

Disclosures

No pertinent financial disclosures

Objectives

- Understand the diagnostic criteria for the recognition of PSH
- Review the most commonly used abortive and preventive pharmacological agents for the management of PSH

A relatively common problem

- It can occur in up to a third of patients with severe TBI
- Can happen after brain anoxia
- More common in younger patients
- Often misdiagnosed and underdiagnosed
- Nomenclature and diagnostic criteria have lacked uniformity

A messy literature

- **Paroxysmal Sympathetic Hyperactivity**
- Autonomic storms
- Sympathetic storms
- Diencephalic seizures
- Autonomic dysfunction syndrome
- Dysautonomia
- Paroxysmal autonomic instability with dystonia (PAID)

Diffuse/multifocal acute brain injury

Disinhibition of sympathetic responses

Paroxysmal Sympathetic Hyperactivity

External or internal triggers

Recurrent episodes

Tachycardia

Hypertension

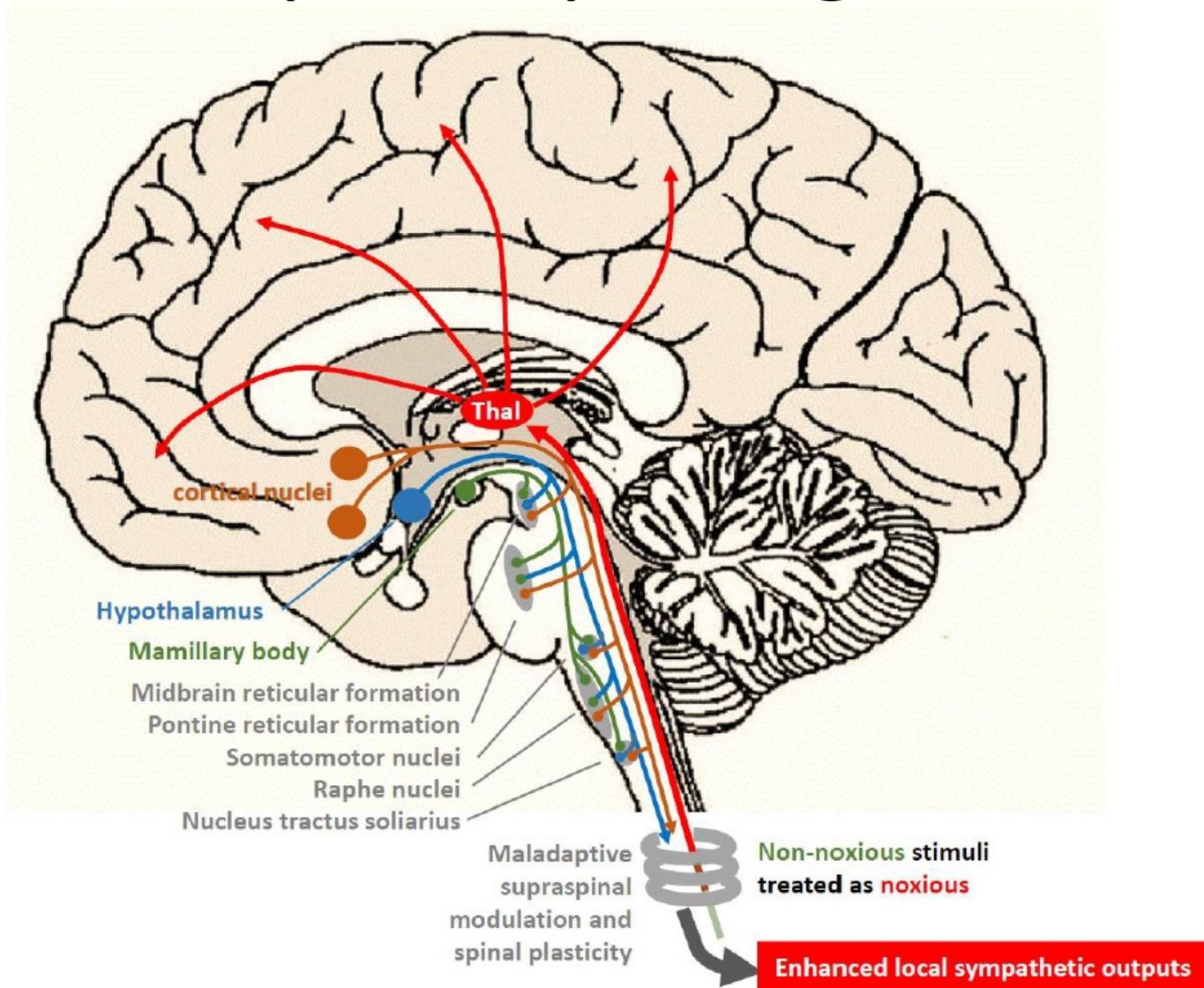
Tachypnea

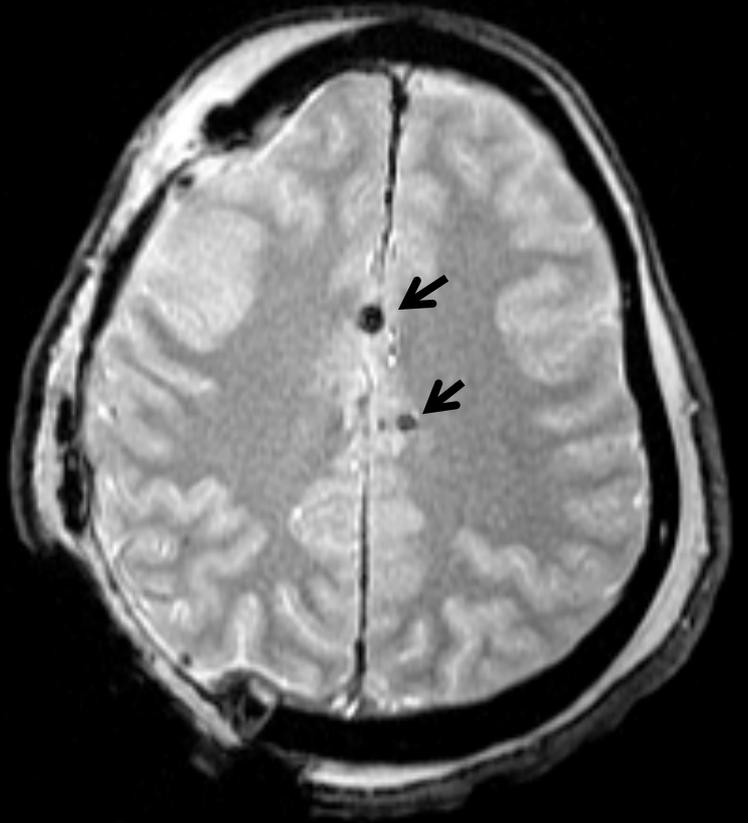
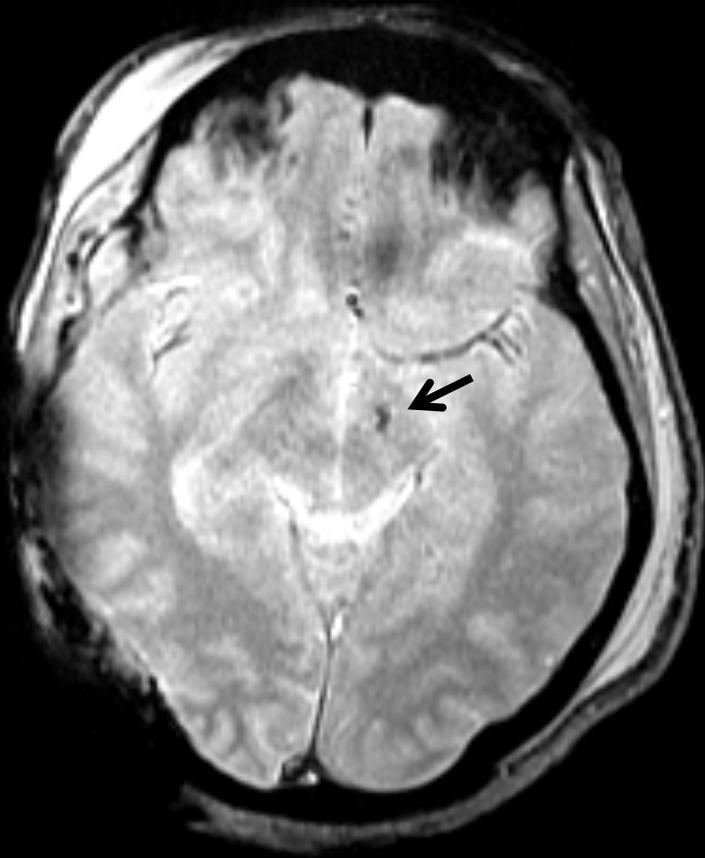
Fever

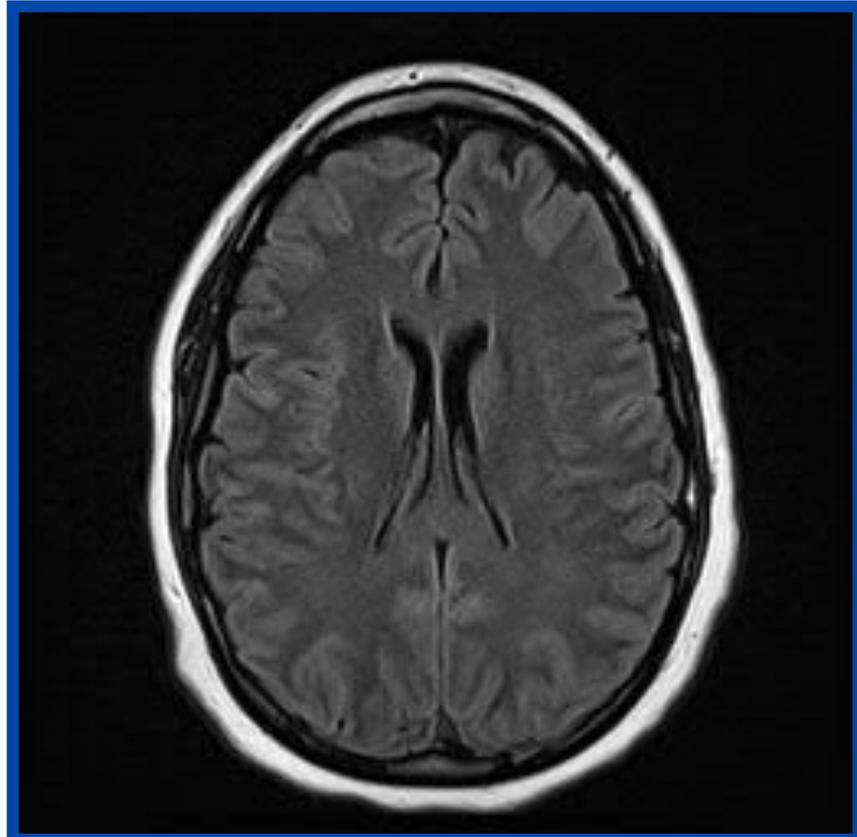
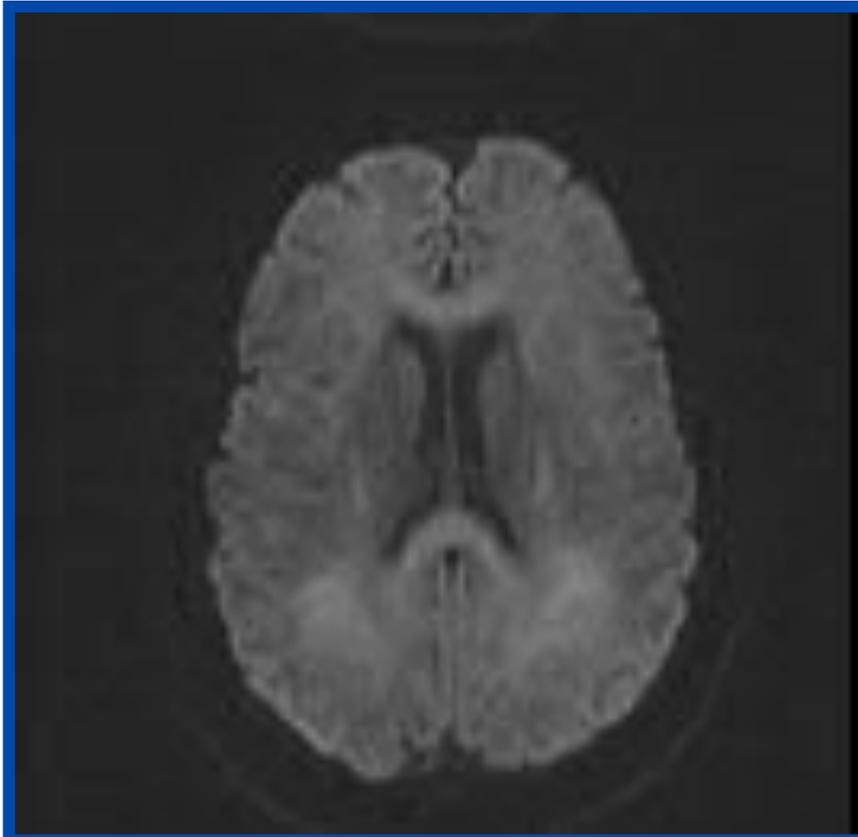
Diaphoresis

Dystonia

Proposed pathogenesis







Diagnostic criteria

Episodic presence of ≥ 4 of the following 6 criteria in the absence of alternative causes:

- Fever ($> 38^{\circ}$ C)
- Tachycardia (>120 x' or > 100 x' if beta-blocked)
- Hypertension (SBP > 160 or PP > 80)
- Tachypnea (RR > 30)
- Excessive diaphoresis
- Severe dystonia

New Consensus Criteria: Assessment Tool

Paroxysmal Sympathetic Hyperactivity - Assessment Measure					
Clinical Feature Scale (CFS)					
	0	1	2	3	Score
heart rate	< 100	100 - 119	120 - 139	≥ 140	
respiratory rate	< 18	18 - 23	24 - 29	≥ 30	
systolic blood pressure	< 140	140 - 159	160 - 179	≥ 180	
temperature	< 37	37 - 37.9	38 - 38.9	≥ 39.0	
sweating	nil	mild	moderate	severe	
posturing during episodes	nil	mild	moderate	severe	
			CFS Subtotal		
Severity of Clinical Features					
			nil	0	
			mild	1 - 6	
			moderate	7 - 12	
			severe	≥ 13	

New Consensus Criteria: Assessment Tool

Diagnosis Likelihood Tool (DLT)			
clinical features occur simultaneously			
episodes are paroxysmal in nature			
over-reactivity to normally non-painful stimuli			
features persist ≥ 3 consecutive days			
features persist ≥ 2 weeks post brain injury			
features persist despite treatment of differential diagnoses			
medication administered to decrease sympathetic features			
≥ 2 episodes daily			
absence of parasympathetic features during episodes			
absence of other presumed cause of features			
antecedent acquired brain injury			
(Score 1 point for each feature present)	DLT subtotal		
Combined total (CFS + DLT)			
PSH Diagnostic Likelihood			
unlikely	< 8		
possible	8 - 16		
probable	> 17		

Common triggers

- Pain
- Bladder distension
- Foley manipulation
- Body turning
- Tracheal suctioning
- Most often unprovoked

Differential diagnosis

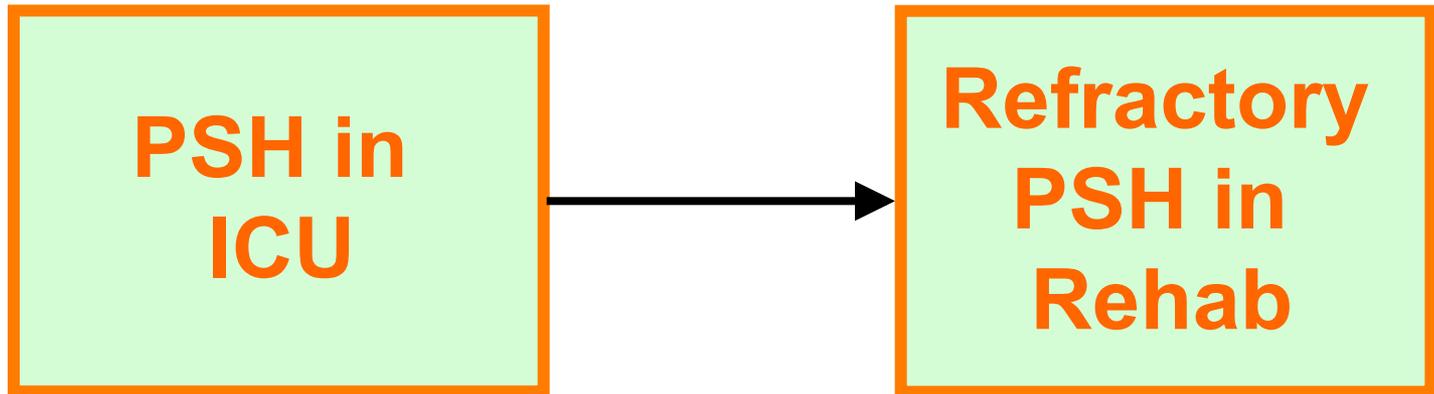
- Sepsis
- Intracranial hypertension
- Seizures
- Rebleeding
- Airway obstruction
- Pulmonary embolism
- Serotonin syndrome/ NMS / Malignant hyperthermia

Diagnosis	Discriminating feature	Confirmatory testing
Intracranial hypertension	Bradycardia may occur Profuse sweating less likely	ICP monitoring Head CT scan
Herniation	Asymmetric posturing Unilateral mydriasis	Head CT scan Brain MRI
Seizures	Clonic movements Shorter duration Profuse sweating less likely	EEG
Intracranial bleeding or rebleeding	Focal deficits	Head CT scan Brain MRI
Pulmonary embolism	Refractory hypoxemia	Chest CT angiography
Severe sepsis	Hypotension	Cultures

Why recognition is important

- **Increases secondary morbidity**
 - Hypermetabolism (↓ body weight)
 - Prolonged hyperthermia
 - Dehydration
 - Neurocardiogenic injury
 - ↑ ICP (?)
 - Contractures
 - Heterotopic ossification
- Inappropriate testing and therapies
- Prolongation of ICU stay

Early recognition → Better Rehab



Our clinical experience in the ICU

- 53 pts – Mean age 33.6 ± 14.5 years (range 16-67)
- TBI in 57% (but also anoxia, SAH, ICH, autoimmune encephalitis, FES, etc)
- Mean time to diagnosis 8.3 ± 11.0 days
- 59% within 7 days and 38% within 3 days

Symptom frequency

Symptom	Frequency
Fever	79%
Tachycardia	98%
Hypertension	72%
Tachypnea	85%
Diaphoresis	79%
Dystonia/Posturing	38%

What to do with the fever?

- 42/53 had fever
- 26 (62%) were treated with antibiotics
- Respiratory infections suspected or confirmed in 24
- In 16 cases antibiotics were started due to symptoms of PSH

Treatments and Outcomes

- Mean duration of episodes 15 ± 20 days (actually 2 weeks if only considered hospital survivors)
- All treated with a mean of 2.1 meds
- 35/37 who survived were discharged on treatment for PSH
- 16 were discharged with ongoing episodes of PSH

Reduce external stimulation

**Paroxysmal Sympathetic
Hyperactivity**

Drug Therapy

Abortive

- IV morphine
- IV beta blockers
- Dexmedetomidine

Preventive

- Gabapentin
- Oral beta blockers
- Clonidine

Drug Treatment of PSH

- **ABORTIVE**
 - Use promptly
- **PREVENTIVE**
 - Start early
 - Requires titration
 - Continue in Rehab

Treatment:

Limitations of the “evidence”

- Case reports and case series
- Lack of diagnostic criteria
- Benefit based on clinical impression (no standardized outcome measures)
- Often treatments only improve specific manifestations
- Absence of controls

Classes of Drugs Tested

- Opiates
- GABA A agonists (BDZs)
- GABA B agonists (Baclofen)
- Alpha 2 agonists
- Beta Blockers
- Dopamine agonists (*and antagonists*)
- Anticonvulsants
- Others (e.g. dantrolene, botulinum toxin A, *hyperbaric oxygen???*)

Abortive Treatments

- Morphine sulfate
 - Most effective abortive agent
 - 2-8 mg IV
- Propranolol / Clonidine / dexmedetomidine
- Benzodiazepines (diazepam)
- Baclofen (IT *but not oral*)
- Dantrolene
- *Chlorpromazine and haloperidol (antidopaminergics) should be avoided*

Prophylactic agents

- Gabapentin

 - Start 300 mg tid and titrate up to 3600-4800 mg per day

- Propranolol

- Clonidine

- Bromocriptine

- Baclofen IT

Support for my choices

- Morphine: multiple case reports and small case series
- Propranolol: multiple case reports and small case series
- Gabapentin: Case series of 6 pts with refractory PSH (Baguley J Neurol Neurosurg Psychiatry 2007; 78: 539–41)

Our Current Study

- Observational, multinational
- Feasibility of application of diagnostic tools
- General assessment of current epidemiology and therapeutic practices
- Formation of a collaborative team for a future interventional trial

Key Messages

- Think of PSH in TBI (and anoxic) patients with episodic changes
- Early recognition of PSH can prevent major short and long term complications
- Use morphine to abort the episodes and gabapentin and propranolol to prevent them
- High quality prospective research is greatly needed

Thank You

