

SURFACE-BASED COMPUTATIONAL ANATOMY TECHNIQUES REVEAL VENTRICULAR AND HIPPOCAMPAL ABNORMALITIES IN ADOLESCENTS WITH SCHIZOPHRENIA

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Using new computational techniques, we created statistical anatomic models that revealed ventricular and hippocampal shape abnormalities in Childhood-Onset Schizophrenia (COS). Longitudinal scanning allowed us to establish the timing and dynamic spread of these disease-specific changes.

3D T1-weighted MRI scans of 12 COS and 12 matched healthy subjects were acquired longitudinally over a 5-year time span (age: $13.9 \pm 0.8SE/18.6 \pm 1.0SE$ years at initial/final scans). When the subjects were scanned, a clinical and cognitive evaluation was made including SANS and SAPS scores, full-scale IQ, and CGAS (children's global assessment scale). All subjects were matched for age, height, gender, follow-up interval, and social background, but not IQ. Scans were normalized by affine transformation to ICBM standardized stereotaxic space. One rater, blind to age, gender and diagnosis, delineated the hippocampus and ventricles at baseline and follow-up. Hippocampal and ventricular volumes (superior horn only) were mapped using a 3D distance field to measure the distance of each surface boundary point to a 3D medial curve derived for each individual structure. Hippocampal and ventricular surface meshes were then spatially registered and averaged across subjects in each diagnostic group. Shape differences and spatial patterns of volumetric loss or gain were visualized using color-coded statistical maps. Distance fields relating surface boundary points to their medial curves were analyzed using surface-based nonparametric regression. Shape differences, visualized in the average anatomical maps, were assessed using permutation tests to compute a null distribution for the total surface area of suprathreshold statistics. Group differences in hippocampal and ventricular volumes were assessed with multivariate regression.

Surface analyses revealed significant bilateral hippocampus volume deficits at time 2 in COS compared to healthy controls ($P < 0.011$ for the right side, $P < 0.042$ for the left side). At baseline, using permutation tests, the group difference on each side was not significant. We also found ventricular enlargement at follow-up in COS compared to healthy controls ($P < 0.037$ for the right side, $P < 0.038$ for the left side) but no enlargement was detected at the first scan, which was shortly after disease onset. The enlargement observed at follow-up was progressive, and diffusely spread over the ventricular surface.

Hippocampal deficits and ventricular enlargement were detected in the COS average shape maps at follow-up. Similar deficits are frequently reported in studies of adult onset schizophrenia. In the course of their illness, COS patients may exhibit decelerated growth in medial temporal lobe structures, regions that are among the last to mature in the teenage years. For the first time, we also report an animation of the progressive ventricular dilatation and hippocampal reductions, over a 5-year period of disease progression.