

Mapping cortical thickness and gray matter density in first episode schizophrenia

Katherine L. Narr, Robert M. Bilder, Roger P. Woods, David Rex, Philip Szeszko, Delbert Robinson, YungPing Wang, Heather DeLuca, Arthur W. Toga, Paul M. Thompson.

Laboratory of NeuroImaging, Departments of Neurology, Psychiatry and Biobehavioral Sciences, Geffen School of Medicine at UCLA, Los Angeles, CA; Department of Psychiatry Research, The Zucker Hillside Hospital, North-Shore Long Island Jewish Health Systems, Glen Oaks, NY.

Abstract:

Introduction: Advanced image analysis tools may be necessary to isolate subtle and regionally-specific cortical gray matter abnormalities in schizophrenia not detectable in volumetric studies. We used novel brain mapping methods to identify and map regional reductions in cortical thickness and gray matter density in first episode schizophrenia. Cortical thickness and gray matter density mapping results were compared.

Methods: High-resolution (256x256x124; 1.5 mm slice separation) T1-weighted MR images were obtained from 72 (51m/21f) first episode patients (mean age = 25.1±4.7 SD) and 78 (33m/44f) healthy comparison subjects (mean age = 27.3±6.6). Scans were corrected for RF inhomogeneities, resliced into a standard orientation using a six-parameter rigid-body transformation and classified into tissue types after editing extra-cortical tissue from the data. Computational cortical pattern matching methods were used to spatially relate homologous cortical regions between subjects. Cortical thickness, defined as the distance from the cortical white-gray matter boundary to the cortical surface, was estimated at sub-voxel resolution from tissue-classified images at thousands of homologous cortical locations in each subject. Gray matter density was also measured at homologous cortical surface points by computing the proportion of gray matter voxels relative to other tissue types within a sphere with a fixed radius. Principal Components Analyses (PCA) were employed to reduce gray matter thickness and density values obtained across the cortex for use as dependent variables in statistical analyses. Diagnosis was included as a predictor variable and sex, brain volume and age as covariates. To reveal regional changes in gray matter thickness and density in first episode schizophrenia, statistical differences were compared at thousands of spatially homologous cortical locations and mapped in 3D.

Results: Global brain tissue volumes were not significantly different between diagnostic groups, although males possessed larger volumes than females. For cortical thickness, the first principal component accounted for 33 percent of the total variance and revealed main effects of diagnosis ($p < .01$); sex ($p < .001$); and age ($p < .001$). Similar results were observed for gray matter density factor scores,

where the first component accounted for 28 percent of the variance and showed significant effects of diagnosis ($p < .0001$), sex ($p < .04$) and age ($p < .02$). For both analyses, diagnosis and age effects remained after brain size correction. Additional principal components accounting for > 5 percent of the variance showed only main effects of sex and/or age. No interactions between sex and diagnosis or diagnosis and hemisphere were observed for any of the components examined. Factor scores for cortical thickness and gray matter density were highly correlated. Cortical thickness statistical maps showed significant regional gray matter thinning in temporal, parietal and prefrontal regions bilaterally in first episode patients. Local reductions in gray matter density were observed in similar regions but were more pronounced in the superior temporal lobe.

Conclusion: Local reductions in cortical thickness and gray matter density are present at disease onset in brain regions linked with functional disturbances in schizophrenia. Cortical thickness and gray matter density mapping produce similar results, although the density metric may be influenced by diagnostic differences in extra-cortical CSF and surface curvature/complexity.