

Adjunctive non-invasive vagus nerve stimulation supports significant improvement in persistent mood and cognition dysfunction in patients with mTBI with comorbid PTSD: a retrospective cohort

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Introduction

Mild traumatic brain injury (mTBI), commonly referred to as concussion, is a major source of prolonged cognitive, emotional, and somatic dysfunction. This burden is often exacerbated in patients with comorbid post-traumatic stress disorder (PTSD), where neuropsychiatric symptoms are more severe and resistant to standard interventions. Non-invasive vagus nerve stimulation (nVNS) has emerged as a promising adjunctive therapy for mTBI, with evidence of neuroprotective effects including modulation of autonomic tone, reduction of neuroinflammation, preservation of the blood–brain barrier, and enhancement of cognitive resilience. Recent preclinical and clinical findings suggest that nVNS may be particularly beneficial in complex mTBI phenotypes such as those involving PTSD.

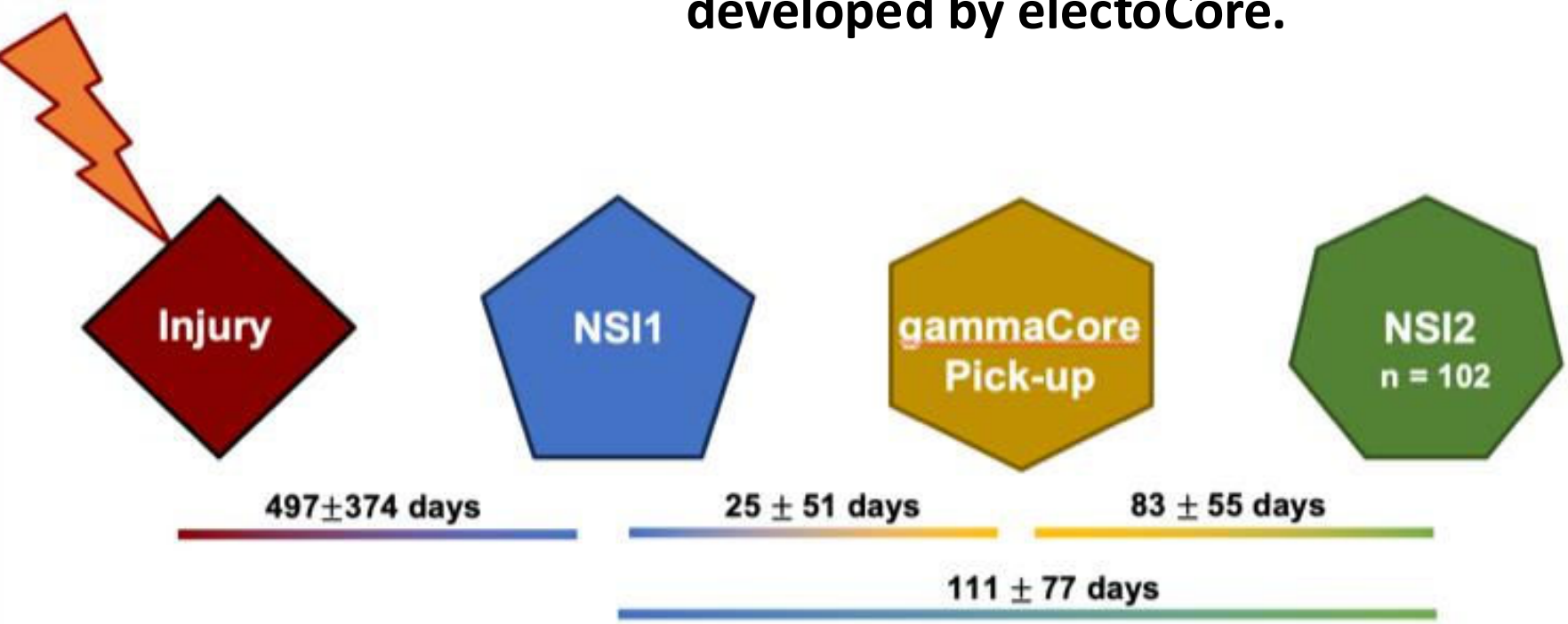
Methods

This retrospective analysis was conducted at Cherry Creek Neurology between October 2020 and September 2024. Patients were included based on clinical diagnosis of mild traumatic brain injury (mTBI), elevated symptom burden as assessed by the Neurobehavioral Symptom Inventory (NSI), and willingness to initiate adjunctive non-invasive vagus nerve stimulation (nVNS) therapy. A subset of patients also completed validated surveys for PTSD (PCL-5), depression, and anxiety at intake.

Patients were prescribed nVNS and were instructed to deliver two consecutive stimulations, twice per day, using the **gammaCore™** device developed by electroCore.



Study Design

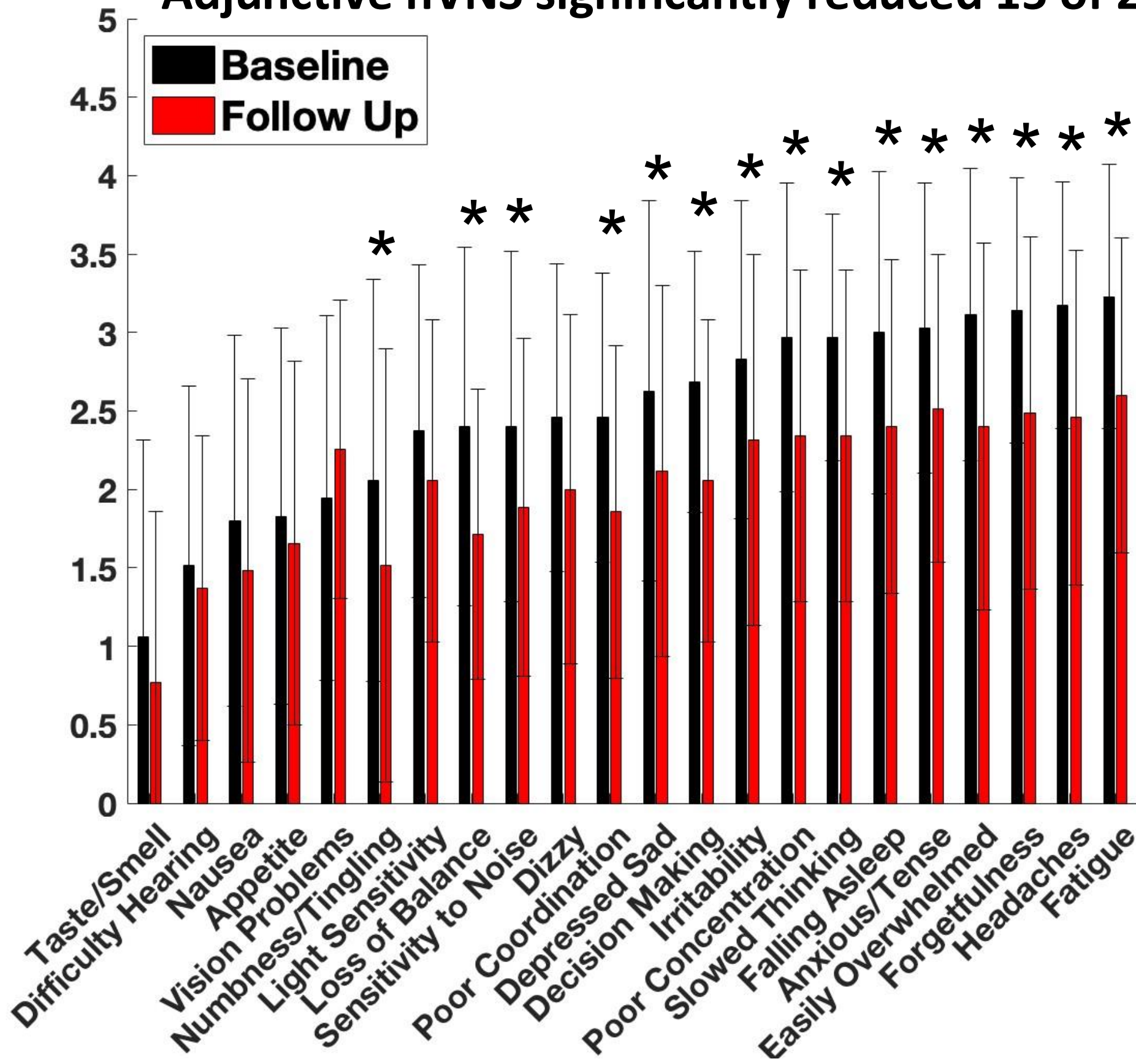


Patients self-administered nVNS (two consecutive stimulations, twice daily) in addition to standard of care (SoC), individualized per clinical discretion. NSI scores were collected at intake (NSI1) and again after approximately 3–4 months of nVNS therapy (NSI2). PTSD was identified in individuals scoring ≥31 on the PCL-5.

Paired NSI scores were compared using Wilcoxon signed-rank tests. Correlations between NSI and psychiatric scales were assessed, and principal component analysis (PCA) was used to explore symptom clustering by PTSD comorbidity. Effects of injury chronicity on baseline severity and treatment response were tested using ANOVA. Among 175 patients screened, 102 had complete pre/post NSI data; of these, 42 had PCL-5 data and 35 met the threshold for comorbid PTSD. Time since injury ranged from 5 days to 3.5 years.

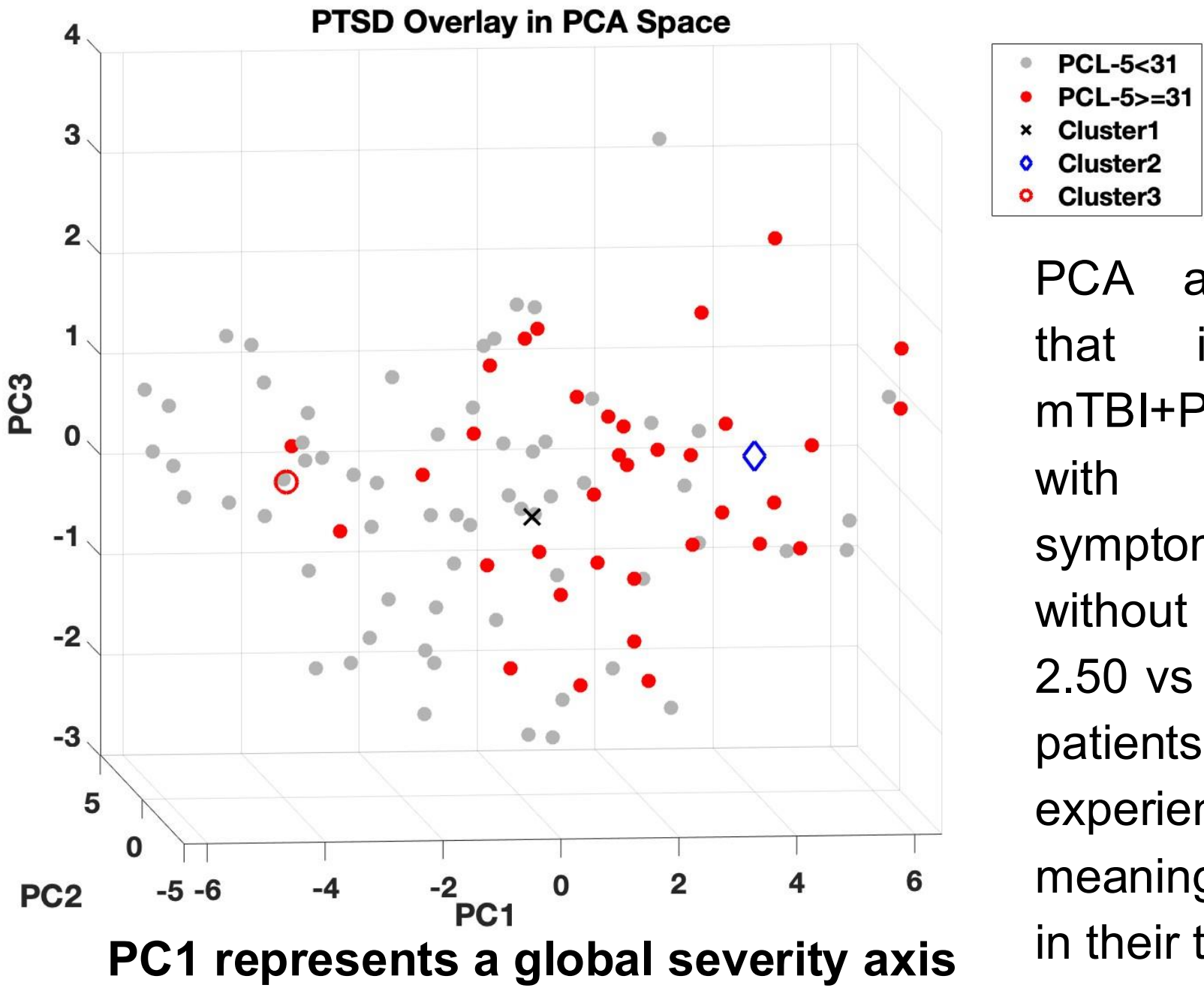
Results

Adjunctive nVNS significantly reduced 15 of 22 NSI parameters from their baseline values in mTBI+PTSD patients.



Among mTBI+PTSD patients, the most significantly improved NSI components were:

- **Easily overwhelmed** (mean change: -0.71 ; $p = 0.0014$)
 - **Poor coordination** (-0.60 ; $p = 0.0024$)
 - **Loss of balance** (-0.69 ; $p = 0.0033$)
 - **Post-traumatic headache** (-0.71 ; $p = 0.0037$)
- The time elapsed since injury did not affect the initial NSI severity ($p = 0.075$ to 0.966) nor treatment efficacy ($p = 0.142$ to 0.987) for all symptoms.



Conclusions

Although patients with comorbid PTSD presented with 38% greater symptom severity compared to those with mTBI alone, adjunctive nVNS combined with SoC produced comparable therapeutic benefit across groups. Significant reductions were observed in affective and cognitive symptom domains. Notably improvements were seen in symptoms of overwhelm, coordination, balance, and post-traumatic headache. Importantly, the duration since injury did not impact baseline severity or treatment efficacy. These findings support the use of adjunctive nVNS in managing persistent neurobehavioral symptoms in complex mTBI phenotypes, including those with comorbid PTSD.

- This mTBI+PTSD cohort presented with 38% more severe symptomatology and nVNS+SoC was effective in reducing the persistent symptom burden at rates similar their counterparts without PTSD
- 40% of patients mTBI+PTSD experienced clinically meaningful improvement in their total NSI score

References

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