

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 behaviour¹.
- Abnormalities of this region have frequently been implicated in the pathophysiology of psychotic disorders², 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 year³, 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^{4,5}.

RESULTS

- Relative to controls, UHR-P individuals showed reduced thickness bilaterally in the r-ACC_P (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_L.
- These thickness increases were associated with greater anxiety ratings in UHR-NP, but not UHR-P, individuals (fig 2D).

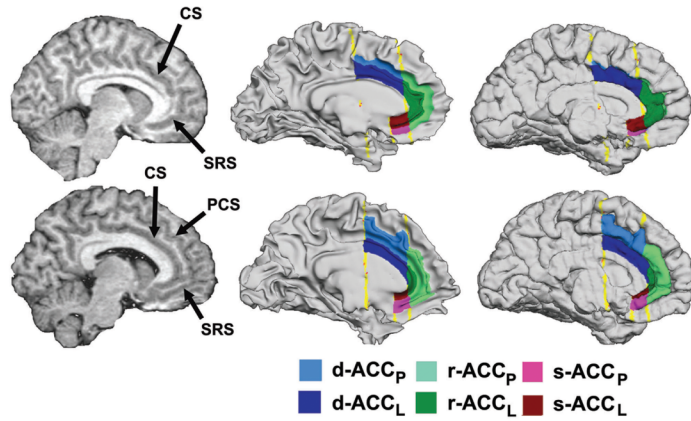
- Sub-diagnostic analysis revealed differences in the UHR-P group were largely driven by individuals who developed a schizophrenia-spectrum psychosis (fig 3).

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

DISCUSSION

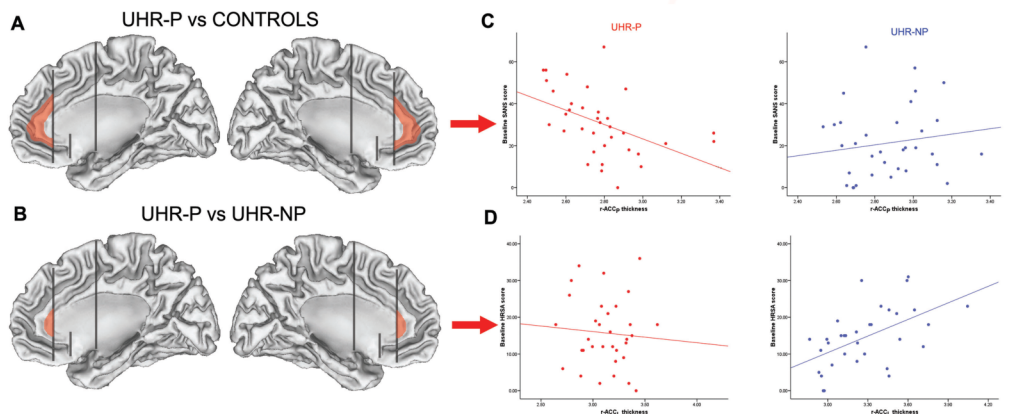
- ACC abnormalities are present before the onset of a frank psychotic episode and are relatively specific to individuals who develop a schizophrenia-spectrum psychosis.

- 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.



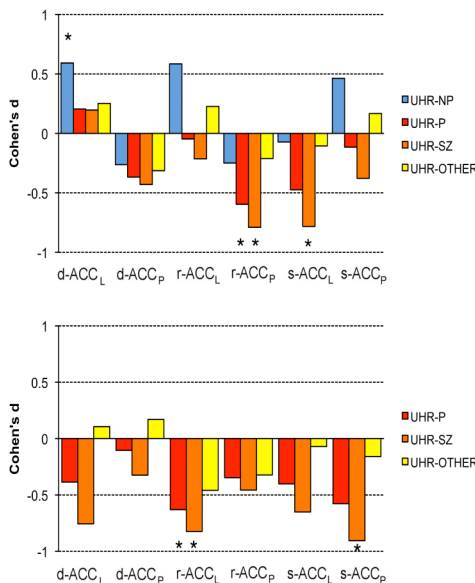
< Figure 1.

The ACC was parcellated into limbic (ACC_L) and paralimbic (ACC_P) 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 paracingulate 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 grey 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. Methods described in 4,5.



^ Figure 2.

A. r-ACC_P region where UHR-P individuals displayed significant cortical thinning relative to controls.
 B. r-ACC_L region where UHR-P individuals showed reduced thickness relative to UHR-NP individuals.
 C. Scatterplots illustrating the correlation between r-ACC_P 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-ACC_L thickness and anxiety ratings in the UHR-P and UHR-NP groups. The correlation was significant in UHR-NP ($r=.54$, $p=.01$, corrected), but not UHR-P individuals ($r=-.08$, $p=.68$). SANS=Schedule for the assessment of negative symptoms. HRSA=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 psychosis (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.

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No potential conflict of interest.