Aberrant modulation of brain activation by emotional valence during self-referential processing among patients with delusions of reference

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1. Introduction

Schizophrenia has been characterized as a disorder of the self (e.g., Sass & Parnas, 2003) that is often accompanied by delusions (Breier & Berg, 1999). Although different types of delusions have long been defined, recent work highlights the potential importance of attending to their distinctions. Delusions of reference are among the most common type of delusions, and refer to instances where mundane events, stimuli, or other persons hold strong personal significance to, or directed at the observer. Here we investigate the emotional modulation of brain activation during self-referential processing. In this context, self-referential processing refers to cognitive mechanisms through which individuals deem the relevance of stimuli to their ‘self’ in a personal and environmental context (Northoff et al., 2006; van der Meer, Costafreda, Aleman, & David, 2010). Cortical midline structures in the brain play key roles in self-referential processing reflect exaggerated or abnormal attribution of salience (Kapur, 2003). David and colleagues (Aleman & David, 2006; Gibbs & David, 2003) have also promoted need to investigate neurocognitive mechanisms underlying such symptoms of psychosis in relation to emotional processes. These features have sparked interest in better understanding the appraisal of self-relevance in psychosis and potential relations to emotional content (e.g., Blackwood et al., 2004; Menon et al., 2011).

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http://dx.doi.org/10.1016/j.jbtep.2016.11.007
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Please cite this article in press as: Girard, T. A., et al., Aberrant modulation of brain activation by emotional valence during self-referential processing among patients with delusions of reference, Journal of Behavior Therapy and Experimental Psychiatry (2016), http://dx.doi.org/10.1016/j.jbtep.2016.11.007
stimuli. Despite some inconsistencies that may relate to specificity in the ventral ACC, with greater decreases in activation to negative stimuli and their patterns of brain activation, as measured by fMRI (functional magnetic resonance imaging) during this self-reflective task. We hypothesized that we would observe aberrant modulation of brain activation by affective valence across cortical-midline structures during self-referential processing among patients with prominent delusions of reference, compared to a healthy sample.

2. Methods

2.1. Participants

The patient sample comprised 14 participants with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder and prominent delusions of reference (score ≥ 4 on this item of the Schedule for Assessment of Positive Symptoms, SAPS; Andreasen, 1984). Additional inclusion criteria included fluency in English and the ability to provide voluntary consent (confirmed using the MacArthur Test of Competence; Appelbaum & Grisso, 1995). Exclusion criteria included serious unstable medical illness, concomitant major medical or neurological illness, history of head trauma that resulted in >30 min of unconsciousness, acute suicidal or homicidal ideation, formal thought disorder rating >2 on the SAPS, DSM-IV substance dependence (except caffeine and nicotine) within one month prior study entry, and MRI-related exclusions (e.g., metal implants, claustrophobia, worked with metal, pregnancy). Inclusion/exclusion criteria for healthy comparison participants (n = 15) were consistent with the above with the addition of no history of any Axis I conditions as determined using the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998), and no reported use of illegal psychotropic drugs within the past two years.

The patient group was recruited through the Centre for Addiction and Mental Health (Toronto, ON) and the non-psychiatric comparison group was recruited through advertisements in the surrounding community. The study was approved by the institutional REB and all participants provided written consent for voluntary participation. The patient and comparison samples were matched on age (Patient, $M \pm SD = 40.6 \pm 12.8; \text{Comparison}, 35.9 \pm 6.9$) and gender (10 males/group). Consistent with the nature of schizophrenia, the patient group had fewer years of education (Patient, $M \pm SD = 12.9 \pm 2.5$; Comparison, $16.9 \pm 2.1$), $t(27) = 4.75, p < 0.001$, $d = -1.76$, and lower estimated premorbid IQ (Patient, $M \pm SD = 97.7 \pm 15.3$; Comparison, 107.8 ± 8.9), t(27) = 2.19, p < 0.05, $d = -0.81$, as estimated by the WRAT-Reading test (Wide Range Achievement Test; Wilkinson & Jastak, 1993). Nonetheless, these means reflect that the patient sample had at least high-school education and were in the Average range of intelligence. All patients were on atypical antipsychotic medication (Mean chlorpromazine equivalent = 413 mg; Woods, 2003). The mean SAPS score for delusions of reference was 4.3 ($SD = 0.9$; See Menon et al. (2011) for further details.

2.2. Self-reference paradigm

The experimental paradigm is described in detail by Menon et al. (2011). Sixty sentence stimuli were presented using E-Prime software (Psychology Software Tools, Pittsburgh, Pennsylvania). Each statement was presented for 5 s, with a variable inter-stimulus interval (ISI) of 1.5–3 s during which participants saw a fixation cross. The sentences described personal characteristics in the third person with the pronoun matched to participant sex, yet ambiguous in reference (e.g., “She is lazy”). Participants completed a detailed instruction phase and three practice trials to confirm that they were to make a binary decision regarding whether they judged each sentence gave rise to the feeling that it was written specifically about them, not just whether it was self-descriptive or true of them. The sentences were presented twice each during scanning (across 2 runs) in order to increase power and reliability of

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