

Causal Associations Between Functional/Structural Connectivity and Dementia Associated Disorders

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Abstract

Background: Disruption of brain resting-state networks (RSNs) is known to be related to some dementia associated disorders, including Vascular Dementia (VD), Alzheimer's Disease (AD), Parkinson's disease Dementia (PD), Lewy Body Dementia (LBD) and Frontotemporal dementia (FTD). However, determining causality can be difficult in epidemiological studies. *Methods:* We used data on genetic variants associated with the levels of functional connectivity (FC) and structural connectivity (SC) within 7 RSNs identified from a genome wide association study (GWAS) meta-analysis among 24,336 European ancestries. The data for VD, AD and PD were obtained from FinnGen database; and the data for FTD and LBD were obtained from IEU OPEN GWAS project database, including 3024 and 6618 participants, respectively. We conducted a two-sample bidirectional Mendelian randomization (MR) study to investigate the causality relationship between FC and SC within 7 RSNs and dementia associated disorders. *Results:* The results showed that lower global mean SC were associated with a higher risk of AD [odds ratio (OR)=2912.261; 95% confidence interval (CI): 52.870-160418.100; P=0.015] and VD [odds ratio (OR)=3.960597e+03; 95% confidence interval (CI): 4.958367e+00-3163608; P=0.015], separately. Furthermore, these result was not affected by heterogeneity, horizontal pleiotropy (MR Egger intercept=0.004, P=0.449; MR Egger intercept=74.015, P=0.445). *Conclusion:* The present study provides genetic support that levels of FC or SC within different RSNs have contrasting causal effects on AD and VD. Moreover, there is a combination of injury and compensatory physiological processes in brain RSNs following AD and VD. Further studies are necessary to validate our results and explain the physiological mechanisms, so as to enhance patients' happiness.

Keywords

Resting-state, Dementia, Mendelian Randomization, Functional Network Connectivity, Happiness