Exploratory Neurophysiological Biotyping of Chronic Traumatic Brain Injury: Observed Divergence from Clinical Severity Scales

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Background

- Traumatic brain injury (TBI) severity is classified using acute injury characteristics
  - e.g., loss of consciousness (LOC), amnesia, confusion
- In chronic phase (≥1 year):
  - Persistent cognitive & functional deficits are present
  - Poor alignment with "Mild" / "Moderate" labels
- Suggests a "Clinical-Neural" gap
  - Clinical history ≠ current brain function

Objective

- Identify latent neurophysiological archetypes
- Use:
  - qEEG (spectral features)
  - ERP (temporal features)
- Evaluate alignment between:
  - The Ohio State University Traumatic Brain Injury Identification Method (OSU TBI-ID) severity labels
  - Objective brain activity

Methods

Participants
- N = 81 Service Members
- 80.2% Male
- ≥1 year post-TBI

Clinical Classification
- OSU TBI-ID
  - Based on retrospective injury history
  - finalized pre-EEG acquisition

EEG Processing
- Automated custom MATLAB pipeline:
  - Artifact Subspace Reconstruction (ASR)
  - Independent Component Analysis Decomposition
  - ICLabel component rejection

Feature Space
- 9 total features:
  - Spectral (e.g., frontal delta power)
  - ERP (N200, P300 timing/amplitude)

Preprocessing
- Z-score normalization

Clustering
- K-means (unsupervised)
- Silhouette optimization:
  - K = 3
  - S = 0.24

Clinical-Neural Gap

- 69.14 % divergence
- Monte Carlo (p=0.41)

Clinical Severity does not predict neurophysiological grouping.

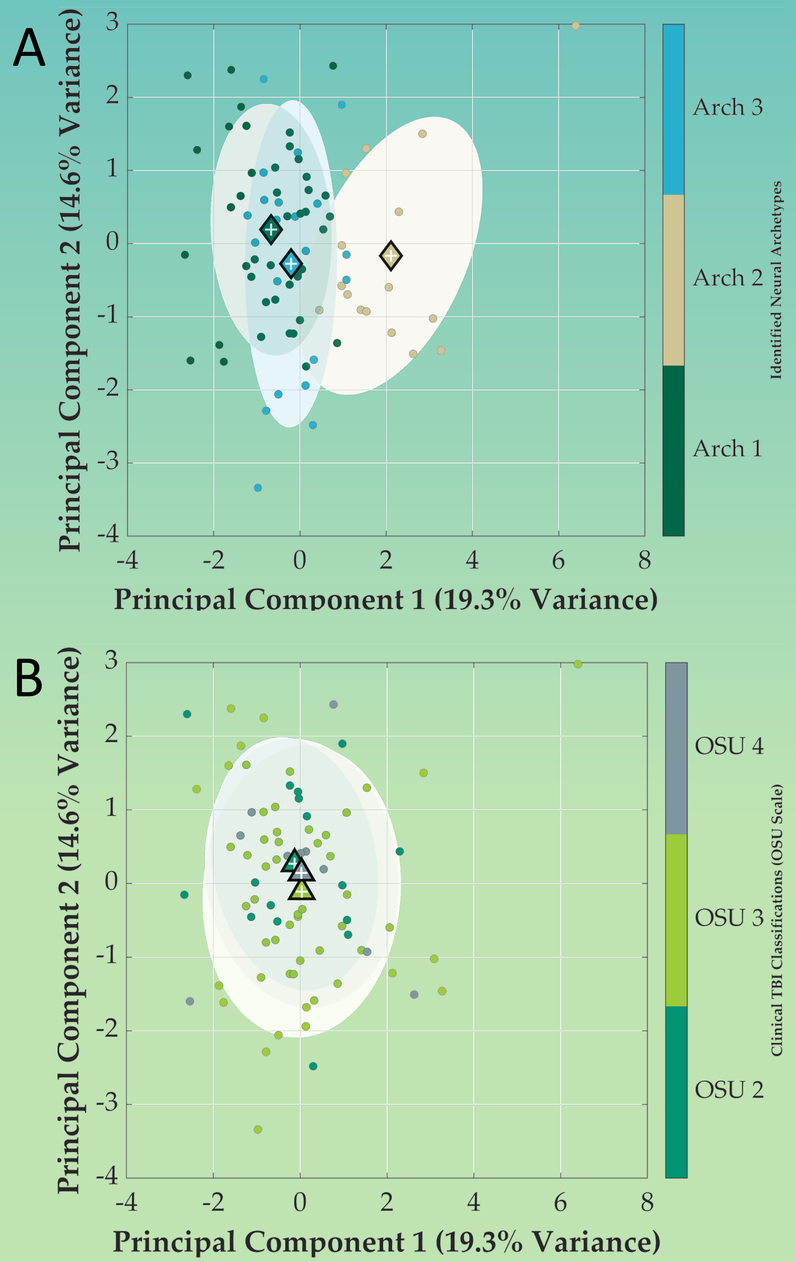

Figure 1. Neurophysiological Archetypes vs Clinical Severity in PCA Space. A) Clustering of participants based on qEEG and ERP features reveals three neurophysiological archetypes. **B)** The same PCA space colored by OSU TBI-ID clinical severity demonstrates substantial overlap across groups.

Neurophysiological Archetypes

- Data-driven clusters → distinct brain profiles
- Not reflected in traditional severity labels (**Figure 1**)
- Capture **latent biological structure (Figure 2)**

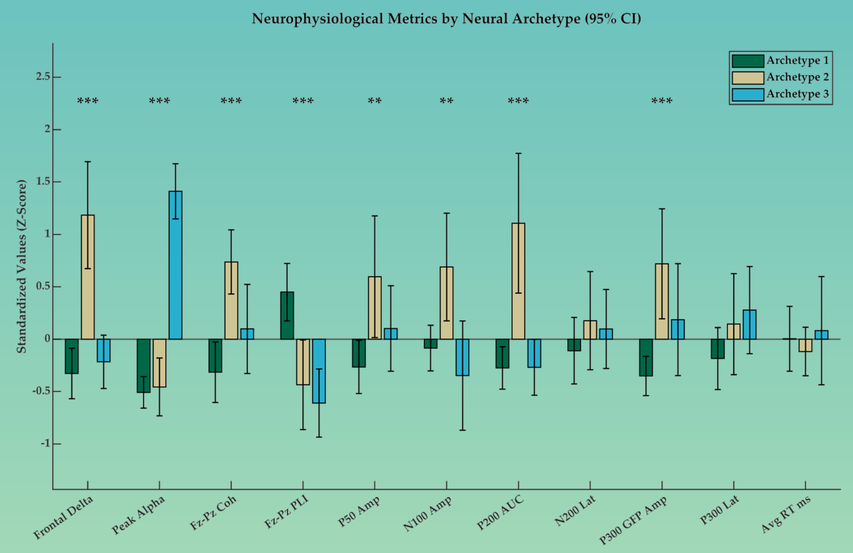

Figure 2. Neurophysiological Feature Profiles Across Archetypes. Grouped bar chart displaying standardized neurophysiological metrics (Z-scores) across archetypes. Each metric (x-axis) is shown for all archetypes with mean ± 95% confidence intervals. Significant differences across archetypes indicated by asterisks (** for p<0.01; *** for p<0.001). Distinct patterns across spectral and ERP features demonstrate that archetypes represent meaningfully different neurophysiological profiles rather than arbitrary groupings.

Conclusion

- Clinical severity ≠ brain physiology
- Evidence of a **Clinical-Neural Gap**
- Archetypes provide:
  - More granular classification
  - Biologically grounded insight
  - Potential sex-specific phenotypes

Implication

- Neurophysiological biomarkers:
  - May outperform clinical severity scales
  - Support precision characterization of chronic TBI

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References