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TITLE: Schizophrenia genetic risk shared with cortical surface area but not cortical thickness: A multiplex, extended pedigree study.

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ABSTRACT: Despite schizophrenia's high heritability ($h^2 = .80$) and patients' regionally reduced cortical volumes, the effect of its genetic risk on the cerebral cortex is poorly understood. To address this question, we employed a multiplex (two schizophrenia probands per family), extended pedigree (first to fourth degree relatives of probands) design that allows the estimation of genetic correlations between schizophrenia and cortical measures in one of the largest such studies to date. A total of 506 participants provided satisfactory MRI scans, consisting of 230 relatives (30 with schizophrenia) from 32 multiplex, extended pedigrees and 276 unrelated controls. Cortical thickness and surface area were estimated using Free-Surfer for 34 bilateral cortical regions. Quantitative genetic analyses using the SOLAR program with False Discovery Rate correction found that thickness and surface area for all cortical regions were significantly heritable. Although nine regions showed significantly lower cortical thickness in schizophrenia, no regions were significantly genetically correlated with schizophrenia. In contrast, 18 regions had significantly lower surface area in schizophrenia patients and

seven regions were significantly genetically correlated with schizophrenia - four of which were in the frontal lobe. These results indicate that schizophrenia genetic risk primarily affects the cortex's surface area, not thickness, and primarily in regions of the frontal lobe, arguing for a focus on specific gene variants relevant to these phenotypes.

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