Correlations between Diffusion Tensor Imaging (DTI) and Magnetic Resonance Spectroscopy (1H MRS) in schizophrenic patients and normal controls

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Introduction: Evidence suggests that white matter integrity may play an underlying pathophysiological role in schizophrenia[1, 2]. N-acetylaspartate (NAA), as measured by Magnetic Resonance Spectroscopy (MRS), is a neuronal marker and is decreased in white matter lesions and regions of axonal loss[3]. It has also been found to be reduced in the prefrontal and temporal regions in patients with schizophrenia. Diffusion Tensor Imaging (DTI) allows one to measure the orientations of axonal tracts as well as the coherence of axonal bundles. DTI is thus sensitive to demyelination and other structural abnormalities. We obtained MRS and DTI data on 43 Normal controls and 44 Patients with schizophrenia. The data was analyzed using regions of interests in the Dorso-Lateral Prefrontal white matter, Medial Temporal white matter and Occipital white matter on both imaging modalities. NAA was significantly reduced in the patient population in the Medial Temporal regions. DTI anisotropy indices were also reduced in the same regions in the patient group. In addition, NAA and DTI-anisotropy indices were significantly correlated. We conclude that both imaging modalities are consistent and may be used to quantify axonal losses.

Methods*:* Schizophrenic subjects (n=44) between the ages of 20-80 were recruited from outpatients psychiatric facilities. Normal Controls (n=43). The diagnosis of schizophrenia was confirmed by a structured diagnostic interview (Comprehensive Assessment of Psychiatric Symptoms and History; CASH) as was the absence of any significant axis I psychopathology in the healthy comparison subject group. Drug testing and medical screening was performed to exclude patients with substance abuse and cardiovascular disease that might affect MRI results. All imaging were performed on a 3T Allegra MRI scanner (Siemens, Ehrlangen, Germany). DTI was acquired using a pulsed-gradient spin-echo sequence with EPI-acquisition (TR=4100ms, TE=80ms, FOV=21cm, matrix =128x128, 28 slices, thickness=3mm skip 1mm, b-factor=1250 s/mm^2, 12 gradient directions, 5 averages). Whole brain Diffusion Tensor data was obtained and fractional anisotropy (FA) indices were computed. ^{1}H spectroscopic imaging (SI) data of the left and right medial temporal lobes were recorded sequentially using the phase-encoded version of the standard PRESS volume localization sequence, with TR = *2000 ms*, TE = 30 ms, *24X24* phase-encoding steps over a field-of-view of 16 cm *(zerofilled to 32X32 phase-encoding steps before 3D Fourier transformation)*, a slice thickness of 10 cm slice, *1 average* per phase-encoding step and circular k-space sampling, to obtain voxels having a nominal size of 0.25 cm^3 (*1.0x0.5x0.5* cm^3). Outer volume saturation bands were prescribed to coincide with all 8 sides of the PRESS box. Water suppression and magnet shimming were automatically performed and adjusted by the host computer. The raw SI data were processed and fitted in the frequency-domain to obtain metabolite peak areas using a manufacturer-supplied MRS data processing software. 2D CSI data was obtained in two slices containing DLPF white matter, Medial Temporal white matter and Occipital White matter. MRS metabolites (NAA, Cho, Cr, Ins1 & Ins2) were obtained from these regions of interests (ROIs). Relative Anisotropy values were obtained in from the same ROIs from matched imaging planes Figure 1.

Results: Significant differences were found in the NAA/Cr ratios in the Medial Temporal regions ($p<0.039$). Relative Anisotropy values in the same region were found to be statistically significant as well ($p<0.006$). The Frontal white matter and occipital white matter were not significant. Correlation between NAA/Cr ratios with RA values in the same regions was also significant ($p<0.039$).

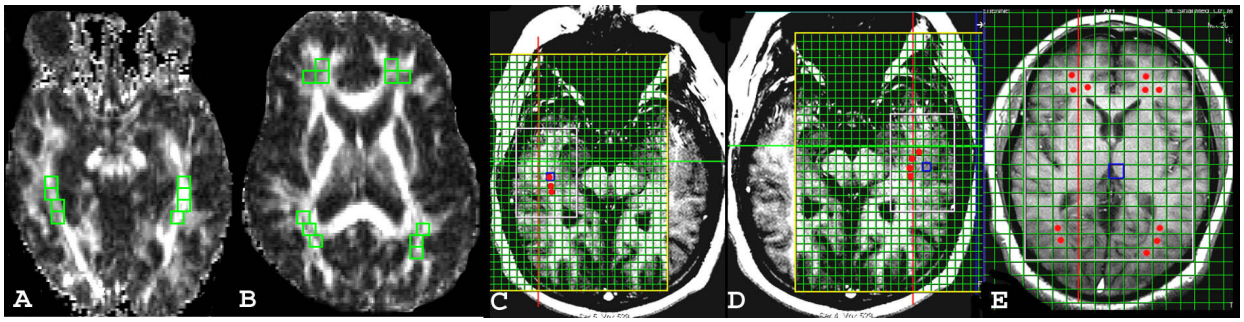

Fig 1: ROI locations for Medial Temporal, Frontal and Occipital white matter. (A,B) DTI-Fractional Anisotropy data, (C,D,E) 2D-CSI ROI placements for metabolite extraction.

Conclusion: The implications of these results are two fold: 1) there is a white matter abnormality in patients with schizophrenia and 2) the biochemical abnormality as detected in MRS is consistent with the DTI results. The biochemical abnormalities likely precede the structural defects. The current results may reflect a disease state that is already in an advanced stage in which both metabolic as well structural abnormalities are present.

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