



# Unrealistic self-overconfidence in schizophrenia is associated with left presubiculum atrophy and impaired episodic memory

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## ARTICLE INFO

### Article history:

Received 8 June 2016

Reviewed 16 August 2016

Revised 14 October 2016

Accepted 25 October 2016

Action editor Peter Kirsch

Published online 17 November 2016

### Keywords:

Schizophrenia

Self-Certainty

Self-Reflectiveness

Hippocampus

Cognitive insight

## ABSTRACT

The study aimed at investigating the role of the hippocampal subfields in cognitive insight and the clinical and neuropsychological underpinnings of the related two sub-dimensions, Self-Reflectiveness (SR), i.e., openness to external feedback, and Self-Certainty (SC), i.e., unrealistic overconfidence in one's opinions. In order to do this, 45 patients with a diagnosis of schizophrenia and 45 age- and gender-matched healthy control subjects (HC) were administered the Beck Cognitive Insight Scale (BCIS), along with neuropsychological, clinical and psychopathological assessment, and underwent an MRI investigation. Hippocampal segmentation was carried out. Regression analyses were performed for BCIS indexes, volumetric parameters of hippocampal subfields and clinical and neuropsychological variables. Results highlighted that in the schizophrenia group, higher levels of SC were related to reduced volume of the left presubiculum, and worse episodic memory. No significant relationship emerged for the SR index. There was no significant relationship between any of the BCIS indexes and volumetric data of the hippocampal subfields in the HC group. Our data support the hypothesis that unrealistic self-overconfidence in schizophrenia is related to the hippocampal presubiculum atrophy, which is involved in episodic memory and cognitive control and is supposed to be underpinned by difficulty in integrating new memories and thus in generating new hypotheses about the self.

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<http://dx.doi.org/10.1016/j.cortex.2016.10.017>

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## 1. Introduction

Autonoetic knowledge is a metacognitive function which involves making judgments about personal memories of one's own past and is considered necessary for remembering self-referential experienced events (Tulving, 1984; 2005; Wells & Purdon, 1999). Disturbances of autonoetic knowledge are believed to underpin lack of insight, a core deficit of schizophrenia which may lead to poor treatment compliance, poor social and interpersonal functioning, a negative prognosis and a higher risk of relapse (Raffard et al., 2008). Realistic self-appraisal cannot be separated from the ability to process information in order to monitor, interpret, appraise and modulate cognitive, emotional and behavioral processes and their organization (Newen & Vogeley, 2003; Wells & Purdon, 1999; Zeman, 2006). Thus, in psychosis, along with the clinical concept of insight (Amador & Strauss, 1993; Marková et al., 2003), this metacognitive orientation led to the development of the construct of cognitive insight (Beck, Baruch, Balter, Steer, & Warman, 2004), i.e., the ability to monitor and correct one's erroneous convictions. Cognitive insight encompasses two abilities, i.e., Self-Reflectiveness (SR), or individuals' capacity and willingness to observe their mental productions and to consider alternative explanations, and Self-Certainty (SC), or overconfidence in the validity of one's beliefs and the reluctance to correct them. High SR may encourage patients to doubt their distorted and unrealistic perceptions or thought productions and lead them to have a more objective attitude towards their illness. On the other hand, high SC indicates resistance to corrective external feedback and thus the maintenance of erroneous beliefs. Thus, in psychosis cognitive insight may provide useful information for cognitive therapy to facilitate compliance and deal with the illness (Granholm, McQuaid, McClure, Auslander, Perivoliotis et al., 2005; Jorgensen et al., 2015; Lam, Ho, Wa, Chan, Yam et al., 2015; Raffard et al., 2013). However, cognitive insight can be considered as a cognitive attitude that can be observed also in healthy subjects (Martin, Warman, & Lysaker, 2010; Orfei, Caltagirone, Cacciari, Assogna, & Spalletta, 2011).

The neuropsychological underpinnings of cognitive insight have been challenged by pointing out the involvement of verbal memory and executive functions (Buchy, Czechowska, et al., 2010; Cooke et al., 2010; Gonzalez-Blanch et al., 2014; Kao et al., 2013; Lepage et al., 2008; Nair, Palmer, Aleman, & David, 2014; Orfei, Spoletini, Banfi, Caltagirone, & Spalletta, 2010). Today, a major challenge is to understand the neural bases of cognitive insight. Very recent functional (fMRI) and structural MRI studies highlighted the relationship between SR and the right ventro-lateral prefrontal cortex (VLPFC) (Buchy et al., 2014; Orfei, Piras, Macci, Caltagirone, & Spalletta, 2013; Pu et al., 2013). The crucial role of this prefrontal cortical area involves cognitive control and the ability to consider several alternative hypotheses simultaneously, the latter being the core aspect of cognitive insight (Gerretsen et al., 2014; Orfei et al., 2013). Few recent studies focused on the role of the hippocampus in cognitive insight. In fact in schizophrenia this brain structure is characterized by both hypermetabolism and reduced size, possibly with hypermetabolism leading to

atrophy and glutamate functioning as a pathogenic driver (Schobel et al., 2013). These abnormalities are supposed to be related to impairments in declarative memory function, especially in the flexible use of event memories (Kuhn et al., 2012; Tamminga, Stan, & Wagner, 2010). Other studies revealed hippocampal dysfunction during semantic word generation (Kircher, Whitney, Krings, Huber, & Weis, 2008). Consistently, Buchy and colleagues, in a study on first-episode patients with psychosis, examined hippocampal volumes as a whole (Buchy, Czechowska, et al., 2010) and found that increased SC was related to reduced hippocampal volume. A second study (Buchy, Luck, et al., 2012) highlighted that SC was significantly correlated with fractional anisotropy (FA) values in the right fornix. Thus, Buchy and colleagues hypothesized that anatomical disconnectivity in the hippocampal network might contribute to maladaptive cognitive inflexibility and overconfidence in psychosis.

Actually, the hippocampal formation consists of functionally and molecularly distinct subfields characterized by complex interconnections (Haukvik et al., 2015; Small, Schobel, Buxton, Witter, & Barnes, 2011). The concept of regional vulnerability within the hippocampus is definitely supported by evidence that specific cognitive operations are linked to specific hippocampal subregions (Small et al., 2011). For instance, the subicular and fimbria-fornix complexes are strictly interconnected with the prefrontal areas (Brasted, Bussey, Murray, & Wise, 2003), in particular with the anterior thalamic nucleus (O'Mara, Commings, Anderson, & Gigg, 2001; O'Mara, Sanchez-Vives, Brotons-Mas, & O'Hare, 2009), and the role of all of these areas in episodic and declarative memory and cognitive control is well known (Aggleton & Brown, 1999; Takei et al., 2008; Thomas, Koumellis, & Dineen, 2011; Tsanov & O'Mara, 2014).

The present study aimed at investigating the possible role of the hippocampal subfields in the cognitive dimensions in schizophrenia. We expected smaller subicular complex and fimbria–fornix complex volumes to be related to higher levels of self-overconfidence. As a secondary aim, we explored the relationship between cognitive insight dimensions and clinical and neuropsychological variables. We expected a relationship between impairments in episodic memory function and higher levels of self-overconfidence and lower levels of SR.

## 2. Material and methods

### 2.1. Subjects and clinical assessment

We recruited 65 consecutive outpatients diagnosed with schizophrenia according to the DSM-IV-TR (APA, 2000) criteria. All patients were diagnosed by one senior clinical psychiatrist (G.S.) using the structured clinical interview for DSM-IV-TR (SCID-I/P) (First, Spitzer, Gibbon, & Williams, 2002). Other inclusion criteria were: 1) age between 18 and 65 years; 2) at least 8 years of education; 3) no dementia or cognitive deterioration according to the DSM-IV-TR criteria, and a Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) score higher than 24, consistent with normative data in the Italian population (Measso et al., 1993); and 4) suitability for a Magnetic Resonance Imaging (MRI) scan.

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