Paroxysmal Sympathetic Hyperactivity and Considerations for Rehabilitation

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Methods

- Literature review of articles from 2007-2017
- Online databases used:
  - PUBMED, MEDLINE, COCHRANE and CINAL
- Terms used:
  - Paroxysmal sympathetic hyperactivity, dysautonomia, brain injury, storming, traumatic brain injury, outcome and rehabilitation
Paroxysmal Sympathetic Hyperactivity

• Characteristic traits were first described by Wilder Penfield in 1929
  • Initially thought to be from a seizure focus
• Over 31 other names identified for the syndrome
• Call for unified term came in 2007 by Alejandro Rabinstein, who suggested use of the term PSH
Definition

“A syndrome, recognized in a subgroup of survivors of severe acquired brain injury, of simultaneous, paroxysmal transient increases in sympathetic (elevated heart rate, blood pressure, respiratory rate, temperature, sweating) and motor (posturing) activity.”

Epidemiology

- 8-33% of acquired brain injuries develop PSH
- Incidence of 15-33% in severe TBI
- Lasts about 18-162 days and resolves within a year

Types of Brain Injury In PSH

- 80% TBI
- 5% Anoxic
- 5% Stroke
- 10% Other
Pathophysiology

• Several proposed mechanisms

• No seizure activity was noted on electroencephalography and noted that the syndrome is not effectively treated with anticonvulsants

• There is no specific lesion designated as the causative factor for the development of PSH, but rather the overall burden of the injury
Pathophysiology cont...

- Sympathetic surge
  - 40% increase from baseline in serum adrenocortical hormones
  - 200-300% increase in serum catecholamine levels during paroxysmal episodes

Systemic Effects

- Elevated catecholamine levels

- Extracranial manifestations
  - Cardiac arrhythmia
  - Pulmonary edema
  - Immunosuppression
  - Focal myocytolysis and myocardial necrosis
Excitatory: Inhibitory Ratio (EIR) Model

• Latest concept is the excitatory: inhibitory ratio (EIR) model

• The model is not specific to PSH and takes into account several neurological disorders that can cause autonomic and muscular overactivity

• 2 part disconnect theory
EIR cont...

- Disconnect theory
  - Injury of higher centers (cortex, diencephalon and upper brainstem)
    - Loss of inhibition over the now unopposed sympathetic outflow from the lower brainstem and spinal cord
  - Loss of ability to modulate the afferent sensory information processed by the spinal cord.
    - Spinal cord circuits to create a positive feedback loop or an amplification of non-noxious or mild noxious stimuli that result in allodynia
  - Allodynic tendency
What is the diagnosis?
Diagnosis

- **Diagnosis of exclusion!**
- No standard criteria or measure
- **Symptoms & Signs**
  - Tachycardia
  - Tachypnea
  - Hypertension
  - Fever
  - Diaphoresis
  - Posturing
<table>
<thead>
<tr>
<th>Differential Diagnoses</th>
<th>Most Common Causes</th>
<th>Least Common Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Constipation</td>
<td>Heterotopic Ossification</td>
</tr>
<tr>
<td></td>
<td>Urinary retention</td>
<td>Neuropathic pain (ie: CRPS)</td>
</tr>
<tr>
<td></td>
<td>Infection</td>
<td>Fractures</td>
</tr>
<tr>
<td></td>
<td>Wounds</td>
<td>Deep venous thrombosis</td>
</tr>
<tr>
<td></td>
<td>Respiratory</td>
<td>Nephrolithiasia</td>
</tr>
<tr>
<td></td>
<td>Metabolic derangements</td>
<td>Cholelithiasia</td>
</tr>
</tbody>
</table>
Key features of PSH

- Features are paroxysmal in nature
- Simultaneity of clinical features
- Sympathetic overactivity to normally non-painful stimuli
- Absence of intra-paroxysmal parasympathetic features during episodes
- Features persist ≥ 3 consecutive days
- Features persist ≥ 2 weeks post-injury
- Features are persistent despite treatment of alternative differential diagnosis
- Medication administered to decrease sympathetic features
- Lack of alternative explanations
- Antecedent acquired brain injury
PSH-Assessment Measure

- PSH-AM

- Clinical tool devised to estimate the probability a patient has PSH and the severity of their symptoms

- Helps to monitor and track patients through their recovery and response to treatments

- Two components
  - Clinical Features Scale (CFS)
  - Diagnosis Likelihood Tool (DLT)
### A Clinical feature scale (CFS) score

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats per min)</td>
<td>&lt;100</td>
<td>100-119</td>
<td>120-139</td>
<td>≥140</td>
</tr>
<tr>
<td>Respiratory rate (breaths per min)</td>
<td>&lt;18</td>
<td>18-23</td>
<td>24-29</td>
<td>≥30</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>&lt;140</td>
<td>140-159</td>
<td>160-179</td>
<td>≥180</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>&lt;37.0</td>
<td>37.0-37.9</td>
<td>38.0-38.9</td>
<td>≥39.0</td>
</tr>
<tr>
<td>Sweating</td>
<td>Absent</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Posturing during episodes</td>
<td>Absent</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
</tbody>
</table>
B  Diagnosis likelihood tool (DLT): one point per feature present

- Antecedent acquired brain injury
- Clinical features occur simultaneously
- Episodes are paroxysmal in nature
- Sympathetic over-reactivity to normally non-noxious stimuli
- Absence of parasympathetic features during episodes
- Features persist for >3 consecutive days
- Features persist for >2 weeks post-brain injury
- Two or more episodes daily
- Absence of other presumed causes of features
- Features persist despite treatment of alternative differential diagnoses
- Medication administered to decrease sympathetic features
C Interpretation of scores

- **CFS subtotal**=
  sum of CFS scores for each of the six features (0–3 points for individual features; maximum subtotal=18);
  **CFS subtotal severity scores**:
  0=nil; 1–6=mild; 7–12=moderate; ≥13=severe

- **DLT subtotal**=
  sum of points for each feature present (one point per feature; maximum subtotal=11)

- **PSH-AM**=
  CFS subtotal + DLT subtotal;
  **PSH-AM score**:
  <8=PSH unlikely; 8–16=PSH possible; ≥17=PSH probable
Supportive Treatment

- Avoid or treat possible triggers
- Proper positioning
- Pain management
- Suctioning
- Nutrition
  - Energy expenditure in PSH has been noted up to three times from baseline
  - Decreases in body weight as much as 25-29% in the acute period
## Treatment

<table>
<thead>
<tr>
<th><strong>Category</strong></th>
<th><strong>Medication</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>IV sedatives</td>
<td>Dexmedetomidine, Propofol</td>
</tr>
<tr>
<td>α2 agonists</td>
<td>Clonidine</td>
</tr>
<tr>
<td>β-blockers</td>
<td>Propranolol</td>
</tr>
<tr>
<td>Opiods</td>
<td>Morphine, Fentanyl</td>
</tr>
<tr>
<td>Neuromodulators</td>
<td>Baclofen, Gabapentin, Bromocriptine</td>
</tr>
<tr>
<td>Peripherally Acting Muscle Relaxants</td>
<td>Dantrolene</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Diazepam, Lorazepam, Clonazepam</td>
</tr>
</tbody>
</table>
Acute PSH Episodes

- Send in the storm troopers!
- Goal is to quiet the sympathetic surge
  - Rule out other causes
  - Few meds to keep in mind
    - Opioids
    - Propranolol
Outcomes

• There are a handful of studies that have looked into outcome of PSH patients

• Type of brain injury matters

• Lower Glasgow Outcome Scale scores and functional independence measures compared to similar patients

• Greater need of enteral nutrition and tracheostomies which lend itself toward further complications

• Higher DRS scores, disorders of consciousness, longer LOS, and mortality in this patient group
<table>
<thead>
<tr>
<th>Publication</th>
<th>Brain Injury</th>
<th>Setting</th>
<th># of Cases with PSH</th>
<th>Incidence</th>
<th>Length of stay (Hosp)</th>
<th>Disability Rating Scale</th>
<th>Glasgow Outcome Scale</th>
<th>Functional Independence Measure</th>
<th>Mortality</th>
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</thead>
<tbody>
<tr>
<td>Mathew et al(^\text{a})</td>
<td>TBI</td>
<td>ICU</td>
<td>29/343</td>
<td>8%</td>
<td>Longer</td>
<td>Higher</td>
<td>Worse</td>
<td>NA</td>
<td>Higher</td>
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<tr>
<td>Lv et al(^\text{a})</td>
<td>TBI</td>
<td>ICU</td>
<td>16/79</td>
<td>20.3%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Laxé et al(^\text{a})</td>
<td>TBI</td>
<td>Rehab</td>
<td>13/39</td>
<td>33.3%</td>
<td>Longer</td>
<td>No significant difference</td>
<td>No significant difference</td>
<td>No significant difference*</td>
<td>NA</td>
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<tr>
<td>Hinson et al(^\text{a})</td>
<td>TBI</td>
<td>ICU</td>
<td>19/167</td>
<td>11%</td>
<td>Longer</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Baguley et al(^\text{a})</td>
<td>TBI</td>
<td>ICU</td>
<td>6/79</td>
<td>8%</td>
<td>Longer</td>
<td>No significant difference</td>
<td>Worse</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Fernandez-Ortega et al(^\text{a})</td>
<td>TBI</td>
<td>ICU</td>
<td>18/80</td>
<td>22.5%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Fernandez-Ortega et al(^\text{a})</td>
<td>TBI</td>
<td>ICU</td>
<td>18/179</td>
<td>10.1%</td>
<td>Longer</td>
<td>NA</td>
<td>No significant difference</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Hendricks et al(^\text{a})</td>
<td>TBI</td>
<td>Acute care</td>
<td>9/76</td>
<td>11.8%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Rabinstein et al(^\text{a})</td>
<td>Varied TBI,SAH,ICH, anoxia</td>
<td>NICU</td>
<td>17/93</td>
<td>18%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Dolce et al(^\text{a})</td>
<td>Vegetative</td>
<td>ICU</td>
<td>87/333</td>
<td>26.1%</td>
<td>Longer</td>
<td>NA</td>
<td>Worse</td>
<td>NA</td>
<td>Higher</td>
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<tr>
<td>Pozzi et al(^\text{a})</td>
<td>Varied</td>
<td>Rehab</td>
<td>26/407</td>
<td>6.4%</td>
<td>NA</td>
<td>Higher</td>
<td>NA</td>
<td>NA</td>
<td>Higher</td>
</tr>
</tbody>
</table>
Rehabilitation

- Multidisciplinary approach
- Uncontrolled PSH episodes interfere with therapy and can cause long term consequences
- Nursing and therapy staff can help point triggers
- Identify parameters of when to hold therapy
Key Takeaways

- Severe brain injury can result in episodes of sympathetic hyperactivity
- Nomenclature varies but PSH is rising as the preferred term
- Diagnosis of exclusion
- Several options for management
- Negative impact on LOS, medical course, and functional outcome measures
References


Thank you.