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Neurocognitive capabilities modulate the integration of evidence in schizophrenia

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ABSTRACT

Previous studies have demonstrated a cognitive bias in the integration of disconfirmatory evidence (BADE) in patients with schizophrenia. This bias has been associated with delusions. So far, it is unclear how the integration of evidence is associated with neurocognitive capabilities. In the current study, 31 patients with schizophrenia and 29 healthy controls, matched on age, gender, education and premorbid verbal intelligence, underwent a BADE task. Written scenarios of three consecutive sentences each were presented, which progressively reduced the ambiguity of situations. Participants were asked to rate the plausibility of four possible interpretations and adjust their ratings in response to the provided sentences. Psychometric rating scales and a neuropsychological test battery were applied. Patients displayed a bias in the integration of confirmatory, but not disconfirmatory evidence and a liberal acceptance of belief formation. Correlation analyses revealed no associations of evidence integration with the severity of positive symptoms, but with neurocognitive domains, especially with processing speed, executive functioning, vigilance and working memory. In conclusion, patients with schizophrenia show a bias in evidence integration. Neurocognitive functioning emerged as a modulatory factor that should be considered in further research. Studies investigating BADE in earlier stages of psychosis will be necessary to reveal causal relationships.

1. Introduction

Holding beliefs with strong conviction in spite of contradictory evidence is a key feature of delusional thinking and a symptom of schizophrenia spectrum disorders. In recent years cognitive models of delusions have been developed suggesting that reasoning biases contribute to the development and maintenance of delusional thinking (Garety and Freeman, 1999; Freeman et al., 2004). Among other biases (Garety et al., 2001; Freeman et al., 2002; Moritz et al., 2005) a deficit in belief flexibility has been reported. Belief flexibility describes the metacognitive ability to reflect one's beliefs, adapt them to changing evidence and knowledge and generate new beliefs in case of better alternatives (Garety et al., 2005). Independent studies have shown that patients with schizophrenia presented deficits in belief flexibility. This has been linked to difficulties in their competence to reflect evidence, consider alternatives and integrate them into existing beliefs (Garety et al., 2005; So et al., 2012).

One aspect of belief flexibility is a metacognitive bias called the bias against disconfirmatory evidence (BADE) (Woodward et al., 2006b). Patients with schizophrenia have especially displayed deficits in the integration of newly achieved evidence which contradicts held beliefs. This inflexibility in adapting the reasoning process to new evidence consequently leads patients to stick to their incorrect convictions (Woodward et al., 2006b). BADE is often assessed by confronting patients with successive sentences or pictures which progressively disambiguate a scenario. When patients with schizophrenia have to decide which of four interpretations describes a scenario best, they often stick to their first plausible decision, ignoring subsequent contradicting interpretations. This bias has been found in schizophrenia patients with and without current delusions (Moritz and Woodward, 2006; Veckenstedt et al., 2011; Riccaboni et al., 2012), in groups of healthy people with delusion ideation and patterns of schizotypy

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(Buchy et al., 2007; Woodward et al., 2007; Orenes et al., 2012; Zawadzki et al., 2012), but not in healthy and psychiatric control groups (Woodward et al., 2006b; Woodward et al., 2008; Veckenstedt et al., 2011; Speechley et al., 2012). It has been especially discussed as an important cognitive bias associated with the maintenance of delusions (e.g. Woodward et al., 2006b; So et al., 2012). To assess delusional severity, different symptom rating scales can be used. Most prior studies reported using a single measure. However, it has been proved useful to implement multiple measures of delusion severity as well as multidimensional scales to investigate associations between BADE and symptomatology (So et al., 2012). In contrast, regarding the integration of confirmatory evidence (BACE), results are more diverging. Some studies found BACE to be intact (Woodward et al., 2006b; Veckenstedt et al., 2011) while others reported a BACE in schizophrenia samples (Riccaboni et al., 2012). Adding to diverging results, Speechley et al. (2012) discuss a bias against disambiguating evidence rather than disconfirmatory evidence which was described as *bias in evidence integration*.

Differing from classical neurocognitive testing, the assessment of metacognition rather evaluates the ability of information acquisition, processing and adjustment in everyday situations. Undoubtedly, close influences between neurocognitive abilities and metacognitive performance have to be assumed, but findings from currently available studies are heterogeneous. In a sample of healthy individuals prone to delusional thinking, BADE and neurocognitive measures (executive function, intelligence, and verbal memory) loaded on independent factors in the exploratory factor analysis (Woodward et al., 2007). In accordance, Moritz et al. (2010) did neither find associations of BADE with verbal learning and premorbid intelligence, nor with set-shifting abilities (Trail Making Test) in a sample of patients with schizophrenia spectrum disorders. However, Riccaboni et al. (2012) investigated associations between BADE and a set of neurocognitive tests and reported correlations between BADE and executive functions as well as verbal memory. It seems likely that both evidence integration and neurocognitive performance, especially executive functions, need to work in close alliance for a cognitive system to operate effectively (Bewick et al., 1995). Until now, studies have however addressed only small numbers of neurocognitive domains. The use of varying combinations of neurocognitive measures complicates comparisons even more. Further research is needed for a better understanding of the interplay between BADE and neurocognitive performance, as well as the severity of illness and antipsychotic therapy.

The first aim of the current study was to reanalyze BADE and BACE in a well characterized sample of patients with schizophrenia compared to healthy controls. We expected to replicate prior findings of a BADE in schizophrenia. Second, we aimed at investigating associations between evidence integration processes and the severity of current positive symptoms, especially delusions. Third, we intended to evaluate associations between evidence integration and neuropsychological performance with a comprehensive test battery specified for the assessment of neurocognition in schizophrenia to gain insight into the neurocognitive modulation of evidence integration.

2. Methods

2.1. Study design and participants

Thirty-one patients with the diagnosis of schizophrenia according to the Diagnostic and Statistical Manual (DSM-IV-R; (Saß et al., 2000)), reporting current or prior delusions, and 29 healthy controls matched regarding age, gender, years of education and premorbid verbal intelligence were included in the study. Patients with schizophrenia were recruited during in-house treatment at the Central Institute of Mental Health in Mannheim, Germany. Inclusion criteria were defined as follows: age between 18 and 60 years, ability to provide informed consent, sufficient German language skills, residence within a radius of 50 km around Mannheim, and antipsychotic monotherapy with a second generation antipsychotic agent (SGA). Current antipsychotic treatment was quantified using chlorpromazine (CPZ) equivalents (Andreasen et al., 2010). We excluded patients with substance dependence (excluding nicotine) or other disorders of the central nervous system requiring treatment.

Healthy control subjects were carefully screened for psychiatric disorders using the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998) as well as family, current and previous medical history. Subjects with suicide, schizophrenia and bipolar disorder in first-degree relatives, as well as subjects with disorders of the central nervous system, inpatient treatment in psychiatric hospitals, current treatment with psychotropic agents, substance dependence (excluding nicotine) and abuse of illegal substances within the four weeks before investigation were excluded.

This cross-sectional study was designed as part of a comprehensive investigation of metacognition in schizophrenia and was approved by the ethical board of the Ruprecht-Karls-University Heidelberg (accession number: 2009-296N-MA). Participants were informed about procedures and aims of the study and provided their written consent after a sufficient period of consideration and resolving open questions.

2.2. Assessments

2.2.1. Psychopathology

Psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS; (Kay et al., 1987)), the Scale for the Assessment of Negative Symptoms (SANS; (Andreasen, 1989)), the delusion part of the multidimensional Psychotic Symptom Rating Scales (PSYRATS; (Haddock et al., 1999)), and the Calgary Depression Scale for Schizophrenia (CDSS; (Addington et al., 1993)). Social and global functioning were rated using the scale for the General Assessment of Functioning (GAF; (Jones et al., 1995)) and the Personal and Social Performance Scale (PSP; (Patrick et al., 2009)). Severity of illness was assessed using the Clinical Global Impression Scale (CGI; (National Institute of Mental Health, 1970)).

2.2.2. BADE task

Metacognitive performance was assessed using a German variant of the BADE task (Woodward et al., 2007, Veckenstedt et al., 2011). Within this task, 12 written scenarios were presented. Three consecutive sentences, which progressively reduced the ambiguity of the given situation by providing additional information, were shown within one scenario. After each sentence, participants were asked to indicate plausibility ratings to four possible interpretations (true, neutral lure, emotional lure, and absurd). Plausibility for each interpretation could be indicated with ratings between zero (implausible) to 10 (most plausible). After the consecutive sentences two and three, participants were asked to adjust their ratings in response to the newly provided information. The BADE task was constructed as follows: after the first sentence the true interpretation was less or equally plausible as lure interpretations and gained plausibility with consecutive sentences. While the absurd interpretation was implausible across all stages, the lure interpretations seemed plausible after the first sentences but lost plausibility when more information was given by sentence two and three. In four control scenarios the true interpretation was most plausible from the first sentence on. These control items were included to mask the pattern of the task and to diversify responding and were excluded from statistical analyses. The current BADE task composed scenarios, which were tested and validated by Veckenstedt et al. (2011). An example of the task is given in the Appendix A.

Each participant was individually tested in a quiet room. One practice trial was administered before introducing the experiment. Plausibility ratings could be given by using a mouse to move a slider from zero to 10 in 0.1 steps. The current point of the slider on the rating scale was expressed in numbers on the right end of the scale, indicating the plausibility. As optional process, in case participants had decided in favor for one interpretation, they could mark this one interpretation by clicking a box to the right of the sentence at any time point. Decision marks after the first sentence can be used as valid indicators for the jumping to conclusion bias (Moritz et al., 2010; Veckenstedt et al., 2011), namely accepting hypotheses on the basis of a very small of amount of information (Fine et al., 2007). However, this evaluation goes beyond the scope of the current article. Trial order and position of the four scenario interpretations were randomized. Participants were randomized to one of three equivalent versions of the task with regard to follow-up measurements.

BADE and BACE measures were calculated using change scores from sentence one to sentence three in accordance to previous studies (Woodward et al., 2008; Veckenstedt et al., 2011). To indicate a BADE, the decrease of plausibility ratings from sentence one to sentence three for the lure interpretations (mean of neutral and emotional lures) was generated. A BACE was determined by the increase in plausibility ratings from sentence one to three for the true interpretations. Higher change scores were indicators of a higher flexibility in evidence integration, whereas low scores indicated little integration.