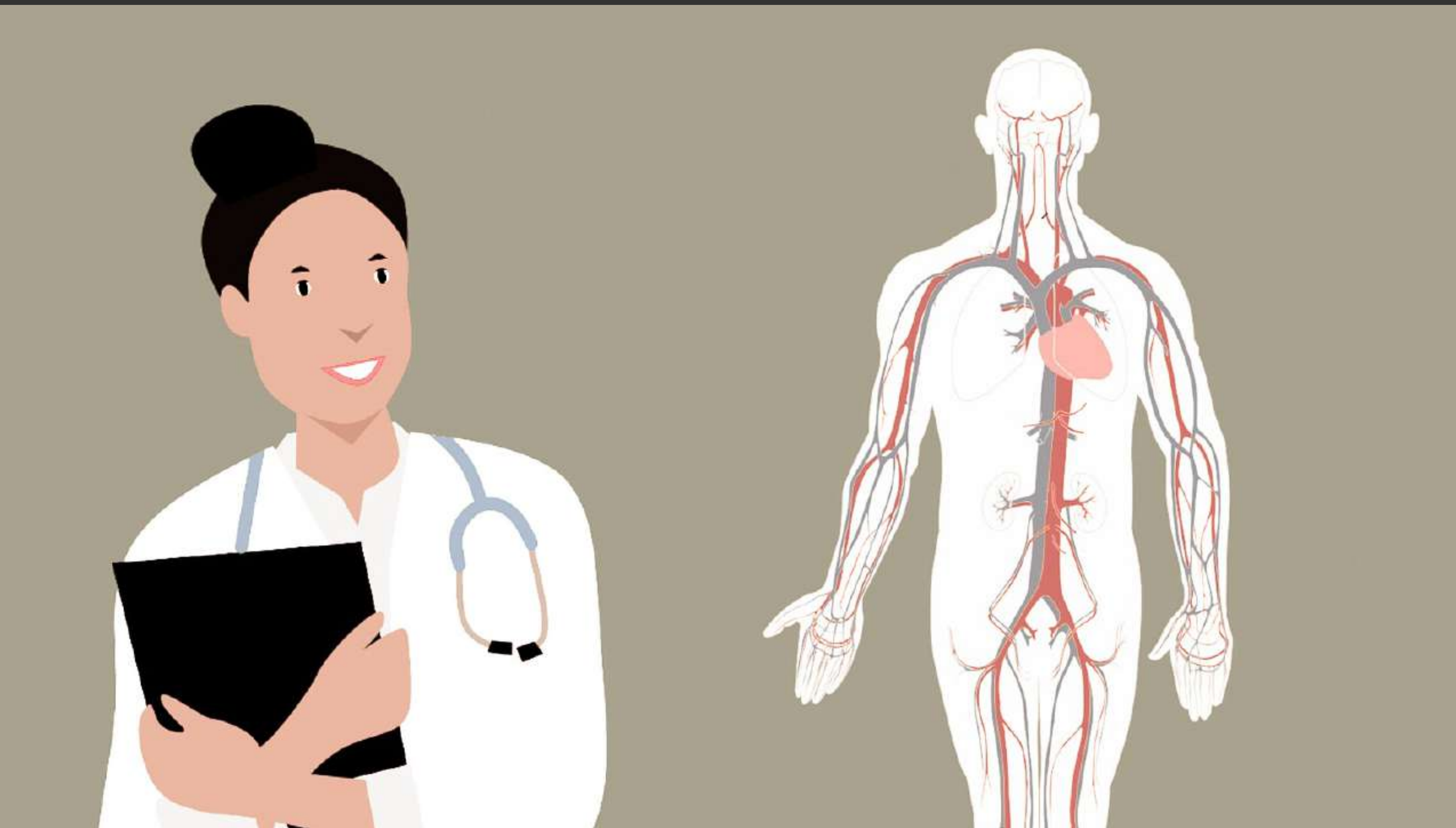
The Vagus Nerve: Considerations for Physical Therapists



Introduction 3
Section 1: Understanding the Vagus Nerve 1 3
Neuroanatomy 2,3 3
Neurophysiology 1,2 7
Sympathetic Nervous System (SNS) 7
Parasympathetic Nervous System (PNS) 6,7 12
Upregulation and Downregulation of the Vagus nerve 14 13
Section 1 Summary 14
Section 1 Key Words 14
Section 2: Clinical Presentation 14
Cervical Spine and the Vagus Nerve 2,15 14
Imbalance and the Vagus Nerve 20,21 17
Signs of Vagus Nerve Impairment and Referred symptoms 6,11,21 18
Section 2 Summary 20
Section 2 Key Words 20
Section 3: Intervention 20
Vagus Nerve Stimulation (VNS) 22–24 20
Modalities for Vagus Nerve Imbalance 24
Case Study and Reflection 26
Section 3 Summary 27
Section 3 Key Words 27
Section 4: Future Considerations 28
VNS 21,34,35 28
Other Considerations 28

Section 4 Summary 29
Section 4 Key Words 29
Conclusion 29
References 30

Introduction

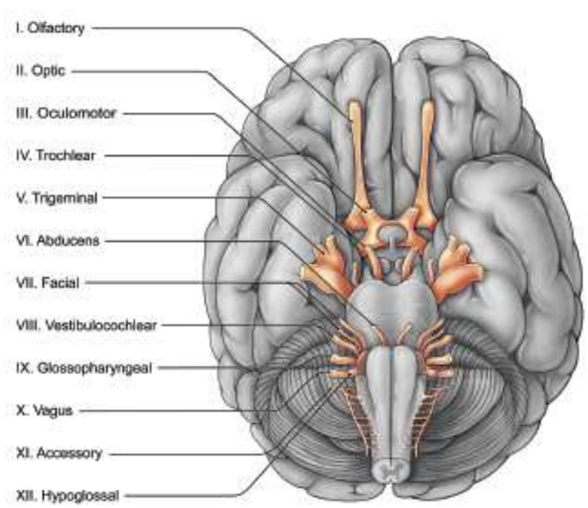
The vagus nerve is called the wandering nerve because it reaches and affects so many physiological processes in the human body. The vagus nerve is cranial nerve number 10 out of 12 cranial nerves, begins at the brain and terminates with branches throughout the neck, thorax and abdomen. Due to the high complexity of this nerve on sensory and motor function, Physical Therapists and Physical Therapist Assistants should be aware of the general anatomy and physiology, signs and symptoms of vagus nerve dysfunction and novel treatments for improving motor function in patients with vagus nerve dysfunction.

Section 1: Understanding the Vagus Nerve [1]

The vagus nerve is one of twelve cranial nerves in the human body and has a large impact on regulating function of several body systems. These include but are not limited to the cardiovascular, respiratory, immune and endocrine systems. The vagus nerve continues to be researched due to its complexity and is involved in regulation of homeostasis. The vagus nerve has motor and sensory components. Motor components are also called efferent nerves and sensory components are also known as afferent nerves.

Neuroanatomy [2,3]

The vagus nerve is cranial nerve ten and is the longest out of twelve cranial nerves. Due to it passing through several systems from the brain to the abdomen it covers the most area out of any cranial nerve.



https://www.enttoday.org/article/using-the-vagus-nerve-to-help-hearing/2/

Path of the vagus nerve

1. The vagus nerve originates at the medulla oblongata between the inferior cerebellar peduncle and the olive of the medulla oblongata

2. The nerve travels through the skull at the jugular foramen and here the nerve has superior and inferior ganglions which are described below. Each of these ganglion bodies also has sensory nerve cell bodies. These sensory cell bodies are pseudo unipolar, meaning there is one nerve cell body which has two axonal branches that separately connect to the central nervous system and the peripheral nervous system.

    a. Superior ganglion – “jugular ganglion”; a 0.5 cm ganglion that contains sensory cell bodies that collect information from the auricle and meningeal branch of the vagus nerve

        i. Auricular branch – gathers sensory information from the auditory canal and tympanic membrane in the ear and interacts with the facial and glossopharyngeal nerves (cranial nerves seven and nine respectively)

        ii. Meningeal branch – gathers sensory information from layers surrounding the brain such as the dura mater and meninges

    b. Inferior ganglion – “nodose” ganglion; a 2.5 cm ganglion that contains sensory cell bodies that collect information from the cardiovascular, respiratory and gastrointestinal systems

3. The spinal accessory nerve (cranial nerve eleven) travels with the vagus nerve distal to the inferior ganglion. After splitting into superior and inferior branches past exiting the skull with the vagus nerve, the superior branch collects sensory information from the pharyngeal, laryngeal and cardiac smooth muscle and the inferior branch innervates the motor function of the sternocleidomastoid and trapezius muscles. The spinal accessory nerve is mentioned here because of its shared involvement with the vagus nerve in regards to the cardiovascular, respiratory and gastrointestinal function.

4. The vagus nerve continues to travel inferiorly through the body, through the carotid sheath along with the carotid arteries and internal jugular vein

5. Anatomically, the vagus nerve on the right side of the body traverses anteriorly to the subclavian artery to the thoracic cavity near the trachea, to the right lung

and esophagus, forming the esophageal plexus (when conjoined with the left vagus nerve

6. Anatomically, the vagus nerve on the left side of the body traverses anteriorly to the left subclavian artery, travels inferiorly beside the aortic arch and posterior to the phrenic nerve (innervates the diaphragm). It travels posterior to the left lung and then to the esophagus and esophageal plexus to join the right vagus nerve

7. The vagus nerve from components of the esophageal plexus create the anterior and posterior gastric nerves which innervate the gastrointestinal musculature

8. In the neck, there are several branches of the vagus nerve

    a. Pharyngeal

        i. Originate from the inferior ganglion and are comprised of sensory and motor (from spinal accessory nerve) neuron fibers

        ii. The nerve fibers innervate the pharyngeal muscles and mucous membrane surrounding the pharynx. They go on to reach the pharyngeal plexus which is comprised of cranial nerve IX (glossopharyngeal) and the *sympathetic chain*

        iii. The intercarotid plexus is innervated by vagus nerve fibers, which then allow regulation of chemoreceptors in the carotid artery

    b. Superior laryngeal nerve

        i. Courses between the internal and external carotid arteries, crossing path of cranial nerve twelve and innervates larynx and area near the glottis in three divisions

    c. Recurrent laryngeal nerve (inferior laryngeal nerve)

        i. Splits into right and left branches which innervate the smooth muscle of the larynx

        ii. The nerve of Galen connects the superior and inferior laryngeal nerves and allows afferent and efferent output of the lining of the trachea and esophagus

        iii. Superior cardiac nerve

        a. Consists of three branches that interact with sympathetic nervous system

9. Branches in the thorax

    a. Inferior cardiac branch on the right originates from the vagal trunk next to the trachea; on the left it originates from the inferior laryngeal nerve

        i. The branches create the *cardiac plexus*

    b. Bronchial branches

        i. Three branches at the front of each lung root

        ii. Course to form the anterior pulmonary plexus after coursing with the *sympathetic trunk*

        iii. Also form the posterior pulmonary plexus with additions from the sympathetic fibers

        iv. Esophageal branches

            a. Anterior and posterior branches to create the *esophageal plexus*

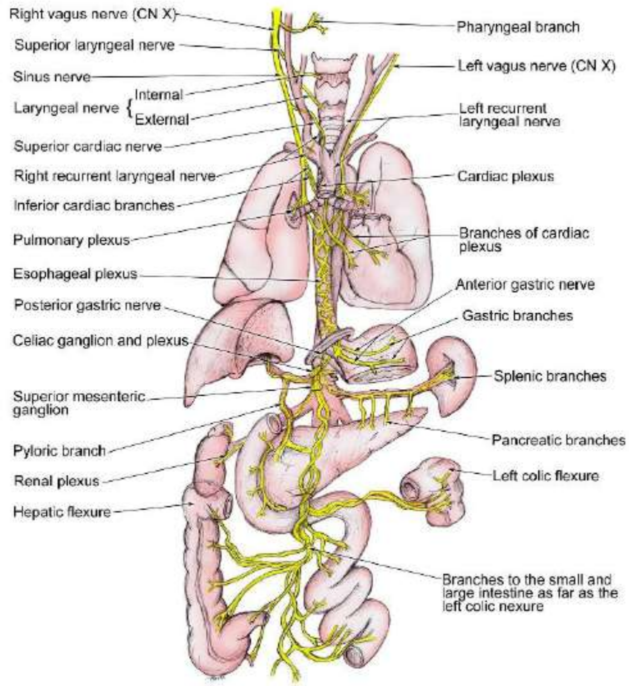
10. Branches in the abdomen

    a. Gastric branches from the vagus nerve supply the stomach and create the posterior gastric plexus and the anterior gastric plexus from the right vagus and left vagus respectively

    b. Celiac branches arise from the right vagus nerve and course with the celiac plexus to innervate several gastrointestinal organs such as the pancreas, spleen, kidneys, adrenal glands and intestine

    c. Hepatic branches arise from the left vagus nerve and course into the *hepatic plexus* to the liver

Branches and distribution of the vagus nerve



https://emedicine.medscape.com/article/1875813-overview#a1

Neurophysiology [1,2]

Physical Therapists and Physical Therapist Assistants should be aware of the general anatomy and physiology, signs and symptoms of vagus nerve dysfunction and novel treatments for improving motor function in patients with vagus nerve dysfunction. The vagus nerve is one of the major components of the Parasympathetic systems. The vagus nerve is comprised of both sensory and motor nerve fibers, with predominantly sensory fibers (around 75%). The nerve contains somatic and visceral afferents which provide sensory information from the body and smooth muscle of organs and visceral efferent fibers which provide motor innervation to smooth muscles and vessels in lungs, heart, gastrointestinal system, liver and pancreas. To better comprehend the involvement of the vagus nerve on these systems, we must first understand much more deeply the Sympathetic and Parasympathetic Nervous Systems. [1,4–8]

The sympathetic and parasympathetic nervous systems (in addition to the enteric nervous system) are part of the autonomic nervous system (ANS) which are responsible for regulation of involuntary processes in the body. These include digestion, breathing, circulation, release of neurotransmitters and a variety of other functions.

Sympathetic Nervous System (SNS)

The SNS is responsible for the fight or flight response for arousal for protection against danger as the heart and muscles receive more circulation and the digestive system receives less circulation and stimulation.

In the discussion of SNS function, it is important to understand the stimulation of various receptors throughout the body. Four specific receptors include the following:

a. Alpha 1 receptor – are found on smooth muscle of vessels throughout the body and determine resistance from arteries and capacity of veins to regulate blood pressure

b. Beta 2 receptor – allows smooth muscle relaxation and dilation of bronchioles in response to neurotransmitter and hormone signaling

c. Muscarinic receptor – parasympathetic nervous system receptors which allow rest and digest function via activation from acetylcholine

d. Adrenergic receptor – catecholamines (norepinephrine, epinephrine) activate

The Sympathetic Nervous Systems can work BOTH in direct opposition to as well as not in opposition to the Peripheral Nervous System (PNS).

The following describes systemic response for when the SNS is stimulated AND DIRECTLY OPPOSES the Peripheral Nervous System (PNS):

1. Gastrointestinal regulation occurs as an inhibitory response for gastrointestinal (GI) muscles. This reduces circulation to the GI muscles via stimulation of alpha 1 and beta 2 receptors and lessens secretion of digestive enzymes and shrinks sphincters throughout the digestive system. This physiology allows increased circulation and energy to be allocated to other systems in preparation for fight or flight.

2. Urinary regulation consists of smooth muscle relaxation of the detrusor muscle when the SNS is stimulated. This increases activation of the sphincter at the urethra, preventing urine from being released. The kidneys will also reach a higher circulatory volume due to increased renin secretion through beta 1 receptor activation.

   The detrusor muscle contracts during urination to allow urine to exit the bladder via the urethra and renin is an enzyme produced by the kidney which assists in blood pressure regulation.

3. Cardiac regulation occurs with increased heart rate and cardiac contraction force through stimulation of beta 1 and 2 receptors. This allows increased cardiac output and more allows oxygen to be delivered to tissues. Cardiac output is the amount of blood pumped per minute by each ventricle in the heart

4. Pulmonary regulation occurs as the bronchiole diameter is widened through stimulation of beta 2 receptors and lessens secretions to lungs. This allows increased oxygen exchange throughout the lungs

The following describes systemic responses for when the SNS is stimulated AND DOES NOT DIRECTLY OPPOSE the Peripheral Nervous System (PNS):

1. The SNS produces strong arterial constriction in skin, abdominal organs and kidney via alpha 1 receptors and less forceful arterial constriction in musculoskeletal system through alpha 1 and beta 2 receptors.
2. The SNS causes glucose production to increase in the liver due to increased energy demand through glycogenolysis and gluconeogenesis
3. The SNS increases whole body cooling through sweat production and the contraction of arrector pili muscles which pull hair away from the body
4. The SNS increases norepinephrine and epinephrine production through the adrenal medulla to move where they are needed in the body via fight or flight response

To better comprehend the influence of the Sympathetic Nervous System, we have outlined the origination and route of the Sympathetic Chain [9–13]

1. Begins at the base of the skull and ends at the coccyx on each side of the vertebrae
2. Sympathetic chain ganglia occur next to the sympathetic chain and include the cervical, thoracic, lumbar and sacral ganglia. The ganglia carry signals from their location to the central nervous system carrying information to fuel the fight or flight response.
3. The sensory pathway involves afferent nerves of the sympathetic nervous system travelling from the involved organ to the dorsal root ganglion to relay sympathetic information to facilitate a motor/efferent response. The motor pathways are described below.
4. Preganglionic neurons occur before the sympathetic chain as nerves leaving the spinal cord and continue as white rami communicates where they are able to communicate/synapse at the sympathetic ganglia. From there, postganglionic fibers communicate with spinal nerves to carry sympathetic signaling throughout the body from the ganglionic levels below. The white rami communicantes

contain SNS fibers from the spinal cord to the sympathetic trunk prior to the ganglia and the gray rami communicantes carry postganglionic fibers from the SNS to the spinal nerves.

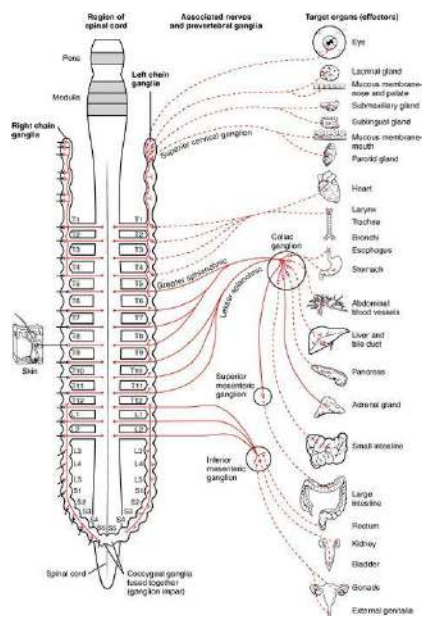
a. Cervical ganglia – there are three total ganglia whose fibers branch after the ganglion (postganglionic) to the head and neck to relay sympathetic information and responses of dilating the pupils, stopping lacrimation, constricting blood vessels of skin and widening opening of eyelids

    i. Superior cervical ganglion – located in front of the transverse processes of C2/3, varies in size, up to 3 cm long, 7 mm long and 3 mm thick

        1. Fibers after the ganglion (post ganglionic fibers) contribute to sympathetic response of tear production, pupil dilation, regulation of circulation to the head and neck, sweating of the face, provide communication to C1 to 4 spinal nerves, and contribute to the cardiac plexus via the superior cardiac nerve

    ii. Middle cervical ganglion – located just in front of C6 vertebra and around 7 mm long and 4 mm wide

        1. Post ganglionic fibers continue down the neural pathway to innervate the pharynx, trachea, larynx and esophagus, provide communication to spinal nerves at C5 to 6 level, and contribute to the cardiac plexus via the middle cardiac nerve



    iii. Stellate ganglion (inferior cervical) – located in front of C6 vertebra and 1.9 cm long, 7 mm wide and 2.5 mm thick.

        1. Post ganglionic fibers provide nerve signaling to the smooth muscle of the subclavian and vertebral arteries, communication to spinal nerves C7 and 8 and T1 and contribute to the cardiac plexus via the inferior cardiac nerve

2. Contribute to the oculosympathetic pathway – three pathways of neurons from the hypothalamus, the level C8 to T1 of the spinal cord and the superior cervical ganglion travel to supply response of the oculomotor pupillary response of dilation

3. Horner Syndrome – results from disruption of the oculosympathetic pathway and includes three signs: ptosis (upper eyelid droops), miosis (pupil constriction) and anhidrosis (unable to sweat and regulate body heat)

b. Thoracic ganglia – from spinal levels T2 to T12 and ganglia arise next to vertebral bodies in the posterior mediastinum

i. Spinal nerves T1 to L2 innervate the wall of the trunk and make up the splanchnic nerves to innervate the organs of the abdomen and pelvis

ii. T5 to 10 form the greater splanchnic nerves and T10 to 11 form the lesser splanchnic nerves

1. The liver, gallbladder, spleen, pancreas, esophagus, stomach, proximal duodenum and adrenal glands are innervated through the celiac plexus

2. The appendix, ascending colon and proximal transverse colon are supplied by the superior mesenteric plexus

3. The kidneys are supplied by the aorticorenal ganglion

4. Levels T12 (least splanchnic) through L2 innervate the upper anal canal and hindgut

c. Lumbar ganglia – comprised of four ganglia; a lumbar sympathetic chain is located anterior and lateral to the lumbar vertebral bodies

i. Spinal nerves L3 and lower innervate the superficial aspect of the lower extremities

ii. The splanchnic nerves begin at the four lumbar sympathetic ganglia which supply motor innervation and contribute to the development of several plexuses throughout the abdomen including the celiac, renal, inferior mesenteric, superior hypogastric. Activity at these plexuses include regulation of abdominal and pelvic organ sympathetic activity, mediated by hormones and neurotransmitters. The main sympathetic function is to redirect circulation from abdominal and pelvic organs to skeletal muscles (fight or flight).

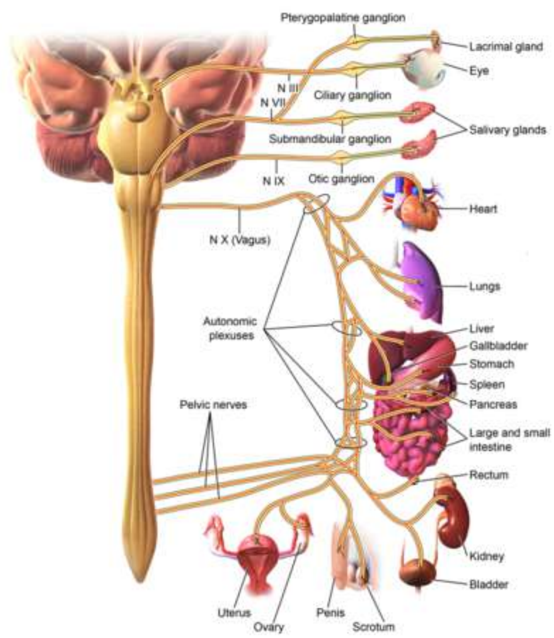
d. Sacral ganglia – levels S1 to S5 and found in front of the sacral foramen of S1 to S2 spinal levels

    i. Innervation of the bladder, rectum, reproductive organs to mediate sympathetic motor response of stopping function of these organs to redirect circulation to skeletal muscle

Parasympathetic Nervous System (PNS)

6,7

The PNS is responsible for the “rest and digest” phase after fight or flight response from the SNS. It is comprised of the vagus nerve (CN 10), oculomotor nerve (CN 3), facial nerve (CN 7) and glossopharyngeal nerve (CN 9). When activated, the PNS provides a complex function of excitatory and inhibitory response on the GI system. The efferent vagus nerve is the major nervous structure of the parasympathetic autonomic nervous system.



Parasympathetic Innervation

https://me-pedia.org/wiki/Vagus_nerve

PNS regulation is outlined below

1. Cardiac regulation occurs as a result of vagus nerve branches for the heart coursing from the thorax to regulate the sinoatrial and atrio ventricular cardiac nodes via muscarinic receptors (M2 receptors). This allows regulation of resting heart rate keeping it right around 70 beats per minute. If the vagus nerve weren’t active in the cardiac system, the resting heart rate may be 100 beats per minute or more.

The sinoatrial node regulates contraction of the atria or upper chambers of the heart (the body's pacemaker) and the atrioventricular node regulates contraction of the ventricles, or bottom chambers of the heart.

2. Gastrointestinal regulation occurs as parasympathetic or "rest and digest" function in the GI system and results in smooth muscle activation and secretions of digestive enzymes to organs via innervation of digestive organs such as the esophagus, stomach and intestines.

There is interplay of the enteric nervous system (ENS) to the sympathetic and parasympathetic nervous system in this area. The enteric nervous system has a vagal nerve plexus along the entire gastrointestinal tract and interacts with the vagus nerve through the secretion of cholinergic neurotransmitters and receptors.

3. Pulmonary regulation in the PNS constricts bronchioles and increases secretions to bronchioles due to low demand for oxygen exchange

4. In addition to these functions the PNS stimulates saliva production, eye lubrication via lacrimation, urine production through smooth muscle activation in the bladder, defecation through smooth muscle activation in the intestinal sphincters

Upregulation and Downregulation of the Vagus nerve [14]

Upregulation and downregulation are important to understand in regard to the vagus nerve and the sympathetic and parasympathetic nervous systems. Upregulation is when the amount of receptors for a neurotransmitter increase and downregulation is when the amount of neurotransmitters decrease for a synapse.

Upregulation

Defined as an increase of the number of receptors for a neurotransmitter or increasing other components of the synapse. Sympathetic upregulation increases the neurotransmitters of norepinephrine and epinephrine which allow quick response of the SNS to prepare for fight or flight. Parasympathetic upregulation involves increased release of the neurotransmitter acetylcholine to prepare for rest and digest function.

Downregulation

Defined as a lower number of neurotransmitter receptors or decrease of another component of the synapse. Sympathetic downregulation decreases the neurotransmitters of norepinephrine and epinephrine which allow reduction of the flight or flight response. Parasympathetic downregulation involves decreased release of the neurotransmitter acetylcholine to block the rest and digest response, and create avenue for fight or flight

Section 1 Summary

The vagus nerve is known as the wandering nerve due to it reaching multiple organ systems throughout the abdomen and pelvis. It is involved a series of complex responses throughout the body through the autonomic nervous system branches of the SNS and PNS.

Section 1 Key Words

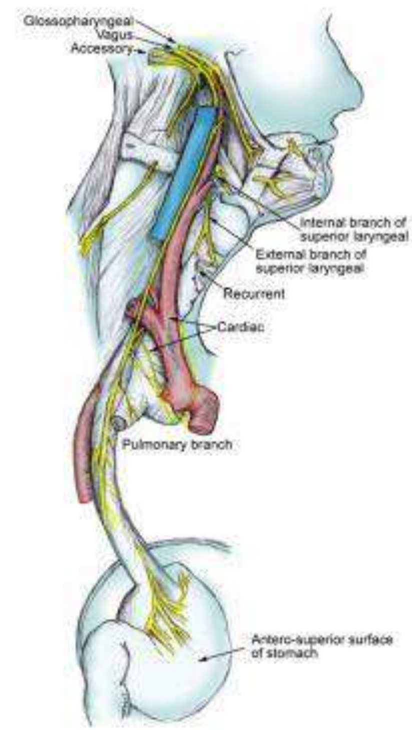
1. Cranial nerve – twelve nerves that exit the brain to elicit function on the head, neck and trunk
2. Ganglia – neuronal cell bodies in a mass found in the peripheral nervous system
3. Pseudo unipolar – neuron with a singular extension from its cell body

Section 2: Clinical Presentation

Due to the complexity of the path of the vagus nerve and its impact on physiology, clinicians should be aware of signs and symptoms of vagus nerve dysfunction and know how to screen for them. It is appropriate in most cases to refer a patient to primary care for work up with symptoms of vagus nerve dysfunction.

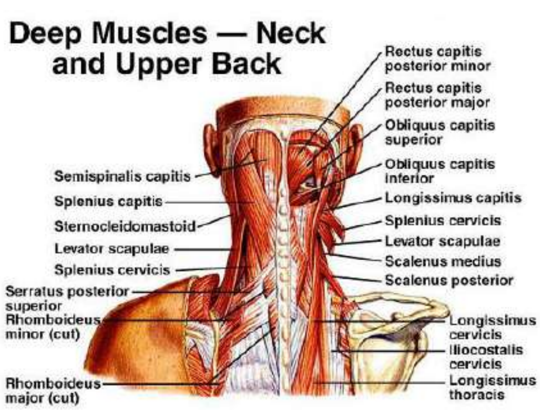
Cervical Spine and the Vagus Nerve [2,15]

The vagus nerve courses from its origin at the medulla oblongata through the jugular foramen then through the carotid sheath (alongside the carotid artery and jugular vein) to branch off as pharyngeal branches, superior laryngeal nerve, recurrent laryngeal nerve and the superior cardiac nerve. The carotid sheath is within the deep fascia of the neck and is located posterior to the sternocleidomastoid muscle. Due to its proximity to cervical musculature and spinal segments, cervical alignment and muscle tension can have a role in vagus nerve dysfunction.



Effect of Cervical Muscular Tension on Vagus Nerve [16]

Patients with muscular shortness or tension in the muscles surrounding and stabilizing the cervical spine may have vagus nerve compression and disruption of nerve signaling. These muscles include the scalenes, splenius cervicus and levator scapulae. It is important for clinicians to screen for muscle shortness, tension and trigger points in these muscles as part of a comprehensive cervical spine examination. Clinicians should screen for symptoms of vagus nerve dysfunction such as dizziness, nausea, digestive problems, and mental health disorders such as anxiety and depression on intake forms. If symptoms of vagus nerve dysfunction are present and severe, a referral to primary care is necessary. Physical therapy should include a comprehensive upper quarter examination and treatment of muscle tension, joint stiffness and poor quality of movement. Physical therapy interventions would likely include soft tissue mobilization, mobilization of joint stiffness and progression of activation and strengthening exercises for cervical, scapular, thoracic and shoulder muscles to achieve balance in the upper quarter.



https://www.raynersmale.com/blog/2016/7/26/cervical-motor-control-part-1-clinical-anatomy

Effect of Cervical Instability on Vagus Nerve [17]

There are many causes of cervical spine instability such as cervical spondylosis and laxity of the ligaments between the top vertebrae and the skull. Cervical spondylosis is progression of disc degeneration and bone spurs along vertebrae in the neck and often worsens with age. With cervical instability, vertebrae deviate from their normal position which can result in compression vasculature or the vagus nerve. The vagus nerve's signaling from sensory and motor response is disrupted when it is compressed by vertebrae in poor position, tension in cervical muscles or bone spurs. This disruption of nerve signaling is called a conduction block, which can alter vagus nerve functioning from the digestive system, thorax or neck. Current evidence is citing cervical spine instability with disruption of vagus nerve signaling at least partially to blame for digestive issues including constipation, stomach pain, bloating, irritable bowel syndrome and gastroesophageal reflux disease (GERD).

How to identify and treat patients with cervical instability [18,19]

1. Special Tests
    a. When cervical spine instability is suspected clinicians should conduct tests prior to treatment to ensure neurologic damage does not occur
    b. Sharp Purser Test
        i. Assesses stability of the joint between C1 and C2 (atlantoaxial joint)
        ii. The clinician instructs the patient to sit in a chair and places the palm of one hand on the patient's forehead, and the index finger of the other hand at the spinous process of C2 to stabilize C2. The clinician then has the patient flex the neck slightly and pushes posteriorly on forehead.
        iii. This test is positive if a patient has reduced symptoms of pain or discomfort in the cervical spine or a click/clunk in the region.
    c. Transverse Ligament Stress Test
        i. Tests for laxity of the atlantoaxial joint
        ii. The clinician instructs the patient to lay supine and supports the skull with the palm. The clinician puts index fingers of both hands

between the base of the occiput and C2 spinous process and raises the patient’s head. This position is held for about 20 seconds and symptoms of a positive test are neurologic signs such as pupil changes, nystagmus, dizziness, nausea, altered sensation of the face or extremities and muscle spasm. The clinician may also feel a soft end feel from C1 to 2 instead of the normal hard end feel.

2. Patients with cervical spine instability should be referred to primary care for imaging. Once cleared by stabilization intervention (surgical, conservative with bracing or in mild cases no intervention) physical therapy can begin.
    a. Exercise program
        i. Gentle active range of motion in cervical spine with careful monitoring of neurological signs
        ii. Activation and strengthening of the deep neck flexors including the longus colli, longus capitus, rectus capitus and longus cervicus
        iii. Scapular and shoulder strengthening with appropriate cervical spine position
        iv. These exercises would progress from gentle range of motion in the cervical spine to strengthening and resistive exercise in the cervical spine, scapula and shoulders when correct form and no neurologic signs are present (paresthesia, dizziness, nausea, etc.)

Imbalance and the Vagus Nerve [20,21]

The vagus nerve passes through the neck and has a large role in regulating blood pressure and heart rate. Therefore, vagus nerve dysfunction can impact a person’s perception of balance through processes of the vasovagal response and disruption of sensory information from the abdomen and thorax to the brain. Imbalance can also occur from vestibular migraines and postural perceptual dizziness. Each of these causes of imbalance is explained below.

1. Vestibular migraines and other balance problems have been linked to vagus nerve dysregulation. Patients with vestibular migraines will have sudden bouts of imbalance, sometimes severe headache, sensory sensitivity and nausea.

2. Postural perceptual dizziness – increased activity of sympathetic nervous system causing symptoms of dizziness, increased heart rate and sweating

3. Vasovagal Response

   Vasovagal response or vasovagal syncope occurs due to a vasovagal reflex of dilating blood vessels in the lower extremities, lowering blood pressure and slowing down the heart rate. These factors cause a loss of consciousness or syncope. This usually happens when people are standing or sitting. Symptoms that occur prior to syncope include dizziness, sweating, nausea, tinnitus and vision changes. Symptoms that occur after the episode include continued nausea and dizziness and loss of appetite and fatigue. Some triggers of vasovagal syncope are severe pain, difficulty urinating or defecating, traumatic events, heat, hyperventilation and overconsuming alcohol or substances.

   It is important for Physical Therapists and Physical Therapist Assistants to be aware of what triggers and follows a vasovagal response. If this happens to a patient while in clinic, it is important to have them lay down and elevate their legs or sit down with their head between their knees to raise blood pressure. If this is a patient's first vasovagal response or they have recurrent responses that are not managed by a physician, it is important to refer to primary care.

Signs of Vagus Nerve Impairment and Referred symptoms [6,11,21]

If a healthcare provider observes the following signs and symptoms the vagus nerve may be involved. Physical Therapists should consider referral to their patient's primary care physician to treat patients with vagus nerve dysfunction holistically. The rest of the medical team may involve nutrition specialists such as dietitians, physicians specializing in hormone balance, neurology, functional medicine and digestion (gastroenterologist) and psychologists/psychiatrists.

1. Cardiac Symptoms

   a. Abnormal blood pressure or heart rate could be caused by a poorly functioning vagus nerve. Vitals should be monitored as part of a comprehensive physical therapy evaluation and treatment. If abnormal vitals are noted, the patient should be sent to primary care or if emergent or severely abnormal, sent to the emergency room for workup.

2. Vocal Changes

   a. Vocal changes could be related to poor functioning of the cervical vagus nerve branches including the pharyngeal, superior laryngeal and recurrent laryngeal nerve

3. Anxiety and/or depression

   a. Partially caused by imbalances in neurotransmitters of dopamine, serotonin and norepinephrine. When norepinephrine is overactive, anxiety can result due to vascular constriction and heightened blood pressure as part of the vagus sympathetic response.

   b. Intake forms for physical therapy should screen for mental health concerns and therapists should refer to appropriate mental healthcare provider

4. Digestive issues

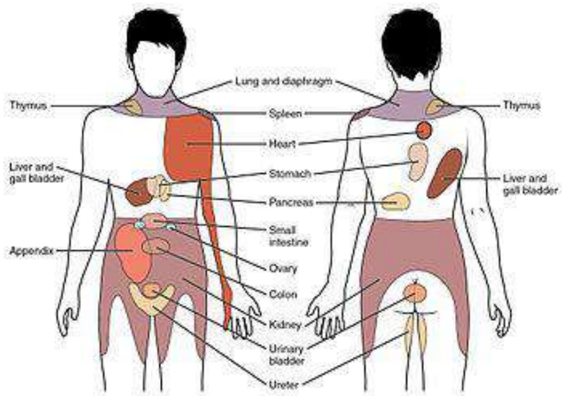
   a. The vagus nerve serves as the main connection between the autonomic nervous system, including the sympathetic, parasympathetic and enteric nervous systems. There can be a disruption of signaling or a conduction block somewhere in the widespread gastrointestinal enteric nervous system plexus or an issue with neurotransmitter communication from the ENS to the PNS. This will result in poor digestion, nausea/vomiting, abdominal pain, constipation and possibly conditions like irritable bowel syndrome.

   b. Physical Therapists should screen for digestive problems on intake forms and through subjective history and refer to primary care for further workup to treat their patients holistically.

5. Referral patterns from vagus nerve and viscera

   a. Sensory/afferent nerve fibers relay information from the abdominal organs to the CNS. This occurs at the same level of spinal nerve afferent fibers in the gray matter of the spinal cord. This close relationship can create diffuse referral patterns of pain or sensation throughout the abdomen but also in areas that the spinal nerves gather sensory information from, on the shin as indicated in the diagram below.

https://en.wikipedia.org/wiki/Referred_pain#/media/File:1506_Referred_Pain_Chart.jpg



Section 2 Summary

The vagus nerve has extensions to organs throughout the abdomen and pelvis including the heart, lungs, abdominal viscera and pelvic organs. Clinically, patients can have dysfunction of any of these areas with a poorly conducting vagus nerve. It is important for clinicians to recognize, refer and treat patients with vagus nerve dysfunction.

Section 2 Key Words

1. Cervical instability – Occurs when ligaments are lax or damaged in the cervical spine, usually between the skull and the first and second vertebrae
2. Vasovagal response – syncope or fainting that occurs as a result of low heart rate and blood pressure in response to a stimulus or trigger

Section 3: Intervention

The treatments in this section are relatively new and continue to be researched in improving quality of life in patients with vagus nerve dysfunction. Vagus nerve stimulation and other modalities will be highlighted in this section.

Vagus Nerve Stimulation (VNS) [22–24]

VNS is a treatment for many conditions where small and steady pulses of electricity are sent to the central nervous system and brain through a vagus nerve stimulator device. It is theorized that VNS works by increasing release of neurotransmitters of acetylcholine and norepinephrine in the cerebral cortex by stimulation of the nucleus basalis and locus coeruleus neurons. Excess neurotransmitters increase the amount of synapses to improve neuronal function. Common disorders that VNS is useful for include epilepsy, depression and chronic heart failure. Patients should not undergo VNS if they have only one vagus nerve, have another type of brain stimulation, have abnormalities in their heart or ANS, have lung disease, vasovagal syncope or ulcers.

Vagus nerve stimulators are implanted by a neurosurgeon as an outpatient procedure under anesthesia. A device called a pulse generator is implanted on the superior left aspect of the chest and wires are connected to the vagus nerve at the inferior aspect of the neck. The battery in the pulse generator typically lasts years and is replaced by a neurosurgeon when it is low.

Patients may experience side effects of VNS implantation including vocal changes, throat and neck pain, headache, problems sleeping, problems digesting, muscle twitching and altered sensation.

Epilepsy

1. VNS aims to decrease the severity, length and recovery time from epileptic seizures
2. VNS is used in combination with antiepileptic drugs
3. VNS typically takes a couple years to have an effect and does not work in reducing seizure severity or frequency in all patients
4. Patients may experience improved mood, memory and cognition and less trips to the emergency room if VNS is working

Treatment Resistant Depression

1. Research continues to follow up on the utility of VNS in treating depression. Contradicting evidence exists on outcomes and benefits to patients
2. Studies indicate that after one year, 30 percent of patients with VNS as a treatment saw large improvements in symptoms and 15% state their depressive symptoms completely went away

VNS on Upper Extremity Limb Function after Cerebrovascular Accident (CVA) [24–27]

CVA can have a profound impact on upper extremity limb function. Just over half of CVAs affect the middle cerebral artery, which supplies the motor cortex of the upper extremity in the brain. Most CVAs are ischemic (near 90%), meaning an occlusion of blood supply to a part of the brain occurs from an embolus or a blood clot. After ischemic CVA over half (60%) of patients experience motor dysfunction of the upper limb. Vagus nerve stimulation is a newly researched treatment method for assisting motor recovery of the upper extremity after CVA.

1. VNS is safe for patients who are six months or greater from the time of their CVA
2. VNS works to improve plasticity in the motor cortex in the area of upper extremity and forearm function. It is best used in combination of specific movement and exercises which emphasize upper extremity coordination, proprioception and functional activity
3. VNS for recovery of upper extremity function after CVA stimulates the cervical vagus nerve and is either implanted or completed transcutaneous
4. Example of protocol
    a. 0.8 mA for intensity, 30 Hz for frequency, 100 pulse width and 0.5 second pulse train
    b. Typically around three times per week for six weeks plus upper extremity specific exercises in clinic including shoulder, wrist and finger coordination, activation and strength
5. Risks of VNS include nausea, vocal problems, skin irritation, taste differences and infection from the wound to implant the VNS device
6. Outcomes to support use of VNS for return of upper extremity function post CVA
    a. Fugl-Meyer Assessment-Upper Extremity (FMA-UE) – assesses upper extremity motor function, sensation, range of motion and pain specifically in people who have hemiplegia post CVA
        i. From an overview of six studies on recovery of motor function post CVA using VNS plus rehabilitation versus rehabilitation alone, patients who received VNS plus rehabilitation significantly

improved upper extremity function via the Fugl-Meyer Assessment at two month follow up

ii. At three months and one year follow up, patients who received VNS plus a home exercise program focused on upper extremity motor control, activation and coordination were able to increase Fugl-Meyer scores by between 9 and 10 points

iii. For the FMA-UE, the minimal detectable change (MDC) is 5.2 and the minimal clinical important difference (MCID) is 10 points. Therefore, an improvement of 9-10 points is statistically significant and just detectable by the patient

b. Other outcomes that studies have examined include Box and Block test, the Nine Hole Peg test, the Stroke Impact Scale, Motor Activity log and the Wolf Motor Function test which did not improve significantly in score after protocol of VNS

i. Box and Block Test – test of upper extremity dexterity

ii. Nine Hole Peg Test – test for finger dexterity

iii. Stroke Impact Scale – subjective reported scale that assesses quality of life and disability after CVA

iv. Motor Activity Log – assessment of functional use of upper extremity

v. Wolf Motor Function Test – assessment of timed upper extremity motor function

7. Transcutaneous VNS improves upper extremity function more than implanted VNS in patients with upper extremity hemiplegia following CVA

8. Overall, research within the past few years supports use of VNS for functional recovery of upper extremity function after chronic CVA. Additional research on parameters of VNS and protocol of upper extremity rehabilitation and assessment of long term follow up are currently being researched

Modalities for Vagus Nerve Imbalance

As the vagus nerve continues to be studied in research, various alternative treatments are being proposed to help stimulate the vagus nerve and elicit parasympathetic response. Patients may ask about these treatments for referral or efficacy at their physical therapy visits.

Acupuncture [28]

Acupuncture is a branch of traditional Chinese medicine where a practitioner uses fine needles to puncture skin in specific areas or acupuncture points. The practitioner can use electrical stimulation or leave needles in the skin to achieve desired effects on the body.

The effects of acupuncture on vagus nerve regulation is being currently investigated. There is evidence of successful treatment of cardiac vagus nerve regulation for conditions such as atrial fibrillation by stimulating the auricular branch of the vagus nerve. Completing acupuncture with transcutaneous electrical stimulation at this point has shown a 5 percent drop in heart rate and a significant increase in heart rate variability by about 20 percent. It is theorized that the stimulation of the auricle branch of the vagus nerve will create activity in the parasympathetic nervous system.

Chiropractic [29]

When done at specific spinal levels, chiropractic adjustment and physical therapist manipulation are theorized to help regulate PNS and SNS functioning. This is due to the release of endorphins and neurotransmitters at the respective spinal level and the effective relay of this information to the CNS. According to recent research29, adjustment and manipulation of the cervical spine has improved symptoms of depression.

Manipulation and adjustment will remediate poor joint alignment. As explained in a prior section, compression on the vagus nerve from poor cervical alignment can alter functioning of the autonomic nervous system and vagus nerve. Manipulation in these areas followed up with stabilization and strengthening exercises can relieve compression on the vagus nerve and any symptoms associated with this (depression/anxiety, poor digestion, abdominal pain).

Dietary, Supplements [30,31]

Evidence supports supplementation of omega 3 fatty acids including DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid). These can assist in reducing stress and inflammation in the body and improve vagus nerve function. In addition, food that regulates the gut microbiome will also improve vagus nerve functioning due to optimizing the interplay between the enteric and autonomic nervous systems. The gut microbiome is involved in immune function and digestion and comprises a complex array of bacteria, viruses and microbes that sit mostly in the large intestine. Prebiotic fiber and probiotics have been shown to increase microbiome activity and improve digestion, stress and vagus nerve parasympathetic response. There is also evidence that diet imbalances including high fat and low carbohydrate or high carbohydrate and low fat diets negatively impact vagus nerve functioning. Clinicians should refer patients to a dietitian for improving gut activity as it influences the vagus nerve and health immensely.

Mindfulness [32]

1. Practices such as meditation, Tai Chi and some types of yoga involve slowing breathing, increasing exhalation time, shifting breath to the diaphragm rather than the chest and practicing mindfulness while completing this breath work with specific movements
2. These practices have been shown to lower resting heart rate, blood pressure and improve the relaxation response of the parasympathetic nervous system.
3. People who regularly practice meditation, tai chi and yoga have lower levels of depression, anxiety and inflammation and less sympathetic nervous system activity than those who have never practiced
4. As an expansion of breath work, humming and singing during yoga or separately can relieve a person's perceived stress via the vagus nerve connection to the larynx. This will stimulate the larynx and send afferent information through activating the parasympathetic and relaxation response to the central nervous system

Cold Water Immersion [33]

Repeated cold stimulation and cold water immersion have been proven to improve cardiac response to stress by lowering resting heart rate and improving heart rate response to stress over time. A higher heart rate variability and a low resting heart rate indicate good cardiovascular health and stress response, and this is associated with parasympathetic relaxation response. Completing regular cold water immersion such as cold showers or application of cold compress to the neck are ways to achieve these physiological benefits. This is an area that is continuing to be studied as a strategy for stress mitigation.

Case Study and Reflection

Brenda is a 45 year old female that comes for physical therapy evaluation direct access due to balance problems. She works as a laborer in a warehouse, stocking packages for delivery. She is obese at a body mass index of 32, has prediabetes and recently diagnosed with atrial fibrillation. Brenda reports at work the past two weeks she has fallen over twice attributing it to poor balance. When asked if she lost consciousness, Brenda states "I woke up within 10 seconds so I didn't think that was an issue." For the past couple years, Brenda has been frustrated by her balance and recalls falling around the house around once per month due to tripping on objects. On her intake form, Brenda indicates she has had a depressive mood four days per week and digestive issues including abdominal pain and bloating.

Q: What additional information should a Physical Therapist ask prior to either treating or referring this patient?

A: A Physical Therapist may inquire what Brenda experienced prior to and after the loss of consciousness, if she has ever experienced this before and if she has sought the opinion of her primary care physician

After asking the above questions, Brenda reveals that all she remembers was being very stressed at work due to the busy season of delivering packages. She states she has never experienced this before and has not gone to her primary care physician because she thought she would be referred to physical therapy for balance.

Q: Based on the information above, what steps should a Physical Therapist take in treating Brenda?

A: Due to the loss of consciousness, new diagnosis of atrial fibrillation and the fact that she has not sought recommendation from a physician, a Physical Therapist should refer this patient to primary care prior to treating.

After Brenda returns from primary care a week later and the physical therapy clinic is able to see the notes from her visit, the cause of fainting was a vasovagal response. Brenda is not able to state what intervention the physician suggested to complete to remediate this.

Q: Brenda inquires what a vasovagal response is and what to do about it. What could a therapist say in response?

A: A vasovagal response is usually caused by an outside trigger, like extreme stress on the body, and happens due to a drop in heart rate and blood pressure. Safety strategies are to sit down with the head between knees or lay down with feet elevated if she feels dizziness or lightheadedness beginning.

Q: How should the Physical Therapist proceed in treating Brenda?

A: A therapist should treat Brenda for her balance difficulties as they are separate from her vasovagal response. Throughout treatment, the therapist should inquire and refer again if she faints another time. A therapist may offer information on vagus nerve functioning, relaxation and meditation strategies, and alternative treatments on improving stress and vagus nerve functioning such as chiropractic, acupuncture and cold water immersion.

Section 3 Summary

Therapists should be aware of treatments that can help with improving vagus nerve functioning including VNS and alternative modalities like chiropractic, acupuncture, supplementation and cold water immersion. Therapists should refer to the appropriate provider and offer information on strategies that assist in improving quality of life in patients with vagus nerve dysfunction.

Section 3 Key Words

1. Vagus nerve stimulation – small pulses of electricity are sent to the central nervous system and brain through a vagus nerve stimulator device

2. Fugl-Meyer Assessment-Upper Extremity (FMA-UE) – an outcome measure used for assessment of upper extremity functioning/hemiplegia after CVA

Section 4: Future Considerations

The vagus nerve is involved in so many physiological processes in the body, as discussed in prior sections. There is an abundance of research currently being completed and will be completed based on those results in the future. This is bound to impact how the medical community understands and treats patients with vagus nerve dysfunction.

VNS [21,34,35]

Researchers have implemented trials on using vagus nerve stimulation on a variety of other disorders. These include inflammation associated with rheumatoid arthritis, diabetes mellitus and Crohn's disease, heart failure and abnormal heartbeat. From a trial in 2016, VNS decreased symptoms and inflammation in patients with rheumatoid arthritis, showing promising results for further research.

As discussed above, VNS will continue to be researched in its effectiveness of returning upper limb function after cerebrovascular accident. Most of the published research on this topic are from the past few years (2019 to 2021) and state that the direction of research will be focused on tailoring VNS parameters and to the development of individualized approach to VNS in patients with upper extremity dysfunction after CVA.

VNS is also being studied in reducing dizziness, imbalance and migraines associated with increased activity of the sympathetic nervous system. Noninvasive VNS has resulted in improvement of imbalance, vertigo and perceived postural sway in early studies.

Other Considerations

As stated throughout this course, new information continues to emerge on the treatment of vagus nerve dysfunction. Areas of research besides VNS include dietary plans to optimize digestion, breathing and stress management techniques to induce parasympathetic response, and specific routines and exercise plans to induce relaxation. As a clinician it is important to keep current on best evidence as patients will ask about the vagus nerve and to direct them to research or another appropriate provider.

Section 4 Summary

The vagus nerve and its complexity continue to be studied by the medical community. Vagus nerve stimulation seems to be the largest area of research, but other studies are investigating factors like stress management and diet on vagus nerve functioning.

Section 4 Key Words

1. Vertigo – sensation of spinning varying in severity from slight spinning to severe perceived movement

Conclusion

As indicated throughout this course, the vagus nerve is a complex cranial nerve known as "the wandering nerve" as it has an impact on most abdominal and thoracic viscera. The vagus nerve is responsible for communication of the autonomic nervous system and the fight or flight sympathetic response and the rest and digest parasympathetic response. It is important for clinicians to be a resource for patients to assist in navigating holistic treatment. Therefore, Physical Therapists and Physical Therapist Assistants should be able to recognize or at least refer when patients present with vagus nerve dysfunction.

References

1. Browning KN, Verheijden S, Boeckxstaens GE. The vagus nerve in appetite regulation, mood and intestinal inflammation. Gastroenterology. 2017;152(4):730-744. doi:10.1053/j.gastro.2016.10.046

2. Vagus Nerve Anatomy: Gross Anatomy, Microscopic Anatomy, Natural Variants. Published online January 21, 2021. Accessed December 6, 2021. https://emedicine.medscape.com/article/1875813-overview#a1

3. Kenny BJ, Bordoni B. Neuroanatomy, Cranial Nerve 10 (Vagus Nerve). In: StatPearls. StatPearls Publishing; 2021. Accessed December 6, 2021. http://www.ncbi.nlm.nih.gov/books/NBK537171/

4. Capilupi MJ, Kerath SM, Becker LB. Vagus Nerve Stimulation and the Cardiovascular System. Cold Spring Harb Perspect Med. 2020;10(2):a034173. doi:10.1101/cshperspect.a034173

5. Vagus Nerve. Physiopedia. Accessed December 10, 2021. https://www.physio-pedia.com/Vagus_Nerve

6. Breit S, Kupferberg A, Rogler G, Hasler G. Vagus Nerve as Modulator of the Brain–Gut Axis in Psychiatric and Inflammatory Disorders. Front Psychiatry. 2018;9:44. doi:10.3389/fpsyt.2018.00044

7. Parasympathetic System. Physiopedia. Accessed December 13, 2021. https://www.physio-pedia.com/Parasympathetic_System

8. Alshak MN, M Das J. Neuroanatomy, Sympathetic Nervous System. In: StatPearls. StatPearls Publishing; 2021. Accessed December 13, 2021. http://www.ncbi.nlm.nih.gov/books/NBK542195/

9. Kattar N, Flowers T. Anatomy, Head and Neck, Sympathetic Chain. In: StatPearls. StatPearls Publishing; 2021. Accessed December 13, 2021. http://www.ncbi.nlm.nih.gov/books/NBK563206/

10. Lykstad J, Reddy V, Hanna A. Neuroanatomy, Pupillary Dilation Pathway. In: StatPearls. StatPearls Publishing; 2021. Accessed December 15, 2021. http://www.ncbi.nlm.nih.gov/books/NBK535421/

11. Jetti R, Kadiyala B, Bolla SR. Anatomy, Back, Lumbar Sympathetic Chain. In: StatPearls. StatPearls Publishing; 2021. Accessed December 15, 2021. http://www.ncbi.nlm.nih.gov/books/NBK539914/

12. Sympathetic Nervous System. Physiopedia. Accessed December 15, 2021. https://www.physio-pedia.com/Sympathetic_Nervous_System

13. Nour D. Sympathetic nervous system | Radiology Reference Article | Radiopaedia.org. Radiopaedia. Accessed December 15, 2021. https://radiopaedia.org/articles/sympathetic-nervous-system-1?lang=us

14. LeBouef T, Yaker Z, Whited L. Physiology, Autonomic Nervous System. In: StatPearls. StatPearls Publishing; 2021. Accessed December 31, 2021. http://www.ncbi.nlm.nih.gov/books/NBK538516/

15. Garner DH, Kortz MW, Baker S. Anatomy, Head and Neck, Carotid Sheath. In: StatPearls. StatPearls Publishing; 2021. Accessed December 30, 2021. http://www.ncbi.nlm.nih.gov/books/NBK519577/

16. Ozel Asliyuce Y, Berberoglu U, Ulger O. Is cervical region tightness related to vagal function and stomach symptoms? Med Hypotheses. 2020;142:109819. doi:10.1016/j.mehy.2020.109819

17. Cervical spine instability and digestive disorders: Indigestion and irritable bowel syndrome caused by cervical spondylosis – Caring Medical Florida. Accessed December 30, 2021. https://www.caringmedical.com/prolotherapy-news/gerd-neck/

18. Cervical Instability. Physiopedia. Accessed December 30, 2021. https://www.physio-pedia.com/Cervical_Instability

19. Sharp Purser Test. Physiopedia. Accessed December 30, 2021. https://www.physio-pedia.com/Sharp_Purser_Test

20. Vasovagal Syncope: A Common Cause of Fainting. Verywell Health. Accessed December 29, 2021. https://www.verywellhealth.com/vasovagal-cardioneurogenic-syncope-1746389

21. Vagus nerve: Function, stimulation, and further research. Published June 28, 2017. Accessed December 28, 2021. https://www.medicalnewstoday.com/articles/318128

22. Hammer N, Glätzner J, Feja C, et al. Human Vagus Nerve Branching in the Cervical Region. PLoS ONE. 2015;10(2):e0118006. doi:10.1371/journal.pone.0118006

23. How Does Vagus Nerve Stimulation Work? Accessed December 17, 2021. https://www.aans.org/

24. Xie Y lei, Wang S, Wu Q, Chen X. Vagus nerve stimulation for upper limb motor impairment after ischemic stroke. Medicine (Baltimore). 2021;100(46):e27871. doi:10.1097/MD.0000000000027871

25. Dawson J, Engineer ND, Prudente CN, et al. Vagus Nerve Stimulation Paired With Upper-Limb Rehabilitation After Stroke: One-Year Follow-up. Neurorehabil Neural Repair. 2020;34(7):609-615. doi:10.1177/1545968320924361

26. Wei-Jiang, Zhang C, Wang JX, et al. The effect of VNS on the rehabilitation of stroke: A meta-analysis of randomized controlled studies. J Clin Neurosci. 2020;81:421-425. doi:10.1016/j.jocn.2020.09.022

27. Kimberley TJ, Pierce D, Prudente CN, et al. Vagus Nerve Stimulation Paired With Upper Limb Rehabilitation After Chronic Stroke. Stroke. 2018;49(11):2789-2792. doi:10.1161/STROKEAHA.118.022279

28. Boehmer AA, Georgopoulos S, Nagel J, Rostock T, Bauer A, Ehrlich JR. Acupuncture at the auricular branch of the vagus nerve enhances heart rate variability in humans: An exploratory study. Heart Rhythm O2. 2020;1(3):215-221. doi:10.1016/j.hroo.2020.06.001

29. Kiani AK, Maltese PE, Dautaj A, et al. Neurobiological basis of chiropractic manipulative treatment of the spine in the care of major depression. Acta Bio Medica Atenei Parm. 2020;91(Suppl 13):e2020006. doi:10.23750/abm.v91i13-S.10536

30. Foster JA, Rinaman L, Cryan JF. Stress & the gut-brain axis: Regulation by the microbiome. Neurobiol Stress. 2017;7:124-136. doi:10.1016/j.ynstr.2017.03.001

31. Loper H, Leinen M, Bassoff L, et al. Both high fat and high carbohydrate diets impair vagus nerve signaling of satiety. Sci Rep. 2021;11(1):10394. doi:10.1038/s41598-021-89465-0

32. Gerritsen RJS, Band GPH. Breath of Life: The Respiratory Vagal Stimulation Model of Contemplative Activity. Front Hum Neurosci. 2018;12:397. doi:10.3389/fnhum.2018.00397

33. Jungmann M, Vencatachellum S, Van Ryckeghem D, Vögele C. Effects of Cold Stimulation on Cardiac-Vagal Activation in Healthy Participants: Randomized Controlled Trial. JMIR Form Res. 2018;2(2):e10257. doi:10.2196/10257

34. Vagus nerve stimulation inhibits cytokine production and attenuates disease severity in rheumatoid arthritis | PNAS. Accessed December 28, 2021. https://www.pnas.org/content/113/29/8284.full

35. Eren OE, Filippopulos F, Sönmez K, Möhwald K, Straube A, Schöberl F. Non-invasive vagus nerve stimulation significantly improves quality of life in patients with persistent postural-perceptual dizziness. J Neurol. 2018;265(Suppl 1):63-69. doi:10.1007/s00415-018-8894-8

FLEX CEUs