DYSAUTONOMIA IN EDS AND HSD

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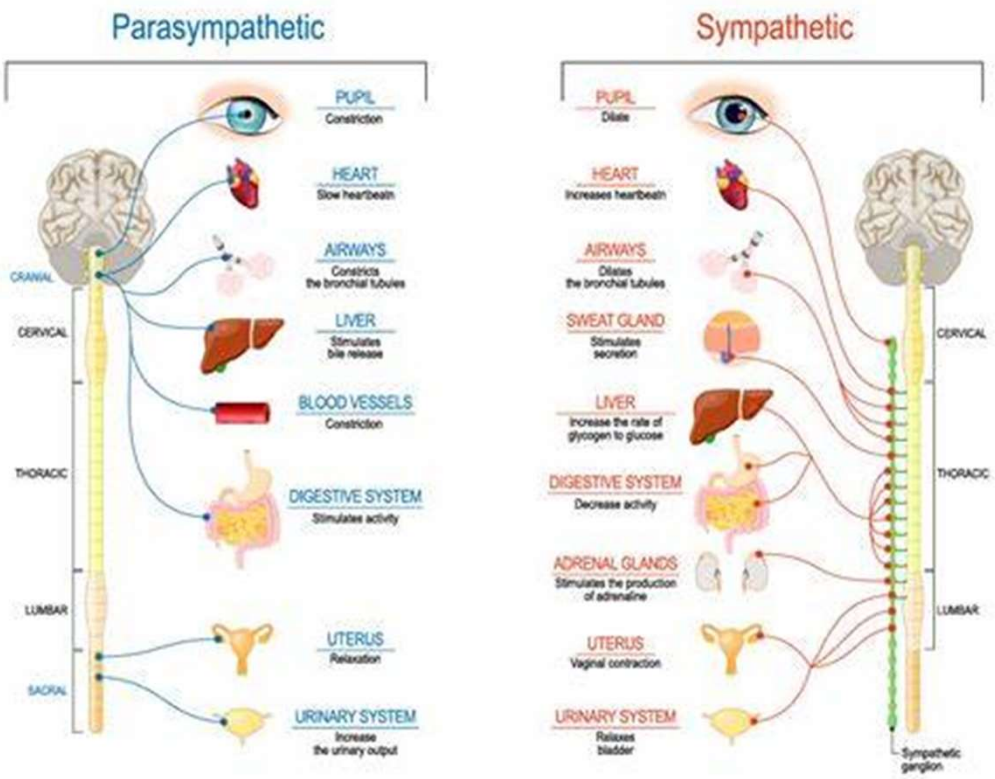
AUTONOMIC NERVOUS SYSTEM



Dysautonomia in EDS and HSD

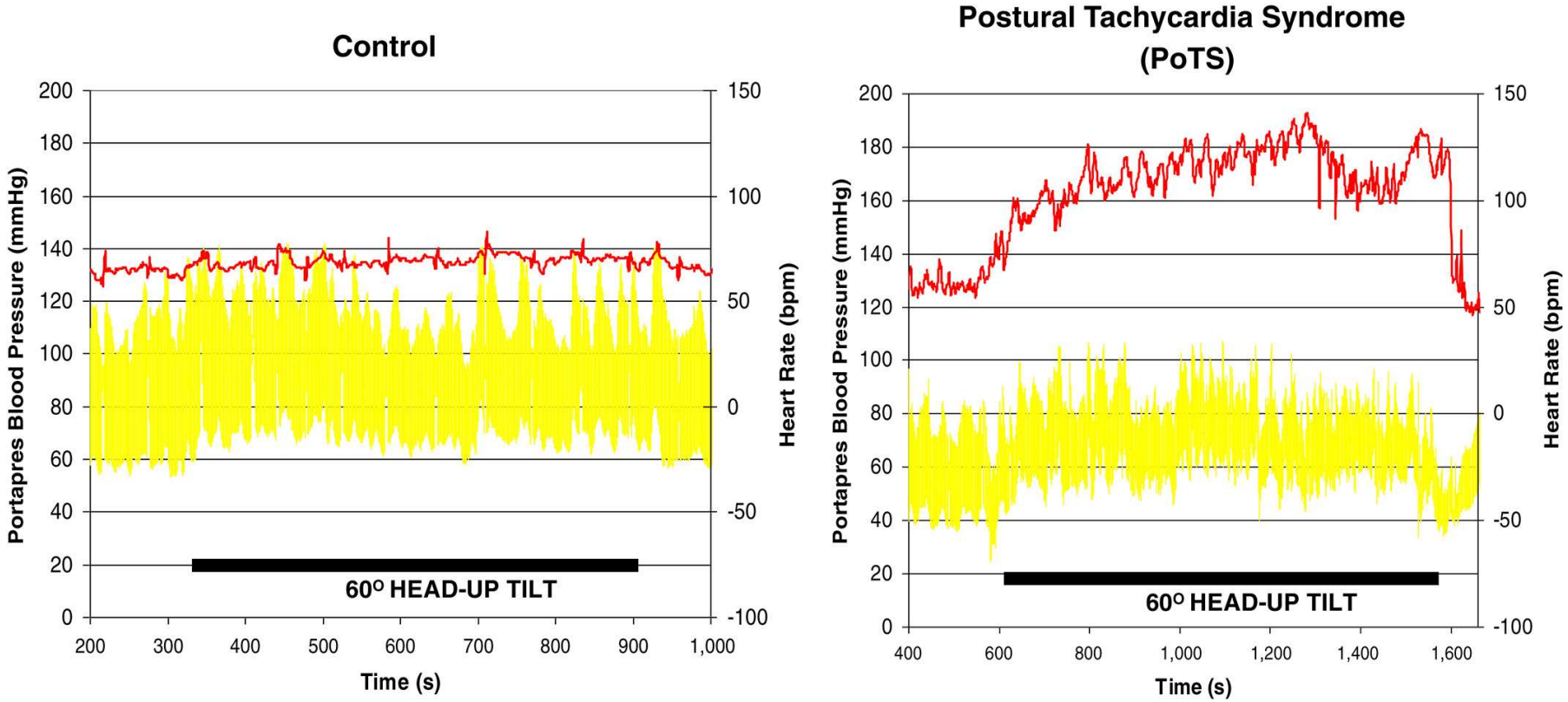
- Gastrointestinal dysmotility
- Disturbed bladder function
- Disturbed sweat regulation
- Cardiovascular autonomic dysfunction
  - Orthostatic intolerance
  - Orthostatic hypotension
  - Neurally mediated hypotension – vaso-vagal syncope/neuro-cardiogenic syncope
  - Postural tachycardia syndrome (PoTS)

-> Focus on PoTS

THE PoTS

- First described 1982 (Rosen and Cryer), later description by Schondorf and Low 1993 as “Postural orthostatic tachycardia syndrome”
- Prevalence estimated 170 cases per 1 million in the general population
- Intermittent autonomic malfunction – between the episodes no autonomic abnormalities (hEDS) Mathias et al., 2011
- PoTS diagnoses: elevation of HR > 30 beats/min in adults and >40bpm in teenagers and adolescents (12-19 years) within 10 min of head-up tilt or standing, or when the HR is over 120bpm while upright

HR & BP measured continuously and non-invasively

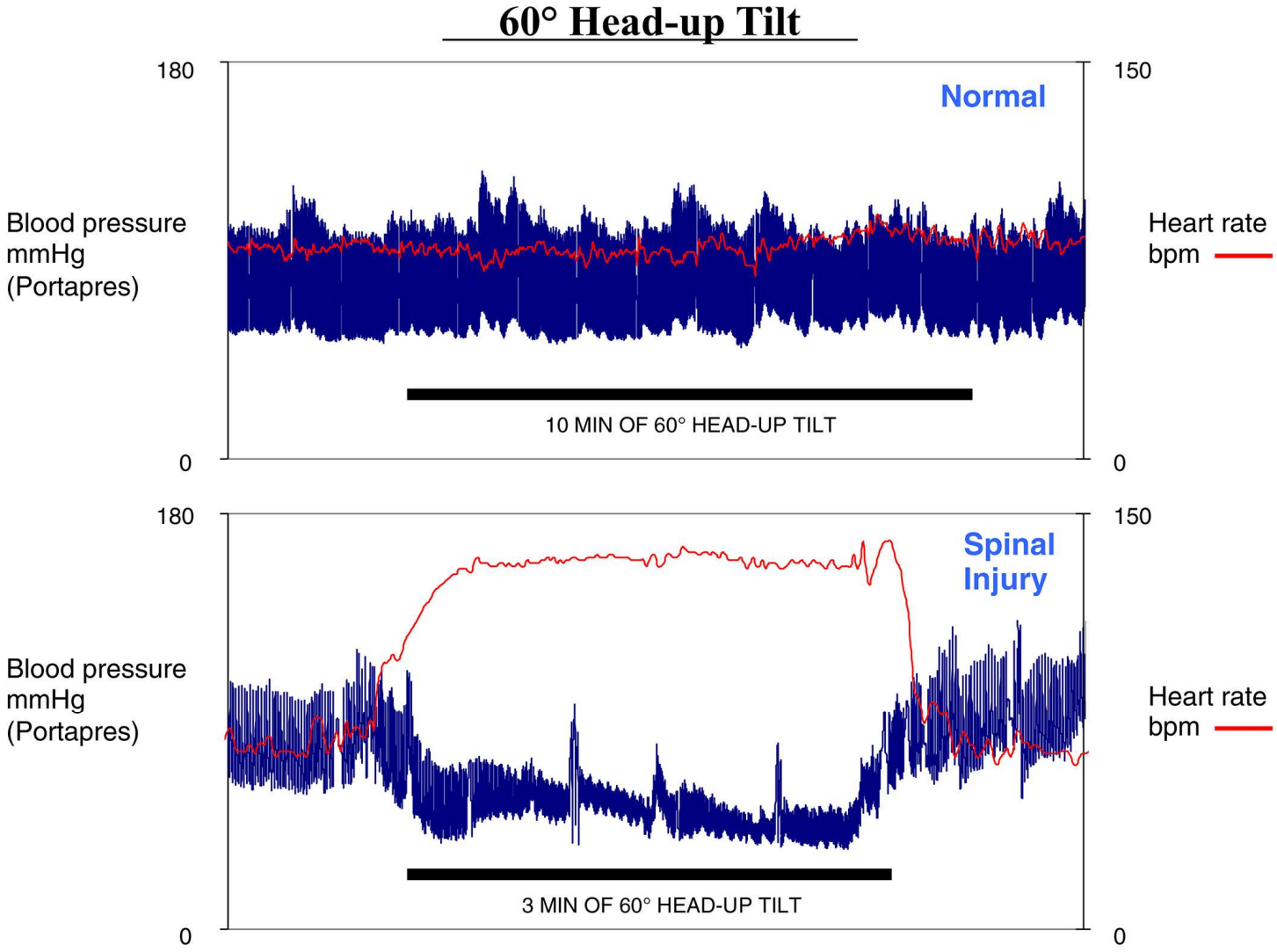


Mathias et al. 2021

- ORTHOSTATIC HYPOTENSION SHOULD NOT BE PRESENT IN UPRIGHT POSITION

- Hyperadrenergic PoTS - orthostatic hypertension (>10mmHg rise in systolic BP while 10min upright position)

SPINAL CORD INJURY



SYMPTOMS OF PoTS

- History of orthostatic intolerance
  - Palpitations
  - Dizziness
  - Visual disturbances
  - Headache
  - Nausea
  - Shortness in breath
  - Pain
  - Presyncope and sometimes syncope
  - Nonspecific – fatigue, brain fog, attentional deficits

FACTORS TO AVOID

- Exacerbating factors
  - Standing still
  - Certain foods (carbohydrates, large meals)
  - Even small amounts of alcohol
  - Physical exertion
  - Dehydration
  - Menstruation
  - Drugs that cause vasodilatation
  - Hot weather

  -> each of this stimuli can cause vasodilatation

PoTS patients and history

- Patients young and more likely to be female
- Onset mostly difficult to pinpoint
- Some report trigger
  - Infection
  - Stress
  - Trauma
  - surgery

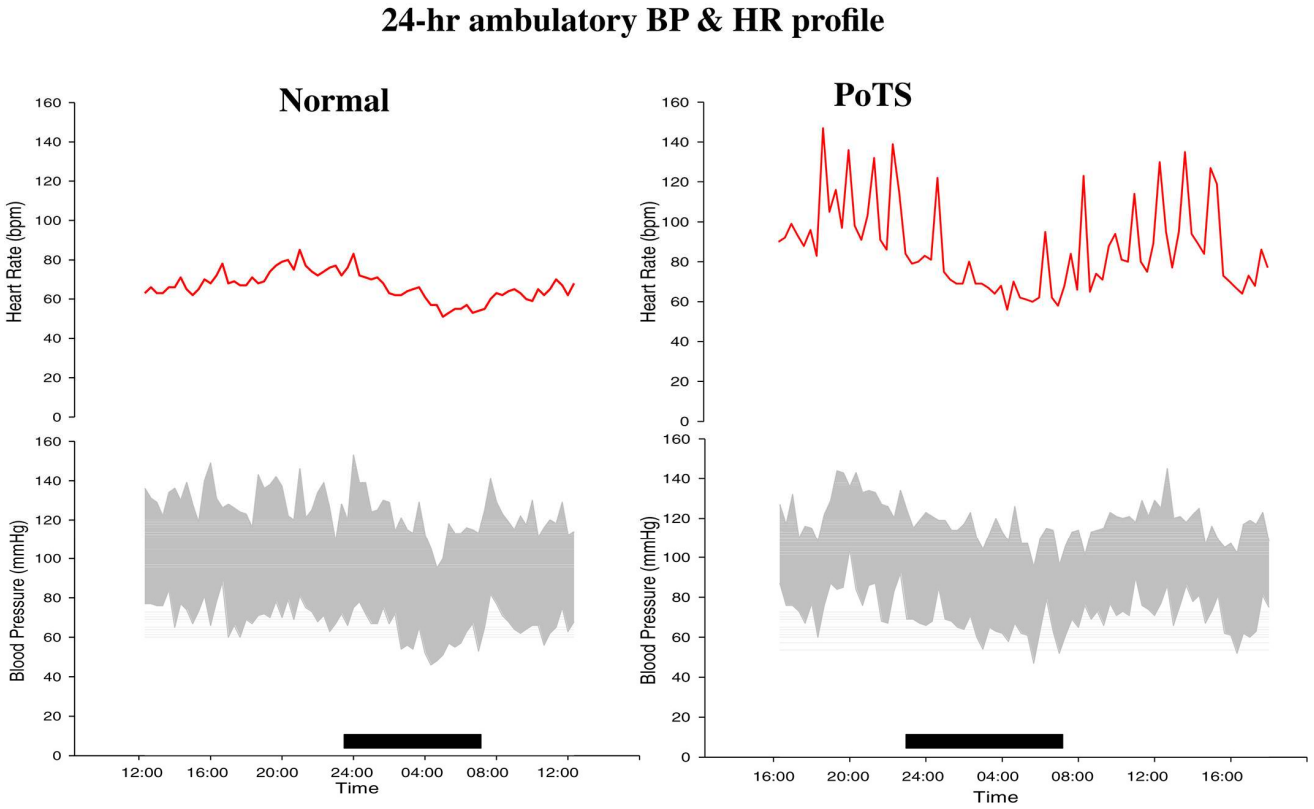
Relationship between joint hypermobility syndrome and PoTS

- Mechanism that cause or contribute to PoTS in EDS unclear
  - Increased peripheral venous dilation and blood pooling
  - Low circulating blood volume
  - Elevated circulating catecholamines
  - Autoimmunity
  - Excess systemic levels of histamine
    - Histamine can induce hypotension and tachycardia
    - Mast cell activation has been identified in cases of hEDS (L.B. Afrin 2021)

Autonomic investigation for PoTS

- Standing test or head up tilt test (10min)
- Pressor stimuli – cutaneous cold, isometric exercise (determine the vasoconstrictor function)
- Heart rate response (determine cardiac parasympathetic responsiveness)
- Plasma noradrenaline and adrenaline levels – supine and upright
- Ambulatory blood pressure and heart rate autonomic monitoring (Mathias et al. protocol)

PoTS – ambulatory RR and HR measurement



Non – autonomic investigations

- Echocardiography (valvular prolapse?)
- Structural neuroimaging – cranio-cervical junction to exclude a Chiari malformation (upright neuroimaging)
- Exclude ‘Small fiber neuropathy’
- Testing of gastrointestinal and bladder function

Differential diagnosis

- Pheochromocytoma
- Adrenocortical deficiency
- Inappropriate ADH secretion…

Treatment – Non pharmacological

To be avoided

- Sudden head up postural change
- Prolonged recumbency
- High environmental temperatures (including hot baths)
- Large meals
- Alcohol
- Undue exertion

To be introduced

- High salt intake
- Water repletion
- Small, frequent meals
- Judicious regular exercise (including swimming)
- Raising the head end of the bed at night
- Physical maneuvers to activate autonomic activity (such as sustained hand grip)
- To be considered – compression stockings

PHARMACOLOGICAL TREATMENT

THERAPEUTIC STRATEGY	DRUG CLASS OR MECHANISM	AGENT
Reducing salt loss and/or plasma volume expansion	Mineralecorticoid	Fludrocortisone
Vasoconstriction	Alpha adrenoreceptors	Midodrine
Reducing tachycardia	Beta2 adrenoreceptor blockers – cardioselective, selective sinus node blockade	Bisoprolol, Ivabradine
Ganglionic nicotinic receptor stimulation	Anticholinesterase inhibitors	Pyridostigmine
Reducing raised blood pressure/heart rate	Central sympatholytic	Clonidine, Moxonidine

CONCLUSION

- Dysautonomia may occur in EDS and HSD
- Often manifests as PoTS
- PoTS symptoms have a negative impact on quality of life
- Non pharmacological treatment first choice
- Pharmacological treatment – individualized depending on
  - Resting, supine BP

  -> objective assessment before start of treatment is necessary