Lateralized Cortical and Subcortical Biochemical Abnormalities in Late-life Major Depression: A Proton MR Spectroscopy Study at 3T

Shaolin Yang[1,2], Olusola Ajilore[1], Minjie Wu[1], Melissa Lamar[1], and Anand Kumar[1]

[1]Department of Psychiatry, University of Illinois at Chicago, Chicago, IL, United States, [2]Department of Radiology, University of Illinois at Chicago, Chicago, IL, United States

Introduction

Late-life major depression is one of the most common mental disorders in the elderly. Magnetic resonance imaging (MRI) has been utilized to study the neuroanatomical correlates of depression in late life, which is found being associated with decreased volume of focal brain regions, such as prefrontal lobe, hippocampus, and the head of caudate nucleus, and increased volume of white matter hyperintensity lesions [1,2]. Proton magnetic resonance spectroscopy (^{1}H-MRS) studies demonstrated increased concentration of choline-containing compound (tCho) and *myo*-inositol (Ins) in the (pre)frontal lobe white matter compared to controls. However, previous ^{1}H-MRS studies used relatively large voxel size (2x2x2 or 3x3x3 cm^3) for data acquisition such that "white-matter" voxels might contain significant portion of gray matter and/or encompass different brain regions. Moreover, previous studies only put voxels on one size (hemisphere) of the brain so there was no chance to study the laterality of brain metabolic abnormalities in late-life major depression. The purpose of this ^{1}H-MRS study was to examine the metabolic abnormalities in the left and right dorsolateral white matter of frontal lobe, the bilateral anterior cingulate gray matter and the left and right head of caudate nucleus of patients with late-life major depression and a healthy comparison group. We hypothesized that the concentrations of tCho and Ins would be higher in the frontal white matter and subcortical gray matter in patients with later-life major depression than the comparison group and we also hypothesized possible laterality of metabolic abnormalities.

Materials and Methods

The study groups consisted of 25 patients with late-life major depression (13 women, mean age=66.44, SD=7.7) and 23 nondepressed comparison subjects (13 women, mean age=65.95, SD=4.1). All subjects were age 60 or older and their mean Mini-Mental State Examination scores were in the normal range (mean±SD=29.16±1.14 in patients; 29.48±0.75 in controls). All depressed patients met DSM-IV criteria for major depression and had scores of 15 or greater on the 17-item Hamilton Depression Ratting Scale (HAM-D). Subjects were also administered the Center for Epidemiologic Studies of Depression (CES-D) scale as an additional measure of depression severity (Radloff LS, 1977). These subjects were recruited from relevant clinics and local area community and the consent form had been acquired from all subjects.

The ^{1}H-MRS scans were performed on a Philips Achieva 3T scanner using a single-voxel point-resolved spectroscopy (PRESS) sequence (TR/TE=3000/35 ms and Nex=128) with an 8-element phased-array head coil. The ^{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). Spectral quantification was carried out in LCModel [3] using unsuppressed water signal for scaling. Only the metabolite concentrations with a Cramer-Rao Lower Bound (CRLB) less than 20% were included in the data analysis.

Differences in the concentrations of metabolites between the 2 subject groups were assessed using analysis of covariance (ANCOVA) controlling for age, sex, and education. Post hoc tests on the metabolites showing significant ANCOVA main effects were performed with Fisher's least significant difference (LSD) test. Correlations between the metabolite concentrations and CES-D and HAM-D were analyzed using partial Pearson's product-moment correlations controlling for age, sex, and education. All statistical analyses were carried out using SPSS for Windows version 18 (SPSS Inc., Chicago, IL, USA). Significant level was set at 0.05.

Results and Discussion

The two groups did not differ in age (F=0.70, p=0.79), gender (χ^2=0.24, p=0.63), and education (F=2.09, p=0.15). The concentration of *myo*-inositol was higher in right frontal white matter (16.7%, $F_{1, 42}$=6.64, p=0.014) and in left head of caudate (18.1%, $F_{1,27}$=3.52, p=0.071, approaching significance) of depressed patients compared to the controls. The ratio of the concentration of *myo*-inositol to total creatine is significantly higher in right frontal white matter (19.3%, $F_{1, 42}$=10.28, p=0.003) and left head of caudate (23.6%, $F_{1,27}$=6.09, p=0.02) too (see Fig. 2). In contrast, both the concentration of *myo*-inositol and its ratio to creatine in the opposite sides, i.e., left frontal white matter and right head of caudate, did not reach statistical significance (all F's <2.46, p's > 0.12), although the means of the concentration and the ratio were higher in the patient group compared to the control group. No other metabolic abnormalities were observed between the groups. The concentration of *myo*-inositol in the right frontal white matter was positively correlated with the depressive symptomatology measures, i.e., the CES-D total score (r=0.46, p=0.038, df=19) and the HAM-D scores (r=0.58, p=0.006, df=19), and the ratio was also positively correlated with the HAM-D score (r=0.48, p=0.028, df=19).
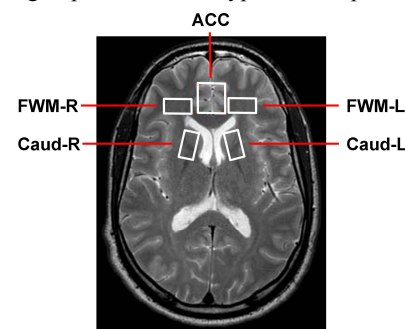

Fig. 1. Voxel placement in five brain regions (anterior cingulate cortex, ACC; frontal white matter left/right, FWM-L/FWM-R; head of caudate left/right, Caud-L/Caud-R)
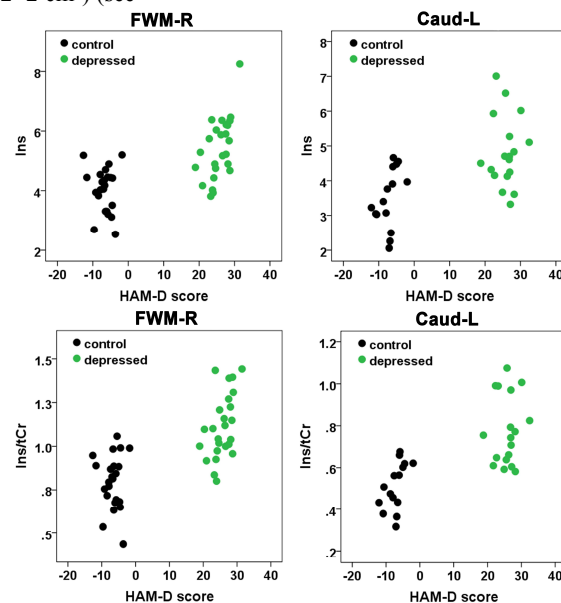

Fig. 2. Concentration of *myo*-inositol and its ratio to total creatine in right frontal white matter and left head of caudate (the HAM-D scores were already adjusted for age, gender, and education)

References

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