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Local contextual processing in major depressive disorder

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HIGHLIGHTS

- Reaction times and P3b latencies of predicted targets were prolonged in depression.
- P3b amplitudes were attenuated in major depressive disorder during processing of predictive contextual information, as well as target N1 amplitudes.
- Processing of local contextual processing is altered in major depressive disorder.

ABSTRACT

Objective: The study investigated local contextual processing in patients with major depressive disorder (MDD). This was defined as the ability to utilize predictive contextual information to facilitate detection of predictable versus random targets.
Method: We recorded EEG in 15 MDD patients and 14 age-matched controls. Recording blocks consisted of targets preceded by randomized sequences of standards and by sequences of standards that included a predictive sequence signaling the occurrence of a subsequent target event.
Results: Both MDD patients and age-matched controls demonstrated a significant reaction time (RT) and P3b latency differences between predicted and random targets. However, patients demonstrated a specific prolongation of these measures during processing of predicted targets, as well as an attenuation of P3b amplitudes for the predictive sequence. In addition, patients target N1 amplitudes were attenuated compared with controls.
Conclusion: MDD patients were able to utilize predictive context in order to facilitate processing of deterministic targets, however, this ability was limited compared to controls, as demonstrated by context-dependent P3b deficits.
Significance: These findings suggest that patients with major depression have altered processing of local contextual processing.

1. Introduction

Contextual processing is considered to be an executive function and a subcomponent of working memory (Cohen and Servan-Schreiber, 1992; Barch et al., 2001). Processing of goal-directed contextual information is essential for the selection of appropriate task behavior and facilitates the detection of task-relevant stimuli (Fogelson et al., 2009b).

Major depressive disorder (MDD) is the most prevalent of all psychiatric disorders and is characterized by a wide range of behavioral, emotional and cognitive symptoms (reviewed by Gotlib and Joormann, 2010; Marazziti et al., 2010; Murrough et al., 2011). Performance on measures of executive function tend to be impaired in depressed patients, and working memory deficits are common (Pelosi et al., 2000; Rose and Ebmeier, 2006; Segrave et al., 2010; Marazziti et al., 2010; Sato et al., 2011) and associated with impairments in attentional control (Pelosi et al., 2000; Rose and Ebmeier, 2006; Segrave et al., 2010; Gotlib and Joormann, 2010; Murrough et al., 2011). However, other studies have demonstrated that there are no impairments in working memory functions in patients with depression (Barch et al., 2003; Holmes et al., 2005).

One measure that has been linked to contextual processing is the event related potential (ERP) called the P300 (Squires et al.,

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1976; Donchin and Coles, 1988). The target P300, known as the P3b, is elicited, among other tasks, by targets in the classical oddball paradigm and has a posterior-parietal scalp distribution (Squires et al., 1975). P3b is thought to be a measure of the evaluation of environmental signals including contextual information (Squires et al., 1976; Donchin and Coles 1988) and is also thought to reflect monitoring processes mediating perceptual analysis and response initiation (Verleger et al. 2005). Findings of P300 abnormalities in patients with depression are inconsistent. Although there is a general trend for patients with depression to show P3b amplitude reductions (Roth et al., 1981; Pfefferbaum et al., 1984; Vandoolaeghe et al., 1998; Urretavizcaya et al., 2003; Campanella et al., 2012), these findings depend on stimulus modality (auditory versus visual), the complexity of the paradigm (oddball versus more cognitively demanding tasks) and on the subtype and severity of the symptoms (e.g., reviewed in Bruder et al., 2012). Studies utilizing more cognitively demanding tasks tend to show more consistent reductions in P3b amplitudes in patients with depression (Bruder et al., 2012).

In the present study, we focus on the ability to process goal-relevant local contextual information. Previous studies have shown that P3b is modulated as a function of local predictive context (Fogelson et al., 2009a,b, 2010). In these studies, targets were preceded by either randomized sequences of standards or by sequences including a predictive sequence, signaling the occurrence of a subsequent target event. Two main neural correlates of contextual processing were identified. First, a facilitated processing of predicted targets was observed, as indicated by faster P3b latencies and reaction times for predicted targets compared with random ones. Second, local contextual processing was associated with the generation of a robust P3b to the final most-informative stimulus of the predicting sequence. Local contextual processing has been shown to be altered by aging (Fogelson et al., 2010) and impaired in patients with lateral prefrontal cortex lesions (Fogelson et al., 2009a), Parkinson's disease (Fogelson et al., 2011a) and schizophrenia (Fogelson et al., 2011b), demonstrating specific alterations in the behavioral measures and neural correlates of local contextual processing in each patient population.

It remains inconclusive whether patients with depression have working memory impairments. Thus, the objective of the current study was to investigate whether patients with major depressive disorder are impaired in their ability to process contextual information, an important subcomponent of working memory, utilizing the previously described paradigm (Fogelson et al., 2009a, 2010, 2011a,b). We evaluated neural correlates of contextual processing based on both behavioral and ERP measures to determine whether a more cognitively demanding version of the oddball task will induce changes in performance in patients compared with controls. Our hypothesis was that if patients with major depression do have contextual processing deficits, we should observe alterations in the behavioral and electrophysiological indices of local contextual processing.

2. Methods

2.1. Participants

15 MDD patients (mean age ± standard error of the mean = 43 ± 4 years, 9 females) and 14 age-matched controls (mean age = 43 ± 4 years, 8 females) participated in the study. Patients were diagnosed with MDD according to DMS-IV-Tr criteria, and were rated for symptom severity using the Hamilton Rating Scale for Primary Depressive Illness (HRSD, Hamilton, 1960). Subjects with past history of neurologic disorders, drug or alcohol abuse were excluded. Mean illness duration was 3 ± 1 years. Mean HRSD scores were 30.2 ± 2.5. Demographics and clinical details of the patients are shown in Table 1. All patients had normal or corrected-to-normal visual acuity. All patients were hospitalized at the time of the experiment due to an episode of major depression and took their regular medications on the day the recordings. Most patients were medicated with a selective serotonin reuptake inhibitor (SSRI), some patients were treated with a mood stabilizer and benzodiazepine. Medication dosages were within regular therapeutic levels, achieving average therapeutic dosage based on blood levels.

Patients were matched by controls for age, gender and education (mean = 14.6 ± .5 and 14.4 ± 1 years of education for MDD and controls, respectively). Age-matched controls had normal or corrected-to-normal visual acuity and had no history of psychiatric or neurological problems. All the subjects were right handed as indicated by self-report. The experimental procedures were approved by the local ethics committees. Written informed consent was obtained from all subjects participating in the study following a complete explanation of the study and procedures.

2.2. Procedure

Subjects were seated 110 cm in-front of a 21-inch PC-computer screen. Stimuli were presented to either the left or right visual field 6° from a central point of fixation. The stimuli consisted of black triangles on a gray background. Subjects were asked to centrally

Table 1
Clinical details of patients with major depression.

Patient (sex)	Disease duration (years)	Diagnosis	HRSD	Medication
1 (F)	1	Major depression	21	Mirtazapine
2 (F)	2	Major depression	26	Lithium
3 (F)	5	Major depression	38	Venalafaxine carbamazepine clonazepam risperidone
4 (F)	1	Major depression	18	Escitalopram
5 (F)	1	Major depression	27	sertraline qutiapin clonazepam
6 (F)	1	Major depression + borderline personality disorder	19	Paroxetine
7 (F)	3	Depression + anxiety	26	Lithium
8 (M)	5	Major depression	17	Qutiapin lithium mirtazapine
9 (M)	1	Major depression + anorexia	27	Venalafaxine mirtazapine
10 (F)	10	Major depression	44	Fluoxetine
11 (M)	10	Major depression	33	Escitalopram
12 (M)	7	Major depression	34	Escitalopram
13 (M)	0.5	Major depression	43	Fluoxetine
14 (F)	1	Major depression	45	Fluvoxamine zolpidem lithium
15 (M)	1.5	Major depression	35	Escitalopram

HRSD, Hamilton rating scale for primary depressive illness (Hamilton, 1960).