

A Multigraph Network Analysis of fMRI Data in Major Depressive Disorder

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Abstract—This study employs a multigraph approach to investigate large-scale network dysfunction in Major Depressive Disorder. We identified significant between-group differences in six key networks—including the Default Mode Network, Frontoparietal Network, and Ventral Attention Network—with patients exhibiting predominantly increased connectivity, particularly in high-level cognitive and attentional hubs. Notably, the Thalamus and Somatomotor networks demonstrated altered self-connectivity, suggesting impaired within-network regulation. Our multigraph model reveals a hierarchical reorganization of network architecture in patients, where hyperconnected core networks may drive global integration-segregation imbalances.

Index Terms—fMRI, MDD, Multigraph, Functional Connectivity, Large Scale Networks, Network Analysis.

I. INTRODUCTION

Major Depressive Disorder (MDD) is a debilitating psychiatric condition with profound impacts on cognitive and emotional functioning, yet its underlying network-level disruptions remain incompletely understood. The rapid development of modern computing technologies has enabled significant progress in a wide variety of fields of research, ranging from physics and electronics [1], [2] to social and human studies [3]–[7]. To date, functional brain networks have consistently shown promise in identifying various brain function disorders [8]. Artificial intelligence and machine learning approaches effectively identify biomarkers of these disorders and can be used to train classifiers and medical decision support systems [9]–[12].

While our previous works [13]–[15] identified localized connectivity alterations, a comprehensive assessment of large-scale network (LSN) dysfunction in MDD requires a systems-level perspective [16], [17]. Here, we expand upon prior findings by employing a multigraph framework to model dysregulated interactions across key LSNs [18], [19]. This approach enables us to capture both localized disruptions and

their broader network consequences, offering new insights into how MDD reshapes the brain's integrative architecture.

II. SUBJECTS

We enrolled a total of 164 participants, comprising 94 individuals without any known psychiatric conditions (Healthy Controls, HC group) and 70 patients experiencing with major depressive disorder (MDD group). Each participant underwent thorough evaluations conducted by experienced psychiatrists, including the administration of the Mini International Neuropsychiatric Interview [20] and the Montgomery–Åsberg Depression Rating Scale (MADRS) [21]–[24]. Exclusion criteria for both groups included a history of comorbid psychiatric conditions, autoimmune diseases, neurological disorders, previous head trauma, or the presence of metal implants incompatible with MRI scans. Prior to participation, all individuals provided written consent in accordance with the principles outlined in the Declaration of Helsinki. The study protocol was reviewed and approved by the Ethical Committee of the Medical University of Plovdiv (Approval No: 2/19.04.2018).

III. METHODS

The brain volume was parcellated into 165 regions according to the automated anatomical labeling atlas AAL3 [25]. To find the connectivity between pairs of brain regions (the so-called, connectivity matrix), we calculated the average BOLD time series for each brain parcellation, detrended them, and estimated Pearson correlation coefficients for all pairs of the averaged parcellation activities [26], [27]. The resulting connectivity matrix represents the functional brain network.

We considered large-scale networks (LSNs) as proposed in the work [28]:

- Auditory Network
- Cingulate Operculum (COper)
- Context Network
- Default Mode Network (DMN)
- Dorsal Attention Network (DAN)

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- Perception Network (perN)
- Somatomotor Network
- Striatum
- Thalamus
- Ventral Attention Network (VAN)
- Visual Network
- Fronto-parietal Network (FPN)
- Salience Network (SN)
- Amygdala Network
- Entorhinal-Hippocampus Network (EHN)

To enhance the interpretation of disturbed communication patterns among large-scale brain networks in Major Depressive Disorder (MDD), we devised a multigraph-based analytical framework. This model was built by integrating only those inter-network linkages that exhibited statistically meaningful differences between individuals with MDD and healthy control subjects.

In our graphical depiction, the weight or thickness of each connecting line (edge) between any pair of LSNs quantitatively reflects the cumulative count of impaired functional connections between them. This visual approach allows for immediate, intuitive evaluation of the degree to which inter-network communication is compromised. A notable advantage of this modeling strategy lies in its capacity to synthesize data across different hierarchical levels—seamlessly merging large-scale shifts in network engagement with intermediate-scale disturbances in functional connectivity. By doing so, this approach vividly demonstrates how localized, individual connection deficits accumulate and propagate, ultimately leading to substantial disruptions in the brain’s critical integration-segregation equilibrium at the LSN level. These disruptions, in turn, contribute to observable changes in the brain’s overarching network architecture.

IV. RESULTS

The analysis of significant network-based statistic connections revealed substantial between-group differences across multiple large-scale networks (LSNs). Notably, out of the 15 examined LSNs, six exhibited marked alterations in functional connectivity: DMN, Thalamus, FPN, VAN, Somatomotor Network, Visual Network, and Striatum. Among these, the Thalamus and Somatomotor networks displayed self-loops, indicating altered within-network connectivity.

The multigraph representation (Fig. 1) offers deeper insight into these connectivity disruptions as identified by the NBS approach. A particularly notable observation was the widespread increase in connectivity within the MDD group, especially among key hub regions such as the DMN, VAN, and FPN. This pattern suggests a fundamental reorganization of network architecture in MDD, wherein certain critical regions—particularly those governing higher-order cognitive and attentional functions—assume a more central role while maintaining their functional independence. These findings highlight a potential shift in the brain’s integrative mechanisms in depression, with implications for both network-level dysfunction and compensatory adaptations.

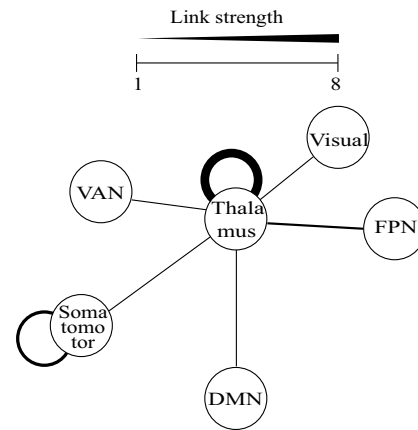


Fig. 1. Example of a figure caption.

V. CONCLUSIONS

Our findings demonstrate widespread disruptions in large-scale network connectivity in Major Depressive Disorder (MDD), particularly affecting the Default Mode Network (DMN), Frontoparietal Network (FPN), Ventral Attention Network (VAN), and sensory-motor regions. A key observation was the overall increase in connectivity among these networks in MDD, suggesting a maladaptive reorganization—where hyperconnected cognitive and attentional hubs may contribute to depressive symptomatology. The presence of self-loops in the Thalamus and Somatomotor networks further indicates impaired within-network regulation.

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