Dissociation Pattern in Resting-State Default Mode Network Connectivity in Type II Diabetes Patients

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Target audience: Endocrinologists, Radiologists and patients with type 2 diabetes.

Purpose: Type 2 diabetes mellitus (T2DM) is associated with an increased risk of cognitive impairment.[1] Patients with impaired cognitive often show default-mode network (DMN) disruption. This study aimed to investigate the integrity of the DMN by using independent component analysis (ICA) methods in patients with T2DM and to correlate the DMN functional connectivity (FC) changes with neurocognitive performance and clinical variables.

Methods: Twenty-nine T2DM patients and thirty well-matched healthy controls were included in the study and underwent rs-fMRI imaging in a 3 Tesla unit. All participants underwent a detailed battery of neuropsychological tests. Clinical parameters such plasma glucose, HbA1c, insulin resistance, BMI and cholesterol levels were also collected. A group ICA method was used to extract the DMN of all participants. Two components were identified to be related to two sub-networks of the DMN, including the anterior and posterior parts of the DMN. Z-maps of the two sub-networks were compared between the two groups and correlated with the neurocognitive performance and clinical parameters by using Pearson correlation analysis.

Results: Patients with T2DM showed significantly increased frontal connectivity around the medial prefrontal cortex (MPFC) in the anterior DMN (aDMN) and significantly decreased connectivity in the posterior cingulate cortex (PCC) and angular gyrus in the posterior DMN (pDMN) (**Fig. 1**). The increased FC in the aDMN was negatively correlated with the neurocognitive performance (i.e. visual memory-related task) and positively correlated with fasting plasma glucose (**Fig.2 A and B**). The reduced FC in the pDMN was negatively correlated with disease duration and positively correlated with neurocognitive performance (i.e. cognitive flexibility) (**Fig.2 C and D**). These associations were independent of vascular risk factors and cerebral small vessel disease.

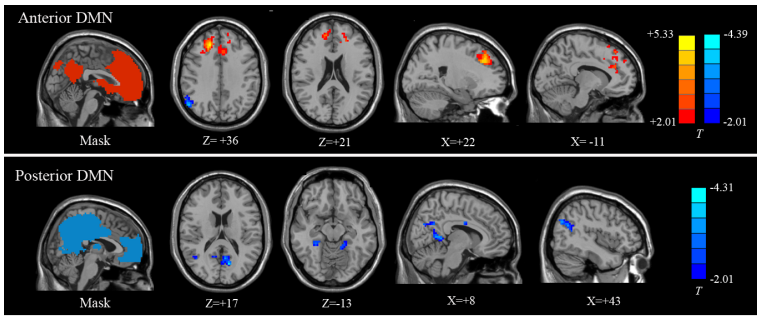

Fig.1 aDMN (upper row) and pDMN (lower row) differences between T2DM patients and healthy controls (P <0.05, AlphaSim corrected)

Discussion: Previous studies have demonstrated that the anterior and posterior sub-networks of the DMN have distinct alteration patterns with different pathologic circumstances.[2] Our study, for the first time, suggested the dissociation between the two DMN sub-networks in T2DM patients. This dissociation pattern has also been observed in several mental disorders, such as Alzheimer's disease, major depression and traumatic brain injury.[2-4] Based on these evidences, we speculate that this disrupted DMN integrity and independence between aDMN and pDMN changes might be a trait of T2MD-related cognitive impairment. Our findings of significant correlations between functional connectivity within DMN, cognitive performance and clinical parameters could also support this hypothesis.

Conclusion: The current study demonstrated the dissociation between anterior and posterior DMN sub-networks in patients with T2DM. Our results highlight the important role of the DMN in the pathophysiology of T2DM-related cognitive impairment and suggest that abnormal DMN activity may be a trait associated with T2DM patients.

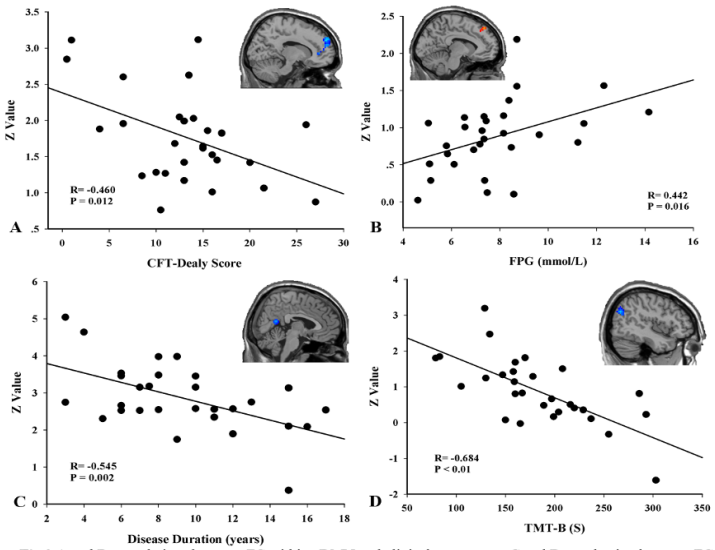

Fig.2 A and B, correlations between FC within aDMN and clinical parameters; C and D, correlation between FC within pDMN and clnical parameter.

References

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