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TITLE: Cortical thickness and cortical surface area show differing genetic relationships with schizophrenia across development: A multiplex extended pedigree study

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ABSTRACT:

Schizophrenia genetic effects on neurodevelopment may remain stable from childhood (as proposed by early neurodevelopmental models; Murray & Lewis, 1987; Weinberger, 1987), increase during adulthood, closer to the peak age-of-onset (as proposed by late neurodevelopmental models; Feinberg, 1983), or increase long after peak age-of-onset (as proposed by neurodegenerative models; Lieberman, 1999). To our knowledge, no study to date has directly tested schizophrenia developmental neurogenetic effects without

confounding illness effects. To examine whether the genetic correlation between schizophrenia and brain morphology changes across peak age-of-onset, 200 relatives from 32 multiplex, extended pedigrees (age range: 12-85 years) and 276 unrelated controls underwent MRI scanning. Quantitative genetic variance decomposition analyses were conducted on MRI cortical thickness (CT) and cortical surface area (CSA) to parse schizophrenia developmental neurogenetic effects that emerge before schizophrenia peak age-of-risk, during peak age-of-risk, and after peak age-of-risk. We found that genetic correlations between schizophrenia and cortical measures changed before, during, and after age-of-risk, suggesting late neurodevelopmental effects on temporal, fusiform, parahippocampal, cingulate, and insula CT and inferior temporal, fusiform, lingual, and pericalcarine CSA, in contrast to neurodegenerative effects on orbitofrontal, inferior frontal, and entorhinal CT. These developmental neurogenetic effects were notably specific to schizophrenia and not found in depression. Our findings suggest that the effects of schizophrenia genetic risk influence different aspects of brain structure before and after schizophrenia age-of-onset, emphasizing the importance of examining whether schizophrenia genetic risk variants change expression similarly across neurodevelopment.

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