Integration of Dynamic Connectivity and Imaging Transcriptome Features in Major Depressive Disorder

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Abstract : Functional connectomics is essential in cognitive science and neuropsychiatry, offering insights into the brain's complex network structures and dynamic interactions. Although neuroimaging has uncovered functional connectivity issues in Major Depressive Disorder (MDD) patients, the dynamic shifts in connectome topology and their link to gene expression are yet to be fully understood. To explore the differences in dynamic connectome topology between MDD patients and healthy individuals, we conducted an extensive analysis of resting-state functional magnetic resonance imaging (fMRI) data from 434 participants (226 MDD patients and 208 controls). We used multilayer network models to evaluate brain module dynamics and examined the association between whole-brain gene expression and dynamic module variability in MDD using publicly available transcriptomic data. Our findings revealed that compared to healthy individuals, MDD patients showed lower global mean values and higher standard deviations, indicating unstable patterns and increased regional differentiation. Notably, MDD patients exhibited more frequent module switching, primarily within the executive control network (ECN), particularly in the left dorsolateral prefrontal cortex and right fronto-insular regions, whereas the default mode network (DMN), including the superior frontal gyrus, temporal lobe, and right medial prefrontal cortex, displayed lower variability. These brain dynamics predicted the severity of depressive symptoms. Analyzing human brain gene expression data, we found that the spatial distribution of MDD-related gene expression correlated with dynamic module differences. Cell type-specific gene analyses identified oligodendrocytes (OPCs) as major contributors to the transcriptional relationships underlying module variability in MDD. In conclusion, this study offers the first comprehensive description of altered brain module dynamics in MDD patients linked to depressive symptom severity and changes in whole-brain gene expression profiles.

Keywords : major depressive disorder, module dynamics, magnetic resonance imaging, transcriptomic
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