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Meta-cognition is associated with cortical thickness in youth at clinical high risk of psychosis

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ABSTRACT

Meta-cognition is compromised in people with schizophrenia and people at clinical high risk (CHR) of psychosis. In the current work in a CHR sample, we hypothesized that meta-cognitive functions would correlate with cortical thickness in five brain regions implicated in the pathogenesis of psychosis: inferior and middle frontal cortices, anterior cingulate cortex, superior temporal cortex and insula. Secondly, we hypothesized that similar neural systems would underlie different meta-cognitive functions. Narratives were gathered for 29 youth at CHR of psychosis using a semi-structured interview. Four meta-cognitive functions within the narratives were measured with the Meta-cognition Assessment Scale and regressed on cortical thickness from our a priori regions of interest using FreeSurfer. Mapping statistics from our a priori regions of interest revealed that meta-cognition functions were associated with cortical thickness in inferior and middle frontal gyri, superior temporal cortex and insula. The distribution of cortical thickness was partially similar across the four MAS items. Results confirm our hypothesis that cortical thickness is significantly associated with meta-cognition in brain regions that consistently show gray matter reductions across the schizophrenia spectrum. Evidence for thickness covariation in a variety of regions suggests partial dependence in the neural architecture underlying various meta-cognitive functions in CHR.

1. Introduction

The term meta-cognition has been used to describe a variety of processes that involve critically reflecting on and monitoring one's own cognition. It involves the ability to select appropriate responses, appraise and weigh information effectively, and cope with cognitive limitations. A series of research reports has documented that relative to healthy people, individuals with chronic (Frith, 1992) and first-episode psychotic illness (Vohs et al., 2014) show widespread deficits in meta-cognition.

Recent studies have explored meta-cognition in youth at clinical high risk (CHR) of psychosis, that is, people who show brief attenuated or sub-threshold symptoms of psychosis, or have a genetic risk with recent functional decline (McGlashan et al., 2010), using the Meta-Cognitions Questionnaire (MCQ) (Cartwright-Hatton and Wells, 1997). In the MCQ, participants rate the degree to which they agree with 65 statements tapping various dimensions of meta-cognition. The scale is designed under the theoretical notion that meta-cognitive beliefs guide ones thinking and coping styles, and those maladaptive meta-cognitions contribute to the maintenance of psychological disorders. MCQ based studies have demonstrated that relative to healthy people, CHR samples endorse high negative beliefs in general (Morrison et al., 2006; Brett et al., 2009; Barbato et al., 2013; Welsh et al., 2013), high negative beliefs about uncontrollability of thoughts and corresponding danger (Morrison et al., 2006; Brett et al., 2009; Barbato et al., 2013), low confidence in the efficiency of their cognitive skills (Morrison et al., 2006; Brett et al., 2009) and diminished cognitive self-consciousness (Morrison et al., 2006; Brett et al., 2009; Welsh et al., 2013). There is also some recent evidence that meta-cognitive abilities in CHR may predict transition to psychosis in CHR youth (Barbato et al., 2013).

Although the MCQ provides useful information on self-rated meta-cognitive judgements, a more ecologically valid approach may be to measure an individual's ability to engage in meta-cognitive acts spontaneously such as would be encountered in everyday life. The Meta-cognitive Assessment Scale (MAS) (Semerari et al., 2003) provides a unique measure of meta-cognition through personal narratives of self and illness in which participants are asked to reflect on their own lives, and may therefore tap into the core processes that underpin real-world meta-cognitive capacities.

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Four aspects of meta-cognition are evaluated: *Self-Reflectivity*, which measures comprehension of one's own mental states, *Understanding Others' Minds*, which evaluates one's comprehension of other individuals' mental states, *Decentration*, or the ability to see the world as existing with others having independent motives, and *Mastery* in the ability to think purposefully about a certain problem, and utilize knowledge of mental states to cope with psychological challenges. Several studies have used the MAS to document deficits in meta-cognition within the narratives of people with schizophrenia (Lysaker et al., 2005, 2007).

The goal of the current study was to examine the brain systems that may be important for MAS-rated meta-cognition in youth at CHR of developing psychosis. This is particularly important, as people at CHR of psychosis show impaired meta-cognitive abilities relative to healthy controls (Barbato et al., 2013) and decreased gray matter volumes in a number of regions implicated in the pathogenesis of psychosis (Fornito et al., 2008; Witthaus et al., 2010; Wood et al., 2010; Mechelli et al., 2011). In particular, the inferior and middle frontal cortices, anterior cingulate cortex, superior temporal cortex and insula appear to be the most affected cortical loci in first- and multi-episode schizophrenia (Ellison-Wright et al., 2008; Bora et al., 2011; Olabi et al., 2011; Radua et al., 2012; Fusar-Poli et al., 2012). A similar pattern of results have been documented in youth at high risk of developing a psychotic illness (Smieskova et al., 2010; Fusar-Poli et al., 2012), and there is strong evidence that structural deficits in prefrontal cortex, anterior cingulate cortex and insula may be predictive for the development of psychosis in high risk youth (Smieskova et al., 2010).

Many of these results have also been observed using fully automated in vivo cortical thickness measurements of magnetic resonance images (MRIs) at a subvoxel resolution. This method provides a metric in millimeters of gray matter morphology, and yields anatomically meaningful results, reflecting cortical laminar structure and integrity. This technique provides an advantage over volumetric measurements such as voxel-based morphometry (VBM) which is sensitive to registration differences, size of the smoothing kernel, shape differences that arise from systematic registration errors during spatial normalization, and image noise (Bookstein, 2001; Jones et al., 2005). Moreover, in VBM, blurring is 3 dimensional and therefore does not respect boundaries along tissue classes, leading to increased probability of either diluting existing signal or misinterpreting boundary shift as signal. In comparison, blurring in cortical thickness analysis occurs in a topographically correct manner along the cortical surface. Research of this kind has demonstrated that individuals at CHR of psychosis who later transition show accelerated thinning in middle frontal cortex (Cannon et al., 2015), anterior cingulate (Fornito et al., 2008; Ziermans et al., 2012), superior temporal cortices and insula as compared to healthy controls (Ziermans et al., 2012), and that cortical thickness in temporal and insular regions allows quantitative prediction of symptom progression in this population (Tognin et al., 2013). Studies in people with schizophrenia have also revealed widespread thinning in frontal and temporal cortical loci (Kuperberg et al., 2003; Narr et al., 2005a; Narr et al., 2005b; Venkatasubramanian et al., 2008; Schultz et al., 2010a; Schultz et al., 2010b). Additionally, we have shown that cortical thickness is a more sensitive measure of clinical insight than VBM in first-episode psychosis (Buchy et al., 2011). Based on this study, it is likely that cortical thickness may further be sensitive to detect brain regions important for other aspects of self-reflection, such as the meta-cognitive variables measured here.

In the current study we evaluated people at CHR for psychosis on the four meta-cognitive processes tapped with the MAS. Given that cortical thickness analyses provide anatomically meaningful measurements of cortical integrity, that the MAS is considered to be sensitive measure of an individual's ability to engage in meta-cognitive acts as would be encountered in everyday life, and that the MAS has been used to document meta-cognitive impairments in people with schizophrenia, we investigated the structural neural correlates of the four MAS rated meta-cognitive processes using a surface-based cortical thickness analysis in our CHR sample. Given the well documented pattern of structural brain abnormalities seen in people with psychoses and at-risk populations, as a starting point we hypothesized that higher meta-cognition would correlate with cortical thickness in five brain regions implicated in the pathogenesis of psychosis: inferior and middle frontal cortices, anterior cingulate cortex, superior temporal cortex and insula. In a secondary hypothesis, we expected any observed associations to be partially overlapping across the four MAS items given the inter-correlations between MAS variables (Lysaker et al., 2005).

2. Materials and methods

2.1. Participants

The sample consists of 29 CHR participants recruited at the University of Calgary. All CHR participants were required to meet the Criteria of Prodromal Syndromes (COPS) using the Structured Interview for Prodromal Syndromes (SIPS) (McGlashan et al., 2010). Twenty-seven participants met attenuated positive symptom syndrome (APSS) criteria, which includes the emergence or worsening of a non-psychotic level disturbance in thought content, thought process or perceptual abnormality over the past year, four participants met criteria for genetic risk and deterioration (GRD), which required either a first degree relative with a psychotic disorder or the subject having schizotypal personality disorder plus at least a 30% drop in functioning on the General Assessment of Functioning (GAF) scale in the past 12 months, and two participants met both APSS and GRD. Participants were excluded if they met criteria for any current or lifetime axis I psychotic disorder, IQ < 70, past or current history of central nervous system disorder or DSM-IV criteria for current substance dependence disorder. A more detailed description of ascertainment, inclusion and exclusion criteria, and participant details are provided elsewhere (Addington et al., 2013).

2.2. Measures

The SIPS and the Scale for Assessment of Prodromal Symptoms (SOPS) (McGlashan et al., 2010) were used to determine criteria for a prodromal syndrome and severity of attenuated positive symptoms. Depression was rated with the Calgary Depression Scale for Schizophrenia (Addington et al., 1990, 2014). The structured clinical interview for DSM-IV (First et al., 1998) was used to assess for current and lifetime schizophrenia spectrum disorders.

Indiana Psychiatric Illness Interview (IPPI) (Lysaker et al., 2002) is the semi-structured interview developed to assess how people understand their difficulties with mental illness generally in their life, in the form of narratives. A research assistant conducts the interview that lasts 30–60 min. Responses are audio taped and later transcribed. Conceptually, the interview is divided into five sections. First rapport is established and participants are asked to tell the story of their lives in as much detail as possible. Secondly, participants are asked if they think they have a psychological problem and, if so, how they understand it. This is followed by questions about how they perceive their condition, how it has or has not affected their psychological and interpersonal life. Third, they are asked whether and, if so, how their condition "controls" their life and how they "control" their condition. Fourth, participants are asked how their condition affects others and is affected