Pathophysiological Insights into Post-Traumatic Amnesia in Mild Traumatic Brain Injury: A CENTER-TBI Study

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Background: Post-traumatic amnesia (PTA) is a state of disorientation, memory loss, and behavioral dysfunction after traumatic brain injury (TBI), but the underlying pathophysiology remains unclear (1). This study evaluated the relationship between PTA status at Emergency Department (ED) admission and 1) blood biomarkers 2) six-month patient-reported outcome measures (PROMs) in mild (m)TBI patients from the CENTER-TBI study (2).

Methods: Data included mTBI patients (Glasgow Coma Scale of 13-15) from CENTER-TBI (n=1,708). PTA status was categorized as ongoing, resolved, or no PTA. The maximum values of acute (<24 hrs) neurofilament light (NfL), glial fibrillary acidic protein (GFAP), ubiquitin carboxyl-terminal hydrolase-L1 (UCH-L1), and tau and subacute (~2 wks) NfL were log-transformed. The relative change (delta) in NfL was also calculated. Blood biomarkers were assessed using Kruskal-Wallis and post-hoc Dunn's tests followed by covariate-adjusted linear models. PROMs were evaluated with univariate and multivariate logistic regressions.

Results: Blood biomarkers were elevated with increasing PTA severity (Figure 1). PTA status remained associated with biomarkers in the linear models (GFAP, UCH-L1, tau (acute); NfL (acute, subacute, delta): $p < 0.001$). While patients with resolved PTA had a lower risk of unfavorable outcomes compared to those without PTA, these findings were largely insignificant in the multivariate models (Figure 2).

Conclusion: PTA status in mTBI patients is associated with a pathophysiological gradient of neuro-axonal and astro-glial injury. PTA status at ED admission is not independently predictive of six-month outcomes. These results further validate blood biomarkers as an objective marker of injury severity along another injury index.

1. Parker, T.D., et al., Post-traumatic amnesia. Pract Neurol, 2022. 22(2): p. 129-137.

2. Steyerberg, E. W., et al., Case-mix, care pathways, and outcomes in patients with traumatic brain injury in CENTER-TBI: a European prospective, multicentre, longitudinal, cohort study. Lancet. Neurol., 2019. 18(10), 923–934.

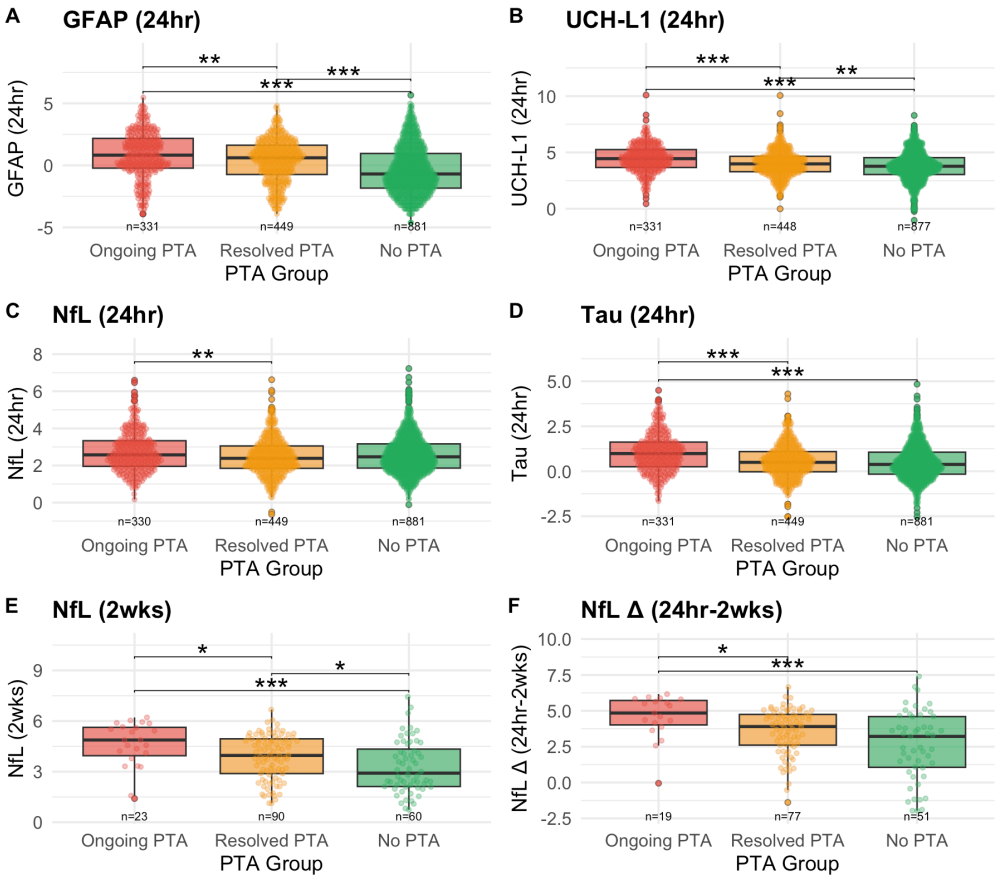

*Figure 1: Boxplots with Beeswarm Jitter of Blood Biomarkers by PTA Status with Significance Annotations from Dunn's tests with Benjamini Hochberg Correction (*p<0.05; **p<0.01; ***p<0.001)*

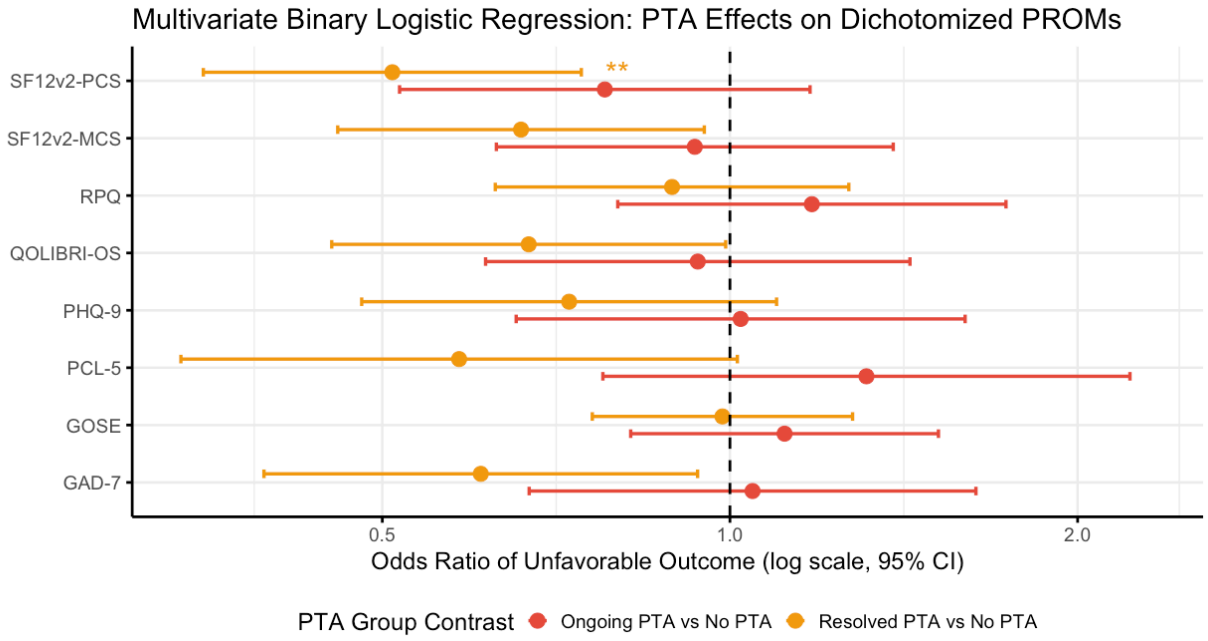

*Figure 2: Forest Plot of Odds Ratios from the Multivariate Logistic Regressions for PTA Effects on PROMs with Benjamini Hochberg-Corrected Significance (*p<0.05; **p<0.01; ***p<0.001)*