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

• Thinely myelinated $A\delta$
  – 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 (1\textsuperscript{st} order efferent)
  - Somatotopic organization
- Preganglionic axons from the cord project to the postganglionic neurons (2\textsuperscript{nd} 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 forth 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
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 $\geq 30$ bpm within 10 min of upright posture in adults. Heart rate increase of $\geq 40$ 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 $\geq 6$ 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

• 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

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 impars
        » 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 $\rightarrow$ 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 $\rightarrow$ posterior gastric plexus
  – Posterioinferior
• Left vagus $\rightarrow$ 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 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