Commentary

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Understanding Age-Related Changes in White Matter-Gray Matter Functional Connectome in Normal Aging

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Description

Functional Connectivity (FC) between separate regions of Gray Matter (GM) in the brain is commonly derived from estimating the statistical correlation between Blood-Oxygenation-Level-Dependent (BOLD) signals in a series of MRI images in a resting state. In our recent cross-sectional study we proposed a novel bipartite graph method to quantify the relationships between the BOLD signals from GM and WM, and in a large set of brains estimate the impact of normal aging on the resting state correlation between GM and WM [1]. WM-GM correlations are a critical yet understudied component of the whole-brain functional connectome and provide insights into the synchronization of BOLD fluctuations between WM and GM regions [2,3].

Our research addresses a significant gap in understanding how aging affects functional signals in WM. We recognized the potential clinical relevance of changes in WM-GM correlations in various neurodegenerative and mental health conditions, such as Alzherimer's disease and schizophrenia [4,5]. Intriguingly, recent research employing deep learning techniques has underscored the unique predictive power of WM-GM correlations, outperforming both GM-GM FC and WM-WM FC in predicting depression [6].

Our dataset included 1,462 cognitively normal subjects aged 22-96 years, drawn from three established repositories (ADNI, BLSA and OASIS-3). This extensive sample size ensures robust and comprehensive insights into aging processes across adulthood and illustrates the value of making such data publicly available.

Our findings are multifaceted. First, at the regional level, we revealed heterogeneous alterations in region-specific WM-GM correlations over adulthood, with a notable predominance of decline during late adulthood (age ≥ 70 years). Second, we highlighted the age-related decline in the density of BOLD correlations of the WM bundles associated with memory, executive function, and processing speed, particularly in late adulthood. Lastly, at system level, we uncovered age-related reductions in the global efficiency of various brain networks spanning the entire adulthood, including the default mode network, attention network, limbic network, somatomotor network and frontoparietal network. We also provided a succinct summary of network efficiencies reported in previous GM-GM FC studies facilitating a direct comparison between our WM-GM correlation results and the prior GM-GM FC observations. Collectively, these results indicate that the brain undergoes a complex aging process during early and middle adulthood, involving local degradation, resilience and compensation. However, in late adulthood, the degradation process appears to surpass resilience and compensation mechanisms in most regions, emphasizing a dynamic age effect on WM-engaged whole-brain functional connectome.

What makes our study particularly remarkable is the pioneering use of a bipartite graph model to quantify WM-GM correlations and interpret those as a form of functional networks. This model offers a novel framework that holds promise for advancing our understanding of intricate brain connectivity patterns, not only in the context of aging but also in various other areas of neuroscience research. The bipartite graph, originally introduced in other fields, addresses the challenge of valuating WM-GM FC network properties, (such as global efficiency), which have been historically inaccessible due to the absence of specific types of connections in the WM-GM network topology. Our proposed bipartite-to-unipartite projection algorithm exhibits sufficient effectiveness in detecting network reorganization during aging. However, future exploration of optimized projection algorithms with enhanced neurophysiological alignment is warranted.

In conclusion, our study provides a comprehensive exploration of age-related changes in WM-GM correlations, offering valuable insights into changes in WM in the aging brain. Additionally, our innovative bipartite graph model introduces a new dimension to the study of brain connectome, with implications extending beyond aging research. These findings contribute to our understanding of brain function across the lifespan and hold promise for future investigations in neuroscience.

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