

Article

Data-Driven Identification of Electrophysiological Subgroups in Chronic Traumatic Brain Injury Using EEG and Behavioral Features

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Abstract

Traumatic brain injury (TBI) is associated with heterogeneous neurophysiological and behavioral outcomes that are not always captured by conventional clinical classifications. This study aimed to characterize electrophysiological patterns in individuals with TBI and examine their alignment with clinical groupings. EEG, event-related potentials (ERPs), spectral features, and behavioral performance were analyzed in 121 participants from a larger clinical cohort. Data were preprocessed using artifact subspace reconstruction (ASR), adaptive mixture independent component analysis (AMICA), and standardized quality control procedures. Spectral power, ERP components, and behavioral metrics were extracted and compared across clinical severity and OSU TBI-ID classifications, and unsupervised k-means clustering was applied to identify data-driven electrophysiological subgroups. Results demonstrated consistent ERP signal quality across participants, with all datasets meeting P300 global field power thresholds. While group-level comparisons revealed distributions of electrophysiological markers across clinical categories, clustering identified two electrophysiological subgroups characterized by differing spectral, connectivity, and ERP profiles that were not significantly associated with OSU TBI-ID classifications. Electrophysiological subgroup assignments were not significantly associated with OSU TBI-ID classifications. These findings suggest that data-driven electrophysiological subgrouping captures variability not reflected in traditional clinical groupings, highlighting the potential utility of electrophysiological measures for characterizing heterogeneity within chronic TBI populations.

Keywords: traumatic brain injury (TBI); electroencephalography (EEG); machine learning; K-means clustering; electrophysiological subgroups; event-related potentials (ERPs)



Academic Editor: Paolo Renna

Received: 30 June 2026

Revised: 27 July 2026

Accepted: 30 July 2026

Published: 1 August 2026

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1. Introduction

Traumatic brain injury (TBI) has been denoted as the signature injury of Operation Enduring Freedom and Operation Iraqi Freedom (later named New Dawn) [1]. While originally associated with the significant increase in blast exposure from improvised explosive devices (IEDs) [2,3], this designation underscores a broader clinical challenge for the modern veteran. Improvements in combat casualty care and personal protection have

led to increased survival rates, yet these advancements often leave veterans with extreme, “invisible” wounds [4]. Approximately 80% of TBIs sustained by service members are classified as mild TBI (mTBI) or concussion, where symptoms often manifest long after the initial event. Despite “normal” results on standard clinical imaging, veterans continue to suffer from significant cognitive and psychological dysregulation that severely impacts quality of life [5–7].

The primary barrier to effective mTBI care is the current reliance on subjective clinical evaluations and patient self-reporting [8,9]. Traditional diagnostics—such as the Glasgow Coma Scale [10,11], documentation of loss of consciousness, and posttraumatic amnesia—are heavily dependent on a patient’s ability to accurately recollect a traumatic event, which is inherently difficult in high-stress environments. Even structured tools [e.g., Ohio State University Traumatic Brain Injury Identification Method (OSU-TBI ID) [12]] are highly reliable for establishing lifetime exposure history, but they remain limited by the patient’s memory and the potential for ambiguity [13–15]. The OSU TBI-ID provides a structured record of lifetime exposure history; however, it does not directly measure current cortical function. This reliance on recall is particularly problematic in cases of polytrauma, where a medical record may be cluttered with concurrent physical wounds [16–18]. In addition to this clutter, the service member themselves may struggle to recollect the cognitive “fog” that may be present if another physical wound is more pressing at the time. In the acute stages of combat injury, overt physical trauma often takes clinical precedence, leading to the “overshadowing” or misdiagnosis of the underlying mTBI. Consequently, many service members may be left without the recognition or treatment necessary for mTBI recovery.

To address this diagnostic gap, there is an urgent need for objective, point-of-care measures that do not rely on patient recall or structural imaging. Standard imaging techniques serve to identify physical damage, but mTBI is fundamentally an issue of neural network desynchronization. In contrast, other functional imaging techniques, such as functional magnetic resonance imaging (fMRI), have limitations. The Blood Oxygen Level-Dependent (BOLD) method used in fMRI produces delayed signals, taking several seconds to peak after stimuli and thereby hampering its ability to monitor the latency of neural responses [19,20]. Additionally, fMRI is cost-prohibitive, with mid-range systems costing approximately \$2 million, along with high operational costs, infrastructure requirements, and limited accessibility outside specialized settings [19–25]. Another technique, functional near-infrared spectroscopy (fNIRS), offers portability for monitoring but suffers from limited temporal resolution compared to EEG. It also experiences motion artifacts; can cause discomfort for participants; and lacks standardization in data analysis, a challenge less prevalent in more established imaging techniques [19,21,23].

EEG, on the other hand, provides a cost-effective and portable measure of cortical physiology with excellent temporal resolution (milliseconds), making it a promising tool for investigating functional neurophysiological alterations associated with TBI. Beyond simple real-time streaming, advanced EEG analysis—specifically functional connectivity—allows for the assessment of how disparate brain regions communicate. Because mTBI often functions as a “disconnection syndrome,” where neural networks are desynchronized despite an intact physical structure [26,27], EEG-based connectivity metrics can identify the functional signatures of injury that standard imaging cannot detect.

To better characterize functional neurophysiological variability following TBI, this study utilized a simple reflexive task as a physiological stress test, demanding rapid neural synchronization that resting-state paradigms may fail to elicit. By extracting electrophysiological measures during task performance, including coherence and phase lag index metrics, the goal was to characterize patterns of network organization associated with a history of TBI. Using an unsupervised clustering approach, EEG-derived measures were

compared with OSU TBI-ID categories to examine whether data-driven electrophysiological subgroups captured variability not reflected in traditional history-based classifications. This exploratory analysis was designed to identify candidate neurophysiological profiles that may contribute to a more detailed characterization of heterogeneity within chronic TBI populations.

2. Materials and Methods

2.1. Participants

Participants ($n = 125$) were recruited as a subset of a larger clinical trial using identical procedures to those described in the parent study [28]. EEG data collection followed the sub-study protocol outlined in Walters et al. [29]. The present study focuses exclusively on baseline session data.

Clinical severity comparisons reflected the grouping structure used in the parent clinical trial, in which OSU TBI-ID scores of 2 and 3 were categorized as mild TBI, and OSU TBI-ID score 4 was categorized as moderate TBI. Additional analyses were performed using the individual OSU TBI-ID categories (2, 3, and 4) to evaluate whether greater stratification of lifetime injury exposure history was associated with differences in electrophysiological measures.

All procedures involving human participants were approved by the University of South Florida Institutional Review Board, approval number STUDY006819, and were conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to participation.

2.2. EEG and Behavioral Data Acquisition

EEG recordings were obtained using a 32-channel Emotiv FLEX 2 saline system (Emotiv Inc., San Francisco, CA, USA), configured according to the international 10–10 electrode placement system. Data were sampled at 256 Hz under standardized recording conditions, with participants seated comfortably in a controlled environment. EEG recordings were acquired using the Emotiv FLEX2 proprietary CMS/DRL mastoid reference configuration. No offline average re-referencing was performed.

Behavioral data were collected concurrently using the Target Game, a simple reaction-time task administered via the NeuroTask platform on an iPad [27,28]. Participants were instructed to tap sequentially appearing visual targets as quickly as possible over a 30 s interval using their dominant hand. Task performance was quantified as the total number of successful responses. Because the task was performance-driven and administered over a fixed 30 s interval, the total number of target presentations and responses varied among participants.

Behavioral outputs were stored as timestamped event logs (.csv files), capturing stimulus presentations, responses, and session boundaries. Custom MATLAB scripts were used to reconstruct trial-level data by temporally pairing stimulus onset with subsequent responses, from which reaction times (time to hit) were derived for successful trials. All timestamps were standardized and aligned with participant records to ensure consistency across EEG and behavioral datasets. Data were organized by participant and session, and only baseline sessions were included in analyses.

2.3. EEG–Behavioral Synchronization

EEG and behavioral datasets were synchronized using a custom MATLAB pipeline. EEG event markers were merged with behavioral logs to create unified event structures. Temporal alignment was achieved through correction of clock offsets using shared reference markers or timestamp-based alignment procedures.

Datasets failing post-synchronization quality control ($n = 4$) were excluded. Three datasets exceeded acceptable post-ASR mean microvolt thresholds, and one dataset contained corrupted event markers that prevented successful epoching.

2.4. EEG Preprocessing

EEG preprocessing was conducted in MATLAB (R2024b; MathWorks, Natick, MA, USA) using the development version of EEGLAB (Swartz Center for Computational Neuroscience, UC San Diego, La Jolla, CA, USA) [30,31]. Continuous data were imported from .edf files, non-EEG channels were removed, and electrode locations were assigned using a standard 10–10 template.

Data were bandpass filtered between 1 and 60 Hz to remove slow drifts and high-frequency noise. Experimental event markers were initially generated within EmotivPRO at the beginning and end of each NeuroTask assessment interval. The NeuroTask platform independently recorded stimulus and behavioral event timestamps on the iPad. During preprocessing, EEG and behavioral datasets were synchronized using a custom MATLAB pipeline. Temporal alignment was achieved using Unix timestamp information recorded by both systems, allowing behavioral event markers to be mapped onto the EEG event marker file. The merged marker file was then used to import event markers into the EEG dataset through sample conversion based on the EEG acquisition rate (256 Hz). The synchronized event structure was subsequently used for stimulus-locked epoch extraction and ERP analysis. Participant metadata (e.g., session and group assignment) were incorporated from external clinical records.

2.5. Data Trimming and Segmentation

EEG datasets were segmented using automated, custom EEGLAB scripts. A 15 s eyes-open baseline period and task-related segments were extracted and concatenated to form a continuous “stitched” dataset representing combined baseline and task activity.

Because the task paradigm lacked inter-stimulus intervals that could provide a stable baseline, the initial 15 s baseline segment was appended to the trimmed task data to ensure that artifact subspace reconstruction (ASR) had an appropriate reference baseline for calibration. This step was necessary to enable accurate artifact correction in the absence of a true baseline within the task itself.

2.6. Artifact Cleaning and Independent Component Analysis

Artifact removal was performed using a standardized automated, custom pipeline in EEGLAB, incorporating the clean_rawdata, AMICA, and ICLLabel plugins [32–35].

Channel-location information was revalidated using a 10–5 electrode template prior to ICA to ensure accurate spatial metadata. artifact subspace reconstruction (ASR) was applied to mitigate transient noise, with variance reduction quantified as a quality metric [36,37]. ASR calibration was performed using the stitched 15 s baseline segment. Processing utilized a burst criterion of 20 and a high-pass transition band of 0.25–0.75 Hz. Flatline, channel, line-noise, and window rejection criteria were disabled. Automatic bad-channel rejection was not performed; artifact mitigation was achieved through ASR, AMICA decomposition, ICLLabel classification, and removal of non-neural independent components.

Independent component analysis (ICA) was conducted using adaptive mixture ICA (AMICA) [38,39]. Components were classified using ICLLabel [34], and non-neural components (ocular, muscular, cardiac, and line noise) exceeding a probability threshold of 70% were removed. Cleaned datasets and processing metrics were retained for reproducibility.

Outlier screening was performed using JMP Pro 19 (SAS Institute, Cary, NC, USA) based on postprocessing quality metrics obtained from the EEG preprocessing log. A robust quartile-based outlier detection method ($k = 4$) was applied to the post-mean

microvoltage variable, which reflects overall signal amplitude and is expected to fall within physiologically typical ranges for scalp EEG (~1–100 μ V). Outliers were identified relative to the sample distribution, resulting in three datasets being classified as outliers and excluded from subsequent analyses.

2.7. Epoching, Trial-Level Processing, and Spectral Analysis

Cleaned EEG data were segmented into epochs from –50 ms to 800 ms relative to stimulus onset. Event markers were curated to retain valid trials with physiologically plausible response times (100–3000 ms). Epochs containing discontinuities were excluded, and additional artifact rejection was applied using a ± 100 μ V threshold. Only artifact-free epochs were retained. Following artifact rejection, an average of 45.3 (SD = 8.8) artifact-free epochs were retained per participant for the valid target condition (range: 13–60).

Behavioral metrics (mean reaction time, variability, and success rate) were computed using retained trials and stored alongside EEG measures. Both trial-level and participant-averaged datasets were exported.

Power spectral density (PSD) was computed using the EEGLAB implementation of Welch's method (spectopo/pop_spectopo) across the 1–50 Hz frequency range. Spectral power was expressed in decibels (dB) and calculated across all channels. Outputs were reformatted into long-format tables containing participant ID, frequency, power, and channel labels for statistical analysis.

2.8. Feature Extraction

Extracted features included spectral, connectivity, and event-related potential (ERP) measures:

Spectral features: Global and regional band power (delta, theta, alpha, beta, and gamma) were computed; linear power values were derived from decibel-transformed data to ensure mathematical validity. Peak alpha frequency (PAF) was localized to posterior sensors (Pz, O1, O2, and Oz) to minimize anterior artifact contamination.

Connectivity metrics (Alpha band): Magnitude-Squared Coherence and Phase Lag Index (PLI) were calculated using windowed FFT.

ERP measures: P50 and N100 amplitudes were extracted at Cz to assess sensory processing. Attentional processing was indexed via the area under the curve (AUC) of the P200 component within the 150–250 ms post-stimulus interval at Cz. Cognitive processing was assessed via N200 latency (Fz) and P300 measures derived from a parietal–occipital region of interest (P3, Pz, P4, O1, Oz, and O2). Global field power (GFP) was calculated as the spatial standard deviation across this electrode array. P300 GFP amplitude was defined as the maximum GFP value within the 250–550 ms post-stimulus interval. P300 latency was defined as the latency of this GFP peak. P300 amplitude was extracted from Pz at the latency corresponding to the GFP-defined P300 peak. EEG datasets were required to exhibit a peak GFP amplitude between 0.01 and 100 μ V within the P300 search window (250–550 ms) to satisfy automated quality-control criteria. P300 amplitude at Pz was extracted as an auxiliary ERP measure; however, the primary P300 metrics used in the reported statistical analyses, PCA visualization, and clustering procedures were P300 GFP amplitude and P300 latency.

ERP analyses were stimulus-locked to target onset rather than response onset. Potential contamination from motor execution activity was further minimized through the use of a posterior parietal–occipital region of interest (P3, Pz, P4, O1, Oz, and O2) for P300/GFP extraction and through trial averaging, which attenuates response-related activity occurring at variable latencies across trials.

ERP measures were extracted from the grand-average stimulus-locked epoch datasets. Connectivity metrics (coherence and PLI) were computed from stacked trial-level epoch matrices to quantify inter-channel phase relationships during task processing. Spectral power measures were derived from exported task-related EEG epoch datasets using Welch's method, thereby restricting analyses to task-related EEG activity rather than resting-state recordings.

2.9. Statistical Analysis

Descriptive statistics were computed for demographic and behavioral variables. Normality was assessed prior to inferential testing. Group differences were evaluated using independent samples *t*-tests or one-way ANOVA for continuous variables and chi-square tests for categorical variables. EEG feature comparisons between clinical severity groups included Cohen's *d* for *t*-tests and Eta-squared (η^2) for ANOVA models. Age-adjusted analyses were conducted using general linear models controlling for age, sex, and clinical history. These models were used to evaluate potential covariate effects and do not represent multiple-comparison corrections. The evaluated EEG, ERP, connectivity, and behavioral features were selected a priori to represent distinct neurophysiological domains commonly examined in TBI research. Accordingly, analyses were intended to characterize relationships across candidate physiological markers rather than to test repeated measurements of a single outcome variable. Statistical results should therefore be interpreted in conjunction with effect sizes, physiological plausibility, and the overall multivariate patterns observed within the dataset.

2.10. Clustering and Electrophysiological Subgroup Identification

Multivariate clustering was performed using k-means on standardized EEG and behavioral features to identify neurophysiological subgroups. Prior to clustering, all features were standardized using z-score normalization. K-means clustering used squared Euclidean distance and a fixed random seed (*rng* = 42) to ensure reproducibility. Candidate clustering solutions (*K* = 2–5) were optimized using 250 random initializations (replicates), selected following a convergence analysis demonstrating stable within-cluster sum of squares across increasing replicate counts. Cluster selection was guided by (1) silhouette coefficients, (2) stability criteria (Jaccard similarity), and (3) minimum cluster size thresholds (~12% of total sample). Cluster characteristics were evaluated using ANOVA with post hoc comparisons. Cluster stability was assessed using a subsampling procedure. For each candidate *K* solution, 100 iterations were performed in which 80% of participants were randomly sampled without replacement, re-clustered using the same k-means procedure, and compared with the original clustering solution. Stability was quantified using cluster-wise Jaccard similarity, calculated as the maximum overlap between original and resampled cluster memberships and averaged across clusters and iterations. Clustering solutions (*K* = 2–5) were evaluated using silhouette coefficients and Jaccard stability indices:

- *K* = 2:0.216/0.767;
- *K* = 3:0.198/0.736;
- *K* = 4:0.191/0.653;
- *K* = 5:0.190/0.580.

Principal Component Analysis was done to create cluster maps. Composite contribution scores were calculated by weighting absolute feature loadings from the first two principal components according to their proportion of explained variance, thereby identifying the neurophysiological metrics most influential in defining spatial separation in the PCA-clustered space.

Associations between derived electrophysiological subgroup assignments and OSU TBI-ID classifications were assessed using χ^2 (chi-square) tests of independence with Monte Carlo permutation testing (10,000 iterations) to obtain empirical p -values.

2.11. Reproducibility and Data Availability

All analyses were implemented using custom MATLAB scripts with standardized parameters applied across participants. Processing logs, structured datasets, and summary outputs were generated to ensure reproducibility. Data, code, and analysis pipelines will be made available upon publication and as requested.

3. Results

3.1. Participant Characteristics and Data Retention

A total of 125 participants with complete datasets across ERP, spectral EEG, and behavioral task measures were included in the preprocessing pipeline. Following EEG preprocessing (including ASR, AMICA, and quartile-based data quality screening, $k = 4$), 122 participants met neurophysiological quality criteria. Behavioral reaction time (RT) data were available for 122 participants. One additional participant was excluded during later-stage preprocessing due to insufficient data quality, resulting in a final analytical sample of 121 participants.

The final analytical sample had a mean age of 48.0 ± 9.6 years and included 21 females and 100 males. Participants were stratified by clinical severity and OSU TBI-ID classification (see Table 1). Age, reaction time, sex distribution, and clinical variables were assessed across groups to evaluate comparability and covariate balance (see Table 2). Distributions are shown in Figure 1.

Table 1. Participant sample sizes for clinical severity, OSU TBI-ID score, and clinical characteristics.

Clinical Severity	<i>n</i>
Mild	103
Moderate	18
OSU TBI-ID	
Score 2	23
Score 3	80
Score 4	18
Clinical characteristics	
Attention-deficit/hyperactivity disorder (ADHD) *	23
Autism spectrum disorder (ASD) *	2
Developmental delay *	4
Cognitive impairment *	2
No reported mental health condition *	90

* These variables were retained for subsequent analyses.

3.2. Spectral and Electrophysiological Features

Descriptive statistics and group comparisons for clustering input features are presented in Table 3 (severity-based comparisons) and Table 4 (OSU TBI-ID comparisons), including mean $\pm$ SD, raw p -values, adjusted p -values, and effect sizes. Grand average ERP waveforms across midline electrodes (Cz, Fz, and Pz) for both clinical severity and OSU TBI-ID groupings are shown in Figure 2. Because the parent clinical trial grouped participants according to mild and moderate TBI categories, analyses were performed using both the parent-study severity groupings and the underlying OSU TBI-ID score categories

(2, 3, and 4) to examine whether greater stratification of lifetime injury exposure history influenced observed neurophysiological patterns.

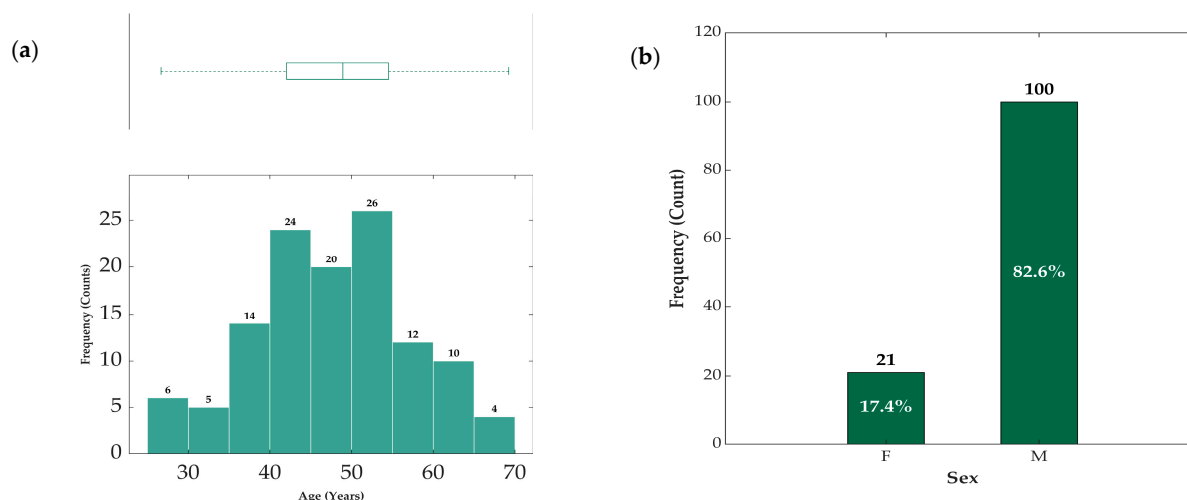


Figure 1. Distribution of demographic variables. The distribution of the age (a) and sex (b) of the 121 participants analyzed.

Table 2. Demographic, behavioral, and clinical characteristics by group.

Clinical Severity (Mild vs. Moderate)	<i>p</i> -Value
Age	0.255
RT	0.806
Sex	0.933
ADHD	0.747
ASD	1.000
Developmental delay	0.105
Cognitive impairment	1.000
No mental health condition	0.061
OSU TBI-ID *	
Age	0.445
RT	0.713
Sex	0.826

* Statistical testing for mental health variables across OSU groups was not performed due to low cell counts.

Table 3. Comparison of neurophysiological features between mild and moderate TBI groups.

Metric	Mild (Mean $\pm$ SD)	Moderate (Mean $\pm$ SD)	Adjusted <i>p</i> -Value	Cohen's <i>d</i>
P50 Amplitude (μ V)	1.18 $\pm$ 2.16	1.64 $\pm$ 2.00	0.428	0.22
N100 Amplitude (μ V)	−1.90 $\pm$ 2.03	−1.70 $\pm$ 2.03	0.643	0.10
P200 AUC (μ V·ms)	−1.95 $\pm$ 37.13	18.85 $\pm$ 43.69	0.035	0.55
N200 Latency (ms)	227.62 $\pm$ 31.08	242.19 $\pm$ 36.57	0.052	0.46
P300 GFP Amplitude (μ V)	1.47 $\pm$ 0.52	1.45 $\pm$ 0.46	0.927	−0.04
P300 Latency (ms)	399.27 $\pm$ 88.36	423.18 $\pm$ 90.51	0.402	0.27
Frontal Delta Power (dB)	8.04 $\pm$ 3.38	9.11 $\pm$ 4.22	0.293	0.30
Peak Alpha Frequency (Hz)	9.22 $\pm$ 1.36	8.68 $\pm$ 0.71	0.110	−0.42
Fz–Pz Coherence	0.73 $\pm$ 0.10	0.74 $\pm$ 0.08	0.981	0.08
Fz–Pz PLI	0.54 $\pm$ 0.06	0.54 $\pm$ 0.05	0.857	−0.04

Note: Values are mean $\pm$ SD. GLM-adjusted *p*-values control for age, sex, and clinical history. Effect sizes: Small (0.2), medium (0.5), and large (0.8); bold indicates *p* < 0.05. Spectral power measures and connectivity metrics (coherence and PLI) were derived from task-related EEG epoch datasets collected during the NeuroTask assessment. ERP measures were extracted from grand-average stimulus-locked target epochs.

Table 4. Comparison of neurophysiological features across OSU TBI-ID groups (2, 3, and 4).

Metric	OSU 2 (Mean $\pm$ SD)	OSU 3 (Mean $\pm$ SD)	OSU 4 (Mean $\pm$ SD)	Adjusted <i>p</i> -Value	η^2
P50 Amplitude (μ V)	1.29 $\pm$ 2.48	1.14 $\pm$ 2.07	1.64 $\pm$ 2.00	0.716	0.007
N100 Amplitude (μ V)	−1.74 $\pm$ 2.08	−1.94 $\pm$ 2.03	−1.70 $\pm$ 2.03	0.845	0.003
P200 AUC (μ V·ms)	−0.69 $\pm$ 28.82	−2.31 $\pm$ 39.35	18.85 $\pm$ 43.69	0.110	0.037
N200 Latency (ms)	234.38 $\pm$ 35.14	225.68 $\pm$ 29.77	242.19 $\pm$ 36.57	0.090	0.037
P300 GFP Amplitude (μ V)	1.33 $\pm$ 0.34	1.51 $\pm$ 0.56	1.45 $\pm$ 0.46	0.283	0.019
P300 Latency (ms)	404.72 $\pm$ 85.98	397.71 $\pm$ 89.50	423.18 $\pm$ 90.51	0.653	0.010
Frontal Delta Power (dB)	7.47 $\pm$ 3.25	8.20 $\pm$ 3.42	9.11 $\pm$ 4.22	0.436	0.018
Peak Alpha Frequency (Hz)	9.70 $\pm$ 1.67	9.09 $\pm$ 1.24	8.68 $\pm$ 0.71	0.046	0.056
Fz–Pz Coherence	0.72 $\pm$ 0.10	0.74 $\pm$ 0.10	0.74 $\pm$ 0.08	0.696	0.007
Fz–Pz PLI	0.55 $\pm$ 0.05	0.54 $\pm$ 0.06	0.54 $\pm$ 0.05	0.448	0.012

Note: Values are mean $\pm$ SD. Raw *p*-values from one-way ANOVA; adjusted *p*-values from GLMs, controlling for age, sex, and clinical history. Effect sizes (η^2): Small (0.01), medium (0.06), and large (0.14). Bold indicates *p* < 0.05.

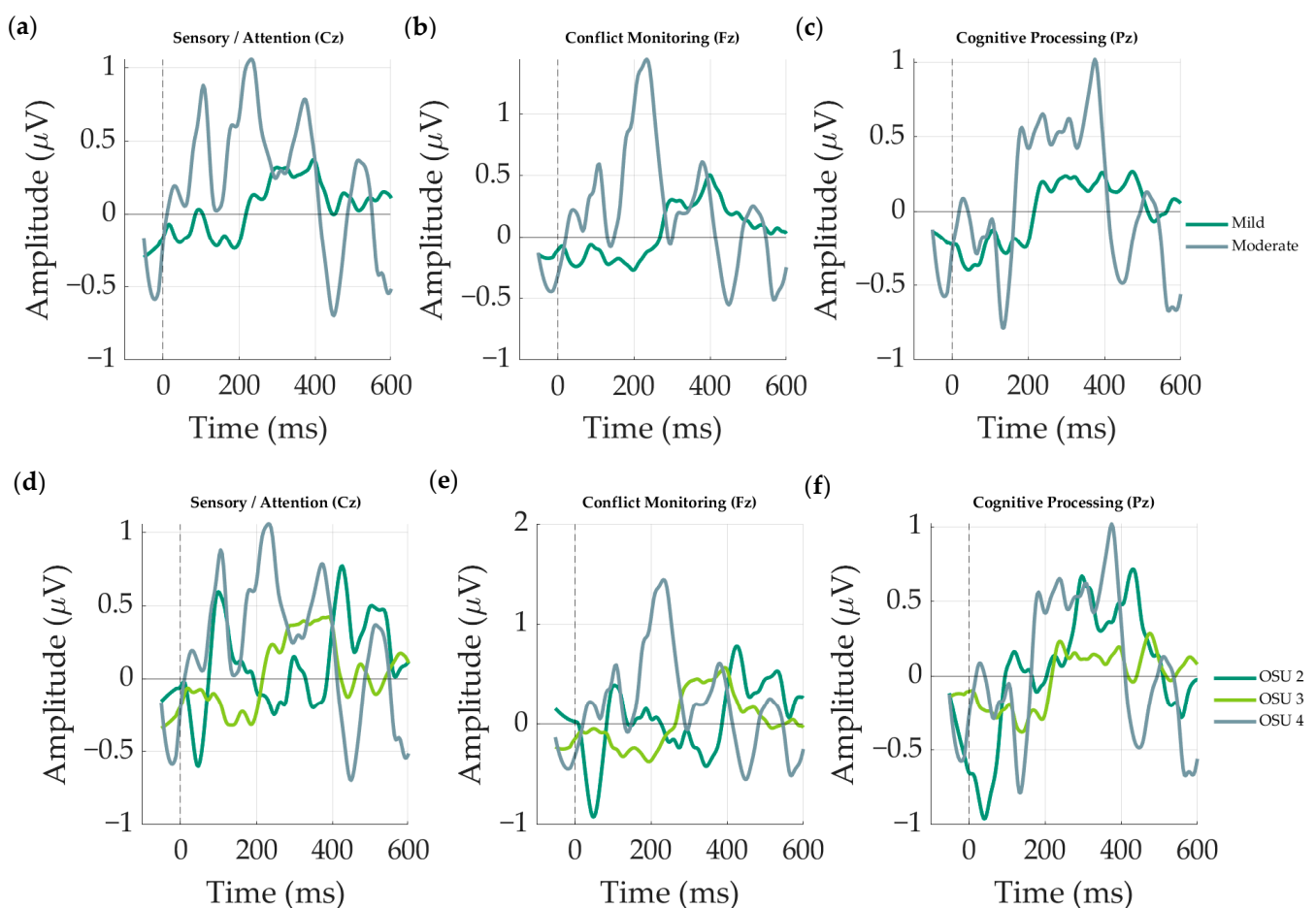


Figure 2. Grand average event-related potential (ERP) waveforms at midline electrodes for clinical severity and OSU TBI-ID classifications. (a–c) ERP waveforms for mild and moderate TBI groups at Cz (a), Fz (b), and Pz (c). (d–f) ERP waveforms for OSU TBI-ID groups (scores 2, 3, and 4) at Cz (d), Fz (e), and Pz (f). Waveforms represent mean voltage (μ V) across time (ms) relative to stimulus onset (0 ms).

3.3. Event-Related Potentials, Global Field Power, and Multivariate Analysis

ERP and GFP measures were extracted for 121 participants, with 121 grand average ERP files processed. All datasets met amplitude-based thresholds for P300 global field power. Distributions of early ERP components (P50, N100, and P200) are presented in Figure 3, and grand-average ERP waveforms at midline electrodes (Cz, Fz, and Pz) are shown in Figure 4.

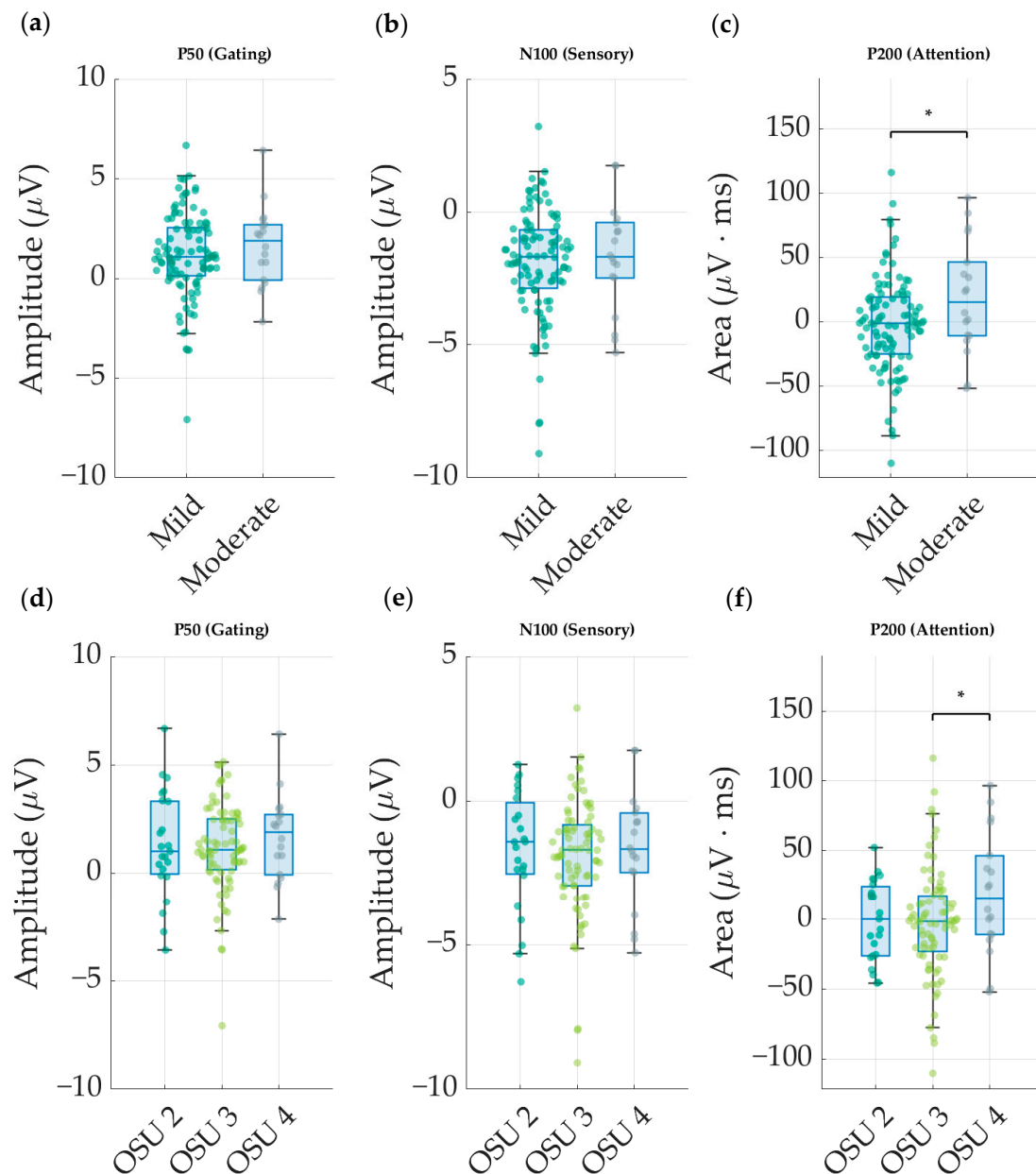


Figure 3. Distribution of early ERP component measures across clinical severity and OSU TBI-ID classifications. (a–c) Comparisons between mild and moderate TBI groups for (a) P50 amplitude (μV), (b) N100 amplitude (μV), and (c) P200 area under the curve ($\mu\text{V}\cdot\text{ms}$). (d–f) Comparisons across OSU TBI-ID groups (scores 2, 3, and 4) for the same measures: (d) P50 amplitude, (e) N100 amplitude, and (f) P200 area under the curve. Boxplots display the distribution and interquartile range of the data with overlaid individual data points. Brackets with asterisks indicate statistically significant group differences ($p < 0.05$).

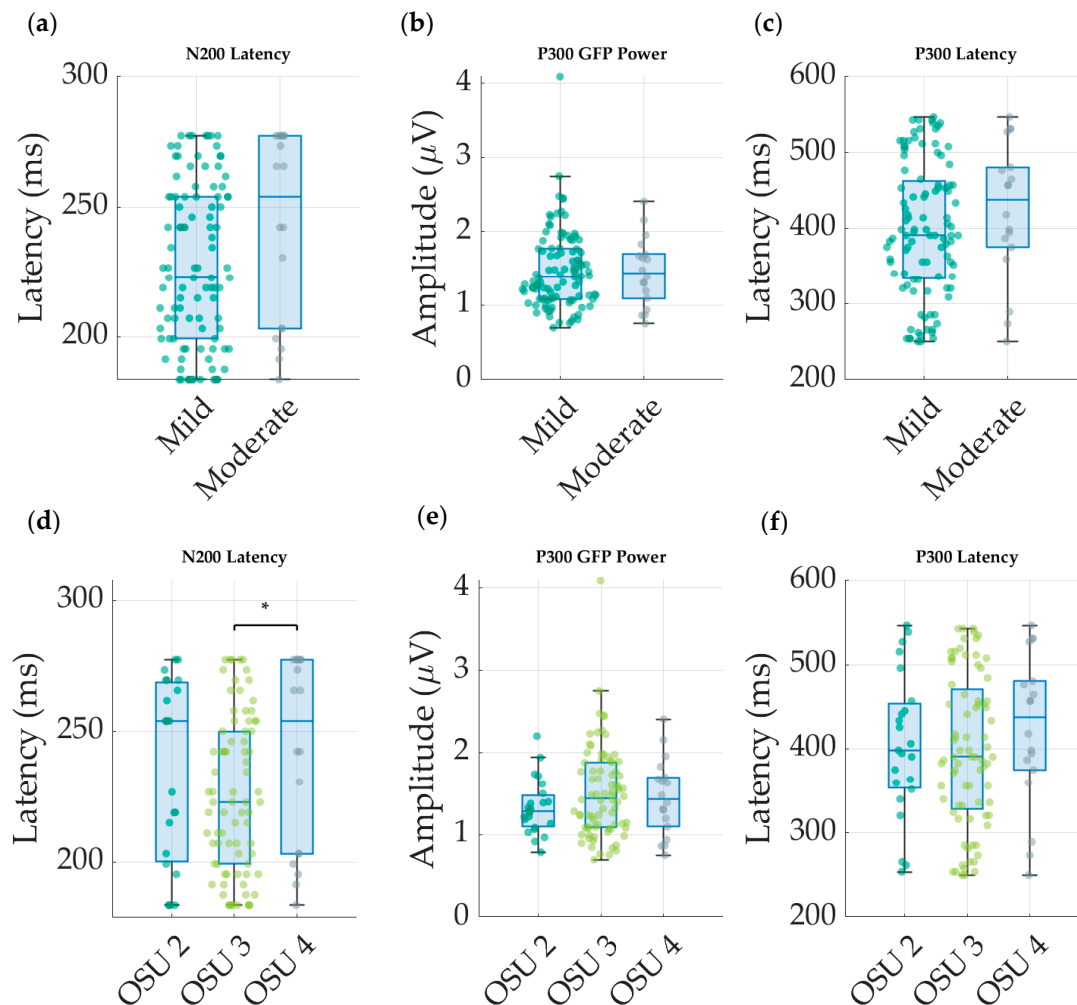


Figure 4. Distribution of late ERP component measures across clinical severity and OSU TBI-ID classifications. (a–c) Comparisons between mild and moderate TBI groups for (a) N200 latency (ms), (b) P300 global field power amplitude (μV), and (c) P300 latency (ms). (d–f) Comparisons across OSU TBI-ID groups (scores 2, 3, and 4) for the same measures: (d) N200 latency, (e) P300 global field power amplitude, and (f) P300 latency. Boxplots display the distribution and interquartile range of the data with overlaid individual data points. Brackets with asterisks indicate statistically significant group differences ($p < 0.05$).

Multivariate comparisons between OSU TBI-ID subgroups (2 vs. 3) for selected neurophysiological markers are shown in Figure 5.

3.4. Electrophysiological Subgroup Identification

The selected solution of the k-means cluster was $K = 2$, with cluster sizes as follows:

- Cluster 1: $n = 68$.
- Cluster 2: $n = 53$.

Participants were assigned to two electrophysiological subgroups identified through k-means clustering. Standardized feature profiles are shown in Figure 6. A two-dimensional PCA visualization of the clustering solution is presented in Figure 7a, where participants are plotted in PCA space and colored by k-means-derived subgroup membership, with centroids and covariance-based density contours overlaid to illustrate cluster structure. The same PCA space is shown in Figure 7b, where participants are instead colored according to their OSU TBI-ID score, enabling direct visual comparison between data-driven clustering and clinical categorization.

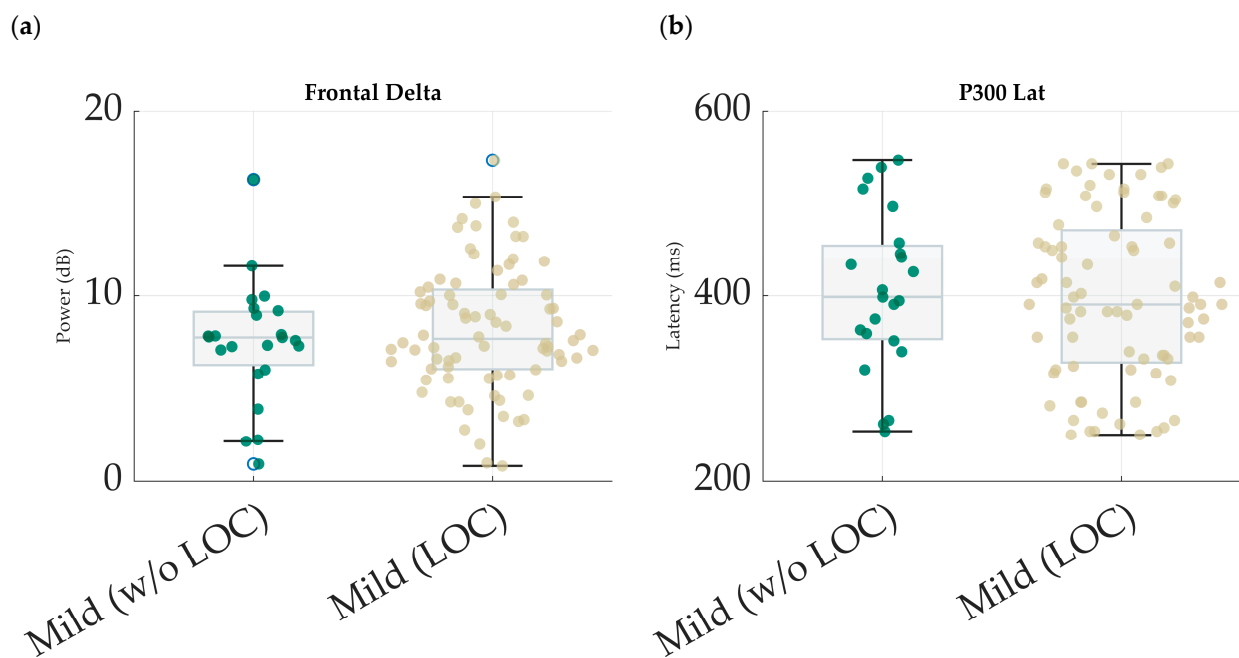


Figure 5. Comparison of neurophysiological markers between OSU TBI-ID mild subgroups. (a,b) Comparisons between individuals classified as mild without loss of consciousness (OSU 2) and mild with loss of consciousness (OSU 3) for (a) frontal delta power (dB) and (b) P300 latency (ms). Boxplots display the distribution and interquartile range of the data with overlaid individual data points.

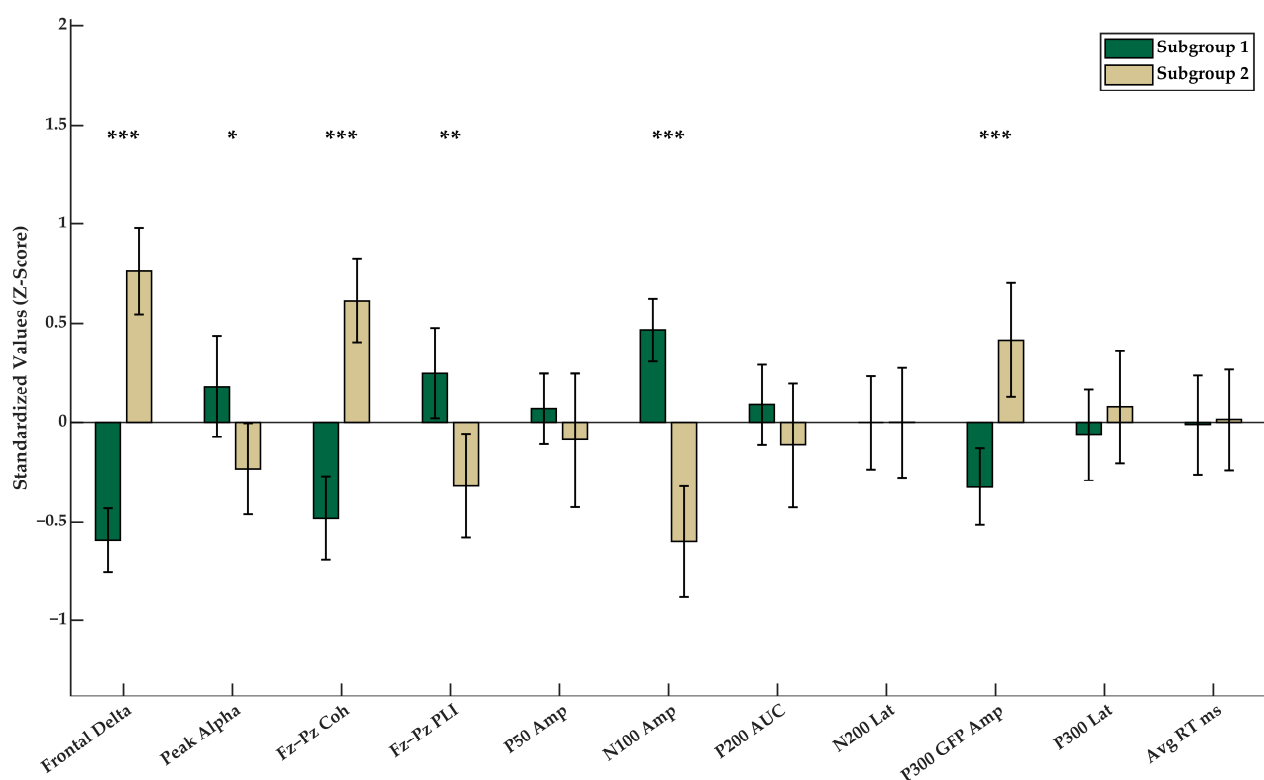


Figure 6. Multi-Metric Signatures by Electrophysiological Subgroup Assignment. Standardized values (Z-scores) comparing qEEG, ERP, and behavioral performance (Reaction Time) metrics across the discovered Electrophysiological Subgroups. Error bars denote 95% confidence intervals. Asterisks indicate statistical significance across groups for a given metric (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

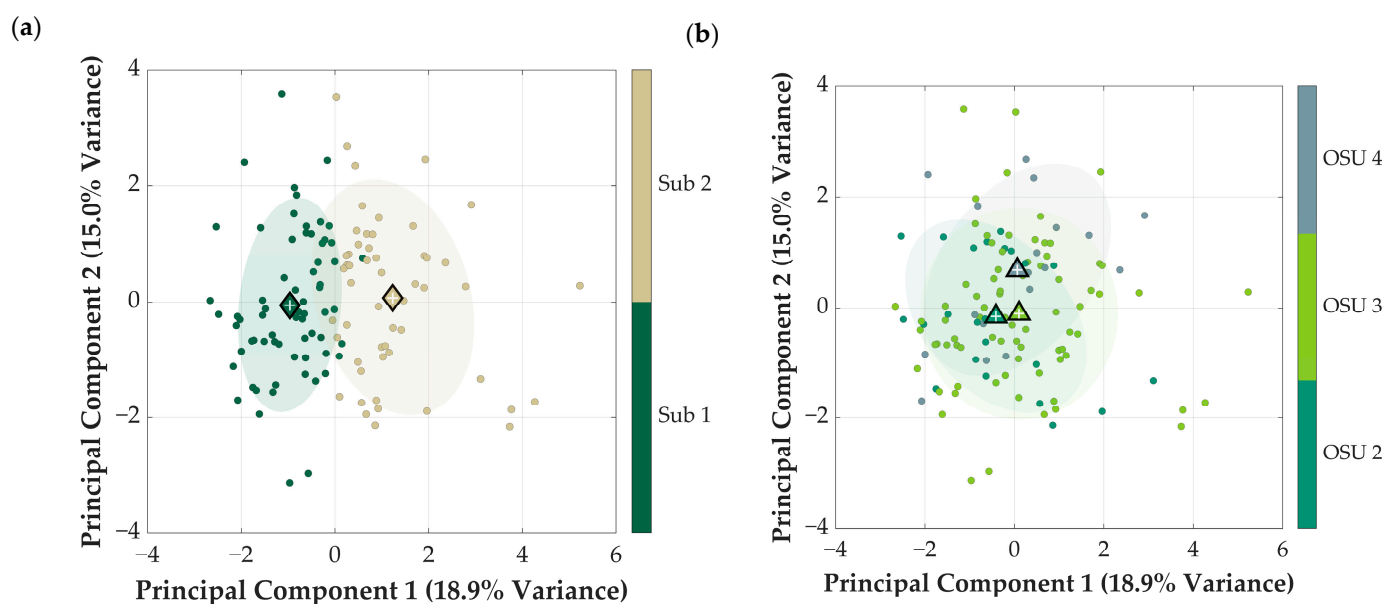


Figure 7. Comparison of data-driven clustering and OSU TBI-ID classifications in PCA space. (a) K-means cluster assignments with centroids (diamonds) and 1.5 SD dispersion clouds. (b) The same participant coordinates labeled according to OSU TBI-ID classifications, with centroids shown as triangles. The underlying participant coordinates are identical in both panels; only the labeling scheme differs.

Comparisons across electrophysiological subgroups revealed no differences in reaction time ($p = 0.890$), age ($p = 0.551$), or sex ($p = 0.924$). Cross-tabulation analyses indicated no significant association between electrophysiological subgroup membership and clinical severity ($p = 0.276$) or OSU TBI-ID classification ($p = 0.256$). Cross-tabulation matrices of clinical severity and OSU TBI-ID categories across electrophysiological subgroups are shown in Figure 8. A summary of PCA-derived feature weights contributing to the two-dimensional clustering structure is provided in Table 5.

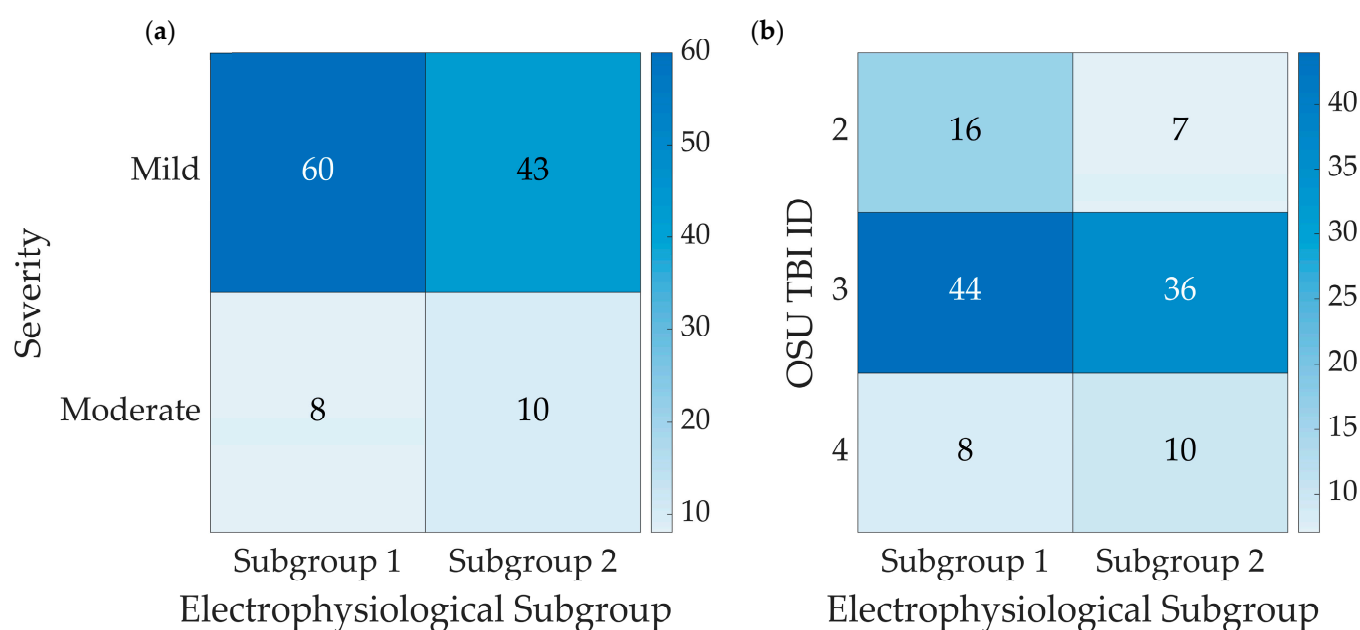


Figure 8. Distribution of clinical groupings across electrophysiological subgroups. (a) Clinical TBI severity categories. (b) OSU TBI-ID classifications. Values represent participant counts.

Table 5. Feature-loading profiles across the 11-metric suite, sorted in descending order of their contribution to the composite 2D PCA space.

Neurophysiological Metric	Composite 2D Feature Loading
N100 Amplitude	0.423
Frontal Delta	0.411
Fz-Pz Coherence	0.339
P50 Amplitude	0.312
P200 AUC	0.286
P300 GFP Amplitude	0.284
Peak Alpha	0.196
N200 Latency	0.179
Avg RT ms	0.099
P300 Latency	0.097
Fz-Pz Phase Lag Index	0.092

3.5. Results Summary

Across 121 participants meeting neurophysiological quality criteria, EEG, ERP, spectral, and behavioral measures were successfully extracted and analyzed. Group-level comparisons across clinical severity and OSU TBI-ID classifications revealed distributions of spectral and electrophysiological features (Tables 3 and 4; Figures 1 and 2), while ERP analyses confirmed consistent signal quality, with all datasets meeting P300 global field power thresholds (Figures 3 and 4). Multivariate comparisons between OSU TBI-ID subgroups demonstrated differences in selected neurophysiological markers (Figure 5). Unsupervised clustering identified two electrophysiological subgroups ($n = 68$; $n = 53$) characterized by differing spectral, connectivity, ERP, and behavioral profiles (Figure 6). The variance weights of the 11 constituent features were quantified across a composite 2D Principal Component Analysis (PCA) space (Table 5), with the data-driven cluster boundaries, centroids, and variance clouds mapped in Figure 7a. The identical coordinate space was utilized to map the clinical group distributions and centroids by the OSU TBI Scale (Figure 7b). These data-driven subgroup assignments were not significantly associated with clinical severity or OSU TBI-ID classifications. The distribution of participants across clinical categories and electrophysiological subgroup assignments is shown in Figure 8.

4. Discussion

Clinical assessments such as the OSU TBI-ID attempt to measure the lifetime exposure of TBI in individuals. The OSU TBI-ID utilizes lifetime exposure and LOC-based indices to classify chronic TBI into a severity category. It is a structured interview using a self- or proxy-report [12,40]. The score assigned to individuals is determined based on their recall of prior injuries, specifically those involving a blow to the head or neck or high-velocity mechanisms that may result in shear injury. Individuals are asked to recall details such as amnesia, LOC, and treatment received. For the most severe injuries, additional details are collected to refine classification. However, in cases of TBI—where common characteristics include post-traumatic amnesia, LOC, and altered states of consciousness—reliance on retrospective recall may introduce limitations. Asking individuals to accurately report these details may be unreliable due to the very nature of the injury itself [41–43]. The OSU TBI-ID has not been validated against objective indices of TBI severity and frequency [44].

The lack of validation leaves this method susceptible to underrepresentation of severity or misclassification, as it is based on subjective reporting. Objective neurocognitive measures provide a clearer representation of an individual's current brain state [9]. When measures are derived directly from the organ itself, there is reduced potential for bias compared to categorization scores based on retrospective reporting [45]. This distinction

highlights a critical difference between lifetime exposure and current physiological state. While the OSU TBI-ID provides an estimate of cumulative exposure, it does not directly assess present neural function, which may evolve over time following injury [46,47].

Within the TBI literature, EEG findings demonstrate recurring trends despite overall variability. In the power spectrum, reductions in mean alpha frequency and posterior dominant rhythm slowing, often accompanied by increased theta and sometimes delta activity, are frequently reported across studies [48–50]. However, these findings are not uniform across individuals, and there is often substantial overlap between patient and control groups, limiting single-variable classification accuracy [49,51].

Inconsistencies across EEG studies are attributed to multiple factors, including differences in hardware, recording conditions, electrode montage, preprocessing pipelines, and frequency band definitions [48–50]. In addition, variability in injury severity and time since injury further contributes to heterogeneous findings across studies [23,52].

Connectivity-based metrics also demonstrate variability. Trends reported in the literature include hypocoherence and reduced synchronization, particularly in theta bands, although findings differ in direction, with both hypo- and hyper-connectivity reported depending on network definitions and study populations [53,54].

For event-related potentials (ERPs), P300/P3 components frequently demonstrate prolonged latency and/or reduced amplitude depending on task paradigm and population [55–57]. In some cases, changes are observed in only one parameter (latency or amplitude), while in others, topographic sub-patterns emerge that are not evident in group-level averages [57,58].

Despite these inconsistencies, EEG remains a valuable tool for assessing neural function. As both hardware and analytical approaches continue to evolve, the ability to detect and interpret meaningful neurophysiological patterns is expected to improve [52,59]. However, current limitations stem not only from participant variability but also from differences in acquisition methods, environmental factors, and study design [60].

To address this variability, clustering approaches provide an alternative framework by identifying patterns across multiple features simultaneously. Rather than relying on individual metrics or predefined categories, clustering allows for the identification of latent groupings based on overall neurophysiological profiles.

In the present study, clinical assessment scores did not effectively separate individuals across key neurophysiological trends commonly associated with TBI, such as increased frontal delta power. Additionally, inconsistencies were observed across classifications based on mild versus moderate severity and OSU TBI-ID levels (2, 3, and 4), as reported in Section 3.5. Importantly, this lack of alignment should not be interpreted as evidence that one approach is inherently superior to the other. The OSU TBI-ID and electrophysiological subgroup assignments capture different aspects of TBI, with the former emphasizing lifetime injury exposure and the latter reflecting current neurophysiological status during task performance. As a result, disagreement between these approaches may be expected and may provide complementary information regarding injury history and present neural function.

In contrast, unsupervised clustering identified two electrophysiological subgroups. This organization is visualized in Figure 7, where participant distributions are displayed within the same PCA space used to compare subgroup assignments and OSU TBI-ID categories. Quantitative evaluation of the clustering solution yielded the highest silhouette coefficient (0.216) and cluster stability (Jaccard = 0.767) among the tested solutions ($K = 2-5$), supporting selection of the two-cluster model. Although the silhouette coefficient indicates substantial overlap between participants, the $K = 2$ solution demonstrated the strongest combination of separation and stability among the evaluated clustering solutions. Consis-

tent with this observation, overlap between participants remained present, yet the subgroup assignments exhibited greater consistency with the observed multivariate structure than the clinical classification labels. This dissociation suggests potential limitations of clinically derived severity groupings in capturing underlying neurophysiological organization. As shown in Section 3.5, the identified electrophysiological subgroups were characterized by differing profiles across multiple metrics commonly reported in the TBI literature, including frontal delta power, peak alpha frequency, and midline connectivity.

The electrophysiological subgroups were characterized by relative differences across multiple features rather than absolute thresholds. Compared to Subgroup 2, Subgroup 1 exhibited approximately 44% lower frontal delta power (6.11 vs. 10.88 dB) and a ~6% higher peak alpha frequency (9.38 vs. 8.84 Hz). These shifts indicate reduced slow-wave activity and relatively faster alpha dynamics in Subgroup 1, whereas Subgroup 2 was characterized by elevated frontal delta and slower alpha frequency. These patterns are consistent with previously reported markers of cortical slowing and altered neural efficiency [61–64].

Connectivity measures also differed between the identified subgroups. Subgroup 1 demonstrated lower midline coherence (Fz-Pz = 0.69) but higher phase lag index values (Fz-Pz PLI = 0.55) relative to Subgroup 2. Although both metrics assess functional connectivity, they quantify different aspects of interregional synchronization and are not directly interchangeable. Coherence reflects the consistency of phase and amplitude relationships between signals, whereas PLI emphasizes non-zero-lag phase relationships and is less influenced by common-source effects and volume conduction [65–70].

The divergence observed between these metrics suggests differences in network organization rather than a simple increase or decrease in connectivity strength. One possible interpretation is that Subgroup 1 exhibited relatively greater phase-lagged synchronization between frontal and parietal regions despite lower overall coupling, whereas Subgroup 2 exhibited stronger overall synchronization that may include a greater contribution from zero-lag interactions. Accordingly, these findings are interpreted as evidence of differing connectivity profiles rather than superior neural efficiency or more precise neural communication.

Subgroup 1 displayed lower N100 amplitude ($-0.93 \mu\text{V}$) and reduced P300 global field power ($1.30 \mu\text{V}$) relative to Subgroup 2. In contrast, Subgroup 2 demonstrated larger N100 amplitude ($-3.08 \mu\text{V}$) and increased P300 global field power ($1.68 \mu\text{V}$). These observations characterize differences in task-related neurophysiological responses between the identified subgroups. However, the functional significance of these differences should be interpreted cautiously, as ERP amplitude measures do not directly establish underlying neural efficiency, resource allocation, or processing capacity.

Importantly, behavioral performance, as measured by reaction time, did not differ between subgroups. This suggests that equivalent behavioral outputs may be achieved through distinct underlying neural processes. Reliance solely on behavioral metrics may therefore obscure meaningful differences in neural function [71,72].

Together, these findings indicate that the identified electrophysiological subgroups were characterized by differing patterns of neural activity during task performance that were not captured by traditional severity classifications. Connectivity differences further suggest variation in the temporal organization of functional connectivity, as phase-based measures such as PLI reflect phase-lag relationships and are less influenced by volume conduction than coherence-based metrics. The divergence between coherence and PLI should be interpreted cautiously, as these metrics quantify complementary aspects of functional connectivity and may be differentially influenced by network topology, oscillatory amplitude relationships, and volume-conduction effects [73,74]. Accordingly, the observed

differences are interpreted as evidence of alternative patterns of network organization rather than superior neural efficiency or more precise neural communication.

The task employed in this study was a simple reflexive visuomotor paradigm requiring rapid responses to spatially unpredictable stimuli. This task engages distributed neural systems, including frontal regions involved in decision-making and motor planning, parietal regions associated with spatial processing, and occipital regions contributing to visual input.

Within this framework, the N100 component may reflect early sensory processing and reflexive spatial attention, while the P300 component is associated with cognitive updating and allocation of neural resources required for response execution [75–80]. The observed differences between subgroups in these components suggest divergence at both early sensory processing and later stages of cognitive resource allocation.

From a clinical perspective, the lack of alignment between OSU TBI-ID classifications and electrophysiological subgroups highlights a potential limitation of relying solely on historical injury metrics. Individuals with similar reported injury histories may exhibit substantially different neurophysiological states, suggesting that lifetime exposure measures may not fully capture current functional status.

These findings support a shift toward individualized, physiology-informed assessment approaches, consistent with precision medicine frameworks [81–83]. Rather than relying exclusively on categorical severity classifications, incorporating objective measures of current neural function may improve characterization of TBI and inform more targeted interventions.

Limitations

Despite the promising results, several limitations should be noted. EEG is inherently limited in spatial resolution. While it provides high temporal resolution, it is less precise in localizing deeper neural structures. The 32-channel montage used in this study, although typical, limits spatial resolution compared to higher-density systems such as 64-channel configurations [84]. Clinical severity groups also demonstrated imbalance, likely influenced by the limitations of the OSU TBI-ID. While clustering appeared to mitigate this imbalance, it does not eliminate underlying sampling constraints or the clinical presentation of diagnoses. Additionally, the findings are specific to a single visuomotor task. Future work should examine whether these subgroups are stable across multiple cognitive paradigms. This study is further limited by the absence of a non-TBI comparison group, which restricts comparison with normative populations. In addition, the identified electrophysiological subgroups were derived and evaluated within a single cohort and therefore require independent replication and external validation before any diagnostic or clinical application can be inferred. Furthermore, baseline data reflect current state only, as pre-injury measurements were not available. The present study focused on objective electrophysiological measurements rather than comprehensive modeling of all potentially relevant clinical variables. Several factors that may influence EEG measures, including psychiatric comorbidities, sleep-related variables, medication use, and chronic pain, were not explicitly incorporated into the clustering framework. In addition, many commonly reported TBI descriptors, including time since injury and number of prior TBIs, are derived from retrospective self-report and may be subject to recall-related limitations. Future work integrating objective neurophysiological, clinical, and outcome measures may provide additional insight into the sources and significance of observed subgroup variability.

5. Conclusions

Since the OSU TBI-ID categories were not significantly associated with the electrophysiological subgroups identified in this study (Figure 8), lifetime injury history and current neurophysiological status may represent complementary aspects of TBI characterization. Within this chronic TBI cohort, these findings suggest that objective electrophysiological measures may provide information not fully captured by historical exposure classifications alone.

Author Contributions: Conceptualization, K.F.W. and N.D.S.; methodology, K.F.W.; software, K.F.W.; validation, K.F.W. and N.D.S.; formal analysis, K.F.W.; investigation, K.F.W.; resources, N.D.S. and J.M.T.; data curation, K.F.W.; visualization, K.F.W.; writing—original draft preparation, K.F.W.; writing—review and editing, H.V.L., J.M.T., and N.D.S.; supervision, N.D.S.; project administration, N.D.S.; funding acquisition, H.V.L. and N.D.S. All authors have read and agreed to the published version of the manuscript.

Funding: Funding for this work was made possible by the State of Florida who funded this multi-year randomized clinical trial through the legislative appropriations process during state fiscal years 2022–2024. The subsequent budgets were signed by the Governor, and the funding was allocated to the USF Morsani College of Medicine to conduct the five-year trial. Funding support was also provided by the Florida Dept. of State Center for Neuromusculoskeletal Research.

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the University of South Florida (protocol code STUDY006819; Date of Approval: 16 July 2024). Participants ($n = 125$) were recruited as a subset of a larger clinical trial using procedures described in the parent study [28], with EEG data collection following the sub-study protocol outlined in Walters et al. [29]. The present analysis includes baseline session data only. Written informed consent was obtained from all participants prior to participation.

Informed Consent Statement: Written informed consent was obtained from the participants to publish this paper.

Data Availability Statement: The data supporting the findings of this study are not publicly available due to ethical and privacy restrictions but may be made available from the corresponding author upon reasonable request and with appropriate institutional approvals.

Acknowledgments: The authors thank the research staff and participants who contributed to data collection and study coordination, and the technical team for support with EEG acquisition and data management. Generative AI and AI-assisted technologies were utilized during the preparation of this manuscript. Specifically, Microsoft Copilot (bizchat.20260701.51.4; powered by OpenAI's GPT-5 chat model) was used by the authors for English grammar and language-editing assistance to improve overall text readability and flow. Additionally, Elicit was employed during the literature review process to summarize existing published research and assist the authors in contextualizing the findings within the current scientific literature. These tools were used strictly to refine and synthesize author-generated text and concepts; no original scientific data, statistical analyses, or literature citations were generated by AI. The final manuscript was completely reviewed, verified, and approved by the human authors, who accept full accountability for the integrity and accuracy of the submitted work. The views expressed herein are solely those of the authors and do not reflect an endorsement by or the official policy or position of the U.S. Department of War, Department of Veterans Affairs, or the U.S. Government or State of Florida.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

TBI	Traumatic brain injury
EEG	Electroencephalography
ERP	Event-related potential
ASR	Artifact subspace reconstruction
RT	Reaction time
AMICA	Adaptive mixture independent component analysis
OSU TBI-ID	The Ohio State University TBI Identification Method
IEDs	Improvised explosive devices
mTBI	Mild traumatic brain injury
fMRI	Functional magnetic resonance imaging
BOLD	Blood Oxygen Level-Dependent
fNIRS	Function Near-Infrared Spectroscopy
ICA	Independent component analysis
PSD	Power spectral density
GFP	Global field power
ADHD	Attention-deficit/hyperactivity disorder
ASD	Autism spectrum disorder

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