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Insight and emotion regulation in schizophrenia: A brain activation and functional connectivity study

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ABSTRACT

Background: Insight is impaired in the majority of schizophrenia patients. The exact neural correlates of impaired insight remain unclear. We assume that the ability to regulate emotions contributes to having good clinical insight, as patients should be able to regulate their emotional state in such a way that they can adapt adequately in order to cope with impaired functioning and negative stigma associated with a diagnosis of schizophrenia. Numerous studies have shown emotional dysregulation in schizophrenia. We investigated the association between insight and brain activation and connectivity during emotion regulation.

Methods: Brain activation during emotion regulation was measured with functional MRI in 30 individuals with schizophrenia. Two emotion regulation strategies were examined: cognitive reappraisal and expressive suppression. Clinical insight was measured with the Schedule for the Assessment of Insight – Expanded, and cognitive insight was measured with the Beck Cognitive Insight Scale. Whole brain random effects multiple regression analyses were conducted to assess the relation between brain activation during emotion regulation and insight. Generalized psychophysiological interaction (gPPI) was used to investigate the relation between task-related connectivity and insight.

Results: No significant associations were found between insight and neural correlates of cognitive reappraisal. For clinical insight and suppression, significant positive associations were found between symptom relabeling and activation in the left striatum, thalamus and insula, right insula and caudate, right pre- and postcentral gyrus, left superior occipital gyrus and cuneus and right middle and superior occipital gyrus and cuneus. Furthermore, reduced clinical insight was associated with more connectivity between midline medial frontal gyrus and right middle occipital gyrus. For cognitive insight and suppression, significant positive associations were found between self-reflectiveness and activation in pre- and postcentral gyrus and left middle cingulate gyrus.

Conclusions: Our results suggest an association between the capacity to relabel symptoms and activation of brain systems involved in cognitive-emotional control and visual processing of negative stimuli. Furthermore, poorer self-reflectiveness may be associated with brain systems subserving control and execution.

1. Introduction

Clinical insight is impaired in the majority of schizophrenia patients (Dam, 2006). It includes the following dimensions: (i) illness awareness, (ii) attribution of symptoms to the illness, and (iii) awareness of need for treatment (David, 1990). Impaired clinical insight is one of the most common reasons for poor treatment adherence, and a strong association between impaired clinical insight and poorer outcome of the disorder has been shown (Lincoln et al., 2006). Clinical insight is separated from cognitive insight, which relates to patients' attributive metacognitive ability. Cognitive insight is defined as the ability to evaluate and reflect upon one's own aberrant views and interpretations

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(Beck et al., 2004; Cooke et al., 2010). Clinical insight requires the ability to reflect upon oneself (i.e. cognitive insight), but also the abilities to inhibit one's own perspective, to take someone else's perspective and to switch between perspectives until the perspective is found that matches reality best. Consequently, it has been suggested that social cognitive functions such as self-reflectiveness and perspective taking, as well as cognitive functions such as cognitive (inhibitory) control and cognitive flexibility (Pijnenborg et al., 2011) may play an important role in clinical insight. We assume that the ability to regulate emotions contributes to having good clinical insight, as patients should be able to regulate their emotional state in such a way that they can adapt adequately in order to cope with impaired functioning and negative stigma associated with a diagnosis of schizophrenia (Pijnenborg et al., 2011). Better emotion regulation skills may also be associated with being more open to considering the possibility of having a mental disorder. The association between emotion regulation and insight has not been studied before. Results of an earlier study suggested that stigma resistance was associated with emotion regulation in patients with schizophrenia (Raij et al., 2014). A model illustrating the relationship between several processes that may be involved in impaired insight can be seen in Fig. 1.

Numerous studies have shown emotional dysregulation in schizophrenia (Henry et al., 2007; Horan et al., 2013; Morris et al., 2012; Perry et al., 2012; Van der Meer et al., 2014). Emotion regulation refers to an individual's ability to manage their emotional states (Gross, 1998). Several emotion regulation strategies exist and individuals differ in their use of them (Gross, 1998). In this study, we focus on the two most-applied emotion regulation strategies, namely cognitive reappraisal and expressive suppression. Cognitive reappraisal is antecedent-focused (i.e. focused on processes that precede an emotional response) and expressive suppression is response-focused (i.e., focused on response that is already under way). Several studies have shown that schizophrenia patients use reappraisal less frequently and suppression more frequently compared to healthy individuals (Kimhy et al., 2012; Livingstone et al., 2009; van der Meer et al., 2009), while other studies did not find significant differences (Badcock et al., 2011; Henry et al., 2008; Perry et al., 2011).

During cognitive reappraisal, individuals control negative emotions by changing their way of thinking. The neural correlates of cognitive reappraisal of emotional stimuli have been investigated extensively in healthy subjects using functional neuroimaging. These studies found increased activation of the prefrontal cortex (PFC; including the dorsolateral prefrontal cortex (DLPFC), ventrolateral PFC (VLPFC), the dorsomedial PFC (DMPFC) and the posterior prefrontal cortex), inferior parietal cortex, dorsal anterior cingulate cortex (dACC) and reduced activation of the amygdala, ventral striatum, insula and ventromedial

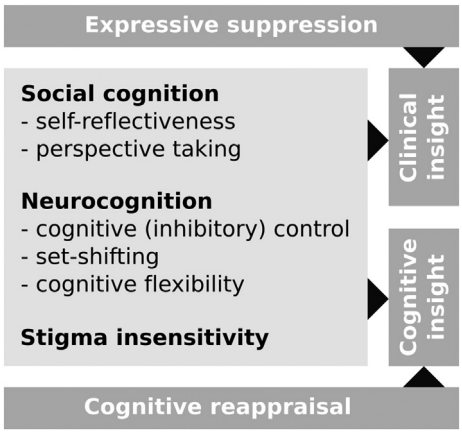

Fig. 1. Model of impaired insight in schizophrenia. Adapted from Pijnenborg et al. (2011).

PFC (VMPFC) during reappraisal (see Diekhof et al. (2011) and Buhle et al. (2014) for meta-analyses). These studies suggest top-down control of the prefrontal cortex on areas involved in emotion processing (e.g. the amygdala). In schizophrenia, neuroimaging studies have reported hypo-activation of the VLPFC compared to healthy controls (Morris et al., 2012; Van der Meer et al., 2014). During expressive suppression, emotion expression is inhibited. Two neuroimaging studies in healthy participants found increased activation of the DLPFC, VLPFC, and insula during suppression (Goldin et al., 2008; Ohira et al., 2006). Findings of these studies on amygdala activation were mixed, with one study finding increased and the other study finding decreased activation during suppression (Goldin et al., 2008; Ohira et al., 2006). No neuroimaging studies on suppression have been conducted in schizophrenia yet.

We assume that emotion regulation by means of cognitive reappraisal requires insight and awareness, as it entails conscious effort in order to initiate it and monitor emotions during its execution. Therefore, we hypothesize that patients with impaired insight are less able to regulate their negative emotions through reappraisal and will make more use of suppression. Specifically, we expect a relationship between reappraisal and cognitive insight since reappraisal is a predominantly cognitive process. We hypothesize that patients with poorer cognitive insight show increased activation of prefrontal and emotional arousal-related areas, as well as more connectivity between prefrontal and emotional arousal-related areas suggesting increased mental effort and top-down control to exert cognitive reappraisal. In addition, we hypothesize that patients with poorer clinical insight will make more use of suppression and, therefore, will show less brain activation of and connectivity between relevant areas (DLPFC, VLPF and insula) during suppression compared to patients with better insight. A visualization of our hypotheses can be seen in Fig. 2.

2. Methods

2.1. Participants

35 individuals with schizophrenia (SZ; 73% men) and 16 healthy controls (HC; 67% men) were included in this study. All patients were diagnosed with schizophrenia by a psychiatrist according to DSM-IV-TR (American Psychiatric Association, 2000) and ICD-10 criteria (World Health Organisation, 2012), which was confirmed with the Mini International Neuropsychiatric Interview (MINI-plus) (Sheehan et al., 1998). Patients were recruited from several mental health institutions in the Netherlands in a consecutive manner. All healthy controls were assessed with the MINI-plus (Sheehan et al., 1998) to confirm lack of personal history of psychiatric, somatic and neurological illnesses. They were matched to the patient group on age, handedness, sex and education. All participants were of ages 18 and above and were able to give informed consent. Exclusion criteria for this study were having an acute psychosis, having a co-morbid psychiatric, somatic and/or neurological disorder, drug use, change of medication within the last week, use of a benzodiazepine equivalent to > 3 mg lorazepam, electroconvulsive therapy within the last year and MRI contra-indications (i.e. metal implants, red ink tattoos, pregnancy or possibility thereof and claustrophobia). All participants provided informed consent and received 45 euros for participation. The study protocol was approved by the medical ethical board of the University Medical Center Groningen and was in accordance with the latest version of the Declaration of Helsinki.

Five patients and one healthy individual were excluded from analyses for different reasons: lack of understanding of fMRI task (2 SZ), MRI artefact (1 SZ), lack of logging of onset times of different conditions fMRI task (1 SZ) and excessive head motion (1 SZ and 1 HC). This left a group of 30 SZ patients and 15 HC for analyses; their clinical and demographic characteristics can be seen in Table 1.