MRI as a tool for finding an anatomical basis for psychotic illness: paracingulate sulcus morphology in individuals with a genetic risk of developing bipolar disorder.

Poster No.: C-1629
Congress: ECR 2011
Type: Scientific Exhibit
Authors: C. Carstairs; Edinburgh/UK
Keywords: Neuroradiology brain, Anatomy, MR, Structured reporting, Imaging sequences
DOI: 10.1594/ecr2011/C-1629

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Purpose

BACKGROUND: MRI IN PSYCHIATRIC RESEARCH

Bipolar Disorder (BD) is a psychotic illness affecting mood and social cognition. MRI studies have shown associations between the development of this illness and morphological variance of the paracingulate sulcus (PCS)[1], a fold in the brain within the anterior cingulate cortex (ACC) (See Fig. 1). The ACC is associated with cognitive and affective regulation [2]. This is the first known MRI study of PCS morphology in individuals at high familial risk of BD.

Using MRI to study folding patterns may indicate whether morphological differences associated with psychopathology precede or occur subsequently to illness onset [1, 3, 4, 5]. As sulci mainly form prenatally [6], and remain stable throughout life [7], it has been established that MRI observation of sulcal variation is a reliable method of rating anatomical differences present from birth [1, 2, 8].

PREVIOUS MRI FINDINGS RELATING TO PATIENTS WITH PSYCHOTIC ILLNESS, AND THOSE AT HIGH RISK

• ACC cortical thickness and volume differences in BD and schizophrenia, thought to be underpinned by PCS morphology [1, 3, 4, 7, 10]
• Less frequent absence of PCS in healthy controls compared to BD patients [1, 9]
• Altered PCS folding patterns in people at high risk of schizophrenia [5], associated with subclinical symptoms
• Specific grey matter variants in people at high familial risk of BD, similar to those found in diagnosed BD patients [11, 12]
• Observed subclinical features of affective instability in unaffected relatives of BD patients.

There is no known study observing PCS differences in people with genetic liability to develop BD. The exploration of anatomical differences is informative in determining structural risk factors for BD [13] and the study of a high genetic risk group may provide further information on the extent to which genetics determine such differences. The investigation of the relationship of PCS morphology with neuropsychological features could give an indication of how far psychotic features are anatomically determined.

PURPOSES OF STUDY:
1. To use MRI to determine whether there are significant differences in PCS morphology in the brains of people at high risk of developing BD compared to healthy controls.

2. To determine whether there is an association between any differing aspects of PCS morphology detected by MRI and the presence of psychopathological symptoms.

**Images for this section:**

![Fig. 1: A sagittal MR image of a left hemisphere, showing the PCS and other local sulci.](image-url)
Methods and Materials

PARTICIPANTS

- Preliminary imaging and neuropsychological data from the Scottish Bipolar Family Study.
- Unaffected relatives (aged 16-25) of known BD patients formed the high-risk group (HR: n=117).
- Healthy controls (HC: n=72) were recruited and group-matched for age, sex and IQ.

IMAGING

- Imaging carried out at the Scottish Brain Imaging Research Centre
- GE 1.5 T Signa scanner (GE Medical, Milwaukee, USA)
- Midline sagittal localization then two further sequences to image the entire brain
- Coronal gradient echo sequence with magnetization preparation
- 128 coronal high-resolution T1-weighted images
- Images were analysed using MRICro software

IMAGING: PCS RATING

- Based on previously established methods [2, 14, 15]
- PCS defined as a clearly identifiable sulcus running parallel and dorsal to the cingulate sulcus (CS) for >20mm, creating two parallel gyri (See Fig.1 [C])
- Visualised in the sagittal view of the hemisphere, sulcus originating at medial aspect and present in #3 slices
- Origin: confluence with the superior rostral sulcus (SRS) (See Fig.1 (D), anterior to the genu.
- Origin of PCS from the SRS defined as the point at which the sulcus extends posteriorly from an imaginary vertical line (Fig. 1 (B)) running perpendicular to the horizontal line passing through the anterior commissure and parallel to the VAC (vertical line through anterior commissure)(Fig. 1 (A)).

IMAGING: PCS SUBCLASSIFICATION

- PCS classified "present" if #20mm (Fig. 2)
- PCS classified "prominent" if #40mm or extending posterior to VAC with not >20mm interruptions anterior to this line (Fig. 3)
• Classified "absent" if no apparent PCS, or PCS<20mm (Fig. 4)
• Interruption >10mm terminates sulcus. Interruptions of #10mm in length result in further subclassification: "interrupted" (as opposed to "continuous").

NEUROPSYCHOLOGICAL TESTING

• TEMPS-A questionnaire: measures minor affective symptoms including cyclothymia (measure of emotional instability). [16]
• Ekman 60 faces test of emotion recognition. [17]
• Rust Inventory for Schizotypal Cognitions (RISC) questionnaire. [18]

ANALYSIS

• Chi-squared tests to analyse intergroup variation in PCS morphology in terms of presence, prominence and interruptions
• dependent-variable tests or ANOVAs used to determine the effects of PCS morphology on neuropsychological features.

Images for this section:
Fig. 1: Sagittal left hemisphere MR image: A = VAC; B = line of confluence of PCS and SRS; C = PCS; D = SRS
Fig. 2: Sagittal left hemisphere MR image showing a "present" PCS (in red). Vertical white line = VAC, horizontal white line highlights distance from anterior commissure to anterior margin of brain - used as reference points.
Fig. 3: Sagittal left hemisphere MR image showing a "prominent" PCS (in red)
Fig. 4: Sagittal left hemisphere MR image rated as PCS "absent." A small length of PCS is shown (in red) though this is
Results

PCS MORPHOLOGY

Table 1: PCS morphology classification frequency data

<table>
<thead>
<tr>
<th></th>
<th>Healthy Controls (n=75)</th>
<th></th>
<th>High-Risk Subjects (n=117)</th>
<th></th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency (%)</td>
<td>Prominent Present</td>
<td>Absent</td>
<td>Prominent Present</td>
<td>Absent</td>
</tr>
<tr>
<td></td>
<td>Left hemisphere</td>
<td>24 (32.0)</td>
<td>12 (16.0)</td>
<td>43 (36.8)</td>
<td>28 (23.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>39 (52.0)</td>
<td>46 (39.3)</td>
<td>(#^2=3.337, p=.198)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Right hemisphere</td>
<td>16 (21.3)</td>
<td>10 (13.3)</td>
<td>49 (65.3)</td>
<td>26 (22.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>49 (65.3)</td>
<td>67 (57.3)</td>
<td>(#^2=1.839, p=.406)</td>
<td></td>
</tr>
</tbody>
</table>

The HC group had a greater proportion of "absent" PCS in left and right hemispheres when compared with proportion of "absent" PCS in HR subjects (52% vs 39.3% in the left hemisphere and 65.3% vs 57.3% in the right hemisphere).

There was no significant difference between groups in terms of the incidence of absent, present or prominent PCS in either the left hemisphere (\#^2=3.337, p=.198) or the right hemisphere (\#^2=1.839, p=.406).

There was a trend approaching significance between groups with regard to overall presence of PCS, (if the data were collapsed down so that PCS was considered "present" if it was "present" or "prominent" in one or both hemispheres) with a trend for PCS to be found overall more frequently in the high-risk group (\#^2=2.872, p=.090).

PCS MORPHOLOGY: PRINCIPAL FINDINGS

A significant difference between HR and HC groups when comparing the presence of continuous PCS (uninterrupted) in the left hemisphere (\#^2=4.358, p=.037). Presence of a continuous left PCS occurred more often in HR subjects (see Fig.2). There was no significant difference with regard to the right hemisphere (\#^2=.740, p=.390).
NEUROPSYCHOLOGICAL FINDINGS RELATED TO PCS MORPHOLOGY

- Fig. 1 shows that subjects with a continuous left PCS scored higher in identifying sadness in the Ekman test (F=6.231, p=.014).

- In the HC group cyclothymia scores were significantly lower (ie less emotional dysregulation) in those with a continuous left PCS (F=4.454, p=.039).

- In the HR group there were significantly lower RISC scores (ie fewer schizotypal symptoms) in individuals with a continuous left PCS (F=4.769, p=.033).

Images for this section:

![Estimated Marginal Means of sadness](image)

**Fig. 1:** A graph showing differences between subject groups and those with, or lacking a continuous PCS, where score in identifying "sadness" in the Ekman 60 faces Trial was the dependent variable.
Fig. 2: A bar graph to show the frequencies of continuous left PCS compared to absent/interrupted left PCS, in high risk (HR) and healthy control (HC) groups.
Conclusion

The non-significant trend for PCS to be present/prominent more frequently in HR subjects compared to controls directly contrasts with the observation of higher PCS presence within healthy controls compared to BD patients in previous studies [1, 9]. It could be speculated that this finding may emphasise a fundamental morphological difference between people at risk of BD and diagnosed patients.

The impact of PCS continuity has not previously been investigated, but interruptions of the CS have been associated with BD [1]. In the current study a continuous, not interrupted, left PCS was more strongly associated with HR subjects than controls. Further work might support evidence that sulcal interruptions are not associated with any common genetic trait, but are due to epigenetic prenatal factors, which could themselves be associated with illness [1, 2].

The association between morphological and neuropsychological findings complement evidence associating ACC and its neural networks with cognitive and affective regulation [2] and seem to indicate that an interrupted or absent PCS is more associated with subclinical features of psychosis. Follow-up of the patient group might clarify this finding, when it is known how many (if any) will later develop BD.

Overall, these entirely novel findings support the hypotheses in that there were significant differences in:

1.) PCS morphology between healthy controls and people at high risk of developing BD, in an element of morphology not previously examined in PCS (continuous/interrupted) and

2.) the presence of psychopathological symptoms associated with these morphological differences.

This study emphasises the potential for MRI to be used to determine the basis of psychotic illness and lead to a further understanding of its development.

References


**Personal Information**

Claire Carstairs BMedSci, University of Edinburgh

Co-author: Dr Goulchira Chakirova, University of Edinburgh

Project Supervisor: Professor Andrew McIntosh, University of Edinburgh