Corpus Callosum Morphometry in Childhood-Onset Schizophrenia

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Introduction: Morphometry of the corpus callosum (CC) is of interest in schizophrenia research as a means to explain abnormalities in communication between brain hemispheres. It is common in clinical studies to analyze the midsagittal cross-section of the CC in terms of area (either whole or regional, defined by Witelson partition (Keller 2003)). For CC, shape features are not only more sensitive than volume, but also more descriptive on the specific changes related to the disease . We have recently developed a shape model based on the continuous description of *medial geometry* of the CC(Yushkevich 2006), from which rich shape features could be derived. In this paper, we use those shape features, along with features derived from boundary representation of the CC, to examine the differences between childhood-onset schizophrenia(COS) patients and normal controls for a large dataset consisting 220 scans, and get some interesting findings.

Methods and Materials: This experiment uses data from the COS imaging study reported in (Keller 2003), where 55 COS patients and 56 matched healthy controls underwent structural MRI over the course of 10 years. Follow-up scans were obtained for many of the subjects, and have been pooled together in this study, yielding 110 COS scans and 86 control scans. As reported in (Keller 2003), the data was normalized to the Talairach space via affine registration to account for differences in head size. The midsagittal cross-section of the CC was segmented by combination of intensity thresholding and manual editing. Deformable Fourier harmonic models (Kelemen 1999) were fitted to the segmentations to generate a continuous boundary parameterization, and points were sampled at equal intervals to produce boundary features. In addition to boundary-based features, we computed *medial features*. These features leverage the rich geometric description of shape called the *medial axis*. The medial axis is obtained from the boundary of an object by thinning; more specifically it is the shock set of the Eikonal equation $|\nabla T| = 1$ with $T = 0$ at the boundary. Medial axes are excellent shape descriptors because they can summarize the complexities of an *N*-dimensional shape in a *N-1* dimensional locus. The bending of the object is summarized by the bending of its medial axis and a local measurement of the thickness of the object is given by the value of *T* along the medial axis. The use of medial features in morphometry has been limited by the fact that data-driven approaches for computing the medial axis (i.e., by simulating the Eikonal equation) can generate medial axes with different numbers of branches for different subjects. We have recently developed a template-based method that allows a consistent set of medial features to be extracted from each subject in a population (Sun 2006). In the current study, we apply this method to the CC and obtain a set of local medial features: coordinates of points sampled along the medial axis; curvature of the medial axis; and thickness of the object. We also obtain several global features, including the total length of the medial axis and average thickness. In this study, we perform a simple *t*-test for each feature to test the null hypothesis that the feature's mean is equal for COS patients and controls. To account for multiple hypothesis testing, we compute corrected *p*-values using the standard Benjamini and Hochberg's step-up procedure, which controls the *false discovery rate* (FDR).

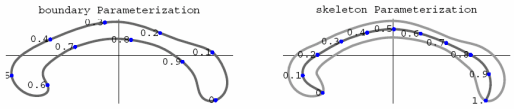

Figure 1: parameterization conventions

Results: For COS/control groups, the overall area of the CCs (post-normalization) did not show significant differences (p-value=0.155). However, the skeleton was significantly longer in the patients (3.1% longer, p = 0.00033). No significant difference in the mean thickness of the CC was detected (p = 0.383).

Local shape features derived from both boundary and medial representation show significant differences for COS/CTL comparisons. The features drawn from medial representation, whose minimal adjusted p-values is 0.00096, are a bit more sensitive than those from boundary representation, whose minimal adjusted p-values is 0.0013. The parameterizations convention of the CC skeleton and boundary which will be used in Fig 2 are showed in Fig.1. And Fig. 2 illustrates both the differences and the significance of the differences between the COS/control groups for thickness, curvature and point distribution for PISA skeleton and object boundary. The greatest differences between groups are detected in the shape of the genu, where the CC appears to be shifted in the anterior direction and in the splenium, where the CC has a similar but less pronounced posterior shift as well as a pronounced elongation, which confirms the global analysis results. These results confirm earlier findings of (Jacobsen 96) which report increased volumes of the genu and the splenium in COS patients.

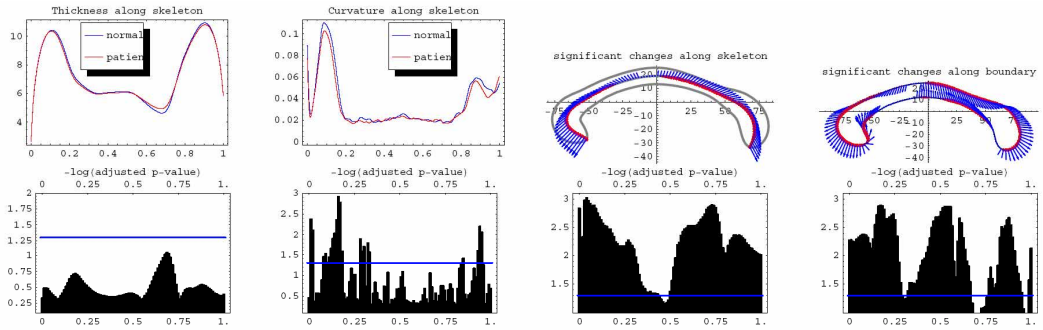

Figure 2: Illustration of COS/control comparisons. Top column shows the changes of features and the bottom column shows the significance of those features by bar charts of their -log(adjusted p-value). The first and second rows are for the thickness and skeleton curvature respectively. The arrow plots in third and fourth rows show the changes from control to COS on the skeleton and boundary respectively. The parameterization conventions used in this figure are explained in Fig.1.

Conclusions: Medial features proved slightly more sensitive than boundary features, and much more sensitive than volume for detecting COS/CTL differences. Together, medial and boundary features provide a rich description of the changes in CC shape in COS, pointing to elongation of the splenium and anterior deformation of the genu.

References:

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