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Defining metabolic abnormalities in acute human traumatic brain injury with cerebral microdialysis and multimodality monitoring

Michael Baker[1], Sara Venturini[1], Caroline Lindblad[1,2,3], Joshua Heihre[1], Ivan Timofeev[1], Mathew Guilfoyle[1], Peter Hutchinson[1], Keri Carpenter[1], Adel Helmy[1]

[1] Division of Neurosurgery, Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom, [2] Department of Medical Sciences, Section of Neurosurgery, Uppsala University, Uppsala, Sweden, [3] Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Objective: We aimed to compare the prevalence and multimodal associations of mitochondrial dysfunction as defined by published cerebral-microdialysis-based criteria versus our novel multimodality-monitoring-based criteria in acute traumatic brain injury patients.

Methods: We retrospectively analyzed neurocritical care monitoring data from 619 acute traumatic brain injury patients. Monitoring modalities included cerebral microdialysis, intracranial pressure, brain tissue oxygenation, cerebral perfusion pressure, and the pressure reactivity index. The cerebral-microdialysis-based criteria we compared combine an elevated lactate/pyruvate ratio (25 or 30) with raised concentrations of lactate (2.5 mM) or pyruvate (70 μM or 120 μM). Our multimodality-monitoring-based criteria comprise a consistent lactate/pyruvate ratio > 25 with intracranial pressure ≤ 20 mmHg, brain tissue oxygenation ≥ 15 mmHg, a pressure reactivity index ≤ 0.3, and cerebral glucose ≥ 1.0 mM.

Results: Across 592 analyzable patients, a lactate/pyruvate ratio > 25 was common, with a median prevalence of 48.9% (41.5% with consistency) and a U-shaped, bimodal distribution. A lactate/pyruvate ratio > 25 was associated with lower glucose and higher glycerol, and when accompanied by high pyruvate (> 120 μM), this derangement was further distinguished by higher glutamate and cerebral perfusion pressure. Using multimodal criteria on a cohort of 268 patients, consistent mitochondrial dysfunction was identified in 25.7% to 41.0% of patients, often in the absence of other physiological derangements.

Conclusions: Many acute traumatic brain injury patients constantly demonstrate neurometabolic derangements, among which clinical mitochondrial dysfunction is highly prevalent despite normal cerebral pressure, oxygenation, and perfusion. There is necessity for targeted, neurometabolic therapies in neurocritical care that address this abnormality.

Defining metabolic abnormalities in acute human traumatic brain injury with cerebral microdialysis and multimodality monitoring

Michael S. Baker Jr.[1], Sara Venturini[1], Caroline Lindblad[1,2,3], Joshua M. Heihre[1], Ivan Timofeev[1], Mathew R. Guilfoyle[1], Peter J. Hutchinson[1], Keri L. H. Carpenter[1], & Adel Helmy[1]

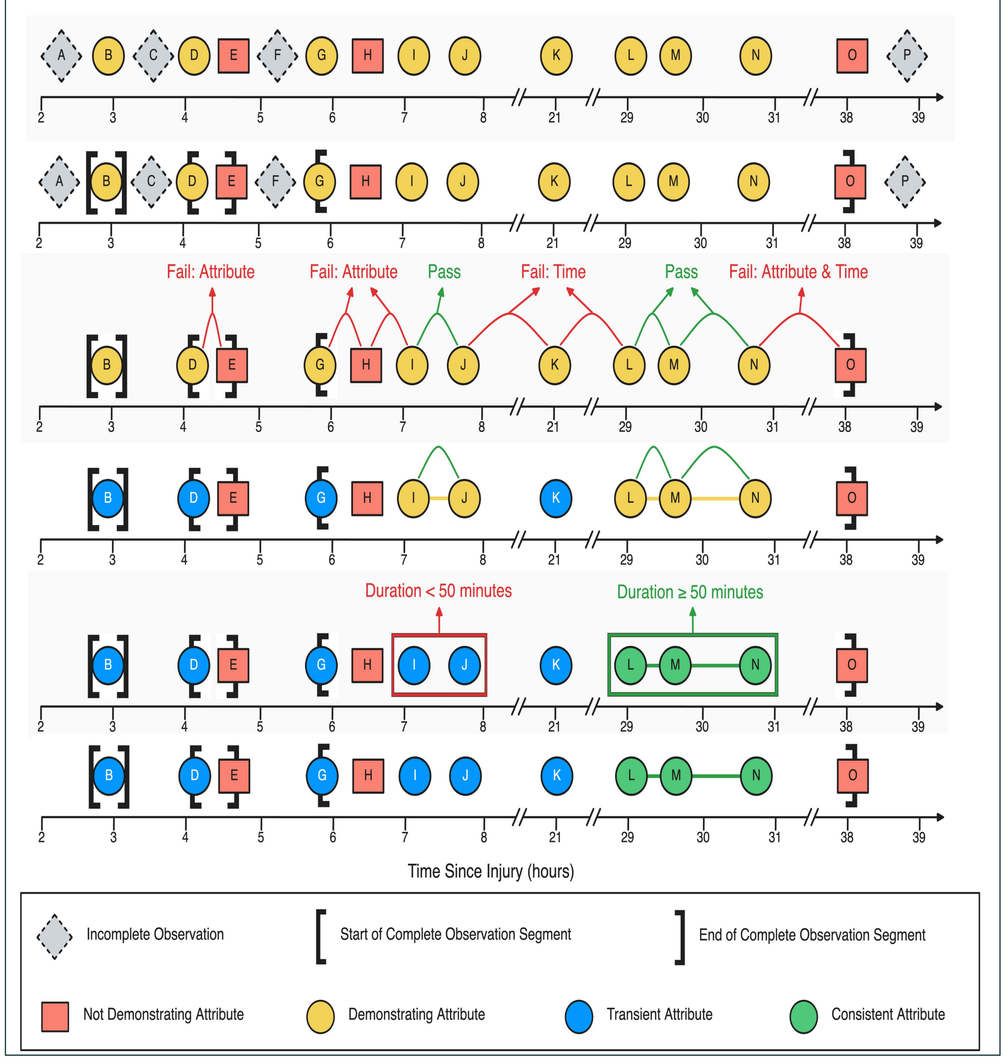
1 Division of Neurosurgery, Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom, 2 Department of Medical Sciences, Section of Neurosurgery, Uppsala University, Uppsala, Sweden, 3 Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Introduction & Objectives

- Traumatic Brain Injury (TBI) causes complex secondary injury, including metabolic energy failure.
- Cerebral microdialysis (CMD) can detect a raised lactate/pyruvate ratio (LPR), indicating a 'metabolic crisis', but this term is used inconsistently.
- A raised LPR can result from distinct states:
  - **Ischemia:** Insufficient oxygen or glucose supply.
  - **Mitochondrial Dysfunction:** Substrates are available but cannot be used effectively.
- **Objective**: Compare existing definitions of mitochondrial dysfunction versus our novel, multimodality monitoring (MMM) framework designed for clinically actionable classification. For brevity, this poster focuses on our MMM-based approach.

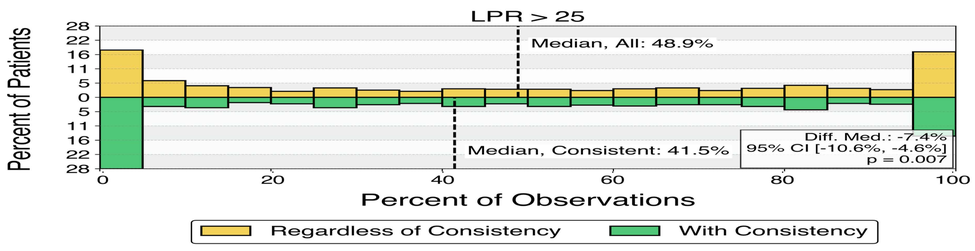
Defining "Consistent" Derangement

- Clinical interventions should target sustained pathophysiology, not transient, spurious fluctuations.
- We developed an algorithm to isolate *consistent* derangements:



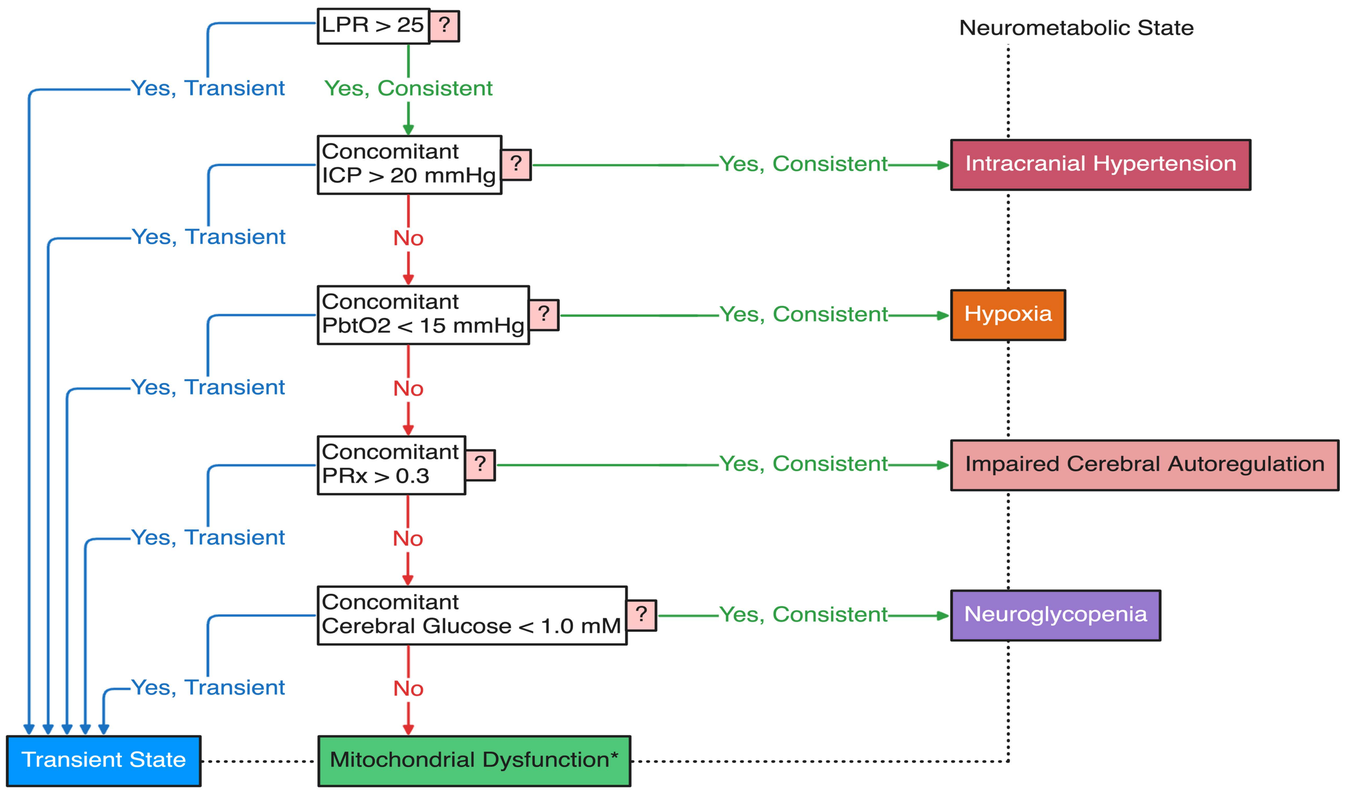
Prevalence of the LPR > 25 Trigger

- Notably, there is a U-shaped distribution of patients **always** vs. **never** demonstrating an LPR > 25.



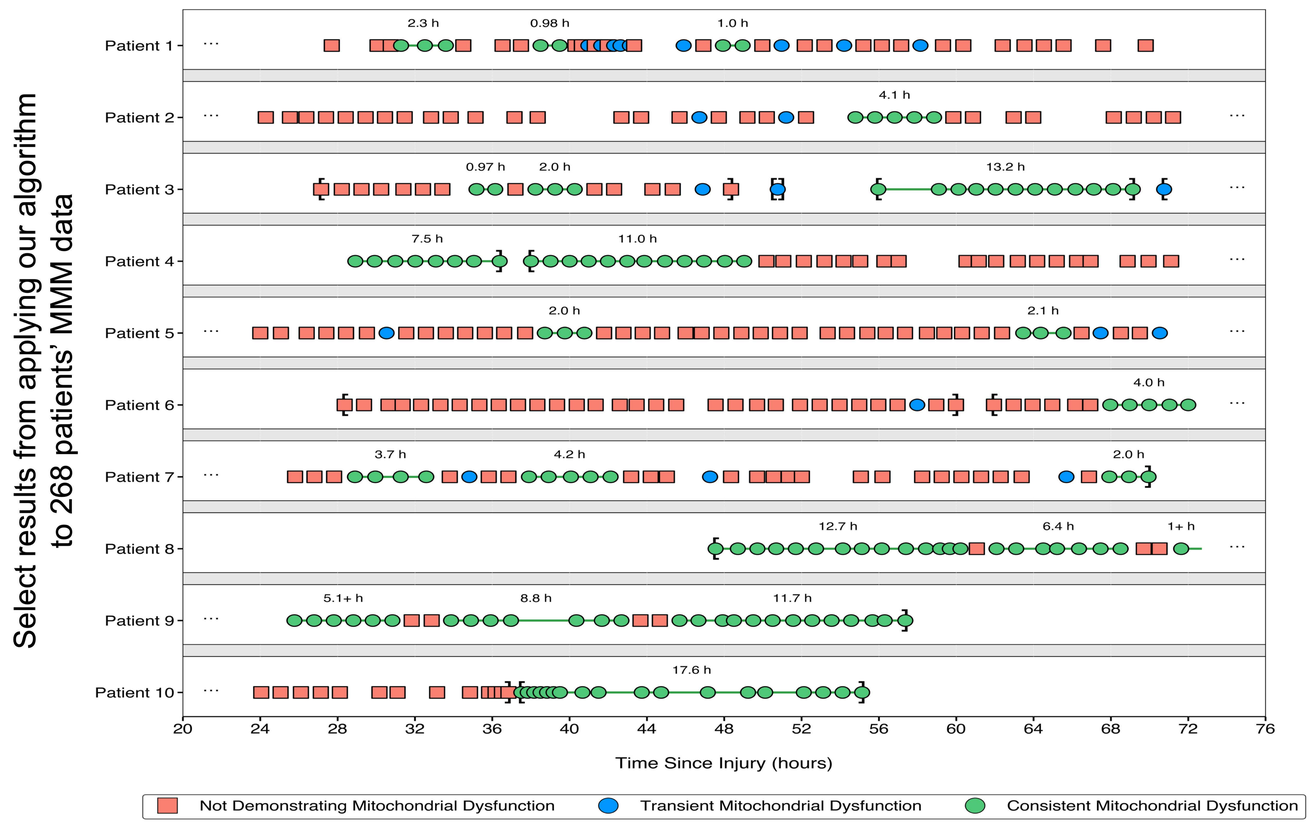
Hierarchical Classification

- We propose a tiered protocol to systematically rule out confounding causes of elevated LPR before identifying mitochondrial dysfunction.
- The hierarchy addresses conditions in a clinically pragmatic order:



- *If LPR remains **consistently > 25** after resolving these preceding states, we classify the derangement as **mitochondrial dysfunction.**

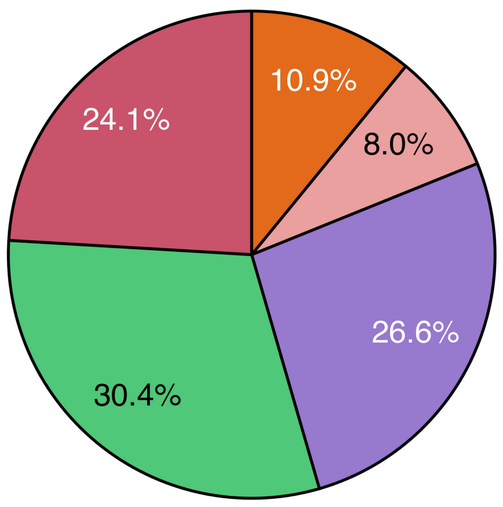
Detecting Consistent Mitochondrial Dysfunction



Prevalence of Hierarchical Neurometabolic States

- After applying our full hierarchical framework, we assessed the relative prevalence of each neurometabolic state.
- Crucially, these neurometabolic states are mutually exclusive, as each observation is assigned only to the first derangement identified in the hierarchical protocol.
- Mitochondrial dysfunction was the most commonly isolated, accounting for 30.4% of all identified consistent derangements.

Deranged CMD Trigger: LPR > 25



Neurometabolic States: Intracranial Hypertension; Hypoxia; Impaired Cerebral Autoregulation; Neuroglycopenia; Mitochondrial Dysfunction

Conclusions

- There is polarization of TBI patients exhibiting our protocol's trigger of LPR > 25, indicating that some patients may never necessitate metabolic interventions, while others frequently may.
- Metabolic derangement (evidenced via LPR > 25) frequently occurs even when pressure, oxygenation, perfusion, and substrate delivery are within normal limits – and we define this as a state of mitochondrial dysfunction.

This study has been recently published:

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