Spherical Registration Distortion and Thalamic Volume in Schizophrenia

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Background: We have reconstructed and registered the cortical surface of schizophrenic and age-matched control brains to a spherical atlas. The metric distortions across the cerebral cortex required to achieve alignment with the population average in spherical space were calculated for both cohorts. The distortions reflect the relative differences in surface geometry of the cortex from the population that makes up the atlas. It has been hypothesized that aberrant cortical development, which in turn affects the morphogenesis of cortical and subcortical connectivity, may contribute to the pathophysiology of schizophrenia [1, 2]. This has been supported by classical cytoarchitectural studies [3, 4] and recently by MRI analysis of the gyrification index of the cerebral cortex [5-7]. More specific geometrical measurements of cortical curvature and folding have been applied to the study of schizophrenia using surface reconstruction tools [8]. Abnormal thalamic volume and shape [9, 10] have also been implicated in schizophrenia. Thus, we have also calculated the thalamic volumes of both patient and control cohorts. We hypothesize that the degree of metric distortion required to achieve optimal registration reflects not only normal but also disease-related variability of cortical geometry. We further hypothesize that greater metric distortion is related to thalamic volume reductions in schizophrenia.

Subjects: Ten (10) patients with schizophrenia (diagnosed any sub-type according to DSM-IV criteria] were recruited from the Erich Lindemann Mental Health Center, Boston. Eight (8) healthy volunteers were recruited by local advertisement. Subjects were age-, gender- and handedness-matched. Handedness was assessed using the Edinburgh Handedness Scale. Exclusion criteria included standard MRI contraindications, significant medical or neurological illness or active substance abuse within the last 3 months. Written informed consent was obtained from all subjects before participation according to the established guidelines of the Massachusetts General Hospital.

Methods: T1-weighted MPRAGE images (TR 2530, TE 3.45, TI 1100, flip angle 7, FOV 256, voxel 1.3x1.0x1.3) were acquired for each subject on a 3T Siemens Trio scanner then subsequently analyzed using the Freesurfer analysis tools (http://surfer.nmr.mgh.harvard.edu). Cortical surface reconstruction and registration algorithms [11-13] created spherical cortical surfaces for the schizophrenic and control cohorts, and metric distortion incurred by the spherical alignment was calculated. Segmentation algorithms calculated thalamic volume in each hemisphere [14]. Cortical thickness and a general linear model (glm) consisting of cohort as factor and metric distortion measures and thalamic volume as regressors was calculated for both cohorts.

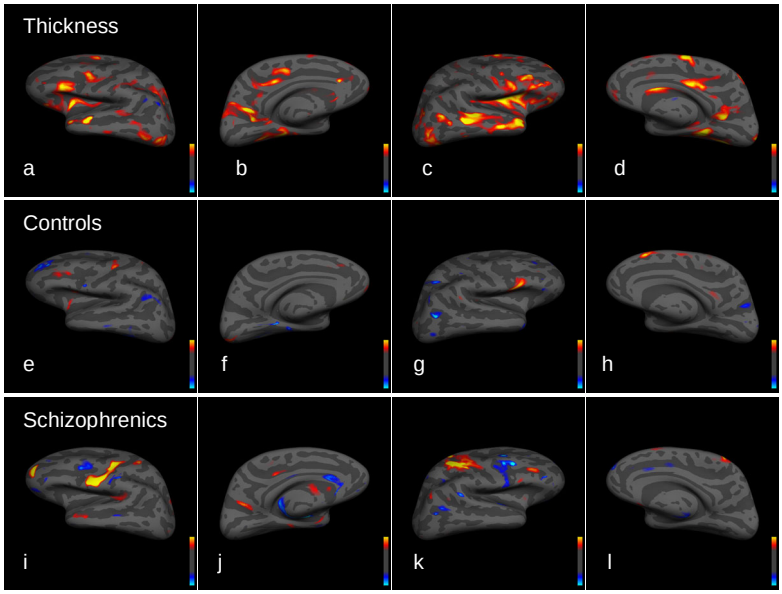

Figure 1: Cohort differences in cortical thickness (a-d), glm model for metric distortion and thalamic volume regression for control cohort (e-f) and schizophrenic cohort (i-l). "Thickness": control-schizophrenic. "Controls" and "Schizophrenic": relationship between metric distortion and thalamic volume. Color bar (red/dark blue: $p<0.05$; yellow/cyan: $p<0.01$). Left hemisphere (a-b, e-f, i-j), Right hemisphere (c-d, g-h, k-l).

Results: Cortical thickness differences between cohorts are most robust in the association and limbic cortices, but there appears to be a larger difference between cohorts in the right hemisphere (Figure 1, a-d). The relationship between metric distortions to accomplish registration and the thalamic volumes for controls is not prevalent, but for schizophrenics is strong near the central sulcus of both hemispheres, the temporal plane and frontal pole in the left hemisphere and the ventral lateral convexity of the prefrontal cortex in the right hemisphere (Figure 1, e-h and i-l).

Conclusions: In our preliminary work, we have shown that the metric distortions required to achieve alignment with the population average in spherical space is greater in selected areas for schizophrenic subjects. These results may reflect anomalous cortical and subcortical development [15, 16] which could contribute to the pathophysiology of schizophrenia. Future work will analyze curvature and folding indices of the cortex in areas where metric distortions are greatest between cohorts. Also, we will investigate the diffusion properties of thalamocortical/corticothalamic tracts that are associated with cortical areas of high geometrical variability.

References:

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