Dizziness, Syncope, and Autonomic Dysfunction in Children

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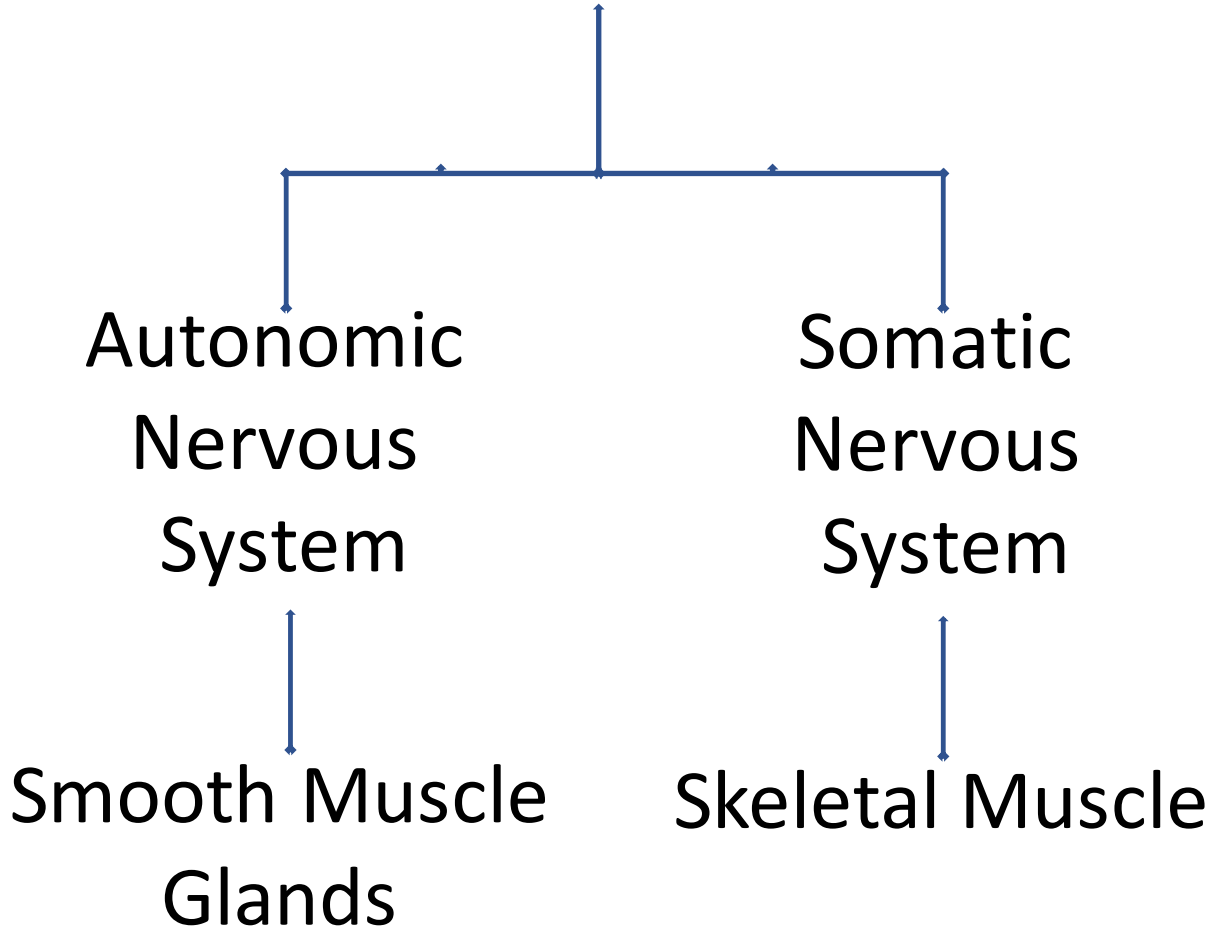
NEMOURS CHILDREN'S HEALTH

No Disclosures

Structure of the Presentation

- Autonomic nervous system
- Physiology of standing
- Orthostatic intolerance
- Autonomic studies
- Therapy

Peripheral Nervous System



Autonomic Nervous System

- Term ANS was coined by John Newport Langley.

- ANS is divided into:
  - Sympathetic
  - Parasympathetic
  - Enteric

ANS

Central

- Forebrain
- Upper brainstem
- Lower brainstem
- Spinal cord

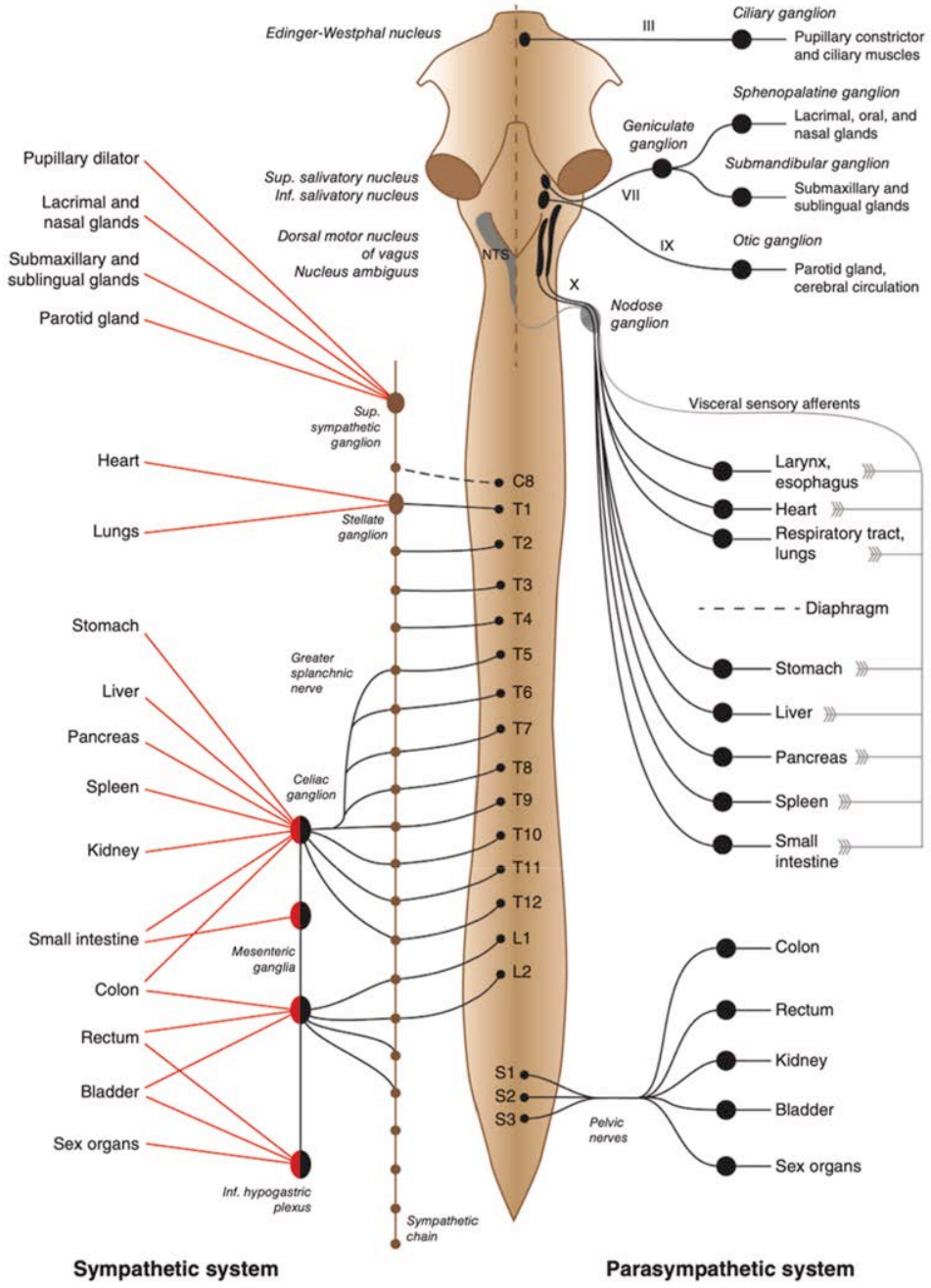
Peripheral

- Sympathetic
  - Sympathetic adrenergic
  - Sympathetic noradrenergic
  - Sympathetic cholinergic
- Parasympathetic
- Enteric

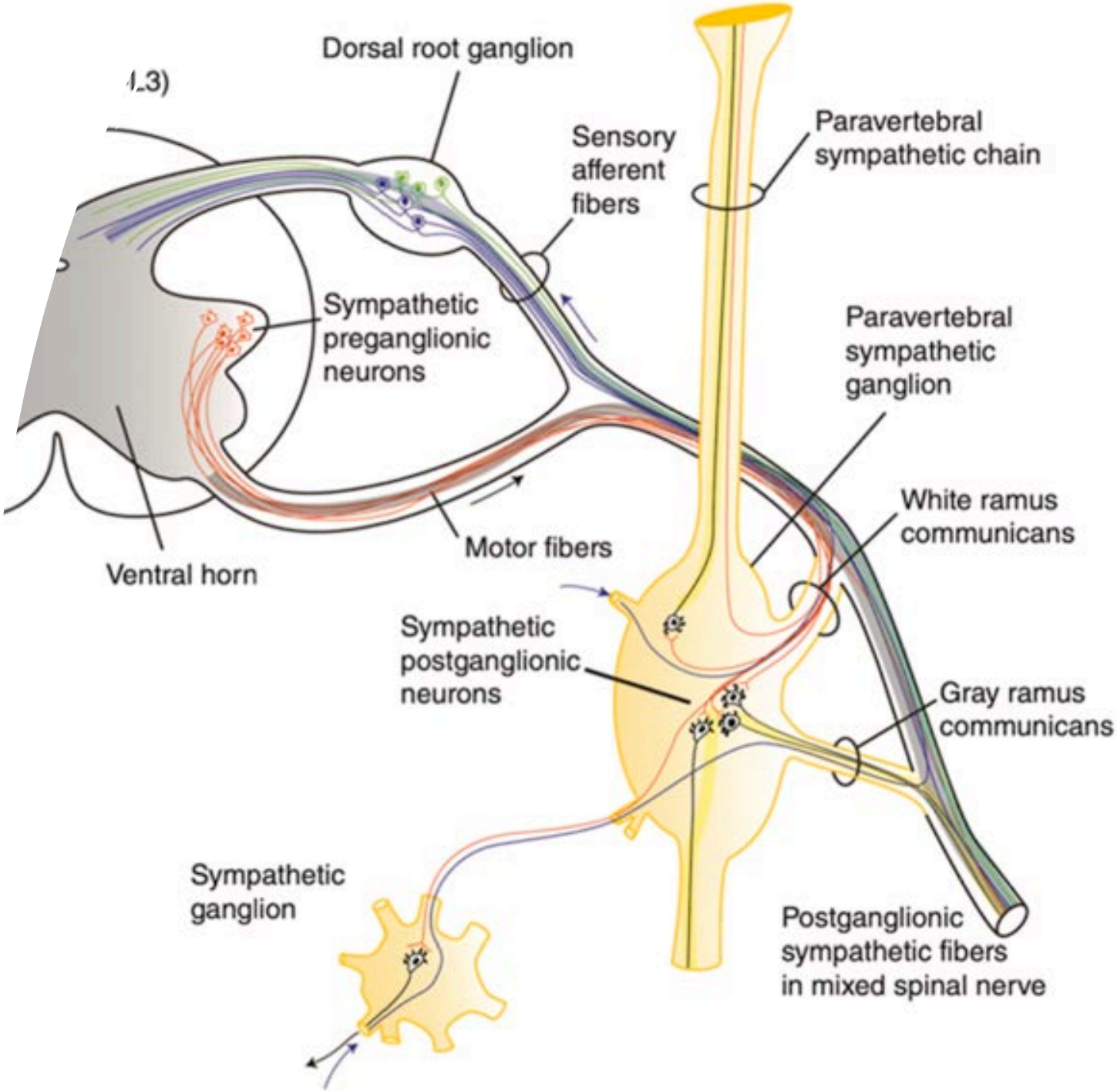
Central ANS

- Brainstem:
  - NTS (nucleus tractus solitarius)
  - Dorsal motor nucleus
  - Nucleus ambiguous

- Spinal cord:
  - Sympathetic: Th1-L2/3
  - Parasympathetic: sacral

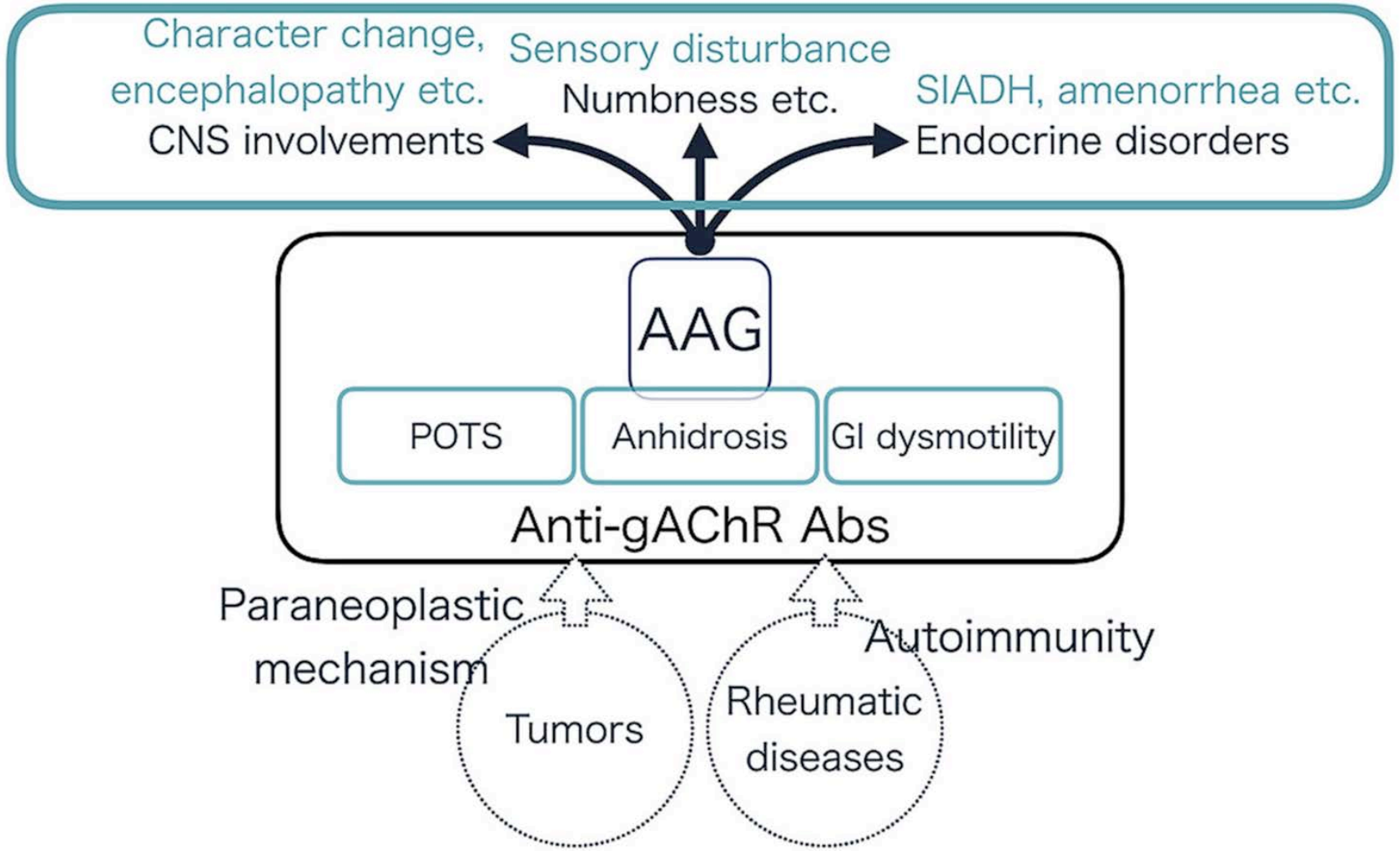


ANS - Spinal Cord



Autoimmune Autonomic Ganglionopathy

AAG



Nakane et al. J Autoimmunity 2020

ANS Functions

Organ	Sympathetic activation	Parasympathetic activation
Eye		
Pupil	Dilation (dilator muscle)	Constriction (sphincter muscle)
Ciliary muscle	Relax (far vision)	Constrict (near vision)
Lacrimal gland	Slight secretion	Secretion
Salivary glands	Slight secretion	Secretion
Heart		
Rate (sinus node)	Increase	Decrease
Contractility (muscle)	Increase	Decreased or none
Lungs	Bronchodilation	Bronchoconstriction
Gastrointestinal tract	Decreased motility	Increased motility
Kidney	Antidiuresis (decreased output)	None
Bladder		
Detrusor muscle	Relaxation	Contraction
Sphincter	Contraction	Relaxation
Penis	Ejaculation	Erection
Clitoris, labia minora	None	Swelling/erection
Nipples	None	Erection
Sweat glands	Secretion	Palmar sweating
Piloerector muscles	Contraction	None
Blood vessels		
Large arteries	Constriction	None
Arterioles	Constriction	None
Precapillary sphincters	Constriction	None
Venules	Constriction	None
Large veins	Constriction, volume mobilization	None
Coronary arteries	Dilatation	None
Muscle		
Arterioles	Dilatation	None
Metabolism	Increased	None
Muscle spindles	Decreased sensitivity	None
Liver	Glycolysis, glucose mobilization	Glycogen synthesis
Fat tissue	Lipolysis	None
Immune system	Suppressed	Activated

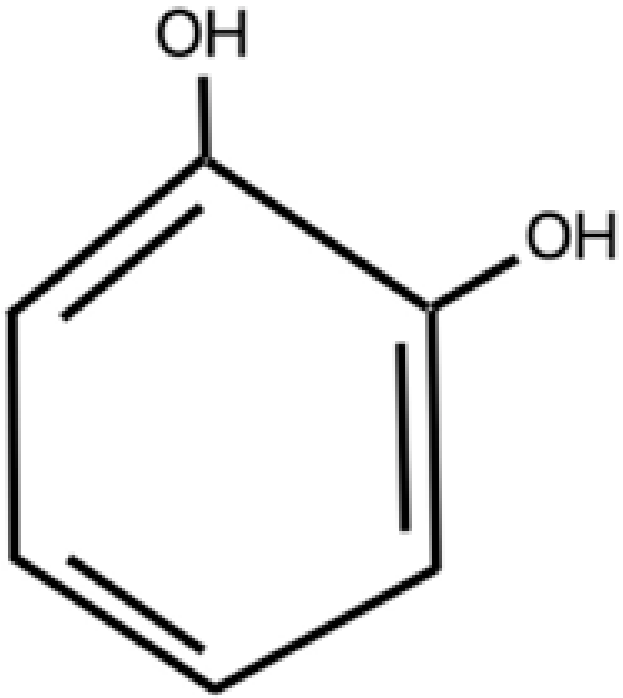
Robertson et al. Primer on Autonomic Nervous System

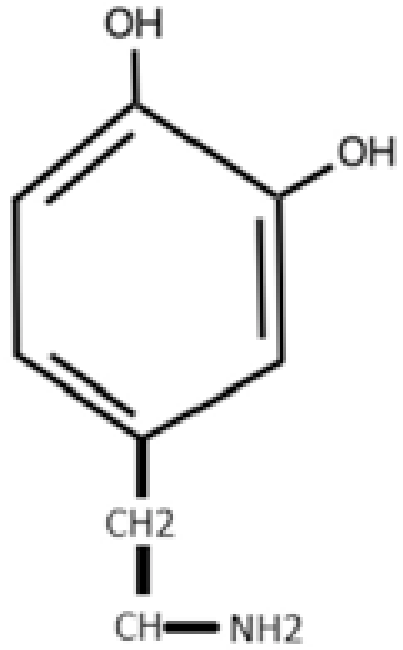
Autonomic Neurotransmitters

- Sympathetic noradrenergic (postganglionic)
- Sympathetic cholinergic (pre- and postganglionic)
- Sympathetic adrenergic (hormone)
- Parasympathetic cholinergic (pre- and postganglionic)

Catecholamines

There are three natural catecholamines and multiple catechols:

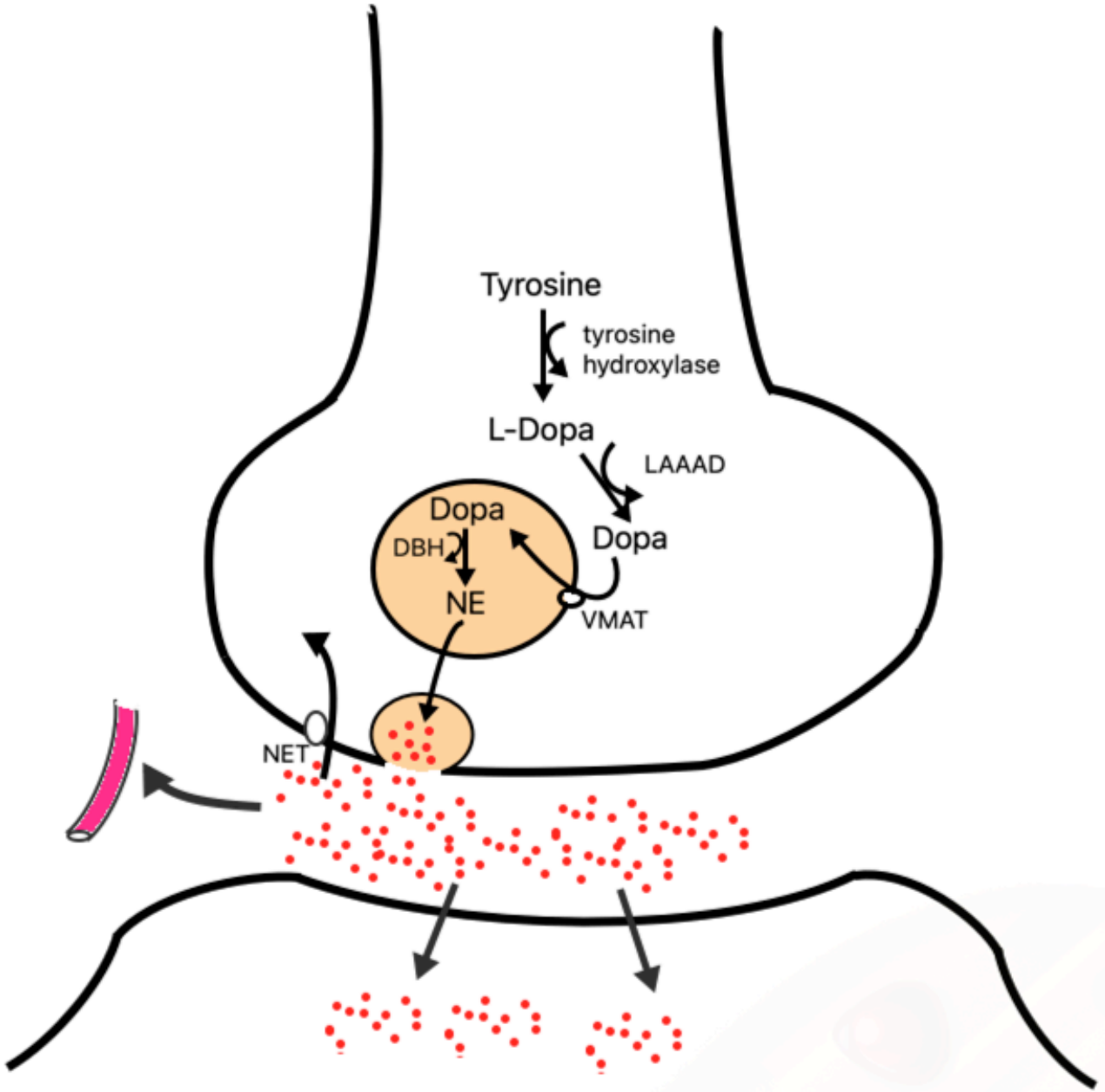




Catecholamines

- Dopamine
- Norepinephrine/noradrenaline
- Epinephrine/adrenaline

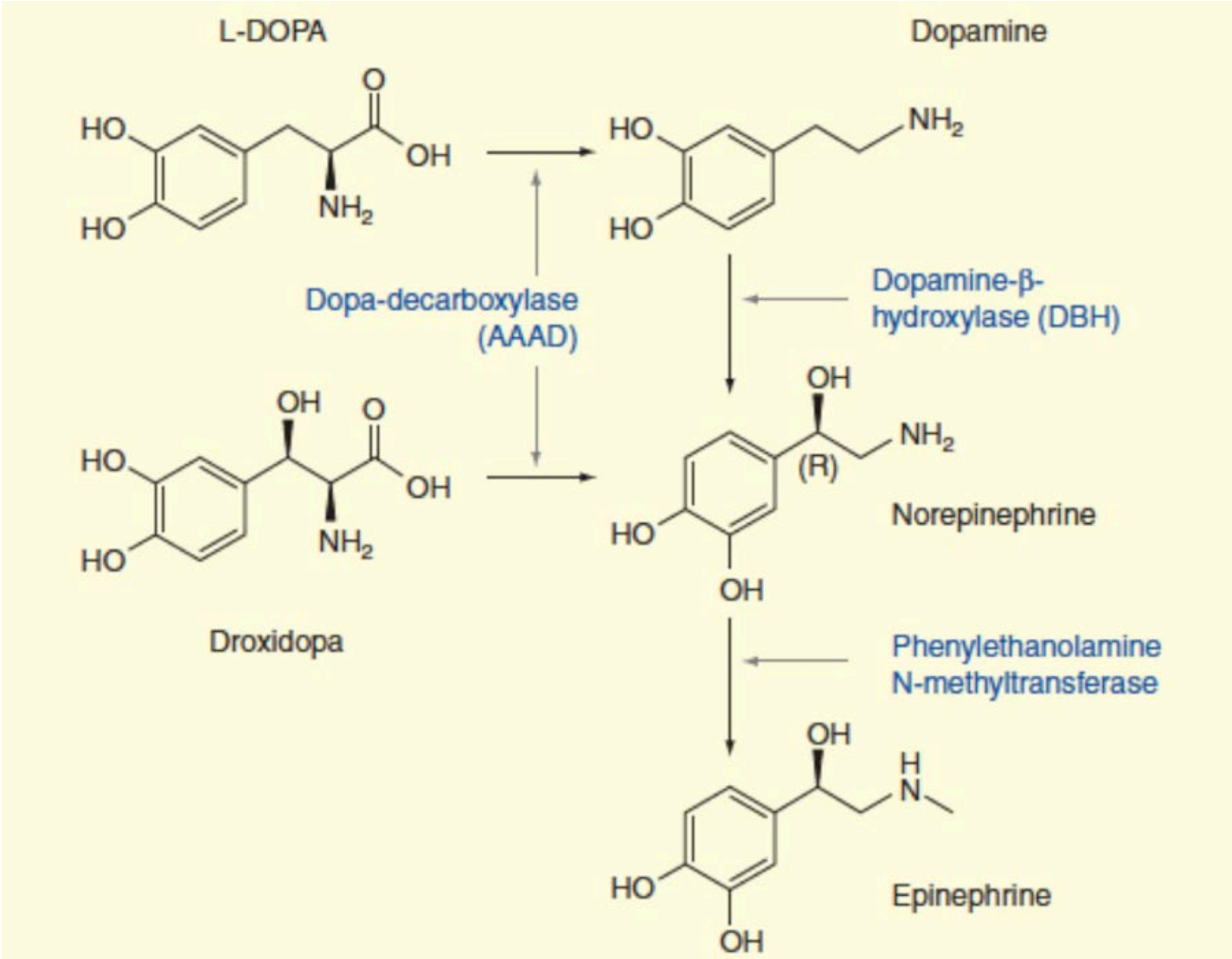
Catecholamines Synthesis



Dopamine Beta-Hydroxylase Deficiency

- Autosomal recessive
- Lack of sympathetic noradrenergic but normal parasympathetic and sympathetic cholinergic function.
- Neonates experience vomiting, hypoglycemia, hypothermia
- Children have reduced exercise capacity and some orthostatic symptoms.
- Adults have severe orthostatic hypotension, pstosis, nasal stuffiness. Symptoms are worse in heat or after alcohol ingestion.
- Droxidopa can reverse much of symptom burden.

Droxidopa



Kaufmann et al. Expert Rev Cardiovasc Ther. 2015

Physiology of Standing

- Standing up results in significant displacement of blood to lower half of the body, as much as 700 ml in adults
- Decreased venous return and preload lead to smaller stroke volume and lower BP.
- Low BP is recognized by high pressure baroreceptors almost immediately. BR blocks the parasympathetic nervous system (higher HR) and activates sympathetic nervous system (vasoconstriction, higher BP).

Prolonged Standing

In addition to blood pooling, plasma extravasation contributes to decreased blood volume and cardiac preload.

High pressure baroreceptors continue to be active.

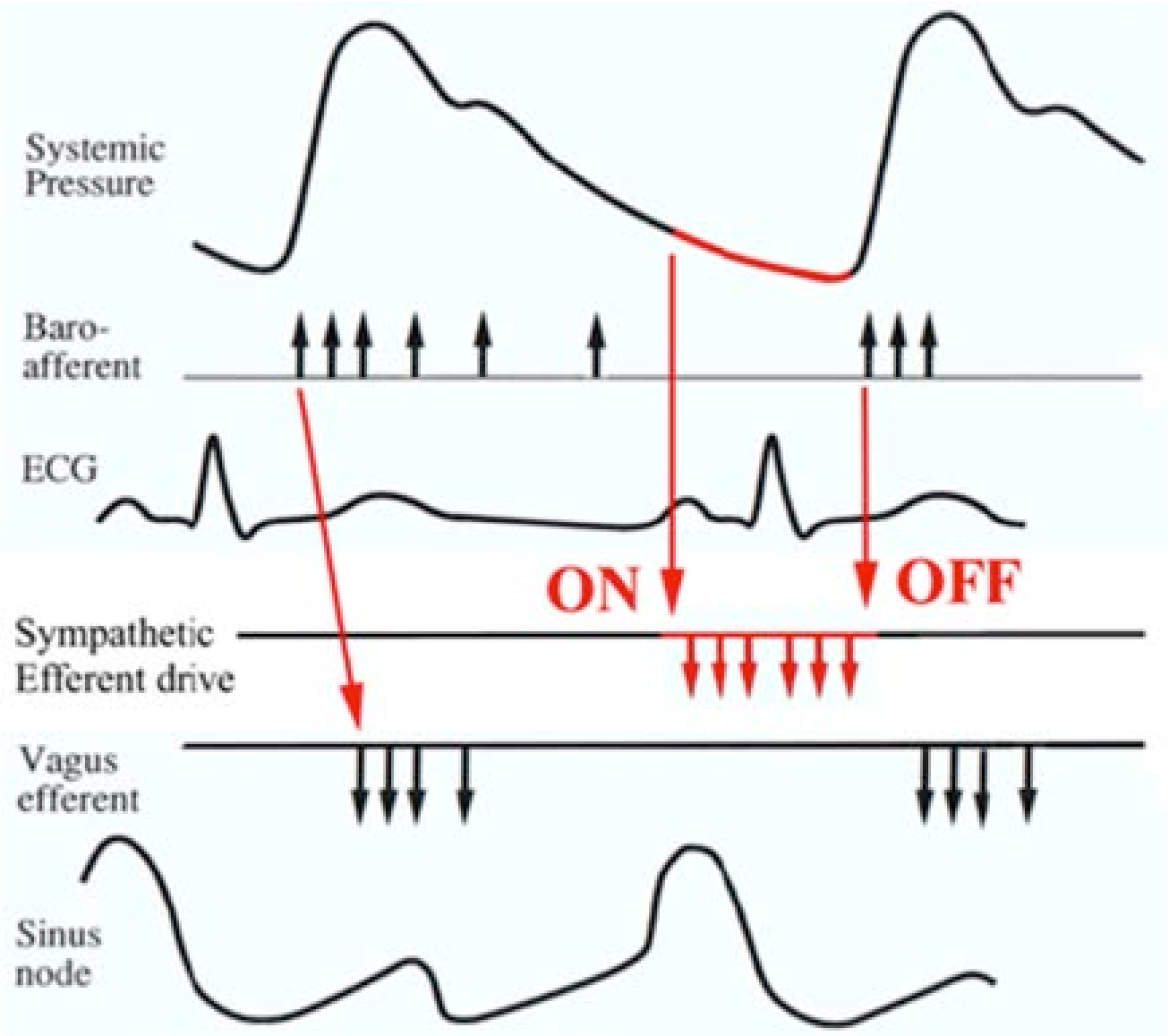
Low pressure BR are activated which in turn activate RAAS and vasopressin secretion. The net effect is blood volume and BP slowly increase.

Baroreceptors

- React to BP pressure via distortion of the cell membrane.

- Aortic arch baroreceptors are connected to NTS via CN X. Carotid sinus baroreceptors send afferent signals via CN IX to NTS.

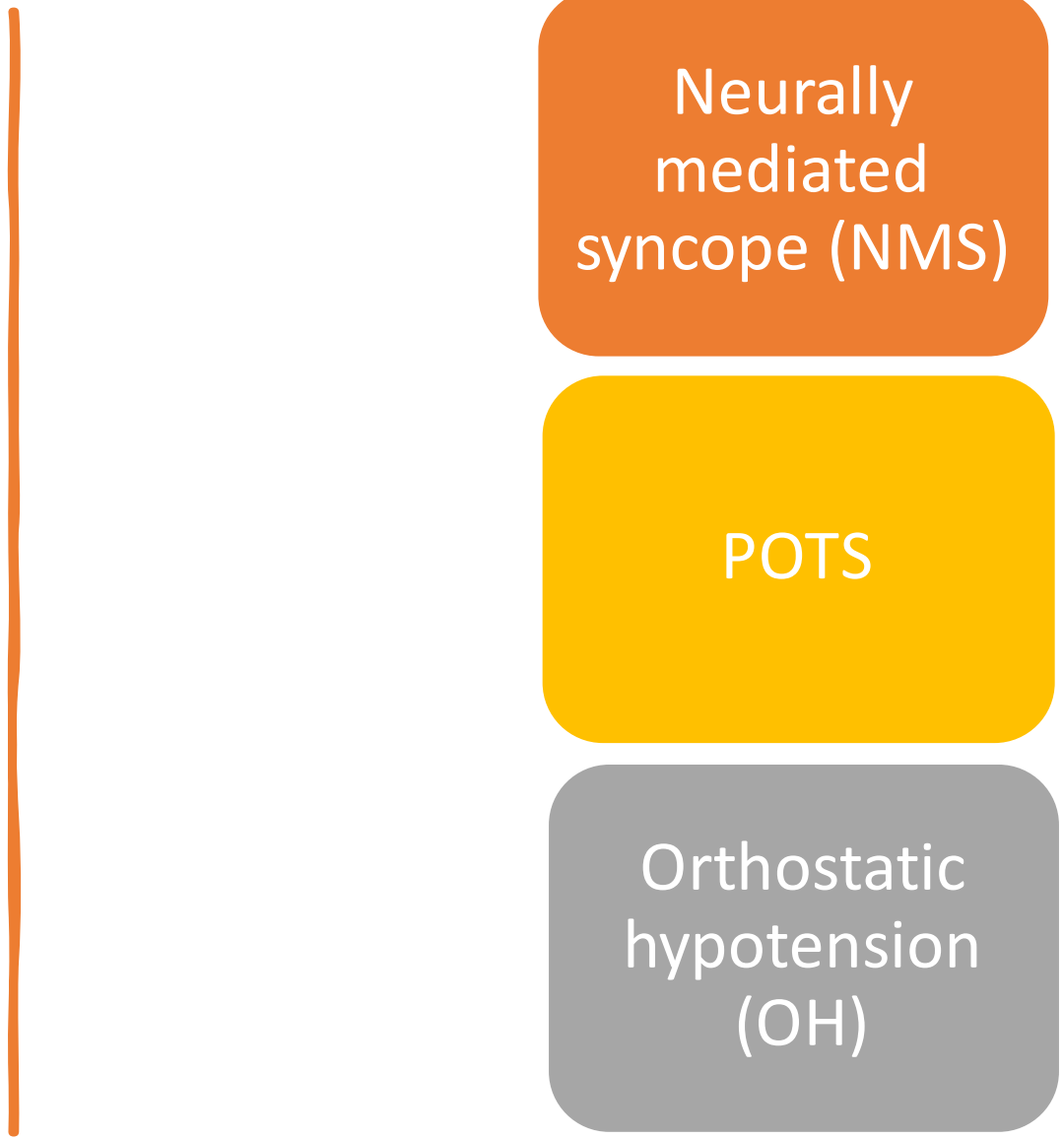
Baroreceptors



Orthostatic Intolerance (OI)

- Not tolerating being upright
- Symptoms include dizziness, palpitation, blurred vision, muffled hearing, nausea, and possibly syncope. Often patients are pale.
- Acute vs chronic OI

OI Subtypes


Neurally mediated syncope (NMS)
POTS
Orthostatic hypotension (OH)

Neurally Mediated (Reflex) Syncope

- Syncope is a form of transient loss of consciousness, accompanied by loss of muscle tone, with rapid onset and full and quick recovery.
- Events usually start with dizziness, palpitation, tunnel vision, pallor, diaphoresis, yawning, etc.
- Post event symptoms: confusion, dizziness, nausea, vomiting, sleepiness.
- “Neurocardiogenic syncope” is not a preferred term.

NMS Subtype

Vasovagal syncope (VVS)	Situational syncope	Carotid sinus syndrome
• Vasodepressor • Cardioinhibitory • Mixed form	• cough • defecation • Urination • Laugh	

NMS Management

- Reassurance
- Antigravity maneuvers
- Hydration
- Medications: midodrine, atomoxetine, fludrocortisone
- (beta blockers)
- (Pacemaker)

Postural Orthostatic Tachycardia Syndrome

- Sustained heart rate increase of at least 30 bpm (40 bpm increase in individuals <19 years) or heart rate increase above 120 bpm (or 140 bpm in children) in upright position without hypotension.

POTS

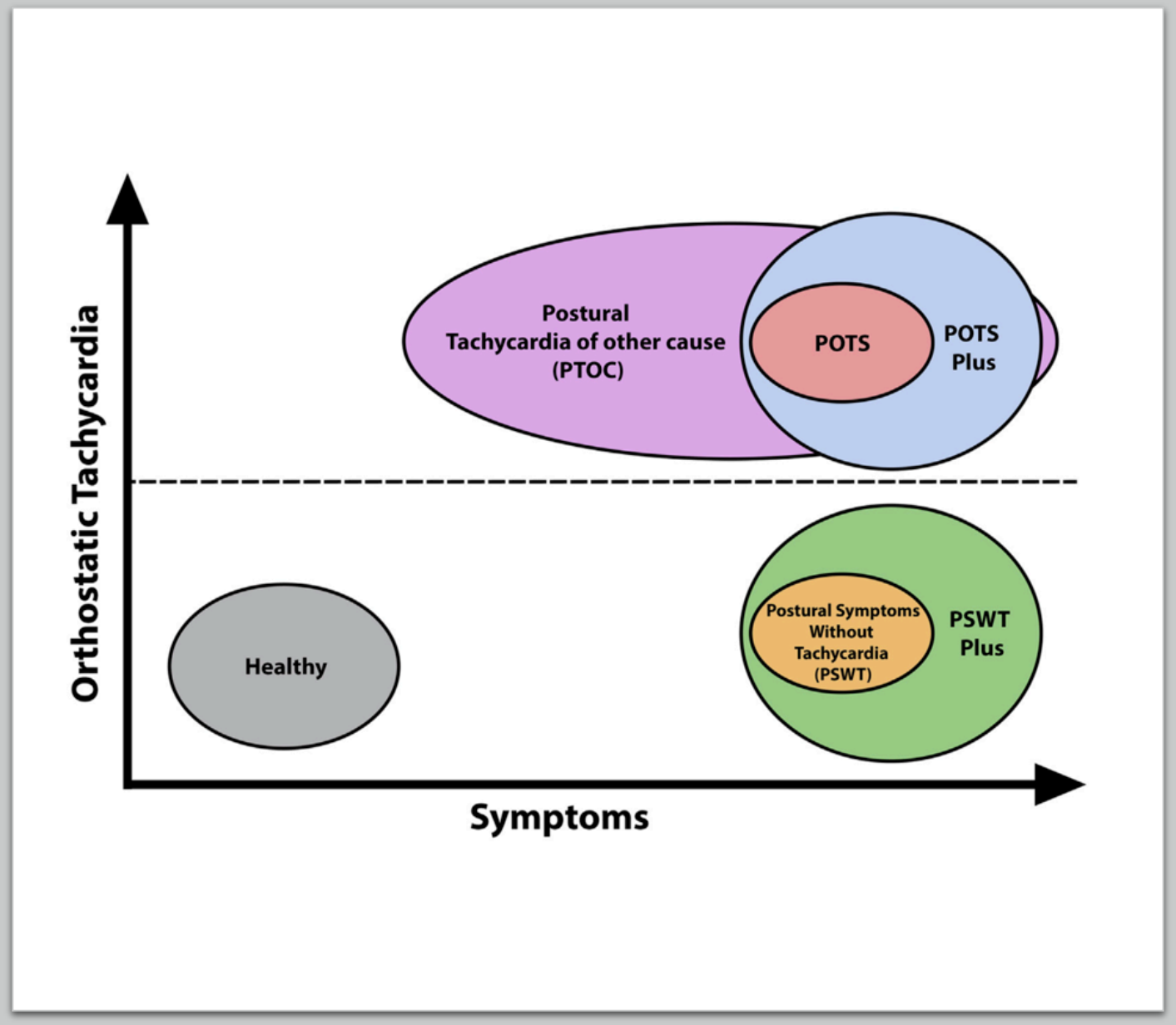
- Females by far more affected.
- Typical age of onset 12-16 years
- Symptoms: dizziness, palpitation, chest pain, HA, nausea, fatigue, insomnia, exercise intolerance
- Associated conditions: hypermobility, mast cell activation, CFS/ME, autoimmune disorder. Celiac disease, mitochondrial disorder

POTS Subtypes

- Neuropathic
- Hyperadrenergic
- Hypovolemia
- Deconditioning

Canadian POTS Classification

- POTS
- POTS Plus
- PSWT
- PSWT Plus
- PTOC



Raj et al. Can J Cardiol 2020

POTS Therapy

- Reassurance does not work here.
- Often multidisciplinary approach (GI, neuro, pain management, PT ...)
- High fluid and salt diet
- Medications: Midodrine, fludrocortisone, beta blockers, pyridostigmine, droxidopa, atomoxetine, carbidopa, ivabradine
- Exercise
- IV fluid?

Orthostatic hypotension

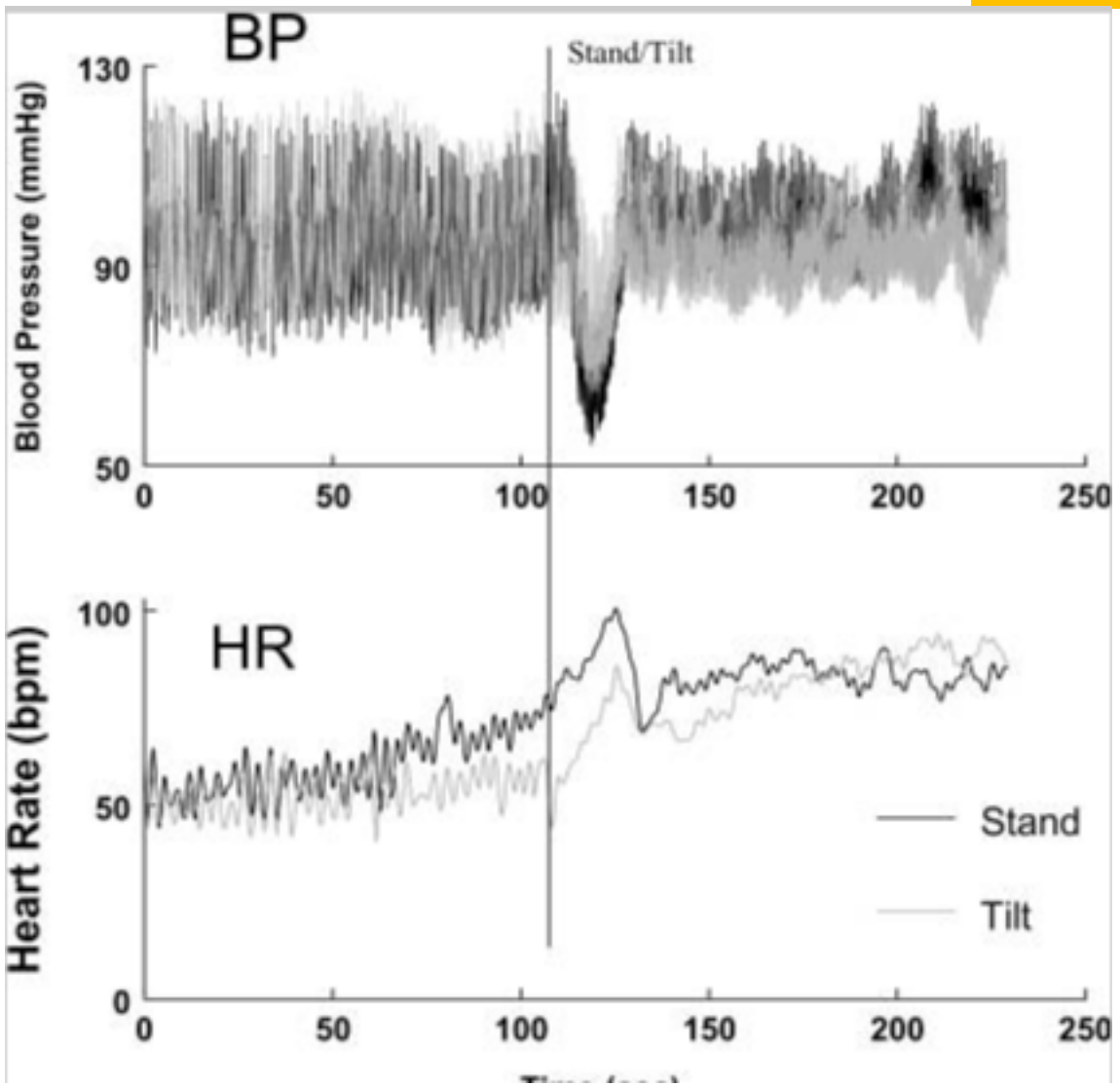
- Classic, neurogenic, orthostatic hypotension (OH) is defined as a sustained, ≥20-mmHg reduction of systolic blood pressure or ≥10-mmHg reduction of diastolic blood pressure within 3 min after standing.

- Delayed OH: hypotension occurs after 3 min. of standing.

- Initial OH: Transient BP fall of >40 mmHg systolic of >20 mmHg diastolic within 15 s of standing and resolves in less than a minute.

iOH

- Common in teens
- Carries good prognosis
- May lead to full syncope



Stewart et al. J Ped 2012

Van Twist et al. Int J Cardiol 2018

iOH Management

- Reassurance
- Hydration
- Exercise (isometric)
- Medication: midodrine

Diagnostic Procedures

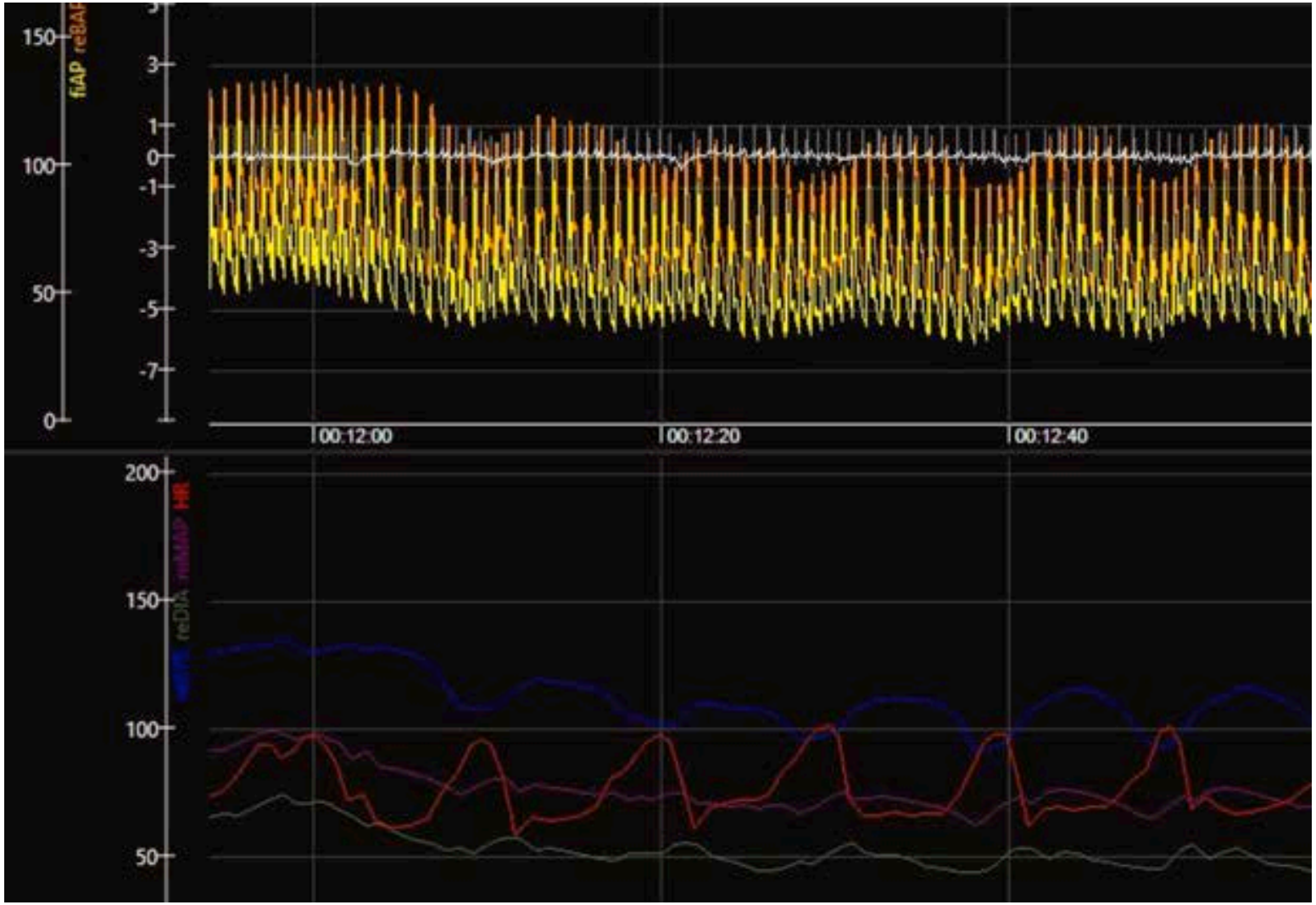
- History still the best tool
- ECG, echo, heart monitors
- Lab studies

Diagnostic Procedures

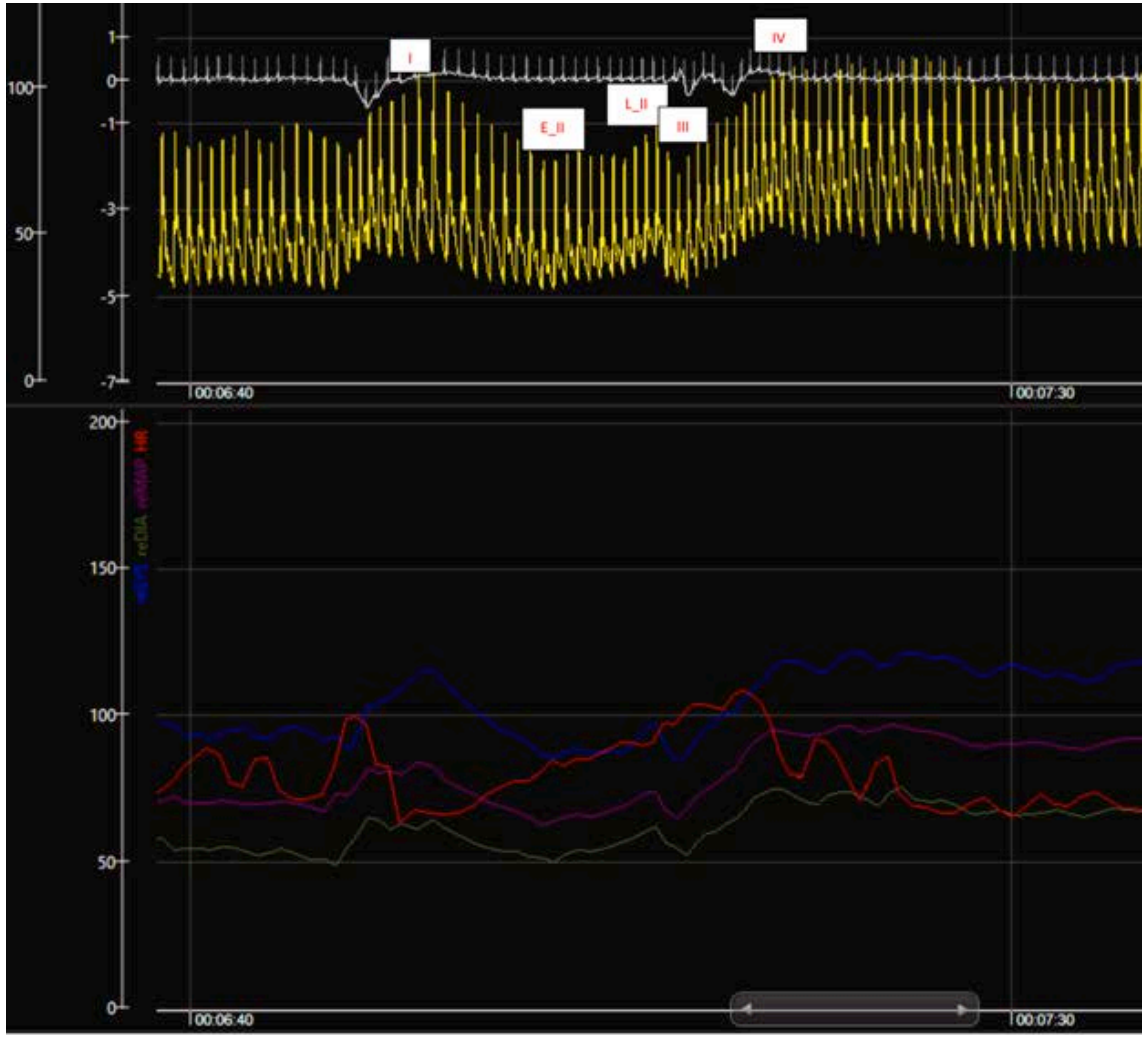
- Autonomic studies
  - Deep breathing test
  - Valsalva maneuver
  - Tilt table test
  - Stand test

- Quantitative sudomotor axonal reflex test (QSART) or quantitative sweat test (Q-Sweat)

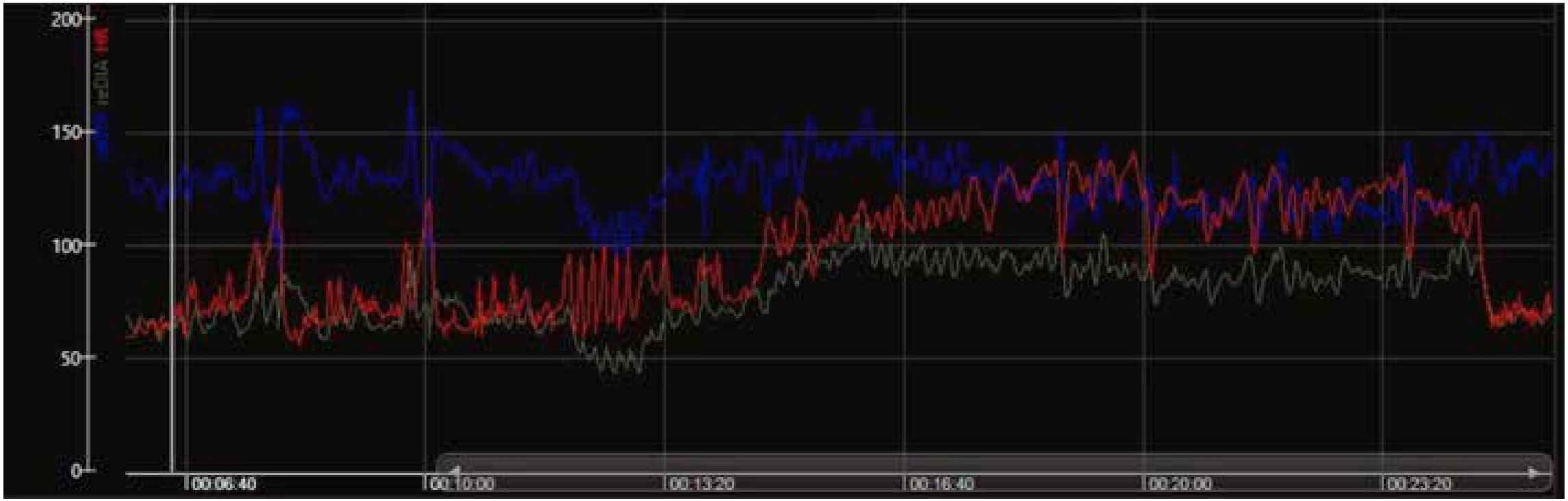
Deep Breathing Test



Valsalva Maneuver



Tilt Table Test



Conclusion

- Orthostatic symptoms and autonomic function are closely involved.
- History is the best tool to the diagnosis
- Autonomic studies are great adjunct diagnostic tools.
- Therapy of chronic orthostatic intolerance can be challenging and protracted.