Personalized Treatment for PTSD: Leveraging Trait-Like and State-Like Biomarkers in Prediction of Prolonged Exposure Therapy Treatment Outcome

Post-Traumatic Stress Disorder (PTSD) is a complex condition with diverse clinical manifestations and neurobiological mechanisms. The heterogeneity of PTSD symptoms, often overlapping with other psychiatric disorders, complicates both diagnosis and treatment. Current treatment approaches rely primarily on subjective symptom reports, overlooking neurobiological factors that could inform personalized interventions. The absence of objective biomarkers contributes to inconsistent treatment responses, underscoring the need for precision medicine in PTSD care.

The ultimate goal of the study is to integrate trait-like and state-like biomarkers to predict treatment outcomes for Prolonged Exposure Therapy (PE), an evidence-based PTSD treatment. Trait-like biomarkers, such as genetic, epigenetic, and baseline neuroanatomical features, help identify individuals at risk for PTSD. In contrast, state-like biomarkers, which reflect dynamic brain changes, track the disorder's progression and response to treatment. By combining these biomarkers, we seek to enhance treatment precision and efficacy.

Specifically, this study aims to (1) identify trait-like biomarkers that predispose individuals to PTSD by examining genetic, epigenetic, and neurostructural factors; (2) track state-like biomarkers reflecting treatment-induced brain changes to assess therapy effectiveness; and (3) integrate both biomarker types to develop predictive models for personalized treatment strategies.

In Study 1, we will compare individuals with PTSD and controls to identify baseline biomarkers distinguishing PTSD-specific changes. We will assess interactions between pre-treatment brain volume and post-treatment structural changes using multiple linear regression models to predict symptom reduction. Study 2 will replicate this analysis, focusing on treatment-related neurobiological changes in regions linked to symptom improvement. Additionally, we will generate state-like biomarkers by analyzing brain changes across treatment sessions, identifying key mechanisms of change.

Using these findings, we will develop predictive models integrating trait-like and state-like biomarkers. Cross-validation techniques will assess model performance and generalizability, while Bayesian networks will capture probabilistic relationships between predisposing traits, treatment-induced neurobiological changes, and clinical outcomes.

Identifying both trait-like and state-like biomarkers can refine PTSD treatment by providing clinicians with objective, neurobiological markers to guide therapeutic decisions. By elucidating the interplay between these biomarkers, this study aims to enhance personalized treatment approaches, improving response rates and reducing the risk of relapse.