Alteration of Brain Metabolites in Patients with Type 2 Diabetes and/or Major Depression Measured by Proton MR Spectroscopy at 3T

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Introduction

Diabetes and major depression are mutual risk factors such that individuals with diabetes are more likely to develop major depression and individuals with major depression are more likely to develop type 2 diabetes [1, 2]. ^{1}H magnetic resonance spectroscopy (MRS) provides a tool by which we can examine possible neurochemical perturbations shared across these disorders by non-invasively measuring neurometabolites in focal brain regions. In the current study at 3T, we measured brain metabolites in the anterior cingulate, frontal white matter, and subcortical regions that encompassed the caudate nucleus to examine the neurochemical basis and the association between type 2 diabetes and major depression.

Materials and Methods

Four groups of subjects, i.e., healthy control (n=17), depressed (n=25), diabetic (n=14), and diabetic depressed (n=10), were recruited from relevant clinics at the University of Illinois at Chicago and the local area community. Each subject group met current clinical standards for a diagnosis of either depression and/or diabetes as determined by formal clinical interview, psychiatric evaluation and medical record review and laboratory testing. Subjects ranged in age from 30 to 71.

The magnetic resonance imaging and spectroscopy scans were performed on a Philips Achieva 3T scanner with an 8-element phased-array head coil. Before MRS scans, an axial T2-weighted image and a high resolution T1-weighted 3D MPRAGE image (voxel size = 0.83×0.83×1.1mm^3, no gap, axial slices, FOV = 240mm) were acquired for placing the voxels, and the latter was also used for image segmentation in post-processing for correction of the CSF in the voxels for MRS scans. A Philips product point-resolved spectroscopy (PRESS) sequence (TR/TE=3000/35 ms) was chosen with four outer-volume suppression bands. The single-voxel ^{1}H-MRS spectra were acquired from the rostral anterior cingular cortex (ACC) (2×2×2 cm^3), the frontal white matter left (FWM-L) and right (FWM-R) (2×1×2 cm^3), and the subcortical regions encompass the caudate nucleus left (Caud-L) and right (Caud-R) (1×2×2 cm^3) (see Fig.1) with and without water suppression. Eddy current correction was achieved using the Philips product spectral correction function. Field homogeneity was optimized automatically using the second-order shimming and "VAPOR" water suppression was performed. Each single-voxel MRS scan included 128 averages (16-step phase cycling) along with 16-TR unsuppressed water scan at the beginning for spectral correction.

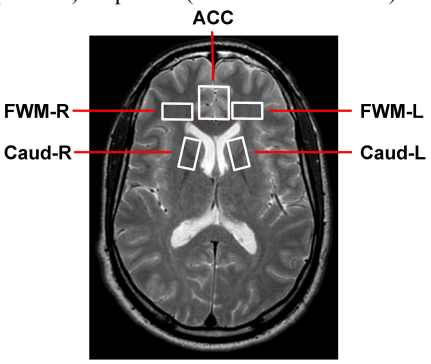

Fig. 1. Voxel placement in five brain regions (anterior cingulate cortex, ACC; frontal white matter left/right, FWM-L/FWM-R; head of caudate left/right, Caud-L/Caud-R)

Spectral quantification was carried out in the LCModel analysis software [3] using unsuppressed water signal for scaling. The basis set consisted of the model spectra of alanine (Ala), aspartate (Asp), creatine (Cr), phosphocreatine (PCr), γ-aminobutyric acid (GABA), glucose (Glc), glutamine (Gln), glutamate (Glu), glycerophosphocholine (GPC), phosphocholine (PCh), *myo*-Inositol (Ins), lactate (Lac), *N*-acetylaspartate (NAA), and *N*-Acetylaspartylglutamate (NAAG). A separate sub-set of macromolecules and lipid were also included in the basis set. Only the metabolite concentrations with a Cramer-Rao Lower Bound (CRLB) less than 20% were included in the data analysis.

Data were analyzed by univariate analysis of variance using SPSS v 17. Based on prior knowledge and hypothesis, we studied the absolute concentrations of NAA, NAA+NAAG, total creatine (Cr+PCr, tCr), total choline (GPC+PCh, tCho), Ins, Glu, and Glx (Glu+Gln), all corrected for CSF in voxels, and their concentrations to tCr ratios. Analyses were performed on both absolute metabolite concentrations and metabolite to tCr ratios. Separate analyses were done on each metabolite of interest and the primary results reported are not adjusted for multiple comparison. Diagnostic group with four levels (control, depressed, diabetic, and diabetic depressed) was the between-groups factor. Age and sex were included as covariates. Significant level was set at 0.05.

Results and Discussion

There was no difference in tCr concentration between the four groups in any of the five regions, ACC, Caud-L, Caud-R, FWM-L, and FWM-R (all F's <1.45, p's > 0.25). Similarly, no difference was found in NAA and NAA+NAAG concentrations or NAA and NAA+NAAG to tCr ratio between the four groups in any of the five regions (all F's <1.72, p's > 0.17). tCho concentration was significantly higher in FWM bilaterally (left: 2.31 a.u., p < 0.04; right: 2.07 a.u., p <0.03) for diabetic depressed patients as compared with healthy controls (left: 2.04 a.u.; right: 1.87 a.u.). tCho to tCr ratio is significantly elevated in bilateral FWM (left: 0.45, p = 0.05; right: 0.42, p = 0.04) compared to control (left: 0.40 and right: 0.37). Ins in Caud-L was significantly increased in diabetic patients (5.71 a.u., p = 0.004) compared to controls (4.58 a.u.). FWM-L Ins was also significantly elevated in diabetic depressed patients (5.79 a.u., p = 0.04) as compared to control (5.06 a.u.). The Ins to tCr ratio was significantly elevated in ACC for depressed (0.96, p < 0.05), diabetic (1.00, p <0.004), and diabetic depressed (0.99, p < 0.02) patients compared to healthy controls (0.9). We also found that the Glx to tCr ratio is significantly elevated in the ACC in diabetic depressed patients (1.83, p < 0.02) compared to healthy control (1.69). The above preliminary results are consistent with our previous work at 1.5T [1, 2]. The findings have broad implications and alterations in those metabolites in focal brain regions provide important neurobiological substrates of these disorders. Further optimization in preprocessing and quantification of MRS data (such as optimization in combining the spectral data from multiple channels) and improved statistical analysis will assist in validating these results in a larger sample.

References

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