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A pilot study of cognitive insight and structural covariance in first-episode psychosis

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ABSTRACT

Cognitive insight is described as a balance between one's self-reflectiveness (recognition and correction of dysfunctional reasoning), and self-certainty (overconfidence). Neuroimaging studies have linked the ventrolateral prefrontal cortex (VLPFC) to cognitive insight in people with psychosis. However, the relationship between cognitive insight and structural connectivity between the VLPFC and other brain areas is unknown. Here, we investigated the modulation of cognitive insight on structural covariance networks involving the VLPFC in a first-episode psychosis sample. Fifteen patients with a first-episode psychosis provided magnetic resonance (MR) scans and completed the Beck Cognitive Insight Scale (BCIS). MR scans were also available for 15 historical controls. Seed-based analysis of structural covariance was conducted using the Mapping Anatomical Correlations Across the Cerebral Cortex (MACACC) methodology, whereby Pearson correlation coefficients were extracted between seed regions in left and right VLPFC and cortical thickness across the brain. Structural covariance maps between groups were compared at each vertex. In first-episode subjects, we evaluated the modulation of BCIS scores on cortical covariance between VLPFC and every other vertex. Findings showed no significant group difference between first-episode psychosis subjects and controls in thickness covariance seeded from left or right VLPFC. However, in first-episode psychosis subjects, a positive association with self-certainty was found in networks seeded from both left and right VLPFC with thickness in medial frontal cortex and right pars triangularis. No significant associations were found for self-reflectiveness. These results suggest that self-certainty, but not self-reflectiveness, positively modulated cortical covariance in a frontal network in patients with a first-episode psychosis.

1. Introduction

The concept of insight in people with psychosis has undergone significant changes over the past century. Initial models of clinical insight held that people with psychosis were either completely insightful of their diagnosis or entirely unaware (Jaspers, 1963; Lewis, 1934). Modern day accounts suggest that clinical insight is multidimensional, encompassing individuals' awareness of their mental illness, their compliance with treatment, and the ability to label psychotic symptoms as pathological (David, 1990). Typically, clinical insight is determined by evaluating an individual's behavior through a clinical interview and is valuable for determining diagnosis, prognosis and treatment.

Essential to the understanding of clinical insight is the evaluation of an individual's ability to critically reflect on, examine, and modify their abnormal experiences and misinterpretation of events. In 2004, Beck and colleagues described this as cognitive insight, and further identified two underlying components: self-reflectiveness, a measure of objectivity, reflection and openness to feedback, and self-certainty, which captures overconfidence (Beck et al., 2004). In their initial study, Beck et al. reported that people with psychosis endorsed significantly lower self-reflectiveness and higher self-certainty as compared to individuals without psychotic disorders, and this has been interpreted as "poor" cognitive insight. Following the results of this study, numerous investigations have reported that in people with psychosis, poorer cognitive insight is associated with greater

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delusion severity, greater negative symptoms, higher depression, and worse functional outcome (Phalen et al., 2015; Riggs et al., 2010).

A more recent and emerging area of interest in this field is the exploration of the neural correlates of cognitive insight in people with psychosis. Studies have shown that the ventrolateral prefrontal cortex (VLPFC) may be particularly important for cognitive insight in this population. For instance, higher self-reflectiveness has been correlated with increased volume in right VLPFC in people with schizophrenia (Orfei et al., 2013). Higher self-reflectiveness has been linked to increased neural activation in the VLPFC in both first-episode (Buchy et al., 2015b) and chronic schizophrenia samples (Pu et al., 2013). Another study found that higher self-reflectiveness modulated right VLPFC activation in people with a first-episode of schizophrenia (Buchy et al., 2015b). To interpret the role of the VLPFC for cognitive insight, most imaging studies have focused on the role of the VLPFC in memory in particular its role in the controlled access to stored conceptual representations (Badre and Wagner, 2004; Levy and Wagner, 2011). The VLPFC mediates the controlled retrieval of semantic knowledge, and in the context of cognitive insight, it has been suggested that the VLPFC is important for the establishment of appropriate confidence levels, certainty about beliefs or judgements, and consideration of others' corrective feedback (Buchy and Lepage, 2015). More specifically, the top-down control from VLPFC may contribute to self-certainty by elaborating or refining cues used to find information in memory.

Several of the abovementioned studies evaluated the structural neural basis of cognitive insight by way of cortical thickness measures. Cortical thickness can be extracted through a fully-automated measurement of magnetic resonance (MR) images at a subvoxel resolution, and is believed to primarily reflect morphometric gray matter features such as the size, density or arrangement of cells (Lerch and Evans, 2005; Parent and Carpenter, 1995). Analysis of structural covariation builds on the cortical thickness technique, by measuring which areas of the cortex are correlated with one another, and thus provides a measure of inter-regional anatomical networks (Lerch et al., 2006). The anatomical associations of particular brain regions involved in cognitive insight, such as the VLPFC, can thus be probed. In addition, this technique allows evaluation of the relationship between the strength of the global connectivity and cognitive insight levels.

Although the microstructural basis of structural covariation is not well understood, it is believed that covariations in gray matter might result from mutually trophic and maturational influences (Mechelli et al., 2005). Diffusion tensor imaging measures direct fibre connections between brain regions, whereas structural covariance measures how cortical thickness in one brain region correlates with thickness in another brain region. Some studies have demonstrated overlap between the inter-regional structural covariance and the underlying connectivity in white matter tracts and functional connectivity networks (Alexander-Bloch et al., 2013; Gong et al., 2015). Hence structural covariance analysis can provide additional information about the structural networks that are important for cognitive insight in people with psychosis.

In the current pilot study in a small sample, we employ structural covariance analysis to evaluate 1) covariance between thickness in the VLPFC and thickness across the entire cortex in people with a first-episode of psychosis relative to a historical control group, and 2) the relationship between VLPFC structural covariance and cognitive insight in first-episode psychosis subjects. Aim one was exploratory, thus no hypothesis was made. For aim two, we tested the hypothesis that higher self-reflectiveness and lower self-certainty would be associated with greater structural covariance between the VLPFC seed regions and cortical thickness across the brain.

2. Materials and methods

2.1. Participants

Fifteen patients with a first episode psychosis participated in the study. All participants were recruited through the Early Psychosis Treatment Service at Foothills Hospital in Calgary, Alberta Canada. For this study a first-episode of psychosis was defined as being within the first three years of receiving an initial diagnosis of a psychosis, which was confirmed through chart records. Inclusion criteria were the diagnosis and aged 16–30. Exclusion criteria were history of neurological disorder, loss of consciousness for more than 5 min, pregnancy for females, IQ < 70, or MRI contraindications such as presence of metal in the body.

All patients provided MR scans. Twelve participants were taking antipsychotic medications and three were not medicated.

Although a control group was not recruited for this study, data was available for 15 historical controls from previous studies conducted at the University of Calgary in the research program of the senior author (J.A). Control subjects could not meet criteria for any prodromal syndrome, any current or past psychotic disorder or a Cluster A personality disorder diagnosis, not have a family history (in first-degree relatives) of any psychotic disorder or any other disorder involving psychotic symptoms. They could not be currently using psychotropic medication. The historical control group was matched to the first-episode psychosis group based on age first and secondly on sex. Unfortunately, the dataset that the historical control group was drawn from was comprised mostly of females over the age of 18 and males under the age of 18. Because we elected to first match on age, this resulted in an over-representation of females in the historical control group. MR data of controls was used in the current study to compare cortical covariance with our first-episode psychosis patients.

All participants provided written informed consent and the study was approved by the University of Calgary Conjoint Health Research Ethics Board.

2.2. Measures

Severity of symptoms was assessed using the positive and negative subscales of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). IQ was assessed with the Vocabulary and Block Design subtests of the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999).

Cognitive insight was assessed with the Beck Cognitive Insight Scale (BCIS) (Beck et al., 2004), a 15-item self-report inventory. Subjects were asked to rate the extent to which they agree with each statement using a 4-point scale from 0 (do not agree at all) to 3 (agree completely). Self-reflectiveness and self-certainty scores were calculated and used in imaging analyses described below.

2.3. Study procedures

PANSS ratings were conducted by experienced research clinicians. First-episode psychosis participants completed the BCIS and provided MR scans on the same day. Participants received monetary remuneration for their participation.

2.4. MRI acquisition

MRI scanning was conducted on a 3 Tesla GE Signa scanner with an 8-channel head coil at the Seaman Family MR Research Centre at the University of Calgary, Alberta. All participants underwent a high-resolution anatomical scan (3D SPGR, 180 slices, FOV = 25.6 cm, 1 × 1 × 1 mm, flip angle = 12°).

2.5. Measurement of cortical thickness

A quality control (QC) procedure was carried out by one rater on all raw T1-weighted images to ensure no visible motion artefacts or poor resolution of gray/white matter contrast. QC'ed MRIs were then submitted to the CIVET processing pipeline (Version 2.0.0) (http://www.bic.mni.mcgill.ca/ServicesSoftware/CIVET) (Ad-Dab'bagh et al., 2006;

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