Anterior Cingulate Metabolic Abnormalities in Late-Life Major Depression

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Introduction

Late-life major depression is accompanied with a number of neuroanatomical changes including white matter hyperintensities, lower fractional anisotropy, prefrontal atrophy, and biochemical alterations. Previous work from our group has shown alterations in prefrontal white matter myo-insoitol at 1.5 T (1). The purpose of the present study was to examine metabolic alterations in the anterior cingulate associated with late-life major depression at 3 T using 2D magnetic resonance spectroscopy.

Methods

40 subjects were recruited through clinic referrals and local advertisements. Subjects were matched by age and gender. All depressed patients were age 60 or older and met DSM-IV criteria for major depressive disorder. All patients had scores of 15 or greater on the 17-item Hamilton Depression Rating Scale. In addition to receiving a detailed mental status examination by a psychiatrist, all patients were assessed with a structured psychiatric interview (Structured Clinical Interview for DSM-IV). Patients and control subjects were free of psychotropic medications for at least 2 weeks before the scan.

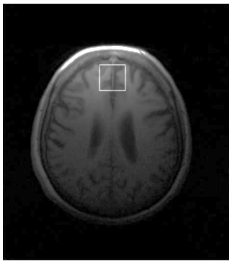
All subjects were scanned on a 3 T GE scanner. A 15.6ml (2.5x2.5x2.5 cm^3) voxel was placed in the anterior cingulate bilaterally (anterior to the anterior margin of the genu of the corpus callosum and symmetrically across the interhemispheric fissure) for all human subjects and other acquisition parameters were as follows: TR/TE=2.5s/30ms, 4 averages/Δt1, 100 Δt1 increments, Spectral width of 2000Hz along the t2 dimension using 2048 complex points, and oversampled to 1000Hz along the t1 dimension. The total duration was approximately 17 minutes. A white matter brain phantom containing more than thirteen metabolites at physiological concentrations (pH=7.3) was used for the validation study. Quantification was performed with ProFit Algorithm (2).

Metabolite concentrations were normalized using ratios to creatine concentrations. T-tests were performed to compare metabolite concentrations in the depressed subject group with the control group. Pearson correlations were used to assess the association between metabolite ratios and depression severity.

Results

Glycine/creatine and glutathione/creatine ratios were significantly increased in depressed subjects compared to control subjects. Glycine/creatine (r=.315, p=.048) and glutathione/creatine (r=.361, p=.022) ratios correlated with depression severity as measured by the Beck Depression Inventory (BDI) across all subjects. There was no significant difference in voxel tissue composition between the two groups.

Figure 1. Voxel placement in the anterior cingulate



	Control (n = 20)	Major Depression (n=20)
Age	68.65 (7.69)	68.60 (7.89)
GM%	59.27 (6.66)	57.41 (5.16)
WM%	21.47 (24.35)	24.36 (5.71)
CSF%	19.26 (4.60)	18.24 (3.72)
Glycine/Cr*	.0399 (.026)	.0630 (.041)
GSH/Cr*	.315 (.052)	.358 (.067)

Table 1. Age, voxel composition, significant metabolite ratios. Values are displayed as means and standard deviations. *, p < .05

Discussion

To our knowledge, this is the first report of alterations in cerebral concentrations of glycine associated with major depression, though plasma glycine changes associated with major depression have been previously reported. Glycine is an important neurotransmitter involved with regulating glutamate transmission. Alterations in this metabolite may contribute to excitotoxic damage which has been hypothesized as a mechanism for gray matter atrophy in the anterior cingulate. Glutathione plays an important role as an antioxidant. Elevations in glutathione may reflect increased oxidative damage in this region of the prefrontal cortex. Further study examining associations with cognitive function and clinical features of major depression are needed to put these findings in context.

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(2) Schulte RF, Boesiger P. ProFit: two-dimensional prior-knowledge fitting of J-resolved spectra. NMR Biomed. 19[2], 255-263. 2006.