Psychiatry Research: Neuroimaging 234 (2015) 328–335

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Is it me? Verbal self-monitoring neural network and clinical insight in schizophrenia

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ARTICLE INFO

Article history:
Received 19 April 2015
Received in revised form
30 September 2015
Accepted 1 October 2015
Available online 13 October 2015

Keywords:
Psychosis
fMRI
Self-awareness
Anterior cingulate
Medial frontal gyrus
Putamen
Birchwood insight scale

ABSTRACT

Self-monitoring, defined as the ability to distinguish between self-generated stimuli from other-generated ones, is known to be impaired in schizophrenia. This impairment has been theorised as the basis for many of the core psychotic symptoms, in particular, poor clinical insight. This study aimed to investigate verbal self-monitoring related neural substrates of preserved and poor clinical insight in schizophrenia. It involved 40 stable schizophrenia outpatients, 20 with preserved and 20 with poor insight, and 20 healthy participants. All participants underwent functional magnetic resonance imaging with brain coverage covering key areas in the self-monitoring network during a verbal self-monitoring task. Healthy participants showed higher performance accuracy and greater thalamic activity than both preserved and poor insight patient groups. Preserved insight patients showed higher activity in the putamen extending into the caudate, insula and inferior frontal gyrus, compared to poor insight patients, and in the anterior cingulate and medial frontal gyrus, compared to healthy participants. Poor insight patients did not show greater activity in any brain area compared to preserved insight patients or healthy participants. Future studies may pursue therapeutic avenues, such as meta-cognitive therapies to promote self-monitoring or targeted stimulation of relevant brain areas, as means of enhancing insight in schizophrenia.

1. Introduction

One important indicator of clinical outcomes in psychotic disorders is the level of insight a patient has into his/her mental condition (Drake et al., 2007). Poor clinical insight has been closely associated with poor medication compliance, more frequent relapses and hospital admissions, poor long-term outcomes and, overall poor global functioning (Amador and David, 2004). Patients with poor insight, characteristically demonstrate a lack of awareness of the presence of a mental disorder, an inability to identify their psychotic experiences as being abnormal (misattribution of symptoms) and/or failure to recognise or identify the need for treatment (David, 1990). As there are limited data on the underlying cause or explanation of this phenomenon, there are few clinical strategies specifically aimed at enhancing insight of affected patients (Shad et al., 2007).

The ability to accurately self-appraise and monitor self-related information may be crucial to having a good insight in psychosis (Kircher and David, 2003; Shad et al., 2007). Kircher and Leube (2003) postulated that intact self-awareness is dependent on intact self-monitoring processes, and that a subconscious inability to label self-generated impulses as originating from "self" underpins core psychotic symptoms such as somatic passivity and thought disorders. In many studies, patients with schizophrenia are found to show poor monitoring of self-generated stimuli in the visual, tactile and verbal domains and misattribute them to other sources (Raveendaran and Kumari, 2007). Shad et al. (2007), in their model of the neurobiology of poor clinical insight in schizophrenia, theorised that impaired self-awareness results in misattribution of symptoms, as awareness of symptoms is crucial in them being correctly attributed to those of the disorder (i.e. good clinical insight). They further linked aberrant functioning of the neural substrates implicated in poor self-appraisal and monitoring to

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http://dx.doi.org/10.1016/j.pscychresns.2015.10.007

misattribution of symptoms, and thus to poor insight, in schizophrenia (Shad et al., 2007).

A number of recent studies (Gerretsen et al., 2014; Shad and Keshavan, 2015; van der Meer et al., 2013) have focussed on the neurobiology of insight in schizophrenia using paradigms that directly or indirectly involve monitoring of the self or self-relevant information. Associations have been found between poor clinical insight and increased connectivity in the self-referential network with the left insula during rest (Gerretsen et al., 2014), better clinical insight and activation of the inferior frontal gyrus, anterior insula and inferior parietal lobule during self-reflection (van der Meer et al., 2013); and between symptom unawareness and activation of many areas, including the prefrontal, parietal and limbic areas, with more specific associations between symptom misattribution and localised regions within the prefrontal cortex and basal ganglia, during a self-awareness task (Shad and Keshavan, 2015).

This present study aimed to investigate the neurobiology of clinical insight in psychosis further by examining functional alterations within the verbal self-monitoring neural network in patients with poor as well as preserved clinical insight, relative to each other and a group of healthy participants. The functional neuroanatomy of verbal self-monitoring in healthy people includes the anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (DLPFC), left inferior frontal cortex, putamen, temporal cortex, posterior cingulate and the inferior parietal cortex (Allen et al., 2005; Kumari et al., 2010b; Raveendaran and Kumari, 2007; Shergill et al., 2001). Functioning of many of these areas, based on recent studies of insight in psychosis (Gerretsen et al., 2014; Sapara et al., 2014; Shad and Keshavan, 2015; van der Meer et al., 2013), appears to be involved in maintaining a good insight in schizophrenia. Previous studies have consistently shown reduced superior-middle temporal lobe activity during variants of the verbal self-monitoring task (Fu et al., 2006; Shergill et al., 2000; Kumari et al., 2010b) but no published study, to our knowledge, has examined verbal self-monitoring performance or the functioning of the associated neural network in relation to the level of insight in schizophrenia.

Based on the existing models implicating self-monitoring deficits in poor insight in psychosis (Shad et al., 2007) and recent fMRI findings (Gerretsen et al., 2014; Sapara et al., 2014; Shad and Keshavan, 2015; van der Meer et al., 2013), we hypothesised that patients with poor insight, compared to those with preserved insight, will show less accurate self-monitoring performance and aberrant fMRI response in the verbal self-monitoring neural network. Poor, but not preserved insight, patients were expected to show markedly impaired performance and performance-related fMRI activations relative to healthy participants.

2. Methods

2.1. Participants and design

The study involved 60 right-handed participants in total. The sample included 40 people with a Diagnostic and Statistical Manual of Mental Disorders (DSM, fourth edition DSM-IV, APA, 1994) diagnosis of schizophrenia (Structured Clinical Interview for DSM-IV, SCID; First et al., 1995). Of these, 20 patients were preselected to have preserved insight and 20 to have poor insight out of a larger pool of 70 patients (see Creation of low and high insight groups). All included patients were required to be on stable doses of antipsychotic medication for at least three months and in the stable (chronic) phase of the illness. Of 40 patients initially included, 14 patients (7 poor and 7 preserved insight) had to be excluded: four patients (2/group) had movement artefacts (i.e. rotations $>5^{\circ}$ or translations >5 mm), four poor insight patients failed to follow the task instructions, and performance data from 1 poor and 5 preserved insight patients were unavailable (equipment failure) during fMRI. Twenty healthy participants, screened to exclude neuropsychiatric conditions using the SCID (non-patient version (SCID-NP) and matched, on average to the two patient groups, for age and sex, were studied for comparison purposes, with 16 providing useable data ($n=3$, movement artefacts; $n=1$ technical failure). Of those remaining in the final sample, 19 patients (9 poor insight, 10 preserved insight) and 11 healthy participants were also included in our earlier study (Sapara et al., 2014).

The study procedures were approved by the research ethics committee of the Institute of Psychiatry and South London and Maudsley NHS Trust, London. All participants provided written informed consent.

2.2. Clinical assessment

Insight was assessed using the Birchwood insight scale (BIS) (Birchwood et al., 1994). The BIS assesses three dimensions of clinical insight (David, 1990), namely (i) the presence of a mental illness (items 2 and 7), (ii) the need for treatment (items 3,4,5 and 6), and (iii) the identification of symptoms as abnormal (items 1 and 8). Each BIS item is rated as 'agree', 'disagree' or 'unsure', giving an item score of 1 for unsure, and 0 or 2 for agree and disagree, depending on whether agreement with the statement indicates good insight (items counterbalanced for response valence). Item 4 "My stay in hospital is necessary" was omitted, as we did not include any inpatients. This yielded a maximum score of 14 (from the remaining 7 items) in this data set instead of 16 observed on the full BIS. For classification of insight levels, Birchwood (1994) suggested a score of 9 (out of 16) as the minimum for good clinical insight. In addition, in all patients symptoms were assessed using the Positive and Negative Syndrome scale (PANSS) (Kay et al., 1987) and predicted IQ was assessed in all participants using the National Adult Reading Test (NART) (Nelson and Willison, 1991).

2.3. Creation of preserved and poor insight groups

We classified patients into "preserved" or "poor" insight groups, rather conservatively by defining preserved insight as a score of 13 or above and poor insight as 8 or less (out of a maximum 14) to ensure distinct insight levels in preserved and poor insight groups (Sapara et al., 2014). Patients were supervised while completing the BIS. The BIS has adequate internal consistency and satisfactory test–retest reliability (Birchwood et al., 1994), and BIS insight scores correlate positively with scores on clinician-rated measures of insight such as the Scale to Assess Unawareness of Mental Disorders (SUMD; Amador and David, 2004) and the Expanded Schedule of Assessment of Insight (SAI-E; David and Kemp, 1997) (Young et al., 2003; Sapara et al., 2007).

2.4. fMRI paradigms and procedure

All participants performed a self-monitoring task (Kumari et al., 2010b) whilst undergoing fMRI. Participants were presented with single words on a computer screen (visible for 750 ms, inter-stimulus interval 16.25 s), viewed (wearing fMRI compatible glasses where needed) via a prismatic mirror fitted in the radiofrequency head coil, as they laid in the scanner, and were instructed to read each word aloud. The participant's speech was transformed in real time through a software programme and a DSP.FX digital effects processor (Power Technology, California, USA), amplified by a computer sound card, and relayed back through an acoustic MRI