleus, and the medulla at this point is continuous with the structures outside the nucleus. This constitutes the so-called hilum (fig. 1) of the nucleus. Dorso-medially, at the tip of the nucleus, nerve fibers also penetrate to the medulla, but the zone of continuity of the medulla with the outside is much narrower at this point than at the hilum.

As seen in Golgi series the dendritic processes of the cortical cells extend into the medulla, while the axones continue outward to form several tracts which will be considered below. The greater number of the axonic processes of the cells in the cortical region pass directly outward and then curve around the superficial surface of the nucleus, to be collected laterally as the tract of the commissura transversa (figs. 2 and 3). The deeper lying cells of the medullary region send their axones in part to the decussatio veli (figs. 4 and 5), and in part to the thalamic region of the diencephalon (fig. 6). The dendrites of the medullary cells are rather large (figs. 4 and 5), but do not extend beyond the limits of the nucleus. They are studded with gemmules. They are directed for the most part caudo-laterally, and appear to come into close relationship with the terminal fibers and collaterals of the lateral lemniscus which enter the nucleus at the hilum. As will be noted from figures 4 and 5, it is these medullary cells which give off axones to the decussatio veli. Whether or not it is similar cells which in the adult send axonic processes into the tractus isthmio-thalamicus could not be determined in the material available. Figure 6, from a larval frog of 40 mm., shows cells in the medulla of the nucleus isthmi, which differ from those just described, only in the absence of gemmules, and in the fact that the axones clearly take part in forming the isthmio-thalamic tract. It is possible that these cells undergo further differentiation before the frog reaches maturity.

FIBER TRACT CONNECTIONS

Lemniscus lateralis

The most prominent afferent tract leading to the nucleus isthmi is composed of fibers from the lateral lemiscus. Joustra ('18) has found a similar prominence of this tract in its relation to the nucleus isthmi in the crocodile and the chameleon, and it is described by Kappers ('21) in fishes. The tract in the frog accompanies the spino-tectal bundle through the portion of the medulla oblongata which lies cephalad to the VIII nerve. The two tracts are closely associated (fig. 1) and their fibers are intermingled. At the level of the hilum of the nucleus isthmi,



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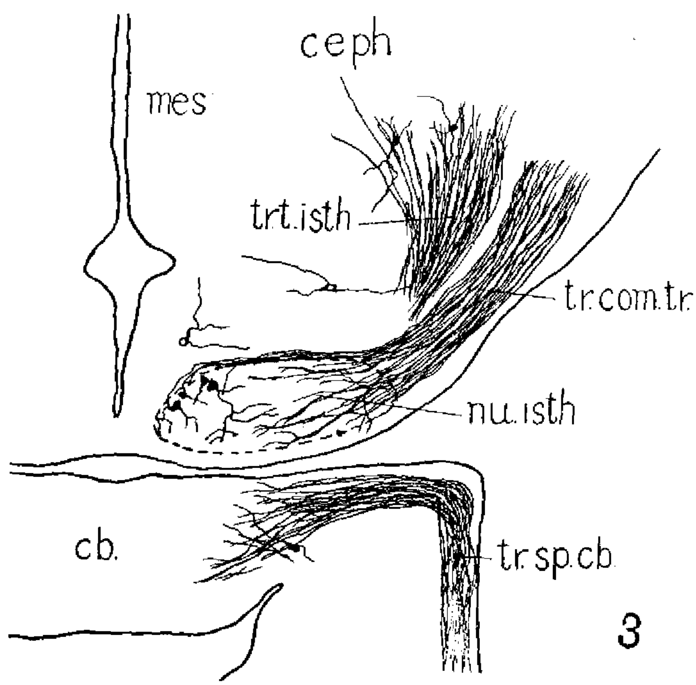

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Fig. 2 Section through the medial part of the nucleus isthmi and a portion of the cerebellum. Some of the cortical cells of the nucleus are shown well impregnated by the stain. Rana pipiens, sagittal series, Golgi method. cam. luc. × 75.

Fig. 3 Horizontal section through nucleus isthmi and neighboring structures, showing cortical cells which give rise to some of the fibers of the tractus commissura transversa, and also showing a portion of the tecto-isthmial tract. Hyla regilla, 32 mm. tadpole. Golgi method. cam. luc. × 64.

collaterals are given off from the fibers of the combined tracts. These collaterals enter the nucleus (fig. 1) and terminate in relation to the dendrites of its cells, as already indicated. It is not impossible that some of these entering fibers are from the spino-tectal tract, but study of Golgi sections of larval stages and of the adult, favors the interpretation that all collaterals and fibers are from the lemniscus lateralis, and therefore are related to the nuclei of the VIII nerve.

Kappers believes that ascending fibers from the spinal V tract possibly also enter the nucleus isthmi, but I have no evidence that such is the case in the frog.

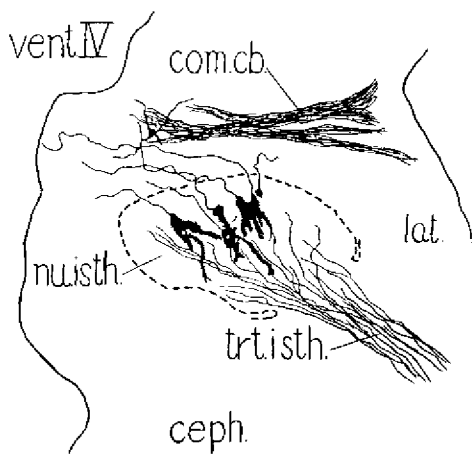

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Fig. 4 Horizontal section through more dorsal portion of nucleus isthmi, showing medullary cells which send axones into the decussatio veli, and also showing the entering tecto-isthmial tract. Acris gryllus. Golgi method. cam. luc. × 60.

Tractus tecto-isthmi

This tract is most easily followed in larval stages stained by the Golgi method. The cells from which its fibers arise are located in the deeper layers of the tectum opticum. The fibers, which are of small size, converge, as shown in figure 3, to form a tract which enters the nucleus isthmi at the dorsal part of the hilum (figs. 4, 6, and 7). They then break up within the nucleus into terminal branches (fig. 8). Gaupp ('99) describes a similar tract.

Quadrigemino-isthmial tract

Cells of the posterior quadrigeminal body give off axones (fig. 9) which pass into the nucleus isthmi, and at least in part, appear to terminate therein. It is possible that some continue through the nucleus to take part in the tract which is designated tractus isthmio-thalamicus in figure 6. Joustra ('18) describes a fiber connection of the nucleus isthmi with the posterior quadrigeminal body in the crocodile and chameleon, but leaves one in doubt

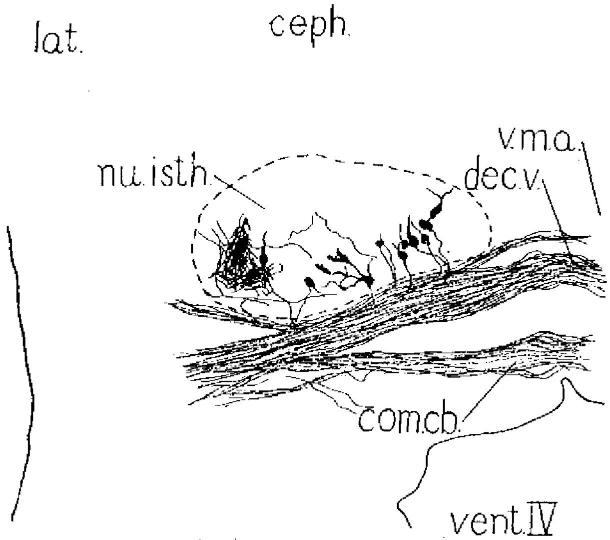

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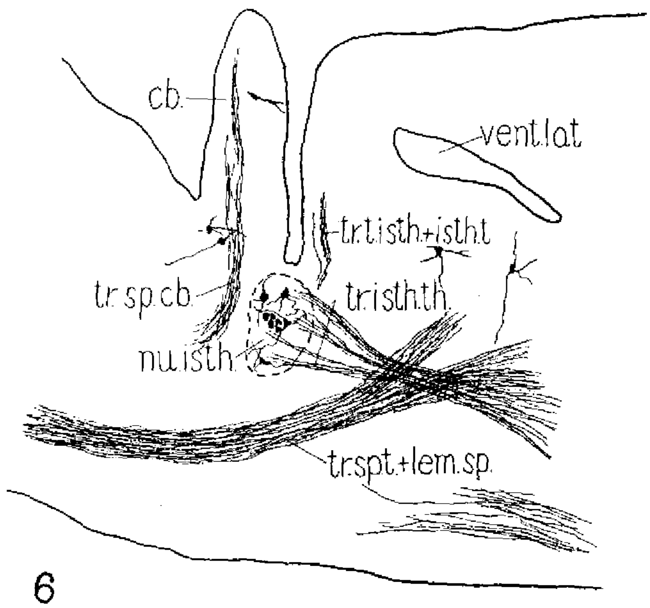
Fig. 5 Horizontal section through nucleus isthmi, showing medullary cells whose axones pass into the decussatio veli. Acris gryllus. Golgi method. cam. luc. × 75.

as to its origin. On another page he describes fibers which pass from the ganglion isthmi, in part to the tectum opticum and in part, to the corpus quadrigeminum posterius. I have not found fibers corresponding to the latter in the frog.

In addition to the foregoing afferent connections, Gaupp states that optic fibers also terminate in the nucleus isthmi. This is denied by Bellonci ('88) and Kappers ('21) makes the statement that he has never seen them. Our transverse Weigert series give



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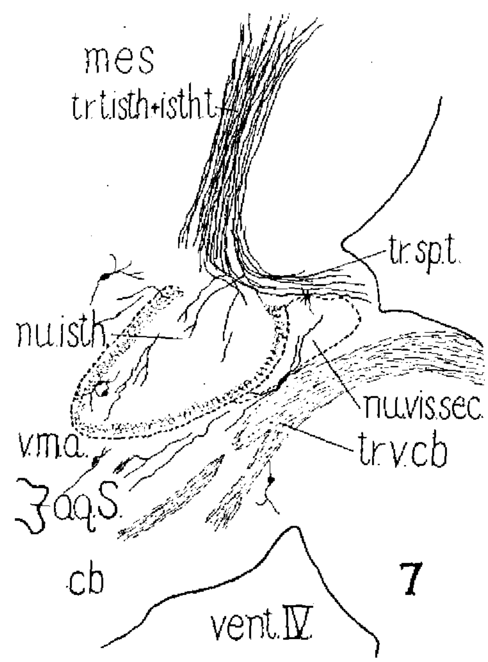

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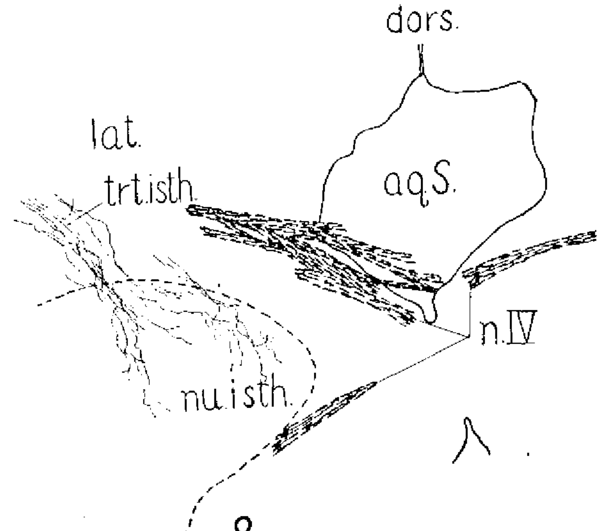
Fig. 6 Sagittal section through cerebellum, isthmus and caudal midbrain region of larval frog of 40 mm. Hyla regilla. Golgi method. cam. luc. × 51.

Fig. 7 Horizontal section through caudal midbrain region, isthmus, and right side of cerebellum of adult frog. Rana pipiens. Golgi method. cam. luc. × 30.



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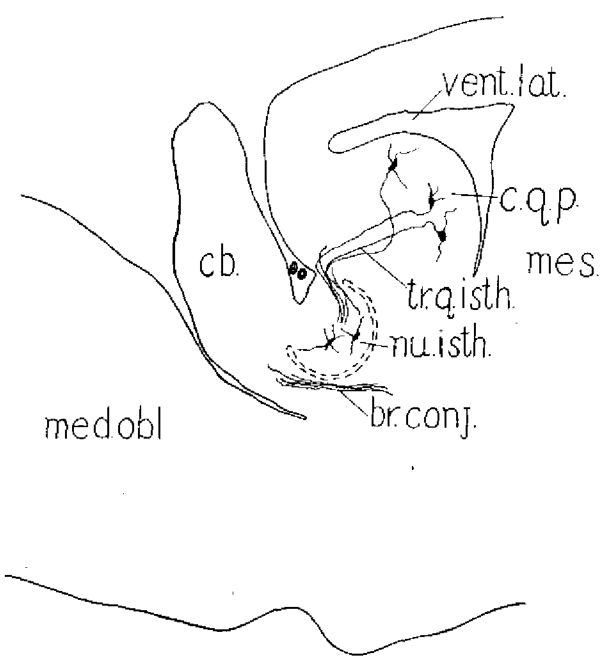

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Fig. 8 From a transverse section through the isthmial region of adult frog, showing the medial tip of the nucleus isthmi, with the terminal fibers of the tecto-isthmial tract. Rana pipiens. Golgi method. cam. luc. × 88.

Fig. 9 Sagittal section through caudal region of midbrain, the isthmus, cerebellum, and cephalad portion of medulla oblongata of larval frog of 40 mm. Hyla regilla. Golgi method. cam. luc. × 51.

the appearance of optic fibers, or at least collaterals from the optic tract, passing into the nucleus, but our Golgi preparations give no indication of such connections. A Marchi series of an adult frog's brain, prepared with the purpose of determining this point, is also negative, both as to collaterals and direct fibers (unless the collaterals are unmyelinated). I find myself therefore in agreement with Bellonci and Kappers that an optico-isthmial connection is absent in the frog.

Tractus isthmio-tectalis

In addition to the fibers which arise from the tectum and pass into the nucleus isthmi as the tecto-isthmial tract, this nucleus gives rise to fibers which pass directly to the tectum (figs. 6 and 7) as our Golgi preparations, especially those of larval stages, indicate. The cells which give rise to these fibers are located in the dorsal part of the nucleus. The fibers terminate in the deeper part of the tectal cortex.

Decussatio veli

Many cells in the caudal part of the nucleus isthmi send their axones into the decussatio veli (figs. 4 and 5). This is especially well shown in Acris gryllus. Some of the fibers pass laterally, without decussation (fig. 5), but the majority pass toward the median line to cross to the opposite side (fig. 4). Both crossed and uncrossed fibers appear to be distributed to the tectum.

Tractus isthmio-thalamicus

This tract (fig. 6) has its origin from cells in the medullary portion of the nucleus. The fibers are slender and usually do not take the stains to advantage. In larval frogs the Golgi method sometimes gives good impregnations. The tract could not be traced as such beyond the thalamic region of the diencephalon, but individual fibers appear to continue farther. These may possibly represent efferent fibers to the retina, corresponding to those which in birds are said to arise in the nucleus isthmi.

Tractus commissura transversa

This tract is made up of fibers from the cortical cells of the nucleus isthmi and from the quadrigeminal body. The fibers from the nucleus isthmi pass rostrally and ventrally (fig. 3) to the region just caudal and dorsal to the optic chiasma. In Golgi series the relations of these fibers can be easily followed. They cross to the opposite side as the commissura transversa (commissure of Gudden) and thence to the nucleus isthmi. The tractus commissura transversa is accordingly made up of both afferent and efferent fibers with respect to either nucleus isthmi. Bellonci and Gaupp have both noted the relation of the commissura transversa to the nucleus isthmi, and Kappers calls attention to it in several classes of vertebrates.

Commissura isthmi

There is a fine fibered commissural connection between the two nuclei isthmi, which is located in the anterior medullary velum and enters the dorso-medial tips of the nuclei. It is more evident in Acris gryllus than in Rana.

Other connections than those above noted for the nucleus isthmi have been described by various workers, both in the frog and in other forms. An intensive study of our material has failed to confirm them for the frog.

SUMMARY

The nucleus isthmi in the frog is entirely distinct from the secondary visceral nucleus which lies just caudal to it. It is made up of a cortex and a medulla, the cortex being rich in cells, while the medulla has scattered cells and numerous nerve fibers. The fibers enter for the most part through the hilum of the nucleus, and terminate in relation to the dendritic processes of both cortical and medullary cells.

The fiber tracts which are connected with the nucleus isthmi include the lateral lemniscus, tractus tecto-isthmi, tractus quadrigemino-isthmi, tractus isthmio-tectalis, tractus isthmio-thalamicus, tractus commissura transversa, and a commissura

isthmi. In addition to the latter, fibers pass into the decussatio veli, to be distributed apparently to the tectum.

The nucleus isthmi appears from its connections and relationships to clearly correspond, in the frog, to the medial geniculate body of mammals.

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