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REVIEW PAPER

A history of the autonomic nervous system: part I: from Galen to Bichat

Peter C. Oakes[1] · Christian Fisahn[1,2] · Joe Iwanaga[1] · Daniel DiLorenzo[2] · Rod J. Oskouian[1,2] · R. Shane Tubbs[1]

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Abstract
Introduction The development of our current understanding of the autonomic nervous system has a rich history with many international contributors.
Conclusions Although our thoughts of an autonomic nervous system arose with the Greeks, the evolution and final understanding of this neural network would not be fully realized until centuries later. Therefore, our current knowledge of this system is based on hundreds of years of hypotheses and testing and was contributed to by many historic figures.

Keywords History · Nerves · Vegetative system · Physiology · Anatomy

Introduction

The history of the autonomic nervous system had its inception quite a long time ago [1]. In fact, the very notion that the body was divided into two systems (an "animal" and an "organic," a somatic and an autonomic) originated with the ancient Greeks [1]. Aristotle (Fig. 1) himself ruminated on the subject and on which bodily functions each system governed [1].

✉ Joe Iwanaga
joei@seattlesciencefoundation.org

1 Seattle Science Foundation, 550 17th Ave, James Tower, Suite 600, Seattle, WA 98122, USA

2 Neuroscience Institute, Swedish Medical Center, 550 17th Avenue, Suite 500, Seattle, WA 98122, USA

Galen

The first known figure of antiquity to truly probe into the nature of this division, however, was Galen [1]. In the second century A.D., Galen was able to follow the vagus into the chest and abdominal cavities, documenting its communications with the organs there within [1, 2]. He depicted the sympathetic trunks as crossing the ribs, connecting with the thoracic and lumbar spinal cord, and continuing on to communicate with organs within the body cavity via plexuses [3]. Galen was also the first to document the superior and inferior cervical ganglia, the "semilunar" (celiac) ganglia, and the rami commmunicantes [2].

Upon observing this system of nerves, Galen arrived at a hypothesis concerning the nervous system [2]. He believed that nerves acted as pipes, allowing the flow of "animal spirits" to pass between organs. This "sympathy," as it was later named, was the notion that when a change in the condition of one organ or part of the body occurred, this in turn caused another organ or portion of the body to react or alter its function [1]. Sympathy was present in a healthy patient but was more commonly believed to be seen in the diseased [1]. During the sixteenth and seventeenth centuries, and before, knowledge on the etiology of diseases was quite sparse [1]. And so, sympathy became an explanation for symptoms appearing far from the actual origin of a disease [1]. However, such an idea most likely drew its roots from a "humoral theory" which was significantly older than Galen [3].

Galen even managed to discover the majority of the cranial nerves—from which he believed the sympathetic trunk originated [2]. Galen grouped the modern glossopharyngeal, vagus, and accessory nerves with the sympathetic trunk into his "sixth cranial nerve," which he believed originated as a single structure from within the cranium itself—a belief that persisted for more than a millennium [4, 5]. This error is most

Fig. 1 Aristotle http://www.biography.com/people/aristotle-9188415

likely attributable to the fact that Galen's dissections did not occur with human subjects but animal subjects, mostly pigs [1, 4].

Vesalius

Over a millennium later, the next man to make any advances in the anatomy of the autonomic nervous system was Vesalius in the sixteenth century [4]. While Vesalius may have improved other points of Galen's anatomical works, he left Galen's sixth nerve largely unaltered (Fig. 2). One reason for Vesalius' acceptance of Galen's description may have been due to the poor quality of material that Vesalius had to work with. Most of his cadavers had been victims of capital punishment, and at the time, execution often consisted of hanging or decapitation, thus rendering Vesalius' task of documenting the anatomy of the neck quite challenging [6]. Nonetheless, Vesalius still performed his own anatomical dissections by which his figures of the sympathetic trunks and peripheral plexuses were drawn [5]. One error of Galen's that Vesalius perpetuated was his belief that the sympathetic trunk was an offshoot of the vagus nerve, branching off at the upper thorax [6]. It was an error that would persist for almost 50 years more [6]. Vesalius' depiction was one of several in Caspar Bauhin's compiled works, which documented the opinions of various anatomists from his era [6]. In these texts, Bauhin describes the sympathetic trunk as it was understood in the late sixteenth and early seventeenth centuries: "the sixth nerve descends from the foramen between the occiput and temporal bone, between the carotid artery and jugular vein, and divides at the clavicle into a large exterior and small interior branch. The latter is the costal, and the former gives rise to the stomachic and recurrent" [6].

Étienne, Eustachi, and Riolan

However, not all sixteenth century anatomists were in agreement with Galen and Vesalius, and several sought to correct

Fig. 2 Vesalius' early drawing of the nervous system based on Galen's description. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2015000200155

the errors they believed persisted. Charles Étienne in 1545 depicted the vagus and sympathetic nerves as originating independent of one another from the cranium [6]. Not long after Étienne, Bartolomeo Eustachi (Eustachius) completed an engraving wherein the sympathetic trunk was distinct from the vagus [6]. Unfortunately, his plates were not published until 1714 [6]. Despite this important discovery, Eustachius persisted in the belief that the sympathetic nerve originated from within the cranium, believing it branched from the abducens nerve [1, 4]. Riolan seems to be the first anatomist to clearly differentiate between the upper and lower sympathetic ganglia and trace the sympathetic trunk [6]. He expressed his opinion that "the costal is produced not from the sixth conjugation, but from the spinal medulla, through the

Fig. 3 Thomas Willis http://www.britannica.com/biography/Thomas-Willis

foramen which is formed between the last vertebra of the neck and the first of the back" [6]. Riolan maintained that the sympathetic trunk originated from spinal nerves rather than from branching off of the vagus, thus resolving one inaccuracy found in Vesalius' book [6].

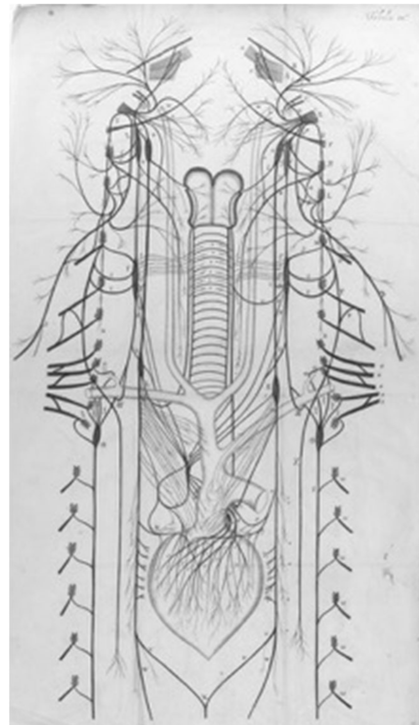

Fig. 4 Willis and his depiction of the autonomic nervous system http://www.indiana.edu/~liblilly/anatomia/head/images/rc340-w7_00001.jpg

Willis

The next major personality in this history is Thomas Willis (Fig. 3), who was most active during the seventeenth century [1]. Willis espoused a "return to Galenic principles" and advanced a mechanical explanation for sympathy [1]. He found that some pathways appeared to allow both sympathy and "reflexion" to take place without cerebral involvement and therefore took place without volition [1]. Willis also tried to establish a physical explanation of physiological and pathological actions, and in doing so, greatly elucidated the exact nature of the vegetative and somatic nervous systems, along with their central organs [1]. He gave a vastly improved description of the plexuses, ganglia, and nerves of the autonomic nervous system as well (Fig. 4). At the time, the term in vogue for the sympathetic nerve (trunk) was the "*nervus intercostalis*" or "*nervus intercostalis magnus*" [1]. There is some disagreement whether Helkiah Crooke (1576–1653) or Reid (1616) actually made first reference to this nerve, but regardless, Willis gave a better description of the nerve and made mention of the rami communicantes [1, 3]. Willis also held the belief that the ganglia and their nerves, which made up this *nervus intercostalis*, were an outgrowth of the central nervous system, describing the autonomic system as a bush growing upon another bush. The ganglia were as knots in a tree trunk, and he believed they received nerve spirits [1]. He also believed that the ganglia guided this flow of spirits in various directions. In a paper published in 1664, Willis described the great mesenteric plexus as being centrally located, similar to a sun, sending its fibers in all directions—earning it the name solar plexus [5]. He believed this plexus was responsible for appropriate control of the heart by the brain. Willis even went so far as to postulate that a branch connecting to the aortic arch might "react to changes in the pulse" [5]. This postulation most likely came from experimentation with dogs. Willis sectioned both vagus nerves and observed a "great trembling" of the heart [5]. He even went so far as to speculate that voluntary movement was controlled by the cerebrum and involuntary movement was subject to the cerebellum, the originating point of the vagus and sympathetic nerves with the rami communicantes acting as bridging points between the two systems. He foreshadowed Brown-Séquard when he postulated that the nerves mechanically constricted the blood vessels on which they traveled [4]. It was Willis who laid the foundation for the modern nomenclature of the cranial nerves and gave a quite accurate account of the "wandering" or vagus nerve [5]. But ultimately, he believed that the cerebrospinal axis was the more important nervous system [1].

One of the next great anatomists that expanded upon Willis' observations of the sympathetic nerve was the Dane J. B. Winslow, active during the early eighteenth century [1]. Winslow called the *nervus intercostalis* "la grande sympathique" to designate it as the major source of sympathetic outflow [1]. This term that has led to the modern nomenclature of sympathetic nerve, or trunk, and was the first documented use of the actual word “sympathy” in relation to the autonomic nervous system [1]. The name originated from the observations of Galen and Willis: the nerve seemed to anastomose with many nerves throughout the body, supporting the existing notion of animal spirits bringing the body into balance. This system of sympathy soon received widespread approval [1].

Winslow and du Petit

Regarding ganglia, Winslow speculated that they were the equivalent of small brains possessing their own “nervous power” and therefore were independent from the cerebrospinal system [1]. By 1732, he declared that the sympathetic trunk did not originate from the cranium but did seem to be composed of ganglia [1]. Winslow was also the first to document the gray and white rami communicantes [4]. One error of Galen’s and Willis’ that eluded Winslow was the incorrect origin of the sympathetic trunk—an error that was finally remedied by Pourfour Du Petit in 1727 (possibly 1729) [1, 7]. Previous anatomists believed that the carotid plexus originated from the cranial nerves [1]. Pourfour du Petit, however, found that the sympathetic trunk joined the fifth and sixth cranial nerves (which many predecessors believed to be the origin of the nerve) in a posterior to anterior orientation, causing the impulses to be carried in a caudal to cranial direction at that location [4, 7]. When observing the thickness of the structures closely, he also noticed that as the sympathetic trunk neared its believed origin at the time, it tapered rather than thickened [1]. Both of these observations thus made Pourfour du Petit skeptical as to the accepted origin of the nerve. In order to convince others, Pourfour du Petit designed an experiment in which he severed the sympathetic nerve of a dog at the level of the neck and observed the effects upon the ipsilateral eye. This eye became “dull, sunken, moist, and mattery” with the nictitating membrane remaining extended over the eye—all of which Pourfour du Petit believed showed “the absence of animal spirits which are supplied by the intercostal nerve” [1]. These results led Pourfour du Petit to believe that the sympathetic trunk had a superficial origin in the spinal cord, and that the branch seen connecting with the fifth and sixth cranial nerves was not the actual origin of the nerve. Pourfour du Petit’s observations of the ipsilateral eye of the sympathectomy also allowed him to speculate that the intercostal nerve may contribute to pupil dilation and blood flow [1]. Unfortunately, this revolutionary finding was not accepted by the greater scientific community for some time, and the belief that the sympathetic trunk originated within the cranium persisted into the nineteenth century [1]. It was not until 1851 when Budge and Waller published their findings that the cervical sympathetic nerve was partly derived from the cord that scientists came to accept Pourfour Du Petit’s conclusions from more than a century earlier [4].

Whytt

Contrasting with Willis and Winslow was Whytt in the eighteenth century, who was more skeptical of the Galenic tradition of spirits [5]. Some of Whytt’s most remarkable advances were in the field of visceral sensation and involuntary movement [5]. He was a pioneer in many fields, being among the first to document skeletal muscle tone, the reaction of pupils to light, and the fact that “the distension of hollow muscle has a remarkable influence towards exciting them into action” [5]. Thus, his observations led him to believe that involuntary motion was actually independent of the cerebellum, which went contrary to the prevailing belief at the time. Whytt altered Willis’ view that sympathy was due to communications of nerves stemming from the brainstem and cerebellum by stating “sympathy presupposed feeling and must therefore be dependent on nerves” [5]. Whytt also concluded from his experiments that nerve fibers were individual units rather than “anastomosing channels” and that their action was subject to the cerebrospinal axis [5]. Whytt thus went on to write, “since every individual nerve appears to be quite distinct from every other, not only in its rise from the medullary substance of the brain or spinal marrow but also in its progress to that part where it terminates, it follows, that the various instances of sympathy, observed between the different parts of the body, cannot be owing to any communication or anastomosis of their nerves” [5]. He concludes that because the nerves do not communicate with one another directly via anastomoses, sympathy in the body is accounted for by having its source somewhere besides the nerves themselves, such as the brain or spinal cord [5].

Johnstone

The eighteenth century English anatomist Johnstone built further upon the assertions of Willis and Winslow in respect to the exact nature of the ganglia and created the most enduring theory on ganglia out of the three men that lasted into the nineteenth century through Bichat [1]. He was mostly in agreement with Winslow’s notion of the ganglia as little brains, going so far as to describe the ganglia as “subordinate springs and reservoirs of nervous power” [1]. However, he differed from Winslow in that he believed the ganglia communicated with the spinal cord and brain [1]. He categorized the spinal root ganglia as part of the ganglionic system, believing they exerted influence over the involuntary movements of the voluntary musculature (i.e., shudders and twinges) [1]. Similarly, he believed that the vegetative or what he called “visceral” ganglia controlled involuntary movement of organs [1]. Johnstone maintained that despite their connection to the central nervous system, the ganglionic system kept a level of autonomy such that the ganglions could continue to communicate with organs where necessary despite being severed from the cerebrospinal nervous system [1]. He further believed that the ganglia acted to convert voluntary motor messages sent from the brain into involuntary messages [1]. These involuntary signals could then be filtered off, preventing contact with vital organs [1]. He believed this played a part to "limit the exercise of the soul's authority in the animal economy and put it out of our power by a single *volition* to stop the motions of our heart and in one capricious instant irrevocably to end our lives" [1]. Furthermore, the reason that viscera were never sensate in non-diseased states was due to the fact that the ganglia were acting as filters in the opposite direction as well—that is, preventing signaling from the viscera from reaching the "*sensorium commune*" or consciousness [1]. Disease caused this filter to become porous and allows such messages of pain through [1]. In terms of their actual makeup, he agreed with those before him by stating that the ganglia were made of a "mixture of cortical and medullary substance nourished by small blood vessels" that he believed was able to generate new fibers and create its own plexuses and nerves, again reaffirming the independence of the ganglia from the cerebrospinal nervous system (a histological error later corrected with the microscope of Ehrenberg in the nineteenth century) [1]. He even attributed the secretion of glands to the ganglia: "the nervous twigs on which they (the ganglia) have been observed, being chiefly distributed to the salivary and mucous glands [sic], about the jaws, tongue, palate, throat, and nostrils, may they not be supposed to have some use in glandular secretion" [1]? But perhaps Johnstone's greatest legacy was his influence upon Bichat's system, which would dominate all thought concerning the autonomic nervous system for decades.

Bichat

Bichat (Fig. 5) presented his immensely influential "*système des* ganglions" or ganglionic system scheme at the very beginning of the nineteenth century (1800) [1, 5]. His basic claim was that life has two facets: animal (somatic) and organic (autonomic) [1]. While his division of life into animal and organic was not unique to him, he expanded upon this notion more than anyone had before [1]. His "*vie animale*" or "*vie de la relation*" resided in the parts of the body that the individual could voluntarily control to react with the world [1]. It was inconstant as it ceased with sleep, and the brain was its governing organ [1]. Its key functions included sensation and movement, but it also oversaw understanding and will. Bichat's "*vie organique*" or "*vie de la nutrition*" was

Fig. 5 Marie François Xavier Bichat https://upload.wikimedia.org/wikipedia/commons/a/a0/Marie_Francois_Xavier_Bichat.jpg

located in an individual's innards [1]. This division of life concerned itself with chemical processes such as catabolism (dissimilative) and metabolism (assimilative) [1]. The governing organ of this system, he believed, was the heart. The sympathetic trunk he labeled as homologous to the spinal cord, and the celiac ganglion as homologous to the brain, so much so that some had come to call it the "*cerebrum abdominale*" [1]. Unlike many of his predecessors who believed that spirits governed these two lives, Bichat claimed that the nervous system itself was ultimately in command [1]. And so, he accorded a different section of the nervous system with each [1]. With the "*vie animale*," Bichat associated the cerebrospinal nervous system, and with the *vie organique*, he associated the vegetative nervous system [1]. This most likely made Bichat the first anatomist to associate the vegetative nerves with metabolism, but more important still was his characterization of the two systems as independent from one another, with each possessing its own separate nervous power [1].

And so, on one hand, there were the ganglia, from which he believed nerve fibers originated [1]. He believed these fibers to be comparable to the cerebrospinal nerves in function [1]. Although not the first to make this claim, his observation that there were more fibers leaving many ganglia than entering them seemed to confirm his belief that they were generated by the ganglion itself, further supporting the system's independent nature [1]. Bichat agreed with Winslow's notion that the ganglia acted as small brains; however, he did consider there to be some communication between the nerves of the two systems, as evidenced by emotions affecting the viscera and involuntary movements of voluntary muscles, for example, but he was inconsistent in his exact explanation of these overlaps or communications [1]. Bichat had considered the rami communicantes running between the spinal roots and vegetative ganglia that Willis had remarked upon, and his opinion on the matter was to deny their being a true functional pathway [1]. He dismissed them as structural anastomoses joining the two systems without functional consequence [1]. He used the same explanation with the decussation of the pyramids of the medulla oblongata to rebuff any attempt to link the cerebrospinal nervous system to the ganglionic system in terms of nervous power [1]. He further bolstered his argument of ganglionic independence by observing that where gaps in the rami occurred, the supplied organs suffered no loss of function—a claim later objected against by many anatomists [1].

Bichat bulwarked his claims with many experiments and observations. He believed the autonomy of his *système de ganglions* was supported by autopsy findings in "idiots" in whom the cerebrospinal system was malformed, but the ganglia were found to be intact [1]. Bichat also observed that the ciliary and sphenopalatine ganglia were always found isolated with their only connection being to cranial nerves [1]. This bolstered his belief that the "great sympathetic nerve does not really exist at all, that the cord it presents is only a series of communications between small nervous systems [ganglia], arranged one above the other, and that these communications are only accessory and perhaps need not exist" [1]. Among his many comparative anatomy experiments, proving this point was one notable experiment involving the chemical and physical irritation of a dog's nervous system [1]. When such stress was applied to the dog's celiac ganglion, almost no signs of pain were observed, and yet when such stresses were placed on the dog's spinal or cranial nerves, a violent reaction was recorded [1]. He thus believed the ganglia to be much less sensate than the cerebrospinal system [1]. This also served to confirm Johnstone's notion of the ganglia stopping pain from reaching the consciousness. Overall, Bichat's published ideas in 1800 won widespread approval, but tragically, he died at a young age in 1802, leaving further clarification of points he raised to others [1]. His notion of how the ganglia functioned denied any dependence on the cerebrospinal nervous system and asserted that the ganglia possessed their own nervous power. This opened a new era in the history of the vegetative nervous system that did not end until the 1880s [1].

Conclusions

As the eighteenth century came to a close, a great deal of progress had been made in the field of gross anatomy of the autonomic nervous system; however, many men of science remained under the influence of Galen and his concept of spirits [1]. Evidence at the time was limited to gross histology and embryology [1]. Without any microscopy, only macroscopic observations of the autonomic nervous system were used, and as such, the ganglia garnered the most interest [1]. Such limitations meant that the leaps made in anatomy were not accompanied by leaps in physiology, and the exact nature of the nervous system's function remained obscure [1]. Experimental methods were not sophisticated enough yet to answer specific questions about the system either [1]. And so, as the nineteenth century opened, Bichat's system soon came to general acceptance in the 1830s, and the rest of the century saw the scientific community's attempt to prove or disprove the system he proposed until its ultimate dismissal half a century later [1].

Compliance with ethical standards

Conflict of interest The authors report no conflicts of interest.

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