

Osteopathic Manipulation in the Management Autonomic Neuropathy

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Objectives

- Differentiate large fiber, small fiber, & autonomic, polyneuropathy
- Describe features of POTS
- Formulate treatment for autonomic neuropathy using osteopathic manipulation

Roadmap

- Basic Polyneuropathy Review
- Small Fiber Neuropathy Refresher
- Autonomic neuropathy
 - All of this is to argue that OMM has a role in management of dysautonomia
- Some Anatomy of course
- Application of osteopathic manipulation

Polyneuropathy

- Impairment of multiple peripheral nerves
 - Sensory, motor, or autonomic
 - Small, large, or autonomic fibers
- Small fibers
 - Pain and temperature carried on small unmyelinated or thinly myelinated fibers
 - Symptoms: burning or temperature changes
- Large fibers
 - A alpha and A beta large fibers – sensory
 - A gamma – motor
 - Vibration, proprioception, touch/2-point discrimination, loss of bulk
 - Symptoms: tingling, pins and needles

Polyneuropathy

- Large Fiber
 - Axonal, Demyelinating, or Mixed
 - Motor vs Sensory vs Mixed
- Autonomic Neuropathy covered in detail later
 - Carried on unmyelinated or thinly myelinated fibers
- Small Fiber Neuropathy and Autonomic Neuropathy often accompany each other
 - More on this in less than a minute

Polyneuropathy

- Anatomic Distribution
 - Typically length dependent affecting the lower limbs first
 - Think Stocking Glove
 - The glove is usually not affected till the the lower limbs are involved up to the knees
 - There are many exceptions
- A good resource is:
<https://neuromuscular.wustl.edu>

Pathophysiology

- Axonal degeneration
 - most common
 - “Dying back”
 - Most distal part of the axon dies
 - Typical distal symmetric polyneuropathy
 - Usually toxic or metabolic
 - Symptomatic/supportive
- Wallerian degeneration
 - Distal degradation
 - Trauma or nerve infarction
 - Symptomatic/supportive/time
- Segmental demyelination
 - Axon spared
 - Nerve sheath impaired
 - Can be focal mononeuropathy but more often seen in immune mediated/inflammatory polyneuropathy
 - Medical management

Small Fiber

- Thinly myelinated A δ
 - Mechanoreceptors and thermoreceptors
 - Pain
 - Cold
 - **Preganglionic fibers (ANS)**
- Unmyelinated C fibers
 - Polymodal receptors
 - Nociception – burning pain
 - Itching
 - Warm
 - Maybe cold
 - **Postganglionic fibers**
 - Sweat glands, blood vessels, heart, etc

Small Fibers

- Sit in the dermis
- Exact pathophysiology of their neuropathy is unknown
 - Autoantibodies to neuronal proteins
 - Inflammatory cytokines
 - Dermal vasculitis

Small Fiber Neuropathy Diagnosis

- Possible
 - Length-dependent symptoms
 - Loss of Pin/temp; allodynia/hyperalgesia
- Probable
 - Length dependent
 - Loss of Pin/temp; allodynia/hyperalgesia
 - Normal NCS
- Definite
 - Length dependent symptoms
 - Loss of Pin/temp; allodynia/hyperalgesia
 - Normal NCS
 - Reduced epidermal nerve fiber density at the ankle (Skin Biopsy) OR abnormal QST (quantitative sensory testing)

Small Fiber Neuropathy Etiology

- Metabolic
 - Pre-diabetes/diabetes/abnormal glucose metabolism or rapid correction
 - Vitamin B12 deficiency
 - Dyslipidemia
 - Hypothyroidism
 - CKD
- Immune
 - Sjogren's
 - Celiac
 - Sarcoid
 - RA
 - SLE
 - Vasculitis
 - Inflammatory Bowel Disease
 - Paraneoplastic
 - Monoclonal Gammopathy
 - Amyloid
- Infection
 - HIV
 - Hepatitis C
 - Influenza
- Toxins
 - ARV
 - Antibiotics
 - Chemotherapy
 - Flecanide
 - Statin
 - EtOH
 - Statin
 - Vitamin B6
- Primary Hereditary
 - Nav 1.7 and 1.8 mutations
 - Familial Amyloid Angiopathy
 - Fabry's
 - Tangier's
- Primary Idiopathic
 - Idiopathic SFN
 - Burning Mouth Syndrome

Autonomic Nervous System

- Sympathetic
- Parasympathetic
- Enteric

Sympathetic

- Hypothalamus to the intermediolateral gray cell column in the spinal cord (1st order efferent)
 - Somatotopic organization
- Preganglionic axons from the cord project to the postganglionic neurons (2nd order efferent) on the paravertebral sympathetic ganglia at their level, above, or below
 - 3 cervical, 10-12 thoracic, 4 lumbar and 4-5 sacral
 - Most are paired ganglia

Sympathetic

- Superior cervical ganglion
- Middle cervical ganglion
- Inferior cervical ganglion
 - Inferior can fuse with
the upper thoracic ganglia

Sympathetic Nervous System

- Caudal most ganglia at the coccyx form the unpaired ganglion impar

Sympathetic Nervous System

- From paravertebral ganglion the sympathetics travel with spinal nerves, cranial nerves, or blood vessel wall to their target

Parasympathetic

- Brainstem and sacrum
- Parasympathetic preganglionic neurons
 - Eddinger-Westphal (III) in rostral midbrain
 - Superior salivatory and lacrimal nuclei (VII) in the pontine tegmentum
 - Inferior salivatory nucleus (IX) periventricular gray – rostral medulla
 - *Nucleus ambiguus (X) – medulla reticular formation posterior to the inferior olivary nucleus*
 - *Oropharynx*
 - *Dorsal Motor Nucleus (X) – floor of the fourth ventricle*
 - *Thorax and abdomen*
 - **CN X has the largest group of parasympathetic fibers in the body**

Nucleus Tractus Solitarius

- Receives sensory input from a number of cranial nerves including Vagus.
- Carotid body, aortic bodies, SA node via the vagus
- Taste, sensation to the middle ear
- Receives input from the heart, lungs, GI, liver, etc
- There is a lot of vagal tone set through here because of this
- Autonomic Reflex zone

Dorsal Motor Nucleus X

- Please reference Netter

ANS

- Bidirectional connected between target and central autonomic network
- Central Autonomic Network (CAN)
 - Medial prefrontal cortex
 - Insular cortex
 - Central nucleus of the amygdala
 - Hypothalamus
 - Periaqueductal gray
 - Parabrachial nuclear complex
 - Nucleus Ambiguus
 - Nucleus Tractus solitarius
- R. Paul Lee, DO describes a release for this CAN
 - We will not do it here

ANS Dysfunction

Dry Mucus membranes

Anhydrosis

Abnormal pupils

Constipation/Diarrhea

Vomiting

Abdominal pain

Early satiety/anorexia

Intestinal pseudo-
obstruction

Urinary retention

Skin color changes

Abnormal heart rate

Orthostasis

Erectile dysfunction

Etiology

- Diabetes
- Multisystem Atrophy
- Guillain-Barre
- Sjogren's Syndrome
- Paraneoplastic
 - Small cell lung cancer
- HIV
- Botulism
- Chagas (now in the US)
- Diphtheria
- Leprosy
- Rabies
- Acute Dysautonomia
- Parkinsonism
- Neuronal intranuclear inclusion disease
- Myopathy and external ophthalmoplegia, neuropathy, gastro intestinal encephalopathy
- A number of hereditary conditions

Autonomic Nervous System

POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME

POTS

- These patients range from mildly impaired to bedridden
- They were usually normal productive people before
 - This can be lost on the medical system
 - In severe cases their lives are usually destroyed and they just want to be normal
 - *Labeled psychiatric*
 - Symptoms confused with anxiety
 - Especially since it affects women more than men
- They will search for exotic diagnoses
- They will need a lot of hand holding and TLC
- Severe cases may take years to recover
 - 1 year OMM, 1 year PT, then additional OMM

POTS - Autonomic Neuropathy

- Some estimates are that 1% of US population has POTS
- Heart rate increase ≥ 30 bpm within 10 min of upright posture in adults. Heart rate increase of ≥ 40 bpm within 10 min is required in adolescents age 12–19 years
- Absence of orthostatic hypotension defined as a sustained drop in blood pressure $\geq 20/10$ mm Hg within 3 min of upright posture
- Symptoms of orthostatic intolerance for ≥ 6 months
- Absence of overt causes for sinus tachycardia such as acute physiological stimuli, dietary influences, other medical conditions and medications
- Tilt table test with or w/o sudomotor testing and transcranial doppler

POTS

- Female:Male 4:1
- Typically 13-50 years old
- **13% with family history**
- Heterogeneous (Cardiogenic vs neurogenic vs **structural***)
- Start after acute stress
 - Surgery, viral illness, MVC etc.
- Blurry vision, brain fog, cognitive dysfunction, chest pain, lightheaded, nausea, fatigue, constipation, acrocyanosis, sleep abnormalities, anxious/brainstem feeling
- Only about 30% have syncope
- Look for **Ehler's Danlos Type III***, Mast Cell Activation Syndrome, Chronic Fatigue Syndrome, migraine, fibromyalgia, Sjogren's and other autoimmune conditions, GI problems (bloating, chronic constipation)

Pathophysiology

- 50% of POTS patients have distal small fiber neuropathy with sympathetic denervation
 - Patient may not be aware of the neuropathy
 - Impaired peripheral vascular resistance in the legs when standing due to blunted norepinephrine there
 - Causes excessive venous pooling →
 - Sympathetic activation →
 - Increase heart rate to maintain blood pressure

Pathophysiology

- 50% have **Hyperadrenergic state**
- Excessive orthostatic tachycardia
- Might be related to excessive interleukin-6
- Usually from hypovolemia or partial sympathetic denervation
- Test orthostatic catecholamines 15 minutes supine then 15 minutes standing (okay to lean against a wall)

Pathophysiology

- Norepinephrine transporter deficiency
 - Causes loss of sympathetic activation by decreasing amount of NE taken up at the synapse
 - Gene SLC6A2
 - Tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, atomoxetine impact NET

Pathophysiology

- Hypovolemia
 - Low blood volume with decreased red blood cell count
 - 13% deficit in plasma volume in POTS
- Thought to cause lower stroke volume and compensatory tachycardia
- Impaired vascular and renal response to hypovolemia
 - Angiotensin II levels are high and BP is normal
- **Fluid responsive**
 - Give Lactated Ringers or isotonic saline
 - Oral rehydration

- Please reference Arnold et al. Postural tachycardia syndrome – diagnosis, physiology, and prognosis. Autonomic Neuroscience: Basic and Clinical. 2018. <https://doi.org/10.1016/j.autneu.2018.02.005>
- Figures 3 and 4

Pathophysiology

- Immune mediated (some studies show 20%)
- Antibodies to ganglionic acetylcholine receptor
- Antibodies to alpha 1 and beta adrenergic receptors and cardiac lipid proteins
- Non-specific markers (e.g, ANA) positive in 25% while 31% have some antibody +
- IgG against cardiac proteins
 - 40 identified

POTS association:

- Sjögren syndrome
- Ankylosing spondylitis
- Antiphospholipid syndrome
- Behcet's disease
- Celiac disease
- Chronic immune demyelinating polyneuropathy
- Inflammatory bowel disease (Crohn and ulcerative colitis)
- Hashimoto's thyroiditis
- Multiple sclerosis
- Neuromyelitis optica
- Rheumatoid arthritis
- Sarcoidosis
- Systemic lupus erythematosus
- Juvenile rheumatoid arthritis
- Adult Still's disease
- Undifferentiated connective tissue disease

Pathophysiology

- Impaired cerebral autoregulation
- Orthostatic intolerance despite normal blood pressure
 - Is this problem central rather than peripheral?

Pathophysiology

- Deconditioning – not sure if this is primary or secondary
- Aerobic exercise is critical
- Is the heart too small?

Structural Associations

- Thoracic Outlet Syndrome
 - Stellate ganglion compression?
- Hypermobility – Ehlers Danlos type 3
 - Also associated with Mast Cell Activation Syndrome
- Maybe Chiari Malformation
- Eagle syndrome
 - Elongated styloid
 - Compression of CN X, IX, carotid

Structural Associations

- Median arcuate ligament syndrome
 - intermittent obstruction of celiac or superior mesenteric arteries by the median arcuate ligament
 - celiac plexus compression
 - postprandial or post-exertional abdominal pain
- Pelvic vein varicosities
 - Venous pooling

A role for the Vagus Nerve in Treatment?

- Vagal nerve stimulation
 - Anti-inflammatory
 - Shown to improve rheumatoid arthritis, Crohn's, Sjogrens
- Regular exercise improves vagal tone
- Anti-inflammatory diet
- Acupuncture
- Biofeedback
- Music therapy
- Meditation

Treatment

- A great cardiologist or autonomic neurologist
- Increased sodium and fluid intake
- Compression stockings
- **Aerobic exercise**
- Isotonic saline/Lactated Ringers infusions
- Beta blockers
 - Metoprolol
 - Corlanor
- Alpha 1 agonist: Midodrine
- Florinef in some cases
- L-Dopa, carbidopa
- SSRI/SNRI
- IVIG/Plasma Exchange/steroids/Rituximab

POTS Additional Information

- Arnold et al. Postural tachcardia syndrome – diagnosis, physiology, and prognosis. Autonomic Neuroscience: Basic and Clinical. 2018. <https://doi.org/10.1016/j.autneu.2018.02.005>
- Vernino and Stiles. Autoimmunity in postural orthostatic tachycardia syndrome: current understanding. Autonomic Neuroscience: Basic and Clinical. 2018. <https://doi.org/10.1016/j.autneu.2018.04.005>
- Goodman. Evaluation of postural orthostasis tachycardia syndrome (POTS). Autonomic Neuroscience: Basic and Clinical. 2018. <https://doi.org/10.1016/j.autneu.2018.04.004>
- Wells et al. Postural tachycardia syndrome: current perspectives. Vascular Health and Risk Management. 2018;14; 1-11.

POTS

IS THERE A ROLE FOR OMT?

OMT for POTS

- Goodkin and Bellew 2014 describe OMT for POTS
 - 26 year old female with fatigue, pre-syncope, heat intolerance, cognitive dysfunction, diffuse joint pain, insomnia, jaw injury
 - POTS diagnosed, partial response to Florinef, midodrine
 - Ligamentous articular strain
 - Osteopathic cranial manipulative medicine
 - **Pre-treatment – could only tolerate 5 minutes in a hot shower**
 - **Post treatment – 45 minutes**
 - Was able to reduce midodrine and amphetamine for 8 days
 - Treated again and this time improved for 8 weeks
 - Treated a 3rd time 28 days later and remained controlled at her 18 month follow-up
 - JAOA Nov 2014;114:874-877

OMT for POTS – GI symptoms

- Cromeens and Gambler 2010
 - 48 year old male with decade of post-prandial abdominal bloating, cramping, nausea and vomiting, and POTS, spine pain throughout
 - By the 3rd treatment patient had reduced GI symptoms
 - 4th Treatment decreased pain
 - Required maintenance treatment
 - Soft tissue, muscle energy, articulatory, ligamentous articular strain, integrated neuromuscular release, articulatory techniques
-
- Osteopathic Family Physician 2010;2:144-147

Polyneuropathy

OSTEOPATHIC MANIPULATION TECHNIQUES

Osteopathic Manipulation

- Large fiber neuropathy
 - **Best to treat the underlying cause**
 - However Treatment of CSF, epineural space and perineural space might be helpful

Today's Lab will focus on Vagus But...

- Autonomic Neuropathy
 - Linea Alba release
 - Release the celiac ganglion and plexus while you are there
 - Correct dysfunction of the respiratory and pelvic diaphragm
 - CV4, might need lots of them
 - Treat ANS and structural abnormalities
 - **Treat the occiput/OA, sacrum, coccyx,**
 - **When the patient is healthy enough integrate the systems**
 - Treat the ganglion impar
 - » Treating hand on the sacro-coccygeal junction and tip of coccyx
 - Treat midline of the sacrum
 - Release the sympathetic chain there
 - Treating the vagus nerve and its nuclei (next slide)

For Images

- Please reference: Netter
- Blumenfeld: Neuroanatomy through Clinical Cases

Vagus Nerve Anatomy

- Exits Medulla
 - Between olive and inferior cerebellar peduncle
- Jugular foramen
 - Sensory ganglia
 - Superior and inferior
- Joins CN XI below the inferior sensory ganglion
- Descends through the carotid sheath posterolateral to carotid
- Medial to internal jugular vein

Right Vagus

- Crosses anterior to subclavian artery
- Fat behind the innominate vessels
- Enters thorax right of the trachea
- Rises behind the hilum of the right lung
- Courses medially toward esophagus
 - Joins the left vagus to form the esophageal plexus

Left Vagus

- Crosses anterior to the left subclavian artery
- Enters the thorax between the left common carotid and subclavian arteries
- Descends on left side of the aortic arch
- Behind the phrenic nerve
- Behind the root of the left lung
- Medially and downward to esophagus
- Meets right vagus → esophageal plexus

Vagus: Gastric Nerves

- Esophageal plexus gives rise to the anterior and posterior gastric nerves
- Supply all abdominal organs and GI tract to the splenic flexure
- Right vagus → posterior gastric plexus
 - Posteroinferior
- Left vagus → anterior gastric plexus
 - Anterosuperior

Vagus: Celiac Nerve

- Right vagus
nerve
- Celiac
plexus

Vagus and the Heart

- Esophageal plexus
 - Supplies posterior pericardium
- Invests in the deep cardiac plexus
 - Anterior to carina
 - Inferior cardiac branch
 - Right side from trunk of vagus at the trachea
 - Left from recurrent laryngeal nerve

Cardiac Plexus

- Superficial
 - Under the aortic arch anterior to the right pulmonary artery
 - Left sympathetic trunk and lower superior cervical cardiac branch of the vagus
- Deep
 - Anterior to the carina, posterior to aortic arch
 - Mix of sympathetic from the and parasympathetic from inferior cardiac branch of vagus

Deep Cardiac Plexus

- Right side
 - Anterior and posterior coronary plexus
 - Right atrium
- Left side
 - Superficial cardiac plexus
 - Left atrium
 - Posterior coronary plexus

Okay let's treat

- Occipitocervical hold or vault – just be comfortable – treat by intention, if you need to treat locally, hands anterior chest wall at the level of the carina (sternal angle) and epigastric area is fine
- DO NOT INVADE; DO NOT RUSH
- Get on the 4th ventricle
- Move anterior and find dorsal motor nerve of the vagus
 - Just lateral to the hypoglossal nucleus – pick one side to treat first then bring in the other
- Bring your attention to the esophageal plexus – bridge to the dorsal motor nucleus of the vagus
- Now bring your attention to the anterior and posterior gastric plexus
- Bridge it to the esophageal plexus then the dorsal motor nucleus
- Now bring your attention to the celiac plexus and do the same as above
- Bring your attention to the superficial and deep cardiac plexus – treat and integrate with the esophageal plexus
- Now see the big picture and put it all together
- Now release the nucleus tractus solitarius then nucleus ambiguus
- THIS IS TOO BIG A TREATMENT FOR A SICK PATIENT
 - Treat the individual components first and over time start linking them together