Understanding the Topography of the Autonomic Nervous System in Humans

Understanding the mechanism of the autonomic nervous system is crucial in the understanding of many disorders and syndromes. This is especially true in our experience of migraine headaches and craniofacial neuralgia treatment, which is based on the malfunction of sympathetic and parasympathetic nervous systems.

The autonomic nervous system is an independent, self-managed, and self-controlled system serving a complex, multi-functional, internal system of organs. Its function continues even when the cognitive cerebral centers are not functioning. The autonomic nervous system demonstrates the dual function of the pro and contra functioning system referred to as the sympathetic and parasympathetic "nervous system". Their activities may affect human and animal emotions, and vice versa.

Embryology development: The ganglion cells of the sympathetic system are derived from the cells of the neural crests. As these crests move forward along the sides of the neural tube and become segmented off to form the spinal ganglia, certain cells detach themselves from the ventral margins of the crests and migrate toward the sides of the aorta, where some of them are grouped to form the ganglia of the sympathetic trunks, while others undergo a further migration and form the ganglia of the Prevertebral and visceral plexuses. The ciliary, sphenopalatine, otic and sub maxillary ganglia which are found on the branches of the trigeminal nerve are formed by groups of cells which have migrated from the part of the neural crest which gives rise to the semilunar ganglion. Some of the cells of the ciliary ganglion are said to migrate from the neural tube along the oculomotor nerve.[3]

The autonomic nervous system is composed of a central and peripheral portion. The central portion is evolutionary transferred mainly to the periphery, located outside the brain. The central intracranial portion is situated in the nuclei of the rhomboid fossa, mid brain, and tuber cinereum: parasympathetic originis nuclei and terminal nuclei of the trigeminal and Vagus nerves, parasympathetic nuclei of the VII and IX. The next central part is located in cells of the lateral horn of spinal cord and spinal ganglia. **Figure 1 & 2**

The peripheral portion is characterized by three major network complexes in the cervical, thoracic, abdominal, and lumbosacral regions. They switch in one of the ganglions prior to approaching the end organ. Preganglionic nerve fibers originate from the central neuron. Preganglionic nerve fibers differ from postganglionic nerve fibers. It is known that the

postganglionic nerves outnumber the preganglionic, e.g., a single preganglionic nerve fiber can nourish several postganglionic nerves. **Figure 1, 2, and 3**

The diffuse and broadband network of sympathetic and parasympathetic nerve fibers, therefore, makes it nearly impossible for surgeons to successfully complete a sympathectomy. The functions return after a while. Reflecting on the complexity of understanding and decoding those interconnections of "rami Communicants" can be extremely challenging for the Neurophysiologist.

Both the sympathetic and parasympathetic nervous systems are highly functional, independent systems working in natural & balanced coexistence. There is physiologically a switching system which genetically determines the silencing or desilencing process, e.g. the Sympathetic nerve innervates the dilator pupillary muscle while the parasympathetic nerve innervates the pupillary sphincter muscle. Their activation by multi-wavelength light (e.g. Radioactive) rays and flashing lights can stimulate the autonomic system toward migraine headaches.

It is physiologically speculated that there are postganglionic intramural microganglia that provide postganglionic switching and certain automatism to the end organ, which can include glands, arteries and veins.

Sympathetic Nervous System

The presence of the sympathetic nerve system demonstrates itself in two major groups of ganglia, the first in the group of sympathetic trunk that lies paravertebrally along the lateral sides of the spinal column and the other, which extends in front of the spinal column as a single Prevertebral ganglion chain. This chain includes the Celiac ganglion, superior, and inferior mesenteric ganglia. The interganglionar fasciculi connect single ganglia as a chain, and rami communicants demonstrate connection between the CNS and sympathetic system. Rami communicant albi called preganglionic redirect connections from spinal cord to sympathetic system, whereby, rami communicantes grisei provides connections from the sympathetic trunk to the spinal cord.

Autonomic ganglia contain from less than ten to more than a million neurons each, as well as satellite or glial cells (Schwann cells). They also contain blood vessels, connective tissue, cells of the immune system and clusters of extra-adrenal chromaffin cells. Preganglionic neurons have their cell bodies in the brainstem or spinal cord. 3 ("The Human nervous system" Juegen K. Mai, George paxinos 3rd edition). The physiologic activity of the ganglia is selectively programmed and coordinated by different types of neurons within each ganglion. It is identified that preganglionic axons branch extensively within ganglia, diverging to provide input for up to several hundred target neurons. In turn, each final motor neuron may receive convergent synaptic inputs from many preganglionic neurons.

The divergence of preganglionic axons permits significant spatial amplification of central commands by a relatively small number of pre-ganglionic neurons. 3 ("The Human nervous system" Juegen K. Mai, George paxinos 3rdedition).

Structure of the sympathetic final motor neurons:

Sympathetic neurons project to most tissues of the body, commonly via major nerves containing predominantly sensory and somatic motor nerve fibers.

Cell bodies of sympathetic neurons range from 15-60μm in diameter, with large cells (35-60 μm) being most common in superior and middle cervical ganglia *(De Castro, 1932).* The neurons are multipolar, bearing up to 12 dendrites, the complexity of which apparently increases with age. Long dendrites may branch considerably forming "dendritic nests" enclosing other ganglion cells. Long branching dendrites from several nearby cells can intermingle to create complex "dendritic glomeruli" *(Ramon Y Cajal, 1911; De Castro, 1932, 1945).* Some multipolar cells also have several short dendrites which do not penetrate the satellite cell capsule. Other cells lack long dendrites and have only short intracapsular dendrites *(Ramon y Cajal, 1911; De Castro, 1932, Kuntz 1945, Botar, 1966).* Axons usually lack collaterals within ganglia and arise from the proximal portion of a large dendrite *(De Castro,1932).* To date, there is no information to address this tissue directly in humans. 3 ("The Human nervous system" Juegen K. Mai, George paxinos 3rd edition*).* Each subtype of the ganglia neuron with its specific neuropeptide may express different levels specific to biogenic activity. The sympathetic ganglia are extraordinarily variable in their number and location of neurons. **For instance, unfused lumbar ganglia contain about 6000-8500 neurons** *(Weber, 1958).* There are numerous "accessory" migroganglia associated with the sympathetic chain and gray communicating rami at all levels and the level of target organs. The migroganglia usually contain from few hundred to a few thousand nerve cell bodies *(Webber, 1955, 1958; Kunz et al., 1956, 1957)*, although some may contain 1000- 2000 neurons (Alexander et al., 1949, Kunz et al, 1957: Webber, 1958). 3 "The Human nervous system" Juegen K. Mai, George paxinos 3rd edition

Peptide expression of the sympathetic nerve endings and synapses:

Various neuropeptides differentially express their bioactivity within the ganglia and end organs. At least 80% of neurons in the superior cervical ganglion are noradrenergic while at the lumbar levels, about 75% of neurons are adrenergic. At all levels of the paravertebral chain, about 50% of noradrenergic neurons contain neuropeptide Y (NPY). A small portion of neurons, presumably cholinergic, contain combinations of VIP, somatostatin or CGRP. Galanin may occur in some neurons. The remaining neurons are probably non-adrenergic

and represent cholinergic sympathetic neurons. They may comprise up to 20-25% in the lumbar ganglia. Most of non-noradrenergic neurons are surrounded by terminals of preganglionic neurons containing encephalin and related peptides.

Anatomic topographically sympathetic trunk differentiates itself in three regions:

Cervical: superior cervical ganglion, mid cervical ganglion, and stellate ganglion

Thoracic trunk: coeliac ganglion, mesenteric superior and inferior, Prevertebral, and paravertebral chain

Lumbosacral: pelvic ganglion and coccyx ganglion

The **superior cervical ganglion** delivers a strong branch of network, namely the Jugular nerve into the internal jugular vein. Interestingly, the Jugular nerve first passes through the parasympathetic communicating nerve fibers of the superior ganglion of the Vagus nerve before supplying the internal jugular vein. Several nerve fibers connect to the cerebral peripheral nerves such as Vagus Glossopharyngeal, and to the trunk of the Hypoglossus nerve as well as Phrenic nerve.

Connections to the cervical nerves going out of the Rr. communicantes grisei include the 3rd and 4th from superior cervical ganglion, the 4th and 5th from mid cervical ganglion, and finally the 6th through 8th from stellate ganglion. There is a high possibility that connections from preganglionic Rr. communicantes albi from cervical spinal cord are present.

The internal carotid nerve is the strongest branch of the superior cervical ganglion. It forms a network with the following outgoing branches:

1. Caroticotympanic nerve, which enters through the Caroticotympanic canal in the middle ear to create tympanic network to supply the ear mucosa.
2. Profound Petrous nerve, which leaves the cranium by lacerum foramen toward the pterygoid canal in order to join the major petrous nerve. It creates at this level the pterygoid canal nerve.

Radices sympathicae of ciliary ganglion extend through the superior orbital tissue toward the ciliary ganglion, which without interruption as ciliary Nn supplies papillary dilator muscle. **Figure 3.** 9

The superior cervical ganglion, alone, provides sympathetic innervation of the head and neck as follows:

Innervates pupillary dilator muscle, orbital muscle, and tarsal muscles. Feeding branches to the glands of oral and nasal mucosa, as well as pharynx, larynx. It supplies thyroid and parathyroid glands. Provides vasomotor fibers to pilomotor and sweat glands of the face and neck.

Mid-cervical ganglion: Often missing in about 60% of individuals, a middle cervical ganglion is about 0.7- 0.8 cm long and located at the level of the sixth cervical vertebra, just superior to the inferior thyroid artery. It has anatomical connections with the fifth and sixth cervical spinal nerves and contributes to the esophageal, tracheal, and aortic plexuses, although the middle cervical ganglion stimulates thyroid hormone secretion through noradrenergic neurons containing NPY. *(*Melander, et al. 1974, Grunditz at al, 1984, and Romaco et al. 1986).

Stellate ganglion and thoracocervical ganglion establishes itself as the main sympathetic innervation source:

1. Innervation of the heart by inferior cervical cardiac Nn. responsible for the acceleration and tachycardia, in addition giving up sensible fibers transferring the cardiac pain.
2. Feeding upper extremities with vasomotor, pilomotor, and fibers to sweat glands.

Provides fibers to the lungs, thyroid, and parathyroid gland. Its fibers penetrate the brain arteries by expanding its fiber network through the vertebral artery.

Parasympathetic Nervous System

There is no way of anatomically differentiating the parasympathetic nerves. The parasympathetic part of the autonomic nervous system is a functional physiologic pattern which is determined by its effect in the end organ. Sympathetic nerves do not originate from cervical or thoracic sympathetic trunk. They innervate the internal organs. Parasympathetic nerves like the sympathetic nervous system are switching in the preganglionic and post ganglionic centers. The pars Cephalica of preganglionic fibers originate from the accessory nucleus (autonomic) through fibers of the occulomotor nerve. Occulomotor nerve fibers reach to the ciliary Nn. breves (internal eye muscle), which then supplies the pupillary sphincter muscle. **Figure 4.**

Parasympathetic and sympathetic nerve fibers are deeply divided, intercepted, and interconnected and co-routed with countless intramural ganglions. Therefore, it is believed that signals are silenced or de-silenced just close to the end organ or at the entering point of the target tissue.

More important relay microganglia stations, especially in the Craniofacial area, may play an important role in diseases such as 'CCSVI", "Tourette Syndrome," and/or Orofacial Myodystonia, too.

Mesencephalic parasympathetic nuclei:

1. Superior Salivatory nucleuses with secretory fibers supply the intermedius nerve, major petrous nerve, and pterygopalatine ganglion. On its way, it gives fibers to the lacrimal n., and through tympanic chorda fibers, to the glandular Rr. to supply submandibular and sublingual glands.
2. Inferior Salivatory nucleus of the glossopharyngeal nerve communicates with glandular Rr. which reaches the parotid gland, passing petrous nerve and Otic ganglion.
3. Dorsal nucleus of Vagus nerve in the medulla oblongata contains numerous parasympathetic nerve fibers which innervate the upper gastrointestinal tract. It demonstrates frequent interconnections by communicating Rr. alongside the sympathetic trunk in thorax and abdomen.

The **sensitive fibers of the parasympathetic** system deliver more specific internal organ receptions than pain delivery. Their fibers penetrate the Vagus nerve and pelvic Nn. The Vagus fibers encounter connections with the sensible trigeminal nucleus and the posterior horn of the 2nd spinal segment. This interception often causes Vagus irritations to be felt at related trigeminal skin zones which may explain nausea and vomiting associated with migraine headaches. **Figure 1, 2, 3**. 8, 9

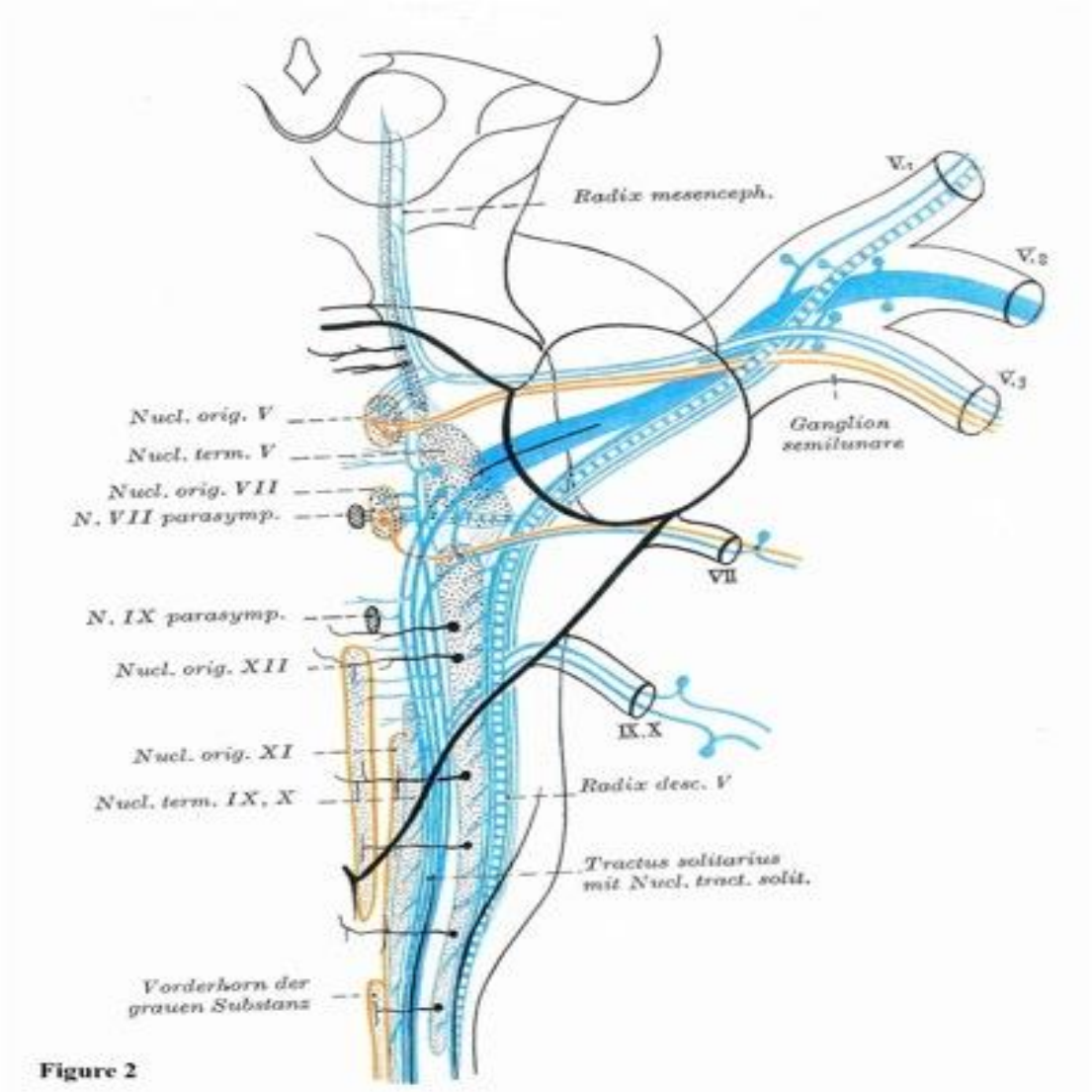

Figure 4: The main sensory nucleus receives its afferents (as the sensory root) from the semilunar ganglion through the lateral part of the pons ventral surface. *

*Sobbota/Becher: Atlas des Anatomie des Menschen, 16 Auflage 1960. Urban und Schwarz, München/Berlin. With friendly permission of Elsevier-de

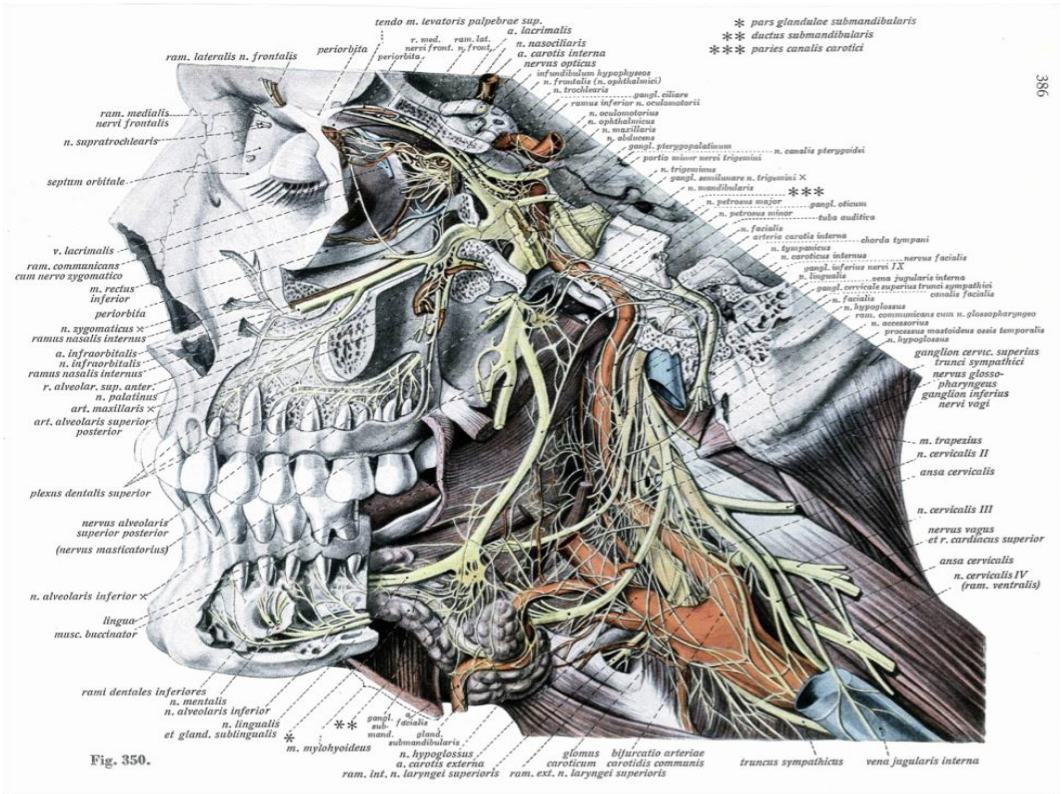

Figure 1: The basic anatomy of craniofacial autonomic nervous system including parasympathetic ganglia in craniofacial variations and contributions. *

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Thoracic trunk and Lumbosacral trunk

The three great gangliated plexuses are situated in front of the vertebral column in the thoracic, abdominal, and pelvic regions and are named, respectively, the cardiac, the solar or epigastric, and the hypogastric plexuses. They consist of collections of nerves and ganglia; the nerves being derived from the sympathetic trunks and from the cerebrospinal nerves. They distribute branches to the viscera.

The thoracic Sympathetic supply accelerator nerves to the heart. They are supposed to emerge from the spinal cord in the anterior roots of the upper four or five thoracic nerves and pass with the white rami to the first thoracic ganglion; here, some terminate, and others pass in the ansa subclavia to the inferior cervical ganglion. The postganglionic fibers pass from these ganglia partly through the ansa subclavia, to the

heart; on their way, they intermingle with sympathetic fibers from the Vagus to form the cardiac plexus.

Inhibitory fibers to the smooth musculature of the stomach, the small intestine and most of the large intestine are supposed to emerge in the anterior roots of the lower thoracic and upper lumbar nerves. These fibers pass through the white rami and sympathetic trunk and are conveyed by the splanchnic nerves to the Prevertebral plexus, where they terminate in the collateral ganglia. From the celiac and superior mesenteric ganglia, postganglionic fibers (inhibitory) are distributed to the stomach, the small intestine and most of the large intestine. Inhibitory fibers to the descending colon, the rectum and internal sphincter ani are probably postganglionic fibers from the inferior mesenteric ganglion.

The thoracolumbar Sympathetic are characterized by the presence of numerous ganglia which may be divided into two groups: central and collateral.

The central ganglia are arranged in two vertical rows, one on either side of the middle line, situated partly in front and partly at the sides of the vertebral column. Each ganglion is joined by intervening nervous cords to adjacent ganglia so that two chains, the sympathetic trunks, are formed. The collateral ganglia are found in connection with three great Prevertebral plexuses placed within the thorax, abdomen, and pelvis, respectively. [3]

The sympathetic trunks (truncus sympathicus; gangliated cord) extend from the base of the skull to the coccyx. The cephalic end of each is continued upward through the carotid canal into the skull and forms a plexus on the internal carotid artery; the caudal ends of the trunks converge and end in a single ganglion, the ganglion impar, placed in front of the coccyx. The ganglia of each trunk are distinguished as cervical, thoracic, lumbar, and sacral and except in the neck, closely correspond in number to the vertebrae. They are arranged as follows:

CERVICAL 3 GANGLIA: SUPERIOR, MID AND STELATE ganglions

THORACIC 12 GANGLIA

LUMBAR 4 GANGLIA

SACRAL 4-5 GANGLIA

In the neck, the ganglia lie in front of the transverse processes of the vertebrae, in the thoracic region in front of the heads of the ribs, in the lumbar region on the sides of the vertebral bodies and in the sacral region in front of the sacrum.

Connections with the Spinal Nerves Communications are established between the sympathetic and spinal nerves through what are known as the gray and white rami communicantes. The gray rami convey sympathetic fibers into the spinal nerves and the white rami transmit spinal fibers into the sympathetic. Each spinal nerve receives gray ramus communicants from the sympathetic trunk, but white rami are not supplied by all the spinal nerves. White rami are derived from the first thoracic to the first lumbar nerves, while the visceral branches run from the second, third, and fourth sacral nerves directly to the pelvic plexuses of the sympathetic and belong to this category. The fibers which reach the sympathetic through the white rami communicantes are medullated; those which spring from the cells of the sympathetic ganglia are almost entirely non-medullated. The sympathetic nerves consist of efferent and afferent fibers, the origin and course of which are described on the next page. 3

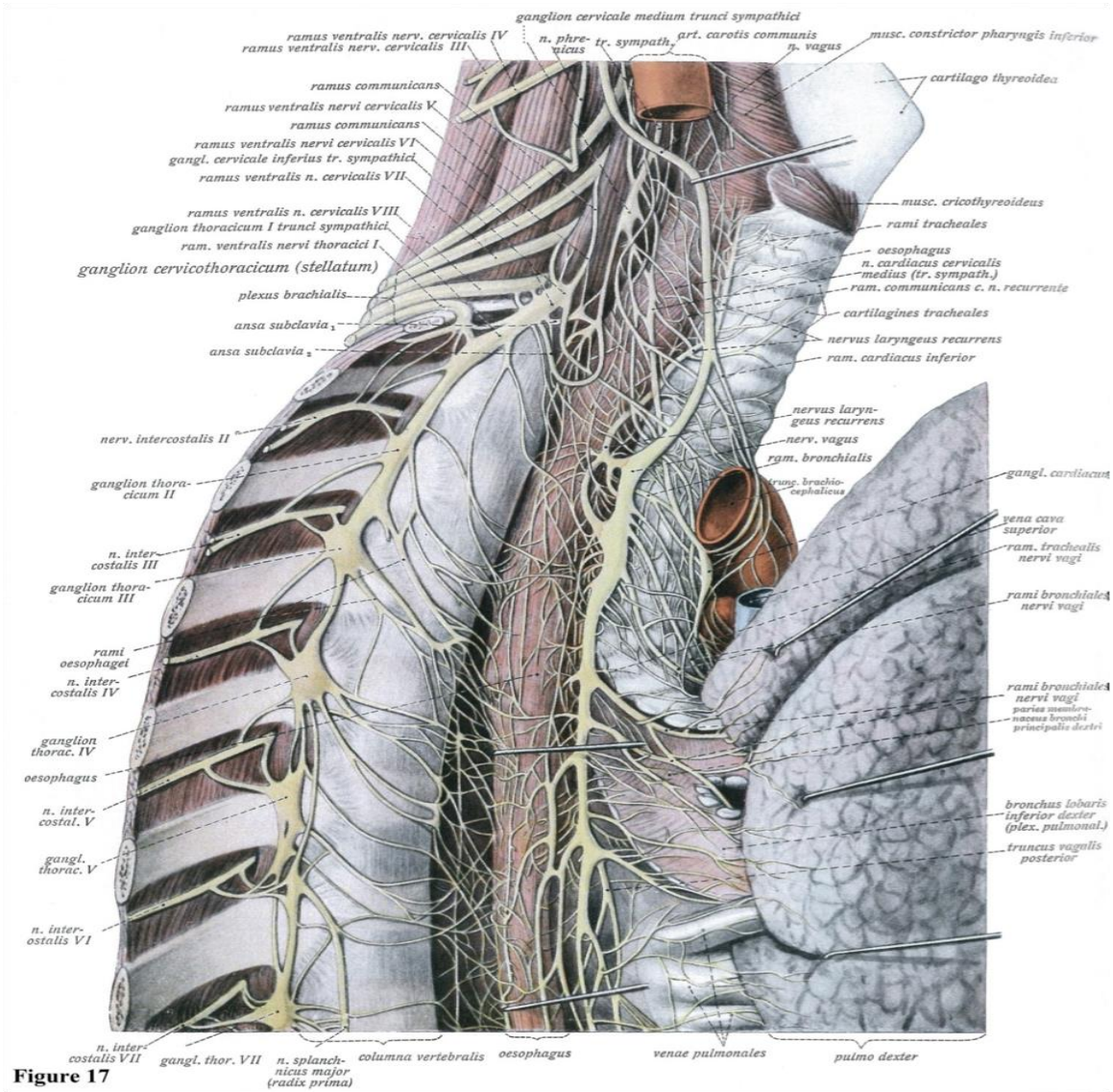

Figure 17

Figure 2 Thoracic sympathetic trunk. *
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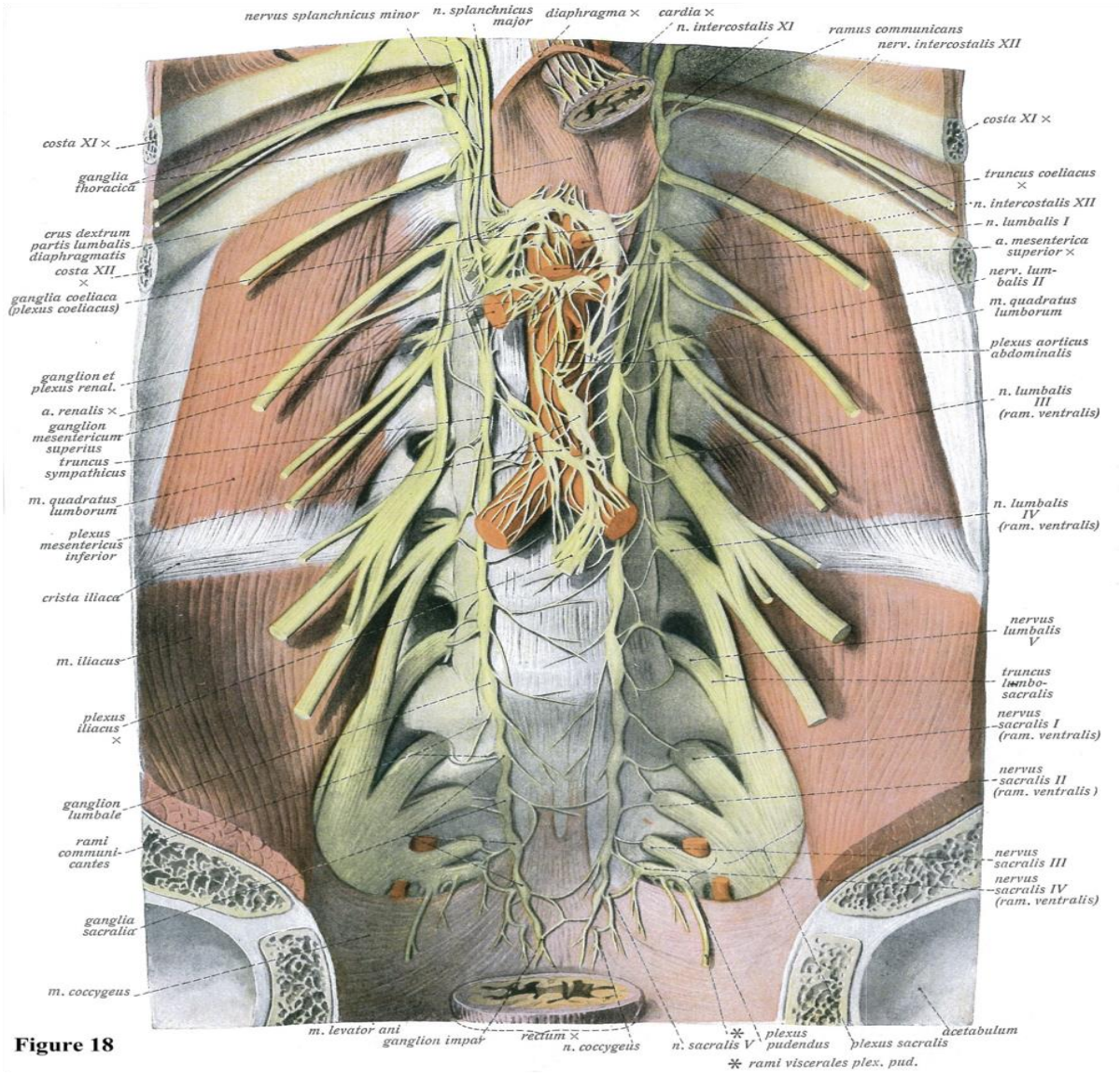

Figure 18

Figure 3: Lumbosacral sympathetic trunk. *
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Target Organ of the Autonomous Nervous System:

The tunica adventitia is the target organ of the sympathetic and parasympathetic nervous system. In addition, its nerve fibers penetrate and are embedded in the smooth muscles, glands, and other complex tissues.

The tunica adventitia, the outer layer of most blood vessel walls, has historically been regarded as a loosely organized collection of fibroblasts, perivascular nerves, and micro-vessels embedded in a collagen-rich extracellular matrix (ECM). Recent studies, however,

suggest a more complex and dynamic picture of the adventitia that emphasizes critical roles played by interacting adventitial cell types in growth, inflammation, repair, and disease of the artery wall. We now know that normal adventitia contains resident macrophages, mast cells, T cells, B cells, and dendritic cells and is a major site for immune surveillance and innate immune responses. [12]

Adventitia may demonstrate important physiologic factors compared to endothelium. The vasoconstrictory-vasodilatory behavior of the human veins of ongoing activity is mostly representative of the Cardiac systolic/diastolic rhythmic behavior. However, environmental, and hormonal factors play additional significant roles in the daily life of the autonomic nervous system. Like most tissues, blood vessels activate intrinsic mechanisms for tissue repair when injured or diseased. This capacity for repair of the artery/vein wall is substantial for continuation of life.

We understand that the adventitia of large elastic arteries is a mechanically active environment. The primary physiological function of these vessels is to absorb ventricular pulse pressures and to dampen the propagation of the pulse pressure gradient. [13] This is accomplished by expansion of the elastic fiber-containing artery wall and its relaxation again with each heartbeat. **The largest changes in wall diameter will occur in the outer layers, e.g., the adventitia.** These mechanisms are regulated directly by sympathetic and parasympathetic impulses, which provide continuation of life, keeping the internal equilibrium in human and animal life.

Concluding Remarks:

The autonomous nervous system is an independent, self-managed and self-controlled system serving a complex multifunctional internal organ system. It responds to internal and external stimuli independent of our consciousness and will. It is genetically determined and programmed. Modifications are possible only on the basis of cell biologic and

molecular evolution. Its dysfunction is the cause of many illnesses in vertebrates and mammals.

The above anatomic pattern and behavior of the sympathetic nervous system demonstrates extremely complex and evolutionary differentiated behavior within the human nervous system. To better understand the nature of craniofacial neuralgia and Migraine headaches, we hypothesized that the Central Nervous System with its 12 expansions are supplied only by their nourishing vasculature, VASA NERVORUM, of the arterial and venous system. Vasa Nervorum is controlled by the sympathetic and parasympathetic network complex, which genetically equilibrates its function by SILENCING AND DESILENCING signals independent of the Central Nervous System.

Biologic signaling system observed as the mechanism of fluency of messaging of biologic system in human and other species.

Recent years have witnessed a growing excitement in the field of mitochondrial biology with a dramatic increase in our appreciation for the diversity and complexity of mitochondrial function as an integrated cell signaling system. Rather than simply acting as isolated energy-generating organelles, as once thought, we now know that these organelles form a dynamic network that is subject to continuous remodeling and is integrated into the cellular signaling pathway. 14

In summary, recent molecular and cell biologic findings suggest that the adventitia maintains multiple types of progenitor cells that appear to act in concert as part of a coordinated healing response to vascular injury. We speculate that disorders such as "Chronic Cerebrovascular Insufficiency (CCSVI)", and "Trigeminal Neuralgia" are acquired events in the process of life and are directly associated with the autonomic nervous system and tunica adventitia of the Vasa Vasorum as well as Vasa Nervorum. **The nature of those disorders is vasoconstrictive, not vasodilative.** However, at this point, many questions will remain to be answered before the picture becomes clearer.

References at the end of part II