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Trait and state aspects of internal and external performance monitoring in schizophrenia

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ABSTRACT

Disturbed internal performance monitoring has been repeatedly demonstrated in schizophrenia. Along with internal monitoring, efficiently processing external task-relevant performance feedback that goes unnoticed by the internal monitoring system is crucial for adequate performance. It is unknown whether external monitoring is disturbed in schizophrenia and whether it is trait or state dependent. The current study investigated the effects of treatment on both internal and external performance monitoring in schizophrenia. Twelve schizophrenia patients and twelve matched healthy controls performed a modified flanker task while ERPs and behavioral measures were obtained. Both groups were assessed twice, with a six-week interval, during which the patients received antipsychotic treatment. Internal monitoring was investigated by means of the response-locked error-related negativity (Ne/ERN), an event-related potential component elicited by erroneous responses. External monitoring was investigated by analyzing the feedback-locked P300 elicited by task-relevant external response-time feedback (late feedback). Compared to controls, schizophrenia patients showed diminished Ne/ERN amplitudes, which were insensitive to six weeks of treatment. Patients also had reduced P300 amplitudes in response to late feedback at the first assessment, but these were normalized at the second assessment. Also, patients showed increased performance following negative external feedback at the second session. This study demonstrates the importance of considering both forms of performance monitoring in schizophrenia. Diminished internal error processing seems to be an important 'trait' marker of the disorder, while processing of externally presented feedback appears to have a 'state' character, susceptible to treatment at both a neurophysiological and a behavioral level.

1. Introduction

In order to adapt in an efficient and flexible manner to a changing environment, humans need to continuously monitor their performance for possible errors and adjust actions when necessary (De Bruijn et al., 2009; Holroyd and Coles, 2002). Previous research in schizophrenia has proposed that failure of internal monitoring of actions plays a part in the generation of some symptoms of the disease, such as delusions of alien control (Frith and Done, 1988) or formal thought disorders (McGrath, 1991). The internal performance-monitoring system can be investigated by means of electrophysiological recordings. More specifically, an event-related potential (ERP) component associated with erroneous responses has been identified. This so-called 'error negativity' (Ne) or 'error-related negativity' (ERN) is a sharp negative deflection in the ERP generated in the posterior medial frontal cortex (pMFC; Debener et al., 2005) that peaks around 50–100 ms after an erroneous response (Falkenstein et al., 1990; Gehring et al., 1993). The Ne/ERN is, for example, thought to result from the detection of a mismatch between a desired and an actual response (Coles et al., 2001; Falkenstein et al., 1991; Gehring et al., 1993) or alternatively, from response conflict generated by two simultaneously activated response tendencies (Botvinick et al., 2001; Yeung et al., 2004).

In line with the assumption that disturbances of the performance-monitoring system play a role in schizophrenia, an initial ERP study by Kopp and Rist (1999) demonstrated reduced Ne/ERNs in schizophrenia patients. Since then, different research groups have replicated this finding using a variety of experimental tasks (Alain et al., 2002; Bates et al., 2002, 2004; Kim et al., 2006; Mathalon et al., 2002, 2009; Morris et al., 2006,

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2008; Perez et al., 2012; Horan et al., 2012; Foti et al., 2012; Simmonite et al., 2012).

A study by Bates et al. (2004) addressed the question of whether attenuated Ne/ERNs in schizophrenia reflect state or trait characteristics of the disorder. The findings revealed an increase in Ne/ERN amplitude in nine patients with schizophrenia after six weeks of treatment with antipsychotics demonstrating the state dependency of the ERN. However, despite this increase, Ne/ERN amplitudes in the patient group remained significantly smaller compared to healthy controls. So, although the Ne/ERN may be modulated by clinical state in schizophrenia, the outcomes of this study seem to suggest that the repeatedly reported reductions in Ne/ERN may reflect an important trait characteristic of schizophrenia. Moreover, the outcomes of a recent study demonstrated that decreased Ne/ERN amplitudes are already present in 9–12 year old children with putative antecedents of schizophrenia (Laurens et al., 2010). Perez et al. (2012) found in their recent study reduced Ne/ERN amplitudes in different samples of patients (schizophrenia patients, early illness schizophrenia patients and clinically high risk patients) and their results also seem to suggest that reduced Ne/ERN amplitudes in schizophrenia is a non-progressive abnormality that is evident well before the sequelae of chronic illness emerge. However, the hypothesis that the Ne/ERN is indeed a strong trait marker of the disease has yet to be replicated in further research.

Importantly, alongside monitoring of internal information, keeping track of external information about one's performance is important for efficient and safe performance. This is most apparent in situations in which the internal performance monitoring system is unable to detect the error at the moment of the actual response. This is for example not only in the case when actions are performed in noisy environments and thus uncertainty about the given response is increased but also when learning is still taking place and people need to rely on external feedback to inform them about the correctness of a given response. In general, external feedback is crucial when the error cannot be detected at the moment when it is made.

However, most studies so far have focused on correlates of internal monitoring processes and disregarded external performance monitoring in patients with schizophrenia. To our knowledge, three recent studies did investigate processing of external error feedback by measuring the Ne/ERN response to the presentation of negative feedback (i.e. feedback-related negativity or FRN). Morris et al. (2008) used a learning paradigm to investigate the Ne/ERN in response to both the erroneous button press and presentation of negative performance feedback. This study showed that both ERP components were reduced in patients with schizophrenia. As they are considered to reflect the same error or performance-monitoring process originating from the same neural structures (Holroyd and Coles, 2002; Holroyd et al., 2004; Mars et al., 2005), this finding is in line with the assumed central role of pMFC in the manifestation of different symptoms in schizophrenia (Fornito et al., 2009; Laurens et al., 2003). In contrast with these results, a more recent study by the same group (Morris et al., 2011) found no difference in FRN amplitudes between schizophrenia patients and a group of healthy comparison subjects using a passive gambling task and a time-estimation task. Finally, using a simple monetary gambling task, Horan et al. (2012) recently reported comparable FRN differentiation between reward and non-reward feedback in a group of schizophrenia patients and a group of healthy controls. These recent findings thus seem to suggest that schizophrenia patients may have specific deficits in response-related error processing and perhaps to a lesser extent in feedback-related error processing regulated by pMFC.

Nevertheless, efficiently processing other task-relevant feedback that goes unnoticed by this medial prefrontal performance-monitoring system is also crucial. The P300 ERP component is an index of endogenous cognitive processes, typically elicited by infrequent sensory stimuli that are either task relevant or novel (Regan, 1989). Previous studies have repeatedly demonstrated reduced P300 amplitudes in schizophrenia patients using auditory (e.g. Jahshan et al., 2012) and visual (e.g. Bestelmeyer, 2012) oddball paradigms. Especially, reduced amplitude of the auditory oddball P300 response seems to be one of the most robust physiological abnormalities observed in schizophrenia (e.g. Ford et al., 2010; Turetsky et al., 2007; Jahshan et al., 2012). Studies that investigated state and trait dependency suggest that P300 amplitudes track fluctuations in clinical state (e.g. Higashima et al., 2003; Park et al., 2010; Mori et al., 2012, but see Molina et al., 2004; Neuhaus et al., 2011). Mathalon et al. (2000) demonstrated this relationship with clinical state to exist for both the more automatically elicited frontocentrally distributed P300 – the so-called P3a – and the more parietally distributed P3b, a P300 elicited by tasks requiring more effort. The neural generators of the P300 are widespread in the brain and largely dependent on the exact task requirements (e.g. Sabeti et al., 2011). Along with oddball paradigms, the P300 ERP component is also elicited when processing feedback signaling unexpected but task-relevant information. It is assumed to reflect context updating and in response to unexpected performance feedback its amplitude reflects the depth of processing of task-relevant stimuli and subsequent updating of the context (de Bruijn et al., 2004, 2006). Yet it is still unknown if this form of external feedback processing is (1) affected in schizophrenia and (2) whether it is trait or state dependent.

The current study aimed at investigating the state and trait dependency of both internal and external performance monitoring in schizophrenia by examining the effects of treatment on the response-locked Ne/ERN and the feedback-locked P300. The relation between the ERP components and behavior was examined by analyzing efficient behavioral adjustments following both response errors and slow response-timing feedback. With regard to internal performance monitoring, we expected to find reduced Ne/ERN amplitudes in patients with schizophrenia compared to healthy controls before and after treatment. Based on the findings by Bates et al. (2004) an increase in ERN amplitude was also expected in the patient group from the first to the second session. This increase was also hypothesized to be reflected in improved behavioral adjustments following response errors. To investigate external performance monitoring, feedback was provided on a trial-to-trial basis informing participants on the correctness of their response, i.e. whether the chosen button was correct or incorrect and whether the response was given on time or not (e.g. De Bruijn et al., 2006). As slow responses are usually difficult to detect at the moment of response onset and are thus associated with increased uncertainty, people need to rely on external feedback to inform them whether the response was on time or not. Indeed, ERPs to negative feedback signaling slow response times are known to elicit a large P300 that is related to the attribution of more meaning to such feedback. Results from a study by De Bruijn et al. (2004) showed that those participants, who made use of unexpected but task-relevant feedback to improve performance by adequately adapting their behavior, were also characterized by larger P300 amplitudes. We expected to find reduced P300 amplitudes in the patient group compared to healthy controls before treatment. Based on the previous work demonstrating the state dependency of the P300 in oddball paradigms (Higashima et al., 2003; Mathalon et al., 2000; Park et al., 2010; Mori et al., 2012), a treatment-induced increase in feedback-locked P300 amplitudes and improved behavioral adaptations were expected for schizophrenia patients.

2. Methods and materials

2.1. Subjects

Twelve patients (11 males; mean age 31.1 years, SD = 11.3) and twelve healthy controls (7 males; mean age 28.0 years, SD = 8.8) participated in the study. Patients with a DSM-IV-TR diagnosis of schizophrenia, as assessed by a semi-structured interview, were included. The patients were recruited in a tertiary psychiatric hospital (St-Norbertushospital, Duffel, Belgium). Patients were excluded on the basis of the following physical, mental, and behavioral criteria. Patients with a concurrent