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Graph Theoretical Analysis of Cognitive Network Reorganization Following Antidepressant Treatment in Major Depressive Disorder

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Background

Cognitive impairments in Major Depressive Disorder (MDD) are a prominent and persistent feature that majorly contribute to poor psychosocial and occupational outcomes—even in individuals who respond to antidepressant treatment. As a systems-level view of cognitive functioning, graph theoretical network analysis provides a framework to investigate the architecture and interconnectivity of cognitive domains and how cognitive changes in different domains evolve together.

Objective

To evaluate how 8 weeks of open-label escitalopram treatment affects the cognitive network properties in individuals with MDD, and to compare these changes to a healthy control group (HC).

Methods

Included participants were 169 adults aged 18-60 yrs with MDD and 100 HC that were recruited across six sites participating in the CAN-BIND-1 study (REF); groups were age, sex and education matched. Participants completed a validated computerized cognitive battery assessing performance across 12 cognitive domains at baseline and after 8 weeks of open-label escitalopram treatment for the MDD group. For each group and timepoint, cognitive networks were constructed using binary adjacency matrices derived from Pearson correlation coefficients of domain-level cognitive performance scores. Key centrality metrics including but not limited to degree centrality, closeness centrality, and betweenness centrality were compared for groups and timepoints.

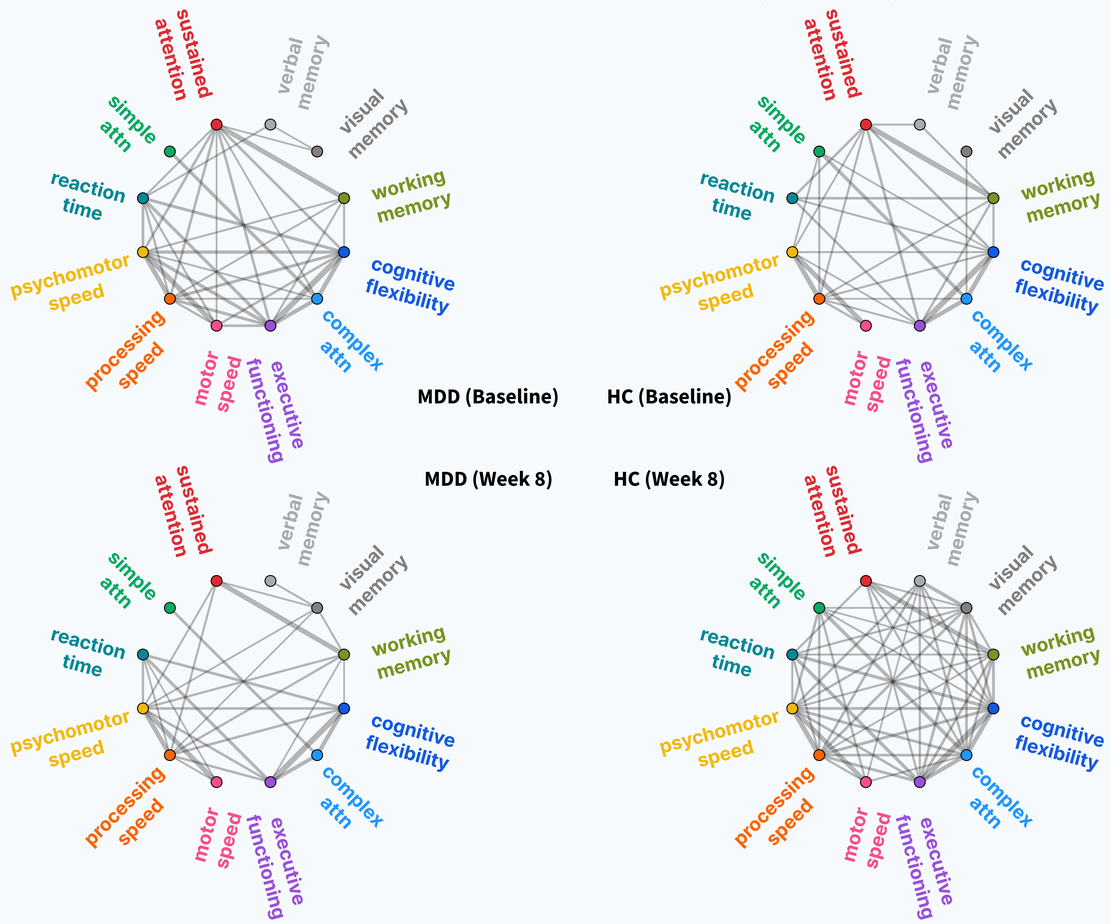

Figure 1 *Representative cognitive networks with at least moderate strength connectivity (Threshold = 0.31)*

Results

A representative cognitive network with a moderate connectivity strength is shown in the Figure 1.

At baseline, network topology measures did not significantly differ between MDD and HC groups. However, following 8 weeks of treatment, the MDD group showed trend-level changes in **degree** centrality, a measure of network **integration** (p=0.083), with decreases observed in most cognitive domains, except for an increase in visual memory and a small increase in working memory. **Closeness** centrality, reflecting network **efficiency**, also decreased significantly across domains in the MDD group, particularly in **sustained attention** (p = 0.004). This is contrasted by the changes in HC where the closeness centrality has increased for almost all cognitive domains with the most increase in visual memory, yet this metric remains unchanged for the sustained attention in HC. By week 8, both degree and closeness centrality differed significantly between MDD and HC groups ($p < 0.001$).

Conclusion

Although cognitive network topology was similar between MDD and HC at baseline, individuals with MDD exhibited treatment-related reorganization characterized by increased memory integration and reduced network efficiency, especially in attentional domains. These findings point to domain-specific cognitive changes in response to antidepressants that may be either adaptive or maladaptive, warranting further investigation into their association with clinical response and functional outcomes.

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Funding
CAN-BIND-1 was supported through grant funding from the Ontario Brain Institute and CIHR.