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Action monitoring in major depressive disorder with psychomotor retardation

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ABSTRACT

Major depressive disorder (MDD) is characterized by disturbances of mood and affect, but also by a distinct pattern of psychomotor and cognitive deficits such as motor retardation and impaired executive functioning. An important aspect of executive functioning is performance monitoring, i.e., a continuous checking whether intended action goals have been reached and whether correction of the applied strategy is necessary. A well-known marker for action monitoring is the error negativity (Ne) or error-related negativity (ERN), an event-related potential (ERP) component generated in the anterior cingulate cortex (ACC) following erroneous responses. To date, Ne/ERN amplitudes have been investigated in moderately depressed patients only. The present study is the first to investigate action monitoring in severely depressed patients (mean Hamilton score = 28.4). In addition, the patients' psychomotor performance was assessed to see whether there is a relationship between action monitoring and psychomotor retardation.

Behavioural and ERP measurements were obtained during performance on a speeded two-choice reaction task in 26 patients with MDD and 25 healthy, matched controls. Psychomotor performance measures were speed of simple movements in various psychomotor tasks and the score on the Salpêtrière retardation rating scale (SRRS).

Relative to the controls, the patients' behavioural results revealed a similar, but slower performance pattern. Overall between-group differences were demonstrated for the error positivity (Pe) amplitudes, but not for the Ne/ERN amplitudes. However, correlations of the Ne/ERN amplitude with several psychomotor variables were strong. In the depressed patients taking benzodiazepines an additional attenuation of Ne/ERN amplitudes was observed.

Only severely depressed patients manifesting retardation showed impeded action monitoring. The correlations between action monitoring and psychomotor performance indicate that in MDD these two processes are highly interdependent, both being deregulated. Moreover, the same network of brain regions is likely to be implicated in both processes.

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1. Introduction

Major depression is a common psychiatric disorder characterized by disturbances of mood and affect, but also by a substantial and distinct pattern of cognitive and psychomotor impairment (Sobin and Sackeim, 1997; Elliott, 1998; Austin et al., 2001). Manifest psychomotor symptoms (Sobin and Sackeim, 1997) as well as deficits in attention and vigilance, memory and executive functions (Austin et al., 2001) have been frequently reported. The latter functions are important in the planning and execution of complex behaviours, in the monitoring of performance and in the revision of strategies and behaviours that cease to be appropriate (Elliott, 1998).

Several experimental studies and reviews reported on different aspects of executive dysfunction in depression (Austin et al., 2001), but very few studies focused on the process of performance monitoring, an important aspect of cognitive control, which entails a continuous checking whether action goals have been reached and correcting the applied strategy when necessary. It has important implications for daily life functioning (Ullsperger, 2006) and should be seen as a crucial evaluation process to gain optimal action outcome (Carter, 2001; Ullsperger, 2006). Performance monitoring has hence become the focus of several recent cognitive studies in different psychiatric disorders such as schizophrenia, anorexia nervosa, obsessive–compulsive disorder, and borderline personality disorder (Gehring et al., 2000; Bates et al., 2004; De Bruijn et al., 2006a; Ullsperger, 2006).

Action monitoring is reflected in behavioural adjustments after an error has been made and occurs in contextual feedback evaluation or in situations in which action outcome is at risk (Ullsperger, 2006). On a neurophysiological level, the error negativity (Ne) or error-related negativity (ERN), an event-related potential (ERP) component associated with error or conflict detection, reflects the process of action monitoring. The integrity of the process can be investigated during speeded choice reaction tasks where an Ne/ERN is elicited when prepotent but incorrect responses are given. It shows a negative peak about 50–100 msec after the erroneous response and has a frontocentral scalp distribution (Falkenstein et al., 1990; Gehring et al., 1993). The Ne/ERN is followed by the error positivity (Pe), a slow positive wave with a more posterior scalp distribution, elicited 200–400 msec after response onset (Falkenstein et al., 1991). Besides the Ne/ERN, a feedback Ne/ERN, i.e., an Ne/ERN-like component following negative feedback, has also been reported (Holroyd and Coles, 2002).

By means of several source localisation and functional magnetic resonance imaging (fMRI) studies, the Ne/ERN is known to be generated in the anterior cingulate cortex (ACC; Dehaene et al., 1994; Ullsperger and von Cramon, 2001), and more specifically in the rostral cingulate zone (RCZ; Ullsperger and von Cramon, 2006).

Recent neurobiological models of depression have highlighted the role of the ACC in the pathogenesis of depression and in the manifestation of its symptomatology (Ebert and Ebmeier, 1996; Mayberg, 1997; Drevets, 2001; Davidson et al., 2002). Functional imaging studies have repeatedly demonstrated decreased ACC activation in patients with a major depressive episode relative to healthy control subjects (Drevets, 2000; Davidson et al., 2002; Mayberg, 2003). Moreover, various reports mention an association between psychomotor slowing in depression and decreased regional cerebral bloodflow in the dorsolateral prefrontal cortex (DLPFC), angular gyrus, paralimbic and supraorbital areas as well as in the ACC (Bench et al., 1993; Dolan et al., 1994; Mayberg et al., 1994; Videbech et al., 2002; Narita et al., 2004).

Three studies were published on the response of Ne/ERN in major depressive disorder (MDD) (Ruchsow et al., 2004, 2006; Chiu and Deldin, 2007). While Ruchsow et al. (2004, 2006) found no overall differences in response of ERN components between depressed patients and healthy controls, Chiu and Deldin (2007) reported greater ERN amplitudes but equivalent Pe amplitudes in the patient group. However, it should be noted that the patients in these studies were all moderately depressed.

In the present study, we investigated the process of action monitoring in MDD patients with a current, severe depressive episode by measuring response-Ne/ERN amplitudes during the execution of a classical Flankers task. We further assessed psychomotor performance to explore the relationship between action monitoring and psychomotor retardation and examined the response-locked Pe and stimulus-locked N1 and N2 to obtain a complete picture of the processes involved. We hypothesized that, compared to healthy controls, patients with MDD would show reduced action monitoring as reflected in reduced Ne/ERN amplitudes, and that this reduction would be greater in patients demonstrating psychomotor slowing.

2. Methods

2.1. Subjects

Participants were 26 patients with unipolar MDD and 25 healthy controls matched for sex, age and education (see Table 1). The patients were recruited from four Belgian psychiatric in- and outpatient clinics and all had a DSM-IV-TR diagnosis of a major depressive (single or recurrent) episode, and a minimum score of 18 on the Hamilton Depression Rating Scale (HDRS); 11 had melancholic and 1 had psychotic features. Patients with concurrent diagnoses of schizophrenia,

Table 1 – Demographic and clinical variables of the patients with MDD and the healthy controls

	MDD group	Control group
N	26	25
Sex (male/female)	5 (19.2%)/21 (80.8%)	6 (24%)/19 (76%)
Age in years	39.76 (11.38)	37.24 (11.51)
Education[a]	2.04	2.36
HDRS total score	28.42 (5.37)	/
BDI-II total score	41.09 (11.61)	2.14 (2.47)
SRRS total score	24.04 (10.58)	/

Standard deviations are given in parentheses.
HDRS: Hamilton depression rating scale; BDI-II: Beck depression inventory; SRRS: Salpêtrière retardation rating scale.
a 1 = low, 2 = average, 3 = high level of education.