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
Diagnosis criteria

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

- Fever (> 38°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

<table>
<thead>
<tr>
<th>Clinical Feature Scale (CFS)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>heart rate</td>
<td>&lt; 100</td>
<td>100 - 119</td>
<td>120 - 139</td>
<td>≥ 140</td>
<td></td>
</tr>
<tr>
<td>respiratory rate</td>
<td>&lt; 18</td>
<td>18 - 23</td>
<td>24 - 29</td>
<td>≥ 30</td>
<td></td>
</tr>
<tr>
<td>systolic blood pressure</td>
<td>&lt; 140</td>
<td>140 - 159</td>
<td>160 - 179</td>
<td>≥ 180</td>
<td></td>
</tr>
<tr>
<td>temperature</td>
<td>&lt; 37</td>
<td>37 - 37.9</td>
<td>38 - 38.9</td>
<td>≥ 39.0</td>
<td></td>
</tr>
<tr>
<td>sweating</td>
<td>nil</td>
<td>mild</td>
<td>moderate</td>
<td>severe</td>
<td></td>
</tr>
<tr>
<td>posturing during episodes</td>
<td>nil</td>
<td>mild</td>
<td>moderate</td>
<td>severe</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severity of Clinical Features</th>
<th>nil</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild</td>
<td>1 - 6</td>
<td></td>
</tr>
<tr>
<td>moderate</td>
<td>7 - 12</td>
<td></td>
</tr>
<tr>
<td>severe</td>
<td>≥ 13</td>
<td></td>
</tr>
</tbody>
</table>

J Neurotrauma 2014;31:1515-20
New Consensus Criteria: Assessment Tool

<table>
<thead>
<tr>
<th>Diagnosis Likelihood Tool (DLT)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>clinical features occur simultaneously</td>
<td></td>
</tr>
<tr>
<td>episodes are paroxysmal in nature</td>
<td></td>
</tr>
<tr>
<td>over-reactivity to normally non-painful stimuli</td>
<td></td>
</tr>
<tr>
<td>features persist ≥ 3 consecutive days</td>
<td></td>
</tr>
<tr>
<td>features persist ≥ 2 weeks post brain injury</td>
<td></td>
</tr>
<tr>
<td>features persist despite treatment of differential diagnoses</td>
<td></td>
</tr>
<tr>
<td>medication administered to decrease sympathetic features</td>
<td></td>
</tr>
<tr>
<td>≥ 2 episodes daily</td>
<td></td>
</tr>
<tr>
<td>absence of parasympathetic features during episodes</td>
<td></td>
</tr>
<tr>
<td>absence of other presumed cause of features</td>
<td></td>
</tr>
<tr>
<td>antecedent acquired brain injury</td>
<td></td>
</tr>
</tbody>
</table>

(Score 1 point for each feature present) | DLT subtotal

| Combined total (CFS + DLT) |          |

<table>
<thead>
<tr>
<th>PSH Diagnostic Likelihood</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>unlikely</td>
<td>&lt; 8</td>
</tr>
<tr>
<td>possible</td>
<td>8 - 16</td>
</tr>
<tr>
<td>probable</td>
<td>&gt; 17</td>
</tr>
</tbody>
</table>
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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Discriminating feature</th>
<th>Confirmatory testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial hypertension</td>
<td>Bradycardia may occur</td>
<td>ICP monitoring</td>
</tr>
<tr>
<td></td>
<td>Profuse sweating less likely</td>
<td>Head CT scan</td>
</tr>
<tr>
<td>Herniation</td>
<td>Asymmetric posturing</td>
<td>Head CT scan</td>
</tr>
<tr>
<td></td>
<td>Unilateral mydriasis</td>
<td>Brain MRI</td>
</tr>
<tr>
<td>Seizures</td>
<td>Clonic movements</td>
<td>EEG</td>
</tr>
<tr>
<td></td>
<td>Shorter duration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Profuse sweating less likely</td>
<td></td>
</tr>
<tr>
<td>Intracranial bleeding or rebleeding</td>
<td>Focal deficits</td>
<td>Head CT scan</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Brain MRI</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>Refractory hypoxemia</td>
<td>Chest CT angiography</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>Hypotension</td>
<td>Cultures</td>
</tr>
</tbody>
</table>
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

PSH in ICU → Refractory PSH in 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

Neurocrit Care. 2014;20(3):454-459
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
</tr>
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<tbody>
<tr>
<td>Fever</td>
<td>79%</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>98%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>72%</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>85%</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>79%</td>
</tr>
<tr>
<td>Dystonia/Posturing</td>
<td>38%</td>
</tr>
</tbody>
</table>
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 $15 \pm 20$ 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
Paroxysmal Sympathetic Hyperactivity

Drug Therapy

Abortive
- IV morphine
- IV beta blockers
- Dexmedetomidine

Preventive
- Gabapentin
- Oral beta blockers
- Clonidine

Reduce external stimulation
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