Altered cortical microstructure in schizophrenia: a diffusional kurtosis imaging study

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Introduction: Schizophrenia is a debilitating illness that affects 1% of the population. Concurring evidence highlights the potential role of neuroinflammation as a significant factor in disease etiology and progression[1] with both astrogliosis and microgliosis reported by histological studies[2-4]. However, these studies, conducted in postmortem tissues, are consistent only in part, most likely due to their relatively small sample sizes. Thus, development of non-invasive imaging biomarkers of inflammation in schizophrenia would be highly instrumental in both identifying affected brain tissue and in providing non-invasive individual assessment of inflammation status. Recent studies have suggested diffusional kurtosis imaging (DKI)[5] as a potential approach to detect inflammation[6], with increased mean kurtosis (MK), a metric of microstructural complexity, found to associate with reactive astrogliosis in a rat model of traumatic brain injury. Thus, the goal of this study was to investigate the utility of MK in assessing gray matter microstructural integrity in schizophrenia.

Methods: Seventeen right handed male patients, with a diagnosis of chronic schizophrenia and eighteen male healthy control (HC) participants 30 to 55 years old participated in the study. The Structured Clinical Interview for DSM-IV (SCID) was used to confirm that subjects in the patient group met the criteria for a diagnosis of schizophrenia. The Non-Patient edition (SCID-I/NP) was used to screen the control subjects for Axis I disorders. All attempts were made to match the two groups in age and parental socio-economic status (SES) by selecting control subjects with similar values for these variables.

Imaging data was obtained using a 3T Trio MRI Scanner (Siemens Medical Solutions, Erlangen, Germany). Images were acquired using a body coil for transmission and a 12-element coil for reception. Approximate full brain coverage was obtained by acquiring 55 contiguous slices with a slice thickness of 2.3 mm (voxel size=2.3x2.3x2.3 mm^2). Other imaging parameters included TR = 8000ms, TE = 97ms and a field of view of 230 x 230 mm^2, and parallel imaging with an acceleration factor of 2. Diffusion weighted data was acquired for a total of 64 uniformly distributed gradient directions and for two b values (b = 1000 s/mm^2 and b=2000 s/mm^2). Additionally, nine sets of images with b=0 s/mm^2 were also obtained. The total imaging time was around 17 minutes. All images were corrected for motion and distortions from B0-field inhomogeneities.

A kurtosis approximation of the diffusion signal was used to calculate the diffusion and kurtosis tensor at each image voxel. MK maps were calculated for each subject. Segmentation of gray matter regions was performed for each subject using the MPRAGE image and the FreeSurfer software package. The segmented maps were then registered to the diffusion data. Automatic and manual approaches were subsequently used to define masks of the prefrontal and temporal gray cortex and of several subregions, which included superior temporal gyrus, parahippocampal and fusiform gyrus, inferior prefrontal cortex (pars opercularis and pars triangularis) and anterior cingulate (rostral and caudal) cortex. These regions have been previously shown to be involved in schizophrenia by both morphological and functional MRI studies. Mean MK values were obtained for each region of interest.

Results: Significantly increased MK was found in the schizophrenia group in temporal gray matter and superior temporal, parahippocampal, and fusiform gyri, pars opercularis, and rostral anterior cinculate cortex ($p<0.05$). Representative results are shown in Figure 1. There were no significant between-group differences in the overall prefrontal gray matter MK ($p>0.05$) suggesting more localized schizophrenia deficits in this brain region.

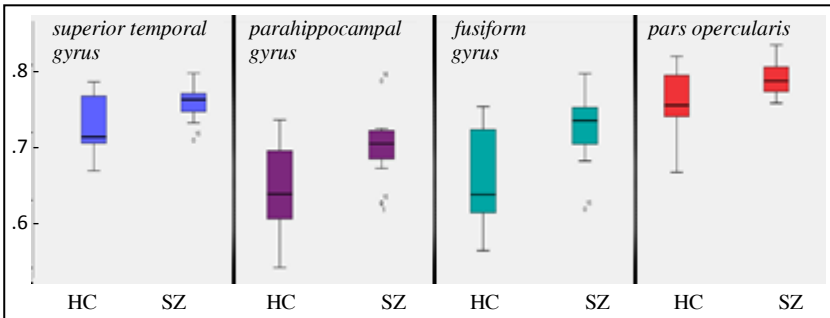

Figure 1. Increase MK is found in SZ compared to HC in several gray matter regions situated in the temporal and prefrontal lobe. From left to right: superior temporal gyrus (p=.006), parahippocampal (p=0.002), fusiform (p=0.001) and pars opercularis (p=0.018). In general, differences were more significant in the temporal than prefrontal lobe.

Discussion: This is the first study, to our knowledge, to examine the microstructural integrity of gray matter in schizophrenia using DKI. Our results suggest increased MK in patients in extended gray matter regions. As increased MK has been found to be associated with reactive astrogliosis[6], these findings may reflect inflammatory processes in schizophrenia. However, increased MK, a marker of structural complexity, may relate to a variety of microstructural changes including alterations in the number of neurons or cortical column spacing. Thus, future studies are needed to corroborate DKI findings with histology or complementary imaging methods in order to establish inflammation as the pathological feature reflected by increased cortical MK in schizophrenia.

References:

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