Feasibility of an Electroencephalography-based Biomarker of Brain Injury Severity in a Preclinical Mouse Model: A First Look

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Abstract— In this work, we investigate the feasibility of a biomarker of brain injury severity extracted from electroencephalography (EEG) data. Preliminary analysis of features extracted from EEG data from a preclinical mouse model of traumatic brain injury shows strong tonotopic clustering of EEG features by injury severity level and future outcome. These promising findings demonstrate the potential to develop an EEG-based biomarker of brain injury severity.

Clinical Relevance— An accurate biomarker of brain injury severity will have a significant impact on neurocritical care by providing clinically meaningful information to optimize care for an individual patient and to facilitate identification of cohorts of patients with similar injury severity levels for clinical trials.

I. INTRODUCTION

Prognosis following acute neurological injury is essential to guide medical decision-making and optimize patient care. While many studies have explored proteins as biomarkers of brain injury [1], electroencephalography (EEG) data analysis has been less studied but is a promising non-invasive means to assess injury as EEG provides a direct, continuous measure of brain function. Here, we focus on developing an accurate EEG-based biomarker of injury severity to predict outcome after traumatic brain injury (TBI). Preliminarily, we used a preclinical animal model of TBI to investigate the feasibility of an EEG-based biomarker of brain injury severity.

II. METHODS

We used a pneumatic impactor [2] to induce controlled TBI in wild-type C57Bl/6 male and female mice. EEG leads were placed and recording started within 3 hours after injury. EEG data were recorded from two electrode channels at a sampling rate of 200 Hz. Mice were trained on a rotating rod (RR) task for 2 days prior to injury to establish a baseline and retested on days 1, 3 and 6 after injury. Using RR performance as a surrogate endpoint, the mice were grouped into four injury severity levels: 1) mild ($\geq$ 200 seconds (sec)); 2) moderate (101-200 sec); 3) severe (11-100 sec); and 4) fatal (0-10 sec). A subset of mice at each severity level was selected for feature analysis. Eight hours of EEG signals from day 1 after injury were normalized and bandpass filtered (0.5-30 Hz). Temporal (variance, skewness, kurtosis), spectral (delta, theta, alpha, and beta) and entropy (sample, frequency, Lempel-Ziv, permutation, and wavelet) features were extracted from 30 sec

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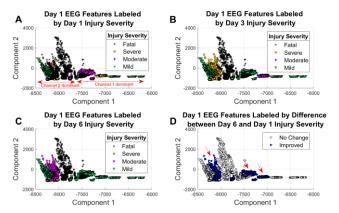
Figure 1. Visualization of the first two principal components (90% variance) of reduced EEG features extracted from day 1 EEG data of mice from each injury level (fatal, severe, moderate, and mild). **(A)** Clustering of day 1 EEG features by injury level and the evolution of injury severity in the day 1 EEG clusters on **(B)** day 3 and **(C)** day 6. **(D)** Day 1 EEG features labeled by the difference in injury severity between day 6 and day 1. Clusters with improved injury severity levels are annotated (arrows).

segments. Principal component analysis was performed to reduce feature dimensions for visualization.

III. RESULTS

Fig. 1A, B and C show clusters of the first two principal components of day 1 EEG features labeled by days 1, 3 and 6 injury severity levels, respectively. Fig. 1D shows the change in injury severity between day 6 and day 1. Mice with mild and fatal injuries are readily isolated and mice with recovery are localized in distinct, channel-specific clusters between clusters of mice with no change in injury severity.

IV. DISCUSSION & CONCLUSION

These preliminary findings show the potential of developing an EEG-based biomarker for brain injury severity as there is strong tonotopic clustering of EEG features by electrode channel, injury severity level and future outcome. Current work includes a robust analysis of the full mouse EEG dataset to develop an EEG-based biomarker machine learning model that predicts brain injury severity. Our ultimate goals are to translate our findings from a mouse to a human model and demonstrate the utility of our novel EEG-based biomarker for optimizing patient care and clinical trial cohort identification.

REFERENCES

[1] Wang, K. K., *et al.* An update on diagnostic and prognostic biomarkers for traumatic brain injury. *Expert Rev Mol Diagn.* 2018.18(2):165-180.
[2] Laskowitz, D.T., *et al.* Traumatic brain injury exacerbates neurodegenerative pathology: improvement with an apolipoprotein E-based therapeutic. *J Neurotrauma*, 2010. **27**(11): 1983-95.