

Identifying PTSD Biotypes Using Explainable AI (XAI) for Personalized Treatment Strategies

Post-traumatic stress disorder (PTSD) is a complex mental health condition with heterogeneous symptom profiles and high comorbidity with major depressive disorder (MDD) and anxiety. This variability complicates diagnosis and treatment, underscoring the need for personalized therapeutic approaches. Explainable AI (XAI) offers a promising avenue for identifying neurobiological biotypes of PTSD, facilitating precision treatment strategies.

This study aims to (1) identify distinct PTSD biotypes based on neurobiological differences in brain structure using deep variational autoencoders (DVAEs) and XAI, (2) evaluate the clinical relevance of these biotypes by comparing PTSD severity, depression comorbidity, and classification performance, and (3) assess their predictive utility in treatment outcomes, particularly responses to prolonged exposure (PE) therapy.

Using data from 3,084 adults (1,298 PTSD patients, 1,786 controls) from the ENIGMA-PTSD working group, we train a DVAE model on control data to establish normative baselines for brain structural features (e.g., volume, cortical thickness, surface area). Latent features extracted from PTSD patients are analyzed via clustering to detect neurobiologically distinct biotypes. Classification models (random forests, support vector machines) assess diagnostic accuracy, quantified by area under the curve (AUC) and accuracy (ACC) metrics using K-fold cross-validation. Lastly, we examine biotype-specific treatment responses to PE therapy. Two PTSD biotypes emerged, differing significantly in PTSD severity and depression comorbidity. Biotype-specific models outperformed general PTSD classification, highlighting their diagnostic potential. XAI analysis identified the pericalcarine region as a key differentiator. Notably, Biotype 2 patients showed a 75% reduction in PTSD symptoms post-PE therapy, compared to 57% in Biotype 1.

By integrating XAI with neuroimaging, this study advances precision psychiatry, enabling targeted PTSD interventions based on individual neurobiological profiles. These findings lay the foundation for personalized mental health care, optimizing treatment efficacy through data-driven insights.