Altered Spontaneous Brain Activity in Type 2 Diabetes Related Cognitive Dysfunction: a Resting-State Functional MRI Study

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Target Audience: Radiologist, MR technologist and clinicians who are interested in diabetes.

Introduction/Purpose: Resting-state functional MRI (rs-fMRI) has been applied to study the spontaneous brain activity in type 2 diabetes (T2DM) [1]. Patients with T2DM have considerably higher risk of developing cognitive impairment and dementia [2]. Differences between impaired and normal cognition among T2DM patients have not been studied yet. This study aims to investigate the possible alterations in spontaneous neural activity of brain through rs-fMRI in T2DM patients with and without cognition impairment (age-, gender- and education-matched). Furthermore, this study also aims at correlating regional homogeneity (ReHo) of blood oxygen level-dependent (BOLD) signals with clinical metrics (disease duration and glycated hemoglobin A1c or HbA1c level).

Methods: ***Patients*** With the approval of the local Institutional Review Board, 34 right-handed T2DM patients (based on diagnostic criteria of American Diabetes Association, 51-73years) were divided into cognitive impairment (DM-CI, n=17) group and normal cognition (DM-NC, n=17) group based on the clinical symptoms and a battery of systematic neuropsychological tests (Montreal Cognitive Assessment, Mini-Mental State Examination, Trail Making Tests, Auditory Verbal Learning Test, Hachinski test, Activity of Daily Living test). Plasma fasting/postprandial glucose and HbA1c were also tested. ***Imaging and data processing*** On a 3 Tesla MRI scanner (Discovery 750, GE Health Care, Wisconsin, USA) with 32-channel head coil, rs-fMRI data were obtained axially using a gradient-echo planar imaging (EPI) sequence with the following parameters: TR/TE =2000/35ms, FOV=24.0×24.0cm^2, 40 continuous slices with 4mm slice thickness, Bandwidth=250kHz, Flip Angle=90°. The registered fMRI data were segmented into 116 brain regions using the anatomically labeled (AAL) template [3]. Based on the estimation of regional mean time series and the coefficients comparisom between each pair of brain regions, the whole-brain partition analysis on functional connectivity [4] was applied to search for significant links. The ReHo value was calculated in different brain areas with the Brainnetome toolkit (BRAT) (www.brainnetome.org/en/brat) and SPM8 (www.fil.ion.ucl.ac.uk/spm) software. Two-sample t-tests were conducted voxel-wise on the ReHo maps to detect the global changes on spontaneous brain activities. The Pearson's correlation coefficients between ReHo value and diabetes duration, HbA1c were computed. The statistical analyses were carried out using SPSS software (SPSS Inc., Chicago, IL).

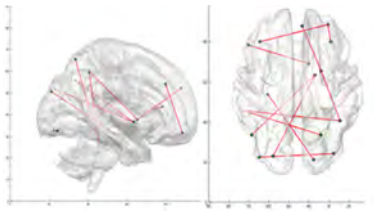

Fig.1 Altered functional connectivity in DM-CI group shown on sagittal and axial views (11-pairs, p<0.01). The dots represent the center of each brain region in AAL template. The lines denote the weaker functional connectivity.

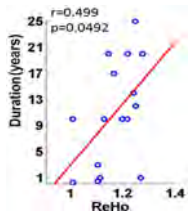

Fig.3 the ReHo value of DM-CI group was positively correlated with diabetic duration in the right inferior frontal gyrus region.

Results: The DM-CI group had longer disease duration (10.4±7.9years) and higher HbA1c (8.4±1.6%) level than DM-NC group (5.8±4.8years; 6.9±1.3%) (p<0.05). Compared to DM-NC group, the DM-CI group showed 11 pairs of weaker functional connectivities in different brain regions (p<0.01) (fig.1). Among which, differences in left-right inferior occipital gyrus, left inferior parietal gyrus-right inferior temporal gyrus were most significant (p=0.001). According to the voxel-based analysis, DM-CI group showed decreased ReHo in right inferior temporal gyrus and middle temporal gyrus, but increased ReHo in bilateral superior frontal gyrus (medial orbital), right gyrus rectus, inferior frontal gyrus (triangular) and superior frontal gyrus (fig.2). ReHo value was found to be correlated with diabetic duration in right inferior frontal gyrus (r=0.499, p=0.0492) (fig.3), one of the increased ReHo regions in DM-CI group. Correlation between ReHo and HbA1c was not significant.

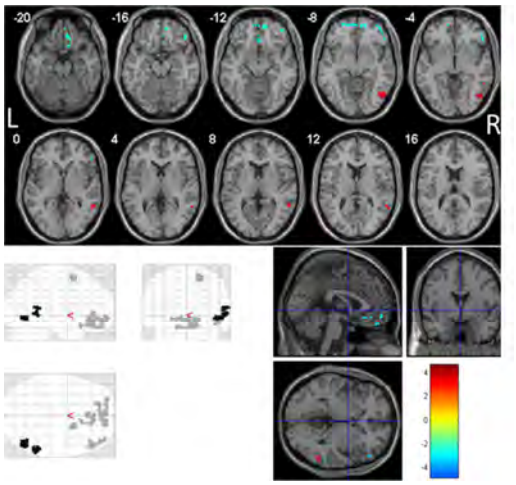

Fig.2 voxel-based maps showing significant differences in ReHo between DM-CI and DM-NC groups. Color scale denotes the t-values of two-sample t-test. Areas in red color means increased ReHo and blue color represents decreased ReHo in DM-NC group. In other words, DM-CI group showed decreased ReHo in right inferior/middle temporal gyrus, and increased ReHo in bilateral frontal regions.

Discussion and conclusion: This study confirmed the intrinsic and spontaneous neural activity alteration in DM-CI patients. T2DM patients with longer duration and poorer glucose control were more likely to have cognitive problems. Alzheimer disease (AD) and mild cognitive impairment (MCI) have been studied to have close relationship with hippocampus and posterior cingulate cortex [5-6]. In our study, based on the ReHo measurements, abnormal spontaneous brain activity was detected to decrease in right temporal regions and to increase in bilateral frontal regions in DM-CI group. These different regions might be most vulnerable to T2DM induced cognitive dysfunction. In addition, the weaker connectivities of multiple brain regions were also revealed through the AAL-based rs-fMRI study. Taking these together, the multi-functional brain disorders revealed by rs-fMRI can help to discover the susceptible regions when some T2DM patients progress into cognition dysfunction, and may provide clues to pathogenesis of T2DM induced cognitive defects. rs-fMRI can be an appropriate approach for studying the spontaneous brain activity alteration in diabetes related cognitive impairment.

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