Proton Spectroscopy Study of Adolescent Depression

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Introduction:

Rates of Major Depressive Disorder (MDD) rise dramatically in adolescence with an estimated lifetime prevalence of 15% in adolescents by ages 15-18.[1] Adolescent MDD is associated with significant morbidity, and most critically, attempted and completed suicides. Furthermore, adolescent MDD is a strong predictor of MDD in adulthood. Converging lines of evidence suggest that significant reductions in regional CNS volume and number and/or sizes of neurons and glia underlie the pathophysiology of MDD.[2] The striatum and the anterior cingulated cortex (ACC), shown in Fig. 1, have been proposed to play a key role in MDD.[2] The dramatic increase in the incidence of depression during adolescence highlights the importance of investigating neurometabolite levels in MDD **during adolescence** to allow the early detection of neurochemical alterations and contribute to the identification of at risk individuals. Proton MR Spectroscopy (^{1}H-MRS) provides a non-invasive *in-vivo* window into brain neurochemistry which reflects neuronal/axonal and glial integrity/viability. The objectives of this study is to explore whether neurochemical alterations exist in adolescents with MDD compared to healthy comparisons in the striatum and the anterior cingulate cortex through the quantification of the concentrations of the N-acetylaspartate (NAA), choline (Cho), and creatine (Cr), examples of which are shown in Fig. 2.

Methods:

Multi-voxel 3-dimensional ^{1}H-MRS acquired at 3 Tesla with high spatial resolution, 0.75 cm^3, voxels focusing on the anterior cingulate cortex (ACC) and striatum are compared between adolescents with MDD and matched healthy controls. Diagnosis of MDD is established by the K-SADS-PL. Children's Depression Rating Scale-Revised (CDRS-R) severity scores $\geq$ 35 are required. The 3D ^{1}H-MRS sequence to be used is described elsewhere.[3] It covered an $7\text{-}8_{LR}\times 10\text{-}12_{AP}\times 6_{IS}$ cm^3 volume-of-interest (VOI) using intermediate TR/TE=135/1600 ms, PRESS. Relative amounts of NAA, Cho and Cr on the voxel level are estimated from their spectral peak areas, examples of which are shown in Fig. 2, using Soher *et al.*'s parametric spectral modeling.[4]

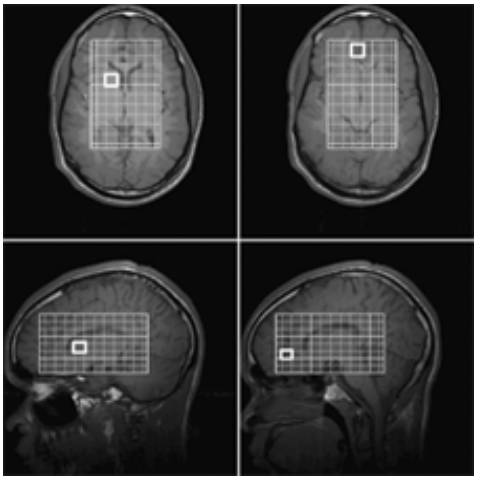

Fig. 1. Left, location of the striatum in a 16 years MDD female patient. Right, location of the ACC T1-weighetd MRI are overlaid with the $7_{LR}\times 11_{AP}\times 6_{IS}$ = 460 cm^3 VOI (white outline) and MRSI grid.

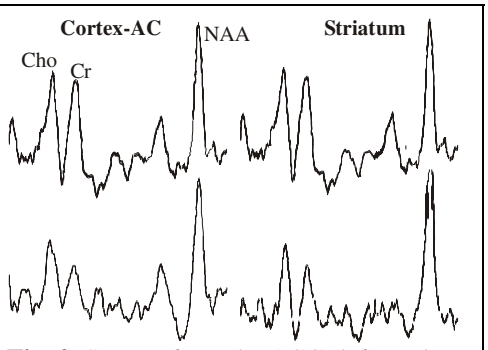

Fig. 2. Spectra from the ACC (left) and striatum (right) in two subjects.

Results: Seven MDD subjects and 7 controls ages 13-19 were scanned. MDD subjects had a significantly higher level of Cho concentrations in the striatum (p=0.012) even in this small sample. There was a trend towards a higher mean for patients with respect to Cho concentrations in the anterior cingulate (2-sided p = 0.07). There was no significant interaction between diagnosis and brain region for any of the three metabolites (p>0.52). Using mixed model analysis to compare patients and controls with respect to the overall mean level of each measure, patients exhibited a significantly greater Cho concentration (averaged over the 2 areas) than did controls (p=0.0004).

Discussion:

This preliminary study suggests Cho abnormalities are present in adolescent MDD, particularly in the striatum. Findings are consistent with greater membrane breakdown and support hypothesis that impaired cellular resilience plays a role in MDD. Confirmation and replication of these results would suggest that MRS is capturing neurodevelopmental pathophysiology in adolescence. Such finding, if validated in a larger cohort, could open the door to objective (instrumental as opposed to clinical) evaluation of MDD patients and quantitative assessment of the efficacy of their individualized treatment.

Acknowledgments:

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References

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