Cortical Thickness Analysis in Patients with Adolescent-Onset Schizophrenia

N. L. Voets[1,2], J. Klein[2], M. Hough[2], G. Douaud[2], S. Smith[2], P. M. Matthews[1], and A. James[3]
[1]GSK, London, United Kingdom, [2]FMRIB Centre, Oxford, United Kingdom, [3]Dept Psychiatry, Oxford University, Oxford

Introduction: In the past decade, there has been increasing interest in the identification of cortical changes in schizophrenia as a potential marker of phenotypic variation. Although voxel-based morphometry (VBM) approaches have been most commonly employed to assess grey matter changes, the interpretation of VBM cortical results may be complicated by the combination of both shape and volumetric measures in analyses. More recently, cortical flattening approaches have been proposed to offer a more direct measure of cortical thickness, potentially facilitating interpretation of apparent changes in regional cortical volume.

Methods: High-resolution T1-weighted MRI images were acquired at 1.5T in 28 healthy volunteers and 23 adolescent patients meeting DSM-IV criteria for schizophrenia (age range: 13-18, age at onset range: 11-17) using a FLASH sequence (TR=12ms. TE=5.6ms, 19° flip angle, 1x1x1mm resolution). Individual subjects' T1 images were input to the FreeSurfer pipeline [http://surfer.nmr.mgh.harvard.edu, refs 1, 2], which carries out a WM segmentation, models the white-grey boundary and the exterior grey boundary with a mesh surface, inflates this surface to a spherical representation for each hemisphere, and then warps to a "spherical template". A study-specific mean group template brain was created and group t-stat maps of cortical thickness (FDR corrected for multiple comparisons (p=0.05)) were generated to test for differences in cortical thickness between healthy volunteers and schizophrenic patients. To verify alignment of individual subject surfaces to the average template, a region-of-interest (ROI) was drawn around a postcentral region showing a significant difference in cortical thickness between patients and controls, which was then projected onto individual surfaces.

Results: Group t-stat maps demonstrated decreased cortical thickness in patients with schizophrenia relative to healthy controls (Figure 1) in rostral medial and orbital frontal gyri in the left hemisphere, and rostral medial frontal gyrus in the right hemisphere. In addition, cortical thickness was reduced in the superior temporal sulcus, postcentral gyrus, inferior/posterior parietal juncion and anterior cingulate in the left, and the inferior temporal, lingual, paracentral and posterior cingulate gyri in the right hemisphere. Bilateral reductions were found in patients in the precuneus. No regions of increased thickness were found in patients relative to controls. Table 1 shows coordinates and peak t-stat values for these regions (MNI 305 coordinates) in schizophrenic patients relative to healthy volunteers. Our results appear consistent with those recently reported by Greenstein et al (2006), demonstrating similar changes in cortical thickness in widespread frontal and temporal regions as well as pre- and post-central gyri. Visual inspection of the postcentral ROI identified on the group t-stat map and back-projected onto reconstructed individual subjects surfaces (examples in Figure 2) suggests good alignment of individual subjects to the group template.

Discussion: Our results show cortical changes, which may account for loss of gray matter previously reported with VBM approaches in schizophrenic populations. Following this initial analysis, schizophrenic and volunteer populations will be age and sex-matched, and results compared with gray matter voxel-wise analyses conducted on the same population with FSL (www.fmrib.ox.ac.uk/fsl/) tools (Douaud et al, abstract ISMRM 2007). In addition, phenotypic information will be used to identify correlates between grey matter volume changes and phenotypic variation.

References: 1. Dale AM et al (1999). NeuroImage 9(2):179-194; 2. Fischl B et al 1999, NeuroImage 9(2):195-207; 3. Greenstein, D. et al (2006). J of Child Psychology and Psychiatry 47 (10): 1003-1012

Figure 1

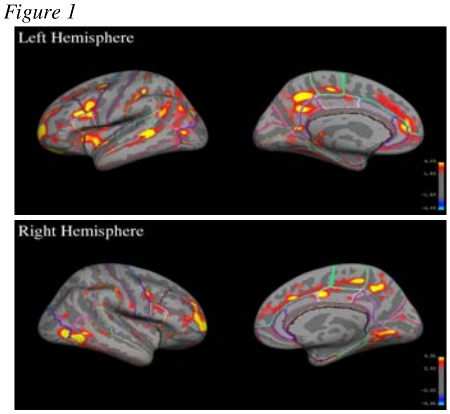

Figure 2

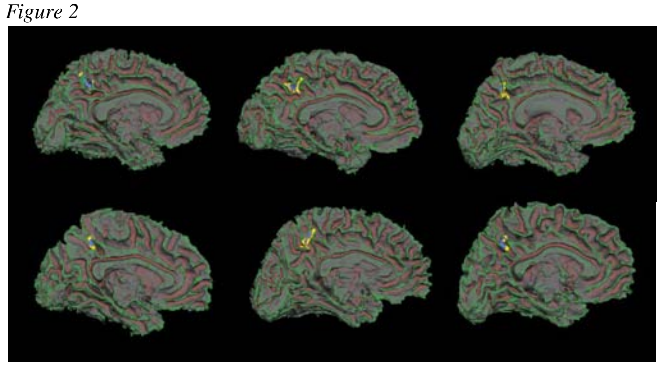

Table 1

LH coordinates (x, y, z)			Tstat	Region	RH coordinates (x, y, z)			Tstat	Region
-24	50	-1	5.38	Rostral Middle Frontal G	49	-57	-2	5.7	Inferior Temporal Gyrus
-22	42	-13	6.05	Lateral Orbital Frontal G	27	49	-1	6.2	Rostral Middle Frontal G
-35	22	21	5.16	Rostral Middle Frontal G	31	48	9	6.2	Rostral Middle Frontal G
-48	-39	8	5.32	Sup Temporal Sulcus	7	-2	38	4.9	Posterior Cingulate Gyrus
-45	-27	34	4.99	Postcentral Gyrus	14	-34	49	5.4	Paracentral Gyrus
-25	-76	19	5.43	Inf/Sup Parietal junction	9	-46	42	5.3	Precuneus
-11	-47	42	6.63	Postcentral Gyrus	5	-65	8	4.69	Lingual Gyrus
-12	42	6	4.22	Rostral Ant Cingulate					