

**Longitudinal mapping of brain development in healthy siblings  
of patients with childhood-onset schizophrenia**

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Childhood-onset schizophrenia (COS) is a rare but severe form of mental illness, impeding a patient's ability to interpret reality and their social environment. Children with COS start to develop hallucinations and other psychotic symptoms before age thirteen. Earlier studies revealed accelerated cortical gray matter (GM) loss and slowed white matter (WM) growth rates in COS compared to normally developing children. The cause of COS is not well-understood but it likely involves a complex interplay between genetic and environmental factors. To better understand how genetic risk for COS impacts brain development in healthy siblings of COS patients, we longitudinally scanned a group of 34 healthy siblings of COS patients (mid-interval age: 17.7±5.0 years; 19 males and 15 females) and 57 controls (16.9±5.3; 28 males and 29 females). Two 3D brain MRI scans were acquired with a 1-4 year interval. All siblings and controls had no history of psychotic symptoms; all had an IQ higher than 70.

3D maps of brain tissue growth were created with tensor-based morphometry. Healthy siblings of COS patients showed slower white matter growth rates than controls, but differences were significant only for the parietal white matter, after multiple comparisons correction. A voxel-wise multiple regression model including age, sex, diagnosis, and a sex x age interaction term, revealed that age effects on growth rates differed between the COS siblings and controls, in a distributed pattern of brain regions including the temporal lobes (GM+WM, critical  $P=0.0002$ ), occipital WM (critical  $P=0.011$ ), parietal WM (critical  $P=0.0036$ ), and temporal WM (critical  $P=0.0016$ ), corrected for multiple comparisons using the false-discovery rate procedure. Growth rates change differently with age in the two groups. Although both groups were normal and showed no psychotic symptoms, they may follow different pathways of brain development, offering insight into how COS-related genes impact brain growth in relatives of patients.

Keywords: Childhood-onset schizophrenia, development, sibling, MRI, tensor based morphometry, genetic risk, age

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Briefly explain (500 characters) the timeliness and importance of your research, and the overall theme of your abstract or group.

**Childhood-onset schizophrenia (COS) arises out of a mix of genetic and environmental causes. To better understand how genetic risk for COS impacts brain development in healthy siblings of COS patients, we examined the brain growth rates in 34 healthy siblings of COS patients and 57 matching controls. Our study revealed that age effects on growth rates differed between the COS siblings and controls in several brain regions, offering insight into how COS-related genes impact brain growth in relatives of patients.**