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The interaction between early sexual trauma and diagnosis of panic disorder on brain structural connectivity: A human connectome study

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Background: Early traumatic experiences are associated with alterations in neural structures that increase risk factors for chronic psychopathology, including a 4- to 12-fold increase in the risk of developing psychiatric disorders (including symptoms of panic disorder (PD)) according to previous research. These early life adversities, such as early sexual trauma (EST), can have a lasting impact on an individual's brain development and functioning throughout adulthood. Although structural alterations in brain regions have been reported in previous studies, to date, no study has investigated connectivity in the brain networks of adult patients with PD experiencing EST through connectome-based analyses of diffusion tensor imaging (DTI) data. We investigated the interaction effects of EST on structural brain networks in PD patients and their relationships with clinical symptoms and trait factors.

Methods: A total of 82 participants with PD patients and 106 healthy controls (HCs) were enrolled in the study (94 men and 94 women; ages= 38.00 ± 12.69 years). Whole-brain structural networks were constructed using white matter tractography and network-based statistical methods were performed. In addition, we conducted exploratory correlation analyses between EST-associated degree in brain connectivity and clinical characteristics related to PD. We performed correlation analyses between the eigenvector centrality of nodes associated with EST and treatment outcomes in patients with PD. The Early Trauma Inventory Self Report-Short Form, Anxiety Sensitivity Inventory-Revised, State-Trait Anxiety Inventory, Neuroticism Scale, and Penn State Worry Questionnaire at baseline were administered. PD symptoms were measured at baseline and follow-up periods of 8 weeks, 6 months, and 1 year using the Panic Disorder Severity Scale.

Results: There were significant interaction effects between EST and the group on the middle temporal gyrus (MTG), parahippocampal gyrus (PhG) and inferior parietal lobule (IPL). Significantly hyperconnectivity in the MTG, PhG, and IPL was shown in patients with PD compared with HCs. Exploratory correlational analysis revealed a positive correlation between the global properties of the interaction networks and trait markers (e.g., neuroticism, anxiety sensitivity) and state markers (e.g., pathological worry) of anxiety levels in PD patients. Furthermore, the eigenvector centrality of the cingulate gyrus and inferior frontal gyrus was negatively correlated with short- and long-term pharmacological treatment responses in patients with PD (FDR passed, q=0.05).

Conclusions: Our findings revealed significant interaction effects between EST and the group on the MTG, PhG, IPL, suggesting that EST may differentially affect structural brain network connectivity in these regions, which are critically involved in memory performance, emotion processing, and regulation in PD patients. Consequently, patients with PD associated EST may have immature emotion processing due to hyperconnected brain regions, which could exacerbate anxiety symptoms and potentially influence treatment prognosis. Furthermore, the partial overlap observed between brain networks associated with EST and regions related to treatment response (e.g. cingulete gyrus, inferior frontal gyrus) suggests that these findings indicate the potential involvement of common neural circuitry in the pathophysiological mechanisms and therapeutic mechanisms of PD. These findings may provide a neuroscientific basis for understanding brain networks through EST.

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