Anatomical abnormalities of the anterior cingulate cortex before the onset of psychosis

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BACKGROUND

- The anterior cingulate cortex (ACC) is critical for integrating cognitive and emotional functions in support of goal-directed behaviour.

- Abnormalities of this region have frequently been implicated in the pathophysiology of psychotic disorders, but it is unclear whether such abnormalities precede illness onset.

- To examine ACC abnormalities before the onset of frank psychosis, we scanned ultra-high-risk (UHR) individuals using MRI and followed them up to ascertain diagnostic outcomes. Baseline ACC changes were compared between UHR individuals who developed psychosis (UHR-P), those who did not (UHR-NP), and healthy controls.

METHOD

- 146 UHR individuals, identified using state and trait criteria associated with a 30-40% rate of transition to frank psychosis within one year, were scanned at baseline.

- They were followed-up for a minimum of 12 months (mean=13; max.=44 months) to ascertain diagnostic outcomes.

- 35 UHR individuals developed a psychosis during the follow-up period.

- Baseline ACC grey matter measures (fig. 1) in this group were compared to 35 UHR-NP individuals, and 33 healthy controls, matched for age sex, and sulcal variability of the ACC.

RESULTS

- Relative to controls, UHR-P individuals showed reduced thickness bilaterally in the r-ACC (fig. 2A; fig. 3, top).

- These thickness reductions were associated with greater negative symptoms in UHR-P, but not UHR-NP, individuals (fig. 2C).

- Relative to controls, UHR-NP individuals showed increased thickness bilaterally in the r-ACC.

- These thickness increases were associated with greater anxiety symptoms in UHR-NP, but not UHR-P, individuals (fig. 2D).

- Sub-diagnostic analysis revealed differences in the UHR-P group were largely driven by individuals who developed a schizophrenia-spectrum psychosis (fig. 3).

- There were no group differences in volume or surface area.

DISCUSSION

- ACC abnormalities are present before the onset of a frank psychotic episode and are relatively specific to individuals who develop a schizophrenia-spectrum psychosis.

- UHR-NP individuals show abnormally increased ACC thickness which may protect them from psychosis but predispose them to other psychopathology, as suggested by correlations with anxiety ratings.

REFERENCES


< Figure 1. The ACC was parcellated into limbic (ACC1) and paralimbic (ACC2) regions. These were then further divided into dorsal, rostral, and subcallosal divisions (denoted d-, r-, and s-, respectively). Boundaries varied depending on sulcal anatomy: top row illustrates ROIs for a case without a paracallosal sulcus (PCS), bottom row shows a case with a PCS. ROIs were traced on cortical surface reconstructions generated using Freesurfer (http://surfer.nmr.mgh.harvard.edu), enabling calculation of regional gray matter volume, area, & thickness. Reconstructed white & pial surfaces are shown in middle and right columns, respectively. Left column shows T1s with PCS. Cingulate Sulcus (CS) and Superior Rostral Sulcus (SRS) highlighted.

< Figure 2. A: ACC1 region where UHR-P individuals displayed significant cortical thinning relative to controls. B: ACC1 region where UHR-P individuals showed reduced thickness relative to UHR-NP individuals. C: Scatterplots illustrating the correlation between r-ACC1 thickness and negative symptoms in the UHR-P and UHR-NP groups. The correlation was significant in UHR-P (r=-.47, p=.03, corrected), but not UHR-NP individuals (r=-.17, p=.33). D: Scatterplots illustrating the correlation between r-ACC1 thickness and anxiety ratings in the UHR-P and UHR-NP groups. The correlation was significant in UHR-P (r=-.54, p=.01, corrected), but not UHR-NP individuals (r=-.08, p=.68). SDS=Schedule for the assessment of negative symptoms. HRTA=Hamilton rating scale for anxiety.

< Figure 3. Effect sizes for differences relative to controls (top) and UHR-NP individuals (bottom). UHR SZ and UHR OTHER correspond to a division of the UHR-P group into individuals who developed a schizophrenia-spectrum (n=21) or other psychosis (n=14). Most of the UHR-P differences were driven by UHR SZ individuals. Few differences were noted in the UHR OTHER group. * p<.05, bonferroni corrected.