THE EVOLUTION OF THE SYMPATHETIC NERVOUS SYSTEM IN VERTEBRATES

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SIX FIGURES

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INTRODUCTION

Animal life consists fundamentally in the adjustment of the organism to two sets of primary conditions: those pertaining to the external environment and those pertaining to the internal environment. In the protozoa and in the primitive metazoa, adjustment to both these sets of conditions is accomplished by a more or less undifferentiated organism. As animals became more complex and correlated responses became necessary, this necessity was met in the organism by the development of a nervous system. Such a nervous mechanism first assumed control of those functions which are concerned primarily with the adjustment of the organism to its external environment. As the interactions between the organism and its external environment became more complex, nervous control of the internal functions also

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became necessary; consequently, these functions also were to a greater or a less extent linked with the nervous system. As specialization advanced a division of labor within the nervous system itself became necessary; consequently, in all the higher metazoa, and more especially in the vertebrates, a division of the nervous system arose which has to a large extent assumed the direct control of those functions which are concerned primarily with the adjustment of the organism to its internal environment. This functional division of the nervous system is known as the sympathetic nervous system.

RELATIONSHIP OF THE SYMPATHETIC TO THE CENTRAL NERVOUS SYSTEM

Modern studies have shown that in all vertebrates the nervous system is derived exclusively from the ectoderm. The area which gives rise to the greater part of the nervous system becomes differentiated on the dorsal surface of the embryo very early in the course of ontogeny. The central nervous system develops very rapidly in the early stages of vertebrate embryos and soon becomes definitely outlined. The further development of the vertebrate nervous system advances from the central nervous organ toward the periphery. The sympathetic nervous system, therefore, arises as an offshoot from the cerebro-spinal nervous system.

In all vertebrates in which the ontogeny of the sympathetic nervous system has been traced, the latter arises from cells which advance peripherally from the cerebro-spinal nervous system. According to the writer's observations, the cells giving rise to the sympathetic trunks and to the prevertebral plexuses migrate peripherally from the spinal ganglia and from the ventral part of the neural tube. The sympathetic plexuses related to the vagi, however, viz., the cardiac plexus and the sympathetic plexuses in the walls of the visceral organs, arise from cells which migrate peripherally from the hind-brain and from the vagus ganglia along the paths of the vagi. The sympathetic nervous system, therefore, bears a direct genetic relationship to the central nervous system.

PROBABLE ORIGIN OF THE SYMPATHETIC NERVOUS SYSTEM IN VERTEBRATES

The most primitive sympathetic nervous system which has been described in the vertebrate series is found in the cyclostomes. In these primitive vertebrates the sympathetic nervous system is so rudimentary indeed that not a few investigators have failed to recognize it as such. By others it has been variously described. The existence of a true sympathetic nervous system in the lower cyclostomes; viz., the myxinoids, has not been clearly demonstrated. According to Johannes Müller, whose opinion has recently been reiterated by Marcus ('09), the functions of the sympathetic nervous system are, in these animals, assumed by the vagi.

The existence of a sympathetic nervous system has not as yet been demonstrated in any of the protochordates. Amphioxus has shed much light on the phylogenetic history of the vertebrate nervous system. As far as the writer is aware, however, no traces of a sympathetic nervous system have as yet been described in this classical object of study.

The facts here pointed out seem to warrant the conclusion that the ancestral vertebrates possessed no nervous structure which was morphologically equivalent to any part of the sympathetic nervous system in the higher vertebrates. It must be conceded, of course, that the facts referred to above do not preclude the possibility of nervous elements wandering into the walls of the internal organs in the ancestral vertebrates, there to take part in the nervous control of the internal functions. Our knowledge of the conditions which obtain in the most primitive vertebrates and in the protochordates is still very incomplete. In view of the fact, however, that in all the higher vertebrates the sympathetic nervous system arises in ontogeny as an offshoot from the cerebrospinal nervous system it is highly probable that this division of the vertebrate nervous system had its origin within the vertebrate series and that it probably arose comparatively late in the course of evolution.

As is well known, many of the higher invertebrates possess a sympathetic nervous system. This system, however, bears no direct phylogenetic relationship to the sympathetic nervous system in vertebrates. Those invertebrates which, like the arthropods, are known to possess a sympathetic nervous system are highly specialized and bear no direct phylogenetic relationship to vertebrates. In the higher invertebrates, as in the vertebrates, the sympathetic nervous system, doubtless, arose in response to the demands of the internal functions. The evolution of the sympathetic nervous system in invertebrates and in vertebrates has, doubtless, been entirely distinct, although in both series the sympathetic nervous system has become specialized along lines which are more or less parallel with each other.

MORPHOLOGY OF THE SYMPATHETIC NERVOUS SYSTEM IN THE CYCLOSTOMES

The real point of origin of the sympathetic nervous system can probably not be determined in modern vertebrates. A knowledge of the conditions which obtain in the cyclostomes, however, may throw some light on this difficult problem. Johannes Müller described an unpaired trunk in the myxinoids which arises by the fusion of a branch of each of the vagi and extends posteriorly along the dorsal surface of the pharynx. Marcus ('09) has recently described this same trunk in Myxine glutinosa and has pointed out the fact that in this species it is connected with certain of the spinal nerves by slender strands of fibers. He has, furthermore, described small groups of cells which he interprets as sympathetic lying along the sides of the aorta.

A true sympathetic nervous system is, doubtless, present in the petromyzonts. Fusari and Giacomini have described, not a unified system, but a scattered system which is composed of sympathetic neurones either isolated or aggregated into small groups associated with plexuses of sympathetic fibers. These sympathetic elements are most abundant in proximity with the aorta and the cardinal veins, along the segmental blood vessels, and in the walls of the visceral organs.

In embryos of Ammocetes, Kupffer observed small aggregates of cells which he interprets as sympathetic lying between the aorta and the jugular veins. These cell-aggregates are connected with the spinal nerves by slender fibrous strands. Furthermore, he described a pair of nerve-trunks which have their origin in the VII cranial nerves and extend posteriorly along the dorso-lateral aspects of the pharynx (fig. 1, *sy.*). In these nerve-trunks he found no ganglia. Ganglion cells were found, however, associated with the fibers which extend from these trunks to the blood vessels associated with the gills. Kupffer interpreted this entire system as a nervous mechanism which is concerned primarily with the control of the blood vessels supplying the branchial apparatus.

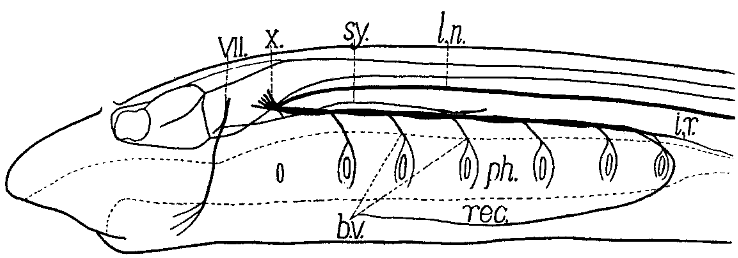


Fig. 1 Diagram showing the distribution of the sympathetic trunks and their relation to the VII and to the X cranial nerves in the petromyzonts. *b.v.*, branches of the vagus; *i.r.*, internal ramus of the vagus; *n.*, lateral line nerve; *ph.*, pharynx; *rec.*, recurrent nerve; *sy.*, sympathetic trunk; *VII.*, seventh cranial nerve; *X.*, tenth cranial or vagus nerve.

In Lampetra wilderi and in Petromyzon dorsatus, Johnston ('08) described a similar pair of nerve-trunks which have their origin in the VII cranial nerves and extend posteriorly along the dorsal wall of the pharynx to the VIII spinal nerves (fig. 1, *sy.*). These nerve-trunks are composed of a series of small ganglia connected by fibers; therefore, Johnston believes them to be homologous with the sympathetic trunks in the higher vertebrates. They are connected with the vagi, but have no apparent connections with the spinal nerves. Fibrous branches may be traced from these trunks to the blood vessels supplying the gills. According to Johnston, "the whole system of fibers seems to be related chiefly or exclusively to the arteries, veins, and blood and lymph sinuses." He is further of the opinion that the cell-bodies of most of the sympathetic neurones in these species are located in the facial ganglia or within the brain.

A review of the literature bearing on the morphology of the sympathetic nervous system in the cyclostomes shows that there has been no attempt on the part of the several investigators to correlate the results of their work with the results of the work which had been previously recorded. It is evident, however, that the sympathetic nervous system in the cyclostomes is still in a very primitive condition, and that in the myxinoids it is still more primitive than in the petromyzonts. Favaro ('10) expressed the opinion that both the scattered sympathetic cells and plexuses described by Fusari and by Giacomini and the sympathetic trunks in the head region (fig. 1, *sy.*) described by Kupffer and by Johnston constitute parts of the sympathetic nervous system as it exists in the petromyzonts, but that these two parts have not yet become intimately connected with each other.

ONTOGENY

Conclusive observations on the development of the sympathetic nervous system in the cyclostomes have not been recorded. Held's ('09) observations on embryos of Petromyzon planeri, however, indicate that the sources of the cells which give rise to the sympathetic nervous system in the cyclostomes are essentially the same as the sources of the cells which give rise to the sympathetic nervous system in the higher vertebrates.

In all the higher vertebrates the sympathetic nervous system consists essentially of a pair of sympathetic trunks lying along the ventro-lateral aspects of the vertebral column, the prevertebral sympathetic plexuses, located in the dorsal region of the abdominal and of the pelvic cavity, the vagal sympathetic plexuses; viz., the cardiac plexus and the sympathetic plexuses in the walls of the visceral organs, the sympathetic ganglia in the head, and the sympathetic cells and fibers associated with the blood-vessels and with the lymphatics.

Practically all investigators since the time of Balfour ('77) have agreed in tracing the origin of the cells giving rise to the sympathetic nervous system to the cerebro-spinal nervous system. They have not all agreed, however, as to the immediate sources and the histogenesis of these cells. The view which has been most generally accepted concerning the histogenesis of the sympathetic nervous system has to a large extent grown out of the work of Balfour, Onodi, and His, Jr. According to this view, the entire sympathetic nervous system is derived from cells which arise in the cerebro-spinal ganglia and advance peripherally primarily along the paths of the spinal nerves and of the communicating rami.

Certain advocates of the theory of local differentiation and of the multicellular nature of nerve-fibers, including Kohn ('05, '07) and Neumayer ('06), have attempted to derive the sympathetic nervous system from elements which arise in situ in the spinal nerves. Their views, however, are obviously influenced by their allegiance to a theory which is opposed to the modern conception of the neurone.

Froriep ('07) advanced a view of the development of the sympathetic nervous system which is based in part on observations made on embryonic material and in part on anatomical and physiological considerations. He succeeded in tracing medullary cells peripherally along the ventral roots of the spinal nerves. With similar cells which wander down from the spinal ganglia, some of these cells enter the anlagen of the sympathetic trunks. Froriep, like Langley, Kölliker, and P. Schultz, advocates the theory that all sympathetic neurones are excitatory in character. He concludes, therefore, that the sympathetic neurones arise primarily or perhaps exclusively from cells which arise in the ventral half of the neural tube and migrate peripherally along the ventral roots of the spinal nerves.

Held ('09) and Marcus ('09) have recently taken exception to Froriep's view. Like the older investigators, they would derive the sympathetic nervous system exclusively from cells which migrate peripherally from the cerebrospinal ganglia. With some modifications, therefore, the views of the older investigators have still been generally accepted.

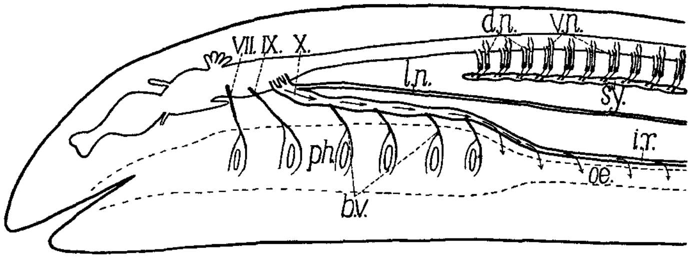
In a series of papers,[1] the writer has recently shown that the sympathetic nervous system in vertebrates is not derived exclusively from the cerebro-spinal ganglia, as the older investigators believed, but that it arises from cells which advance peripherally both from the cerebro-spinal ganglia and from the neural tube. The cells giving rise to the sympathetic trunks advance peripherally either directly through the mesenchyme or more commonly along the paths of the spinal nerves and of the communicating rami. The prevertebral sympathetic plexuses are derived directly from the anlagen of the sympathetic trunks. That the vagi play a large part in the innervation of the vascular system and of the digestive organs in the lower vertebrates is well known. Nevertheless, it has been generally assumed that the cardiac plexus and the sympathetic plexuses in the walls of the visceral organs, which the writer has designated as the vagal sympathetic plexuses,[2] arise from cells which migrate ventrally from the sympathetic trunks and from the prevertebral sympathetic plexuses. My observations on embryos of both the lower and the higher vertebrates have shown conclusively that the vagal sympathetic plexuses bear no direct genetic relationship to the sympathetic trunks, as the earlier investigators believed, but that they arise from cells which have their origin in the hind-brain and in the vagus ganglia and migrate peripherally along the paths of the vagi.

Figs. 2 and 3 have been introduced to illustrate the genetic relationship of the sympathetic trunks and of the vagal sympathetic plexuses to the cerebro-spinal nervous system in the lower and in the higher vertebrates, and to indicate the paths of migration along which the cells giving rise to the sympathetic nervous system advance peripherally. The arrows in the figures indicate the paths and the direction of migration of these elements.

Most of the cells which advance peripherally from the cerebro-spinal nervous system and enter the sympathetic anlagen, like

[1] See bibliography.

[2] The development of the sympathetic nervous system in mammals, p. 235. Jour. Comp. Neur. Psych., vol. 20, no. 3, pp. 211–258.



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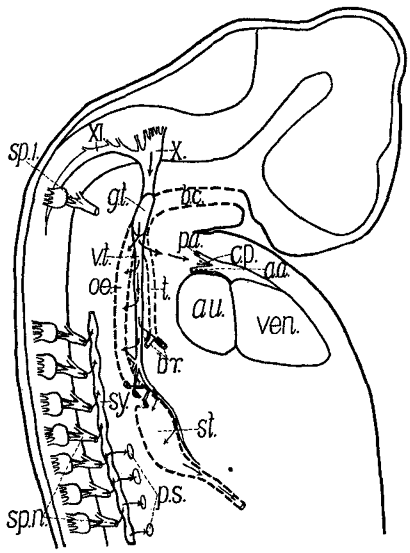

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Fig. 2 Diagram illustrating the genetic relationship of the sympathetic trunks and of the vagal sympathetic plexuses to the cerebro-spinal nervous system in the selachians. The arrows indicate the paths and the direction of migration of the sympathetic elements. *b.v.*, branches of the vagus; *d.n.*, dorsal nerves; *i.r.*, internal ramus of the vagus; *l.n.*, lateral line nerve; *ph.*, pharynx, *oe.*, oesophagus; *sy.*, sympathetic trunk; *v.n.*, ventral nerves; *VII.*, seventh cranial nerve; *IX.*, ninth cranial nerve; *X.*, tenth cranial or vagus nerve.

Fig. 3 Diagram illustrating the genetic relationship of the sympathetic trunks and of the vagal sympathetic plexuses to the cerebro-spinal nervous system in mammalian embryos. The arrows indicate the paths and the direction of migration of the sympathetic elements. *a.a.*, aortic arch; *au.*, atrium; *b.c.*, buccal cavity; *br.*, bronchi; *c.p.*, cardiac plexus; *g.t.*, vagus ganglion; *oe.*, oesophagus; *p.a.*, pulmonary artery; *p.s.*, anlagen of prevertebral plexuses; *st.*, stomach; *sy.*, sympathetic trunk; *t.*, trachea; *sp. 1.*, first spinal nerve; *sp.n.*, spinal nerves *ven.*, ventricle; *v.t.*, vagus trunk; *X.*, vagus nerve, *XI.*, eleventh cranial nerve.

the majority of the cells which remain in the mantle layer in the neural tube, are characterized by very little cytoplasm and by large rounded or elongated nuclei showing a delicate chromatin structure. These cells obviously are the descendants of the 'germinal' cells (Keimzellen) of His; viz., the 'indifferent' cells of Schaper. In the higher vertebrates a few cells may be found among the migrant nervous elements which show distinct protoplasmic processes and may, therefore, be recognized as neuroblasts. These are obviously the 'neuroblasts' of Schaper. Inasmuch as the cells giving rise to the sympathetic nervous system, like the cells giving rise to the neurones and to the neuroglia cells in the central nervous system, are the descendants of the 'germinal' cells of His, these two types of elements are homologous. The sympathetic nervous system is, therefore, homologous with the other functional divisions of the peripheral nervous system, and the sympathetic neurones are homologous with their afferent and their efferent components.

STAGES OF EVOLUTION

The conditions which obtain in the cyclostomes indicate that certain of the cranial nerves, viz., the X and the VII, have played a large part in the evolution of the sympathetic nervous system in the vertebrate series. The only nervous structure which has been definitely interpreted as sympathetic in the myxinoids is the unpaired trunk which arises by the fusion of a branch of each of the vagi. The paired trunks with their branches, which have their origin in the VII cranial nerves and maintain connections with the vagi, constitute the only well developed part of the sympathetic nervous system in the petromyzonts. In both groups these nervous structures are concerned primarily with the innervation of the vascular system supplying the branchial apparatus. The internal rami of the vagi extend posteriorly along the walls of the digestive tube. The scattered sympathetic elements in proximity with the aorta and the cardinal veins in the petromyzonts, doubtless, arise from cells which migrate peripherally along the spinal nerves. Inasmuch, however, as the sympathetic plexuses in the walls of the visceral organs in all the higher vertebrates arise from cells which migrate peripherally along the vagi it is highly probable that the sympathetic neurones associated with the viscera in the petromyzonts also arise from cells which wander out from the cerebro-spinal nervous system along the paths of the vagi.

In all the lower vertebrates the vagi are comparatively large, while the sympathetic trunks are but feebly developed. As the sympathetic trunks become more highly developed the vagi become relatively smaller. This decrease in the relative size of the vagi in the higher vertebrates may be accounted for in part by the fact that the functions of the lateral line organs have been assumed by the sense organs in the head region. Nevertheless, there is a reciprocal relationship between the degree of development of the vagi and of the sympathetic trunks in the vertebrate series.

As already indicated, the vagi are comparatively highly developed in the primitive vertebrates, and their internal rami extend posteriorly along the walls of the digestive tube. These facts indicate that the digestive tube came under nervous control comparatively early in the history of the vertebrate series. Those parts of the sympathetic nervous system, moreover, which are most highly developed in the cyclostomes are closely associated with the vagi and are concerned primarily with the innervation of the blood vessels supplying the branchial apparatus. Furthermore, the cardiac plexus and the sympathetic plexuses in the walls of the visceral organs in the higher vertebrates are genetically related to the vagi. In the course of ontogeny these plexuses arise independently of the sympathetic trunks and, withal, simultaneously with them. All these facts lead us to the conclusion that the vagal sympathetic plexuses; viz., the cardiac plexus and the sympathetic plexuses in the walls of the visceral organs, represent those parts of the sympathetic nervous system which arose earliest in the course of evolution.

In the most primitive vertebrates the nervous control of the internal functions was, doubtless, assumed by the vagi. It is highly probable, however, that in these simple animals the internal functions were not to any great extent subject to nervous control. Even in the most highly specialized animals some of the internal organs, such as the pancreas and certain other glands, whose normal functions were formerly believed to be under the direct control of the sympathetic nervous system, are now known to be stimulated normally by the direct influence of substances, hormones, which are produced by other organs of the body. Muscular organs also are known to respond to direct stimulation. The heart of Salpa carries on its normal functions although it is entirely free from nervous connections. The heart of the chick is known to beat normally for a considerable period before it becomes invaded by nervous elements. In like manner it is highly probable that in the ancestral vertebrates the muscles in those regions of the digestive tube which could not be innervated by the vagi, as well as certain of the other internal organs, carried on their normal functions in response to direct stimulation until the necessity for such direct stimulation was removed by the development of a sympathetic nervous system.

As specialization advanced the control of the internal functions was in part shifted posteriorly. The main blood vessels in the trunk region gradually became innervated by neurones whose cell-bodies remained within the cerebro-spinal nervous system or by cells which migrated peripherally along the spinal nerves. As such cells began to migrate peripherally, many of them were attracted toward the aorta and the cardinal veins. In this manner the location of the cell-aggregates which gradually gave rise to the sympathetic trunks, was in all probability, determined by the location of the main blood vessels. As neurones became aggregated along the aorta they afforded a second link in the viscero-motor apparatus which gradually assumed a share in the nervous control of the visceral organs. The linking of the neurones constituting the viscero-motor apparatus is illustrated diagrammatically in fig. 4, *v.m.f.* As the sympathetic trunks became more highly developed their longitudinal fibers provided a path for the transmission of nervous impulses from one level of the trunk to another. The sympathetic trunks may, therefore, be looked upon as representing the second stage in the evolution of the sympathetic nervous system.

As the internal functions became more complex, sympathetic neurones became aggregated in the dorsal region of the abdominal and of the pelvic cavity. These ganglionic aggregates which finally gave rise to the prevertebral sympathetic plexuses (fig. 4, *p.s.*) afforded a second link in the viscero-motor apparatus

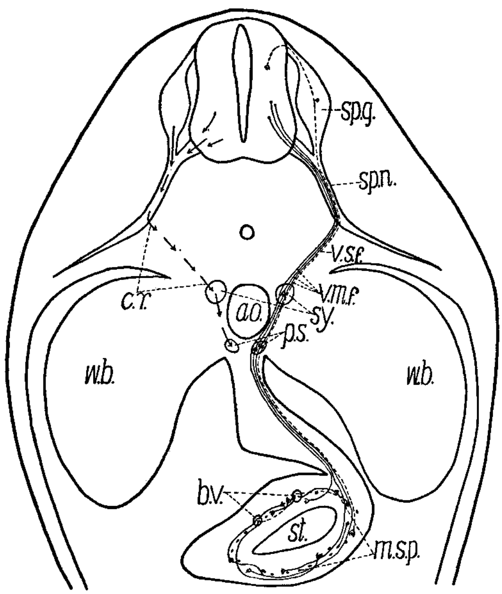

Fig. 4 Diagrammatic transverse section through the trunk region of a mammalian embryo. *ao.*, aorta; *b.v.*, branches of the vagi; *c.r.*, path of communicating ramus; *m.s.p.*, anlagen of myenteric and submucous plexuses; *p.s.*, anlagen of prevertebral plexuses; *sp.g.*, spinal ganglion; *sp.n.*, spinal nerve; *st.*, stomach; *sy.*, anlagen of sympathetic trunks; *v.m.f.*, viscero-motor fibers; *v.s.f.*, viscero-sensory fiber; *w.b.*, Wolffian bodies.

and an intermediate link between the sympathetic trunks and the sympathetic plexuses in the walls of the visceral organs. The development of the prevertebral sympathetic plexuses and of the sympathetic nerves connecting the sympathetic trunks with the vagal sympathetic plexuses probably represents the third stage in the evolution of the sympathetic nervous system.

COMPARATIVE PHYLOGENY

The vagal sympathetic plexuses follow essentially the same course in ontogeny in all the vertebrate embryos in which their development has been investigated by the writer. The fact that no great variations occur in the course of the development of these plexuses in the vertebrate series lends further evidence to the conclusion that they represent those parts of the sympathetic nervous system which arose earliest in the course of evolution. Certain morphogenetic differences occur, however, in the development of the sympathetic trunks and of certain sympathetic ganglia which, doubtless, indicate phylogenetic relationships.

In the fishes, including the selachians as well as the bony fishes, the anlagen of the sympathetic trunks arise as cell-aggregates at the median sides of the spinal nerves. As development advances these cell-aggregates advance mesially until they lie along the lateral aspects of the aorta, each, however, retaining connection with its respective nerve by a fibrous communicating ramus. These ganglionic aggregates are at first independent of each other, but become united later by longitudinal commissures. The prevertebral sympathetic plexuses are not well developed in the fishes.

The course of the development of the sympathetic trunks in the amphibians is essentially the same as the course just outlined in the fishes. The sympathetic trunks in the amphibians are very slender and the sympathetic nervous system as a whole is apparently no more highly developed than in the bony fishes.

The sympathetic nervous system is more highly developed and the sympathetic elements are much more numerous in reptiles than in fishes or in amphibians. In embryos of the turtle, the anlagen of the sympathetic trunks arise as cell-aggregates lying along the lateral surfaces of the aorta and along the dorsal surfaces of the carotid arteries. In the early stages of development cells advance from the distal ends of the spinal ganglia, directly through the mesenchyme, into the anlagen of the sympathetic trunks. After fibers are present in the spinal nerves, cells migrate from the spinal ganglia and from the ventral part of the neural tube along the paths of the spinal nerves and of the communicating rami into the sympathetic anlagen. As development advances, the anlagen of the sympathetic trunks begin to break up and to become more or less scattered. Cell-strands push out from the spinal nerves proximal to the origin of the communicating rami and advance mesially until they appear as irregular cellular tracts extending from the spinal nerves into the anlagen of the sympathetic trunks. As development advances still farther the communicating rami are shifted proximally along the spinal nerves until they fuse with these cellular tracts. The ganglia of the sympathetic trunks do not appear as definitely limited cell-aggregates until comparatively late in the course of ontogeny.

The prevertebral sympathetic plexuses are well developed in the turtle. In the sacral region, cells may be traced ventrally from the anlagen of the prevertebral plexuses into the mesentery where they become aggregated into small cell-groups associated with the rectum (fig. 5, *s.r.*).

In birds two pairs of sympathetic trunks arise in the course of ontogeny. The primary sympathetic trunks arise in the chick about the beginning of the fourth day of incubation, as a pair of cell-columns lying along the lateral surfaces of the aorta and along the dorsal surfaces of the carotid arteries. The anlagen of the secondary sympathetic trunks arise about the beginning of the sixth day, as ganglionic enlargements at the median sides of the spinal nerves. The primary sympathetic trunks reach their maximum development during the course of the sixth day, after which they gradually decrease in size until they disappear. The cells giving rise to both the primary and the secondary sympathetic trunks in the chick migrate peripherally from the spinal ganglia and from the ventral part of the neural tube. In the early stages of development these cells become aggregated along the aorta and the carotid arteries to give rise to the primary sympathetic trunks. As development advances, the cells migrating peripherally no longer wander into the primary sympathetic trunks, but become aggregated at the median sides of the spinal nerves to give rise to the anlagen of the secondary sympathetic trunks. These cell-aggregates later advance mesially for a short distance, each, however, retaining connection with its respective nerve by a fibrous communicating ramus. In the posterior region of the body, the cells composing the primary sympathetic trunks migrate ventrally and give rise to the prevertebral sympathetic plexuses. In the anterior region these elements are withdrawn into the secondary sympathetic trunks.

In the sacral region cells may be traced ventrally from the anlage of the hypogastric plexus into the mesentery where they give rise to the ganglion of Remak which is a large and conspicuous cell-column, more or less oval in transverse section, lying in the

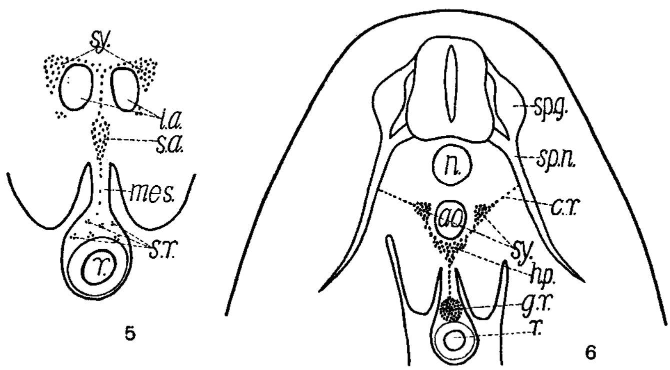

Fig. 5 Diagrammatic transverse section through the anlagen of the sympathetic trunks and through the rectum of an embryo of the turtle. *i.a.*, iliac arteries; *mes.*, mesentery; *r.*, rectum; *s.a.*, aggregate of sympathetic cells; *s.r.*, sympathetic cell-aggregates associated with the rectum; *sy.*, anlagen of sympathetic trunks.

Fig. 6 Diagrammatic transverse section through the sacral region of an embryo of the chick. *ao.*, aorta; *cr.*, communicating ramus; *g.r.*, ganglion of Remak; *h.p.*, anlage of hypogastric plexus; *n.*, notochord; *r.*, rectum; *sp.g.*, spinal ganglion; *sp.n.*, spinal nerve; *sy.*, anlagen of sympathetic trunks.

mesentery along the dorsal surface of the rectum (fig. 6, *g.r.*). This ganglion so enormously developed in birds has no counterpart in any of the other classes of vertebrates. As will be shown presently, however, its prototype is, doubtless, represented in the aggregates of sympathetic cells which are associated with the rectum in embryos of the turtle.

In mammalian embryos, the sympathetic trunks arise as a pair of cell-columns lying along the lateral surfaces of the aorta and along the dorsal surfaces of the carotid arteries. The cells giving rise to the anlagen of the sympathetic trunks migrate peripherally from the spinal ganglia and from the ventral part of the neural tube along the paths of the spinal nerves and of the communicating rami. But a single pair of sympathetic trunks arises in the mammals and development advances regularly. The prevertebral sympathetic plexuses are well developed, but no aggregates of sympathetic cells are found in the mesentery associated with the rectum.

A comparative study of the development of the sympathetic nervous system in the several classes of vertebrates shows that, while the sympathetic system gradually becomes more highly developed as we ascend in the vertebrate series, it also shows some remarkable deviations from the ancestral type.

The sympathetic nervous system is essentially of the same type in the amphibians as in the fishes, and is scarcely more highly developed in the former than in the latter. This simple type of sympathetic nervous system may be easily derived from the type of sympathetic nervous system which was described above in the petromyzonts. The sympathetic plexuses in the walls of the visceral organs, in all probability, had their origin in scattered aggregates of sympathetic cells, such as occur associated with the viscera in the petromyzonts. The sympathetic cell-aggregates which occur in proximity with the aorta in the petromyzonts also afford a basis for the development of the sympathetic trunks. These cell-aggregates, having become somewhat larger and being united with each other and with the primitive sympathetic trunks which were already present in the anterior region of the body by longitudinal commissures, would constitute such simple sympathetic trunks as are found in the fishes and in the amphibians. The prevertebral sympathetic plexuses are still but feebly represented in these two classes of vertebrates.

The sympathetic nervous system in the reptiles is much more highly developed than the sympathetic nervous system in the fishes or in the amphibians. It also shows remarkable deviation from the ancestral type. The phenomena involved in the development of the sympathetic trunks in the turtle are prophetic of still greater deviation from the ancestral type in the development of the sympathetic trunks in birds. As indicated above, the earliest traces of the sympathetic trunks are found along the lateral surfaces of the aorta both in embryos of the turtle and in the chick. In embryos of the turtle these formations early break up to become aggregated once more during the later stages of development. In the chick, the primary sympathetic trunks give way completely to secondary formations which arise as ganglionic enlargements at the median sides of the spinal nerves. In embryos of the turtle no such ganglionic enlargements occur at the median sides of the spinal nerves, but cells deviate from the course of the spinal nerves proximal to the origin of the communicating rami and advance in irregular cellular tracts toward the anlagen of the sympathetic trunks. These phenomena seem to indicate a close phylogenetic relationship between the sympathetic nervous system in turtles and in birds. This does not mean, however, that the sympathetic nervous system in turtles is the direct ancestral type of the highly specialized sympathetic nervous system in birds. The sympathetic nervous system in turtles is itself a specialization of a more generalized type in the ancient reptiles.

The phylogenetic relationship between the sympathetic nervous system in reptiles and in birds is indicated by still another character. As indicated above (fig. 5, *s.r.*), aggregates of sympathetic cells occur closely associated with the walls of the rectum in embryos of the turtle. These cell-aggregates apparently represent the prototype of the ganglion of Remak in birds which is a large and well defined ganglion lying in the mesentery along the dorsal surface of the rectum (fig. 6, *g.r.*). This condition, which probably originated in reptiles and has become so highly specialized in birds, in all probability, represents a specialization which has arisen in response to the demands of a specialized function. The habits of reproduction in turtles and in birds have become specialized along more or less parallel lines. This specialization has, however, advanced much farther in the latter than in the former. The production and deposition of the large avian egg has involved modifications in the structure of the reproductive organs, and has, in all probability, stimulated the development of a more efficient nervous mechanism which might assume the direct control of the reproductive functions. We are led to the conclusion, therefore, that the ganglion of Remak so enormously developed in birds, as well as the aggregates of sympathetic cells associated with the rectum in turtles, is correlated with oviparous habits.

The relationships above pointed out seem to warrant the conclusion that the sympathetic nervous system in birds bears a more or less direct phylogenetic relationship to the sympathetic nervous system in the ancestral type of reptiles and that it has become specialized along lines which are more or less parallel with those followed by the sympathetic nervous system in the Chelonia. This conclusion is none other than should have been anticipated in view of the intimate relationships between these two types of vertebrates in the phylogenetic history of the vertebrate series.

While the sympathetic nervous system in mammals, doubtless, also bears a phylogenetic relationship to the sympathetic nervous system in the ancestral type of reptiles, it has not followed the lines of specialization which are indicated in turtles and in birds, but has become specialized along the lines which are indicated by the simple type of sympathetic nervous system in fishes and in amphibians. We are led to the conclusion, therefore, that in the two most highly specialized classes of vertebrates; viz., mammals and birds, the sympathetic nervous system has departed more widely from the ancestral type in the latter than in the former. This conclusion, again, might have been anticipated in view of the extreme degree of specialization attained by the nutritive functions in the highly specialized avian branch of the vertebrate series.

SUMMARY

1. In all the higher vertebrates the sympathetic nervous system arises in ontogeny as an offshoot from the cerebro-spinal nervous system.

2. The ancestral vertebrates probably possessed no nervous structure which was homologous with any part of the sympathetic nervous system in the higher vertebrates. In these primitive

vertebrates, the nervous control of the internal functions was probably assumed by the vagi.

3. The most primitive sympathetic nervous system which has been described in the vertebrate series is found in the cyclostomes. The part of the sympathetic nervous system which is most highly developed in these animals is closely associated with the vagi and is concerned primarily with the innervation of the blood vessels supplying the branchial apparatus. Scattered sympathetic elements occur in the trunk region.

4. In the lower vertebrates the vagi are comparatively highly developed, while the sympathetic trunks are but feebly represented. As the sympathetic trunks become more highly developed, the vagi become relatively smaller.

5. In all the higher vertebrates, the vagal sympathetic plexuses; viz., the cardiac plexus and the sympathetic plexuses in the walls of the visceral organs, arise from cells which migrate from the hind-brain and from the vagus ganglia along the paths of the vagi. The sympathetic trunks arise from cells which advance peripherally from the spinal ganglia and from the ventral part of the neural tube. The vagal sympathetic plexuses, therefore, arise independently of the sympathetic trunks.

6. The facts above summarized warrant the following conclusions: (a) the sympathetic nervous system in vertebrates probably had its origin within the vertebrate series; (b) the vagal sympathetic plexuses represent those parts of the sympathetic nervous system which arose earliest in the course of evolution.

7. As specialization advanced, the nervous control of the internal functions was in part shifted posteriorly. The sympathetic trunks, therefore, represent a second stage in the evolution of the sympathetic nervous system.

8. The prevertebral sympathetic plexuses and the sympathetic nerves connecting the sympathetic trunks with the vagal sympathetic plexuses probably represent the third stage in the evolution of the sympathetic nervous system.

9. The sympathetic nervous system in the fishes and in the amphibians is essentially of the same type. It is probably

derived from such a simple type of sympathetic nervous system as exists in the petromyzonts.

10. The sympathetic nervous system is more highly developed in the reptiles than in the fishes and in the amphibians. It also shows remarkable deviation from the ancestral type.

11. The sympathetic nervous system in birds shows more or less direct phylogenetic relationship to the sympathetic nervous system in the ancestral type of reptiles. It has become specialized along lines which are more or less parallel with the lines of specialization followed by the sympathetic nervous system in the Chelonia.

12. The sympathetic nervous system in mammals also bears a phylogenetic relationship to the sympathetic nervous system in the ancestral type of reptiles. It has not followed the lines of specialization which were followed by the sympathetic nervous system in turtles and in birds, but has become specialized along the lines indicated by the simple type of sympathetic nervous system in fishes and in amphibians.

13. A comparative study of the development of the sympathetic nervous system in the two most highly specialized classes of vertebrates; viz., mammals and birds, shows that the sympathetic nervous system has departed more widely from the ancestral type in the latter than in the former.

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