

Magnetization Transfer Imaging Reveals Subcortical Biophysical Abnormalities in Patients with Type 2 Diabetes and Major Depression

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Introduction

Type 2 diabetes and major depression are mutual risk factors such that individuals with type 2 diabetes are more likely to develop major depression and individuals with major depression are more likely to develop type 2 diabetes, compared with general population [1,2]. To understand the pathophysiology of depression in type 2 diabetes, we examined the biophysical integrity of white matter and gray matter in critical brain regions in patients with both diseases using magnetization transfer (MT) imaging at 1.5T and found that magnetization transfer ratio (MTR) was significantly lower in the head of caudate nucleus in depressed diabetic patients compared with controls and patients with type 2 diabetes alone and patients with diabetes alone had MTR values between the control and depressed diabetic patients [3]. The current study was to expand our previous observations by adding a patient group with major depression alone to examine if the MTR value of this new group would differ from other 3 groups and study the effects of two diseases on biophysical abnormalities of the human brain.

Materials and Methods

Four groups of subject, healthy control (HC, n=32), patients with major depression alone (MDD, n=30), patients with type 2 diabetes alone, i.e., diabetic controls, (DC, n=18), and patient with both type 2 diabetes and depression (DD, n=15), were recruited for the study (see Table 1) from relevant clinics at the University of Illinois at Chicago and the local area community and consent forms had been acquired from all subjects. Each group of subjects 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. The subjects with major depression met the DSM-IV criteria for major depressive disorder and required a score of 18 or higher on the 17-item HAM-D score.

The MRI scans were performed on a Philips Achieva 3T scanner with a SENSE-Head-8 coil. The MT images are acquired using a three-dimensional (3D) spoiled gradient-echo echo-planar imaging sequence. The sequence parameters are TR/TE = 64/15 ms, flip angle = 9°, FOV = 24 cm, 67 axial slices, slice thickness = 2.2 mm/no gap, off-resonance frequency of the RF pre-saturation pulse = 1500 Hz [4,5]. Regions of interest (ROI) were put in left and right anterior cingulate, dorsolateral frontal white matter, occipital white matter, caudate and putamen, and bilateral genu and splenium.

Two-way analysis of covariance (ANCOVA) was performed on the MTR values, with type 2 diabetes and major depression as the two factors, controlling for age, gender, and education. Differences in the MTR values between groups were assessed using ANCOVA controlling for age, sex. Post hoc tests on the MTR values showing significant ANCOVA main effects were performed with Fisher's least significant difference (LSD) test. All statistical analyses were carried out using SPSS for Windows version 18. Significant level was set at 0.05.

Results and Discussion

The four groups did not differ in age and gender (as shown in Table 1). The MTRs in the right head of caudate nucleus were significantly different between groups ($F_{3, 89}=6.76$, $p<0.001$) and more specifically as shown in Fig. 1, the MTR value was significantly lower in the groups of MDD ($p=0.04$, *), DC ($p=0.002$, **), and DD ($p<0.001$, ***) all compared with the HC group and the MTR value was also significantly lower in the DD group than the MDD group ($p=0.02$, *). The MTR values in the left head of caudate nucleus was also significantly different between groups ($F_{3, 89}=2.71$, $p=0.05$) (data not shown for simplicity), which was mainly driven by lower MTR values in the DD group compared with the HC group ($p=0.007$) and compared with the MDD group ($p=0.06$, approaching significance).

Two-way ANCOVA analysis with type 2 diabetes (combining the DC and DD groups) and depression (combining the MDD and DD groups) as 2 factors found that there was a significant diabetes effect in the lower MTR values in the right head of caudate nucleus in patients with both diseases ($p<0.001$) while the depression effect just reached the significance ($p=0.05$). There was no interaction between diabetes and depression. There was also a significant diabetes effect in the lower MTR value in the left head of caudate nucleus ($p=0.02$). No interaction between diabetes and depression was found in the left head of caudate nucleus either. There were no significant differences in MTR value between groups in the other regions that we examined.

The combined effects of type 2 diabetes and major depression were generally consistent with an additive model, especially in the right head of caudate nucleus. As a result, biophysical abnormalities were the most striking in patients with type 2 diabetes and major depression and patients with type 2 diabetes or major depression alone had the MTR values that fell between the other groups. These data suggested that there is an important subcortical biophysical component to patients with type 2 diabetes and major depression.

References

[1] Ajilore O et al., Neuropsychopharmacology 2007; 32:1224-1231. [2] Haroon E et al., Psychiatry Res. 2009; 171:10-19. [3] Kumar A, et al., Arch Gen Psychiatry, 2009; 66:324-330. [4] Reich DS, et al., Am J Neuroradiol, 2006, 27:2166-2178. [5] Smith SA, et al., Magn Reson Med, 2006, 56:866-875.

Table 1. Demographical variables of 4 groups

	HC n=32	MDD n=30	DC n=18	DD n=15	
Age mean(SD)	55.13 (16.28)	54.90 (13.67)	56.11 (11.06)	54.27 (8.32)	F=0.06 p=0.98
Gender (M/F)	16/16	14/16	9/9	6/9	$\chi^2=0.47$ p=0.93

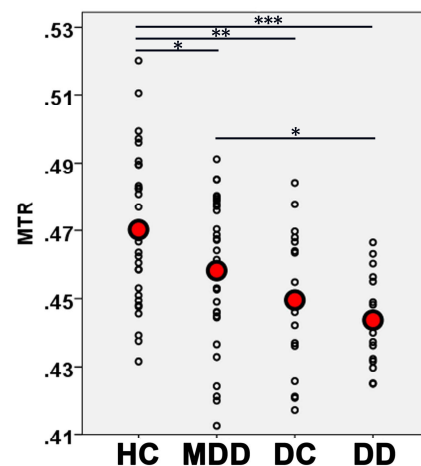


Fig. 1. Scatterplot of MTR values in the right head of caudate nucleus significantly different between 4 groups ($F_{3, 89}=6.76$, $p<0.001$) with MDD<HC ($p=0.04$, *), DC<HC ($p=0.002$, **), DD<HC ($p<0.001$, ***), and DD<MDD ($p=0.02$, *) (mean MTR values marked with enlarged circles)