

Publication

Association of Structural Magnetic Resonance Imaging Measures With Psychosis Onset in Individuals at Clinical High Risk for Developing Psychosis: An ENIGMA Working Group Mega-analysis.

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The ENIGMA clinical high risk (CHR) for psychosis initiative, the largest pooled neuroimaging sample of individuals at CHR to date, aims to discover robust neurobiological markers of psychosis risk.; To investigate baseline structural neuroimaging differences between individuals at CHR and healthy controls as well as between participants at CHR who later developed a psychotic disorder (CHR-PS+) and those who did not (CHR-PS-).; In this case-control study, baseline T1-weighted magnetic resonance imaging (MRI) data were pooled from 31 international sites participating in the ENIGMA Clinical High Risk for Psychosis Working Group. CHR status was assessed using the Comprehensive Assessment of At-Risk Mental States or Structured Interview for Prodromal Syndromes. MRI scans were processed

using harmonized protocols and analyzed within a mega-analysis and meta-analysis framework from January to October 2020.; Measures of regional cortical thickness (CT), surface area, and subcortical volumes were extracted from T1-weighted MRI scans. Independent variables were group (CHR group vs control group) and conversion status (CHR-PS+ group vs CHR-PS- group vs control group).; Of the 3169 included participants, 1428 (45.1%) were female, and the mean (SD; range) age was 21.1 (4.9; 9.5-39.9) years. This study included 1792 individuals at CHR and 1377 healthy controls. Using longitudinal clinical information, 253 in the CHR-PS+ group, 1234 in the CHR-PS- group, and 305 at CHR without follow-up data were identified. Compared with healthy controls, individuals at CHR exhibited widespread lower CT measures (mean [range] Cohen $d = -0.13 [-0.17 \text{ to } -0.09]$), but not surface area or subcortical volume. Lower CT measures in the fusiform, superior temporal, and paracentral regions were associated with psychosis conversion (mean Cohen $d = -0.22$; 95% CI, $-0.35 \text{ to } 0.10$). Among healthy controls, compared with those in the CHR-PS+ group, age showed a stronger negative association with left fusiform CT measures ($F = 9.8$; $P < .001$; $q < .001$) and left paracentral CT measures ($F = 5.9$; $P = .005$; $q = .02$). Effect sizes representing lower CT associated with psychosis conversion resembled patterns of CT differences observed in ENIGMA studies of schizophrenia ($\rho = 0.35$; 95% CI, $0.12 \text{ to } 0.55$; $P = .004$) and individuals with 22q11.2 microdeletion syndrome and a psychotic disorder diagnosis ($\rho = 0.43$; 95% CI, $0.20 \text{ to } 0.61$; $P = .001$).; This study provides evidence for widespread subtle, lower CT measures in individuals at CHR. The pattern of CT measure differences in those in the CHR-PS+ group was similar to those reported in other large-scale investigations of psychosis. Additionally, a subset of these regions displayed abnormal age associations. Widespread disruptions in CT coupled with abnormal age associations in those at CHR may point to disruptions in postnatal brain developmental processes.

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