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Research report

Natural speech comprehension in bipolar disorders: An event-related brain potential study among manic patients

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ABSTRACT

Background: Thought and language disturbances are crucial clinical features in Bipolar Disorders (BD), and constitute a fundamental basis for social cognition. In BD, clinical manifestations such as disorganization and formal thought disorders may play a role in communication disturbances. However, only few studies have explored language disturbances in BD at a neurophysiological level. Two main Event-Related brain Potentials (ERPs) have been used in language comprehension research: the N400 component, elicited by incongruous word with the preceding semantic context, and the Late Positive Component (LPC), associated with non-specifically semantic and more general cognitive processes. Previous studies provided contradictory results regarding N400 in mood disorders, showing either preserved N400 in depression or dysthymia, or altered N400 in BD during semantic priming paradigm. The aim of our study was to explore N400 and LPC among patients with BD in natural speech conditions.
Methods: ERPs from 19 bipolar type I patients with manic or hypomanic symptomatology and 19 healthy controls were recorded. Participants were asked to listen to congruous and incongruous complete sentences and to judge the match between the final word and the sentence context. Behavioral results and ERPs data were analyzed.
Results: At the behavioral level, patients with BD show worst performances than healthy participants. At the electrophysiological level, our results show preserved N400 component in BD. LPC elicited under natural speech conditions shows preserved amplitude but delayed latency in difference waves.
Limitations: Small size of samples, absence of schizophrenic group and medication status.
Conclusions: In contrast with the only previous N400 study in BD that uses written semantic priming, our results show a preserved N400 component in ecological and natural speech conditions among patients with BD. Possible implications in terms of clinical specificity are discussed.

1. Background

Language and speech skills are widely involved in daily-life situations for patients suffering from Bipolar Disorders (BD). They constitute a fundamental basis for social cognition and a crucial condition for accessibility to psychotherapy. In BD, clinical manifestations such as disorganization and Formal Thought Disorders (FTD) may play a role in communication disturbances. A growing body of evidence from clinical and cognitive studies tends to go against the classical distinction between schizophrenic disorganization and cognitively preserved BD (Goodwin and Jamison, 2007; Piguet et al., 2010; Cuesta and Peralta, 2011).

At a clinical level, FTD in affective disorders are typically described in patients with BD, even if their temporal evolution appears less stable than it does for FTD in schizophrenia (Andreasen, 1979; 1986; Harvey et al., 1984). Several thought and language disorders are considered core features of mania including flight of ideas; pressed to incoherent speech; racing, loose or tangential thoughts (DSM IV-TR, APA, 2000); being more talkative than usual; or pressure to keep talking (DSM 5, APA, 2013). Numerous recent studies have detailed clinical manifestations of

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bipolar disorganization (Serretti et al., 2002; Rossi and Daneluzzo, 2002; Schürhoff et al., 2005; Cuesta and Peralta, 2011).

At a neuropsychological level, language skills involve non-linguistic cognitive processes such as working memory, declarative memory, attention and executive functions, which are known to be disturbed in BD (Quraishi and Frangou, 2002; Bora et al., 2010; Aminoff et al., 2013). FTD among patients with BD have been associated with non-linguistic cognitive impairments during manic states (Robinson et al., 2006; Arts et al., 2008; Delaloye et al., 2009; Schouws et al., 2009; Radanovic et al., 2013). Moreover, general cognitive disturbances with moderate severity have also been found among bipolar patients during euthymia (Robinson et al., 2006; Arts et al., 2008; Delaloye et al., 2009) and among non-bipolar people with familial risk (Quraishi and Frangou, 2002; Balanzá-Martínez et al., 2008; Ivleva et al., 2009).

Though non-linguistic cognitive performances have been extensively explored, only a few studies specifically focus on language issues in BD (Goodwin and Jamison, 2007; Cuesta and Peralta, 2011; Radanovic et al., 2013; Wang et al., 2011). At a behavioral level, patients with BD exhibit impaired performances in denomination tasks (Burt et al., 2000; Radanovic et al., 2013), in sentence completion task (Wang et al., 2011) and during semantic priming (Andreou et al., 2013). However, behavioral examination of bipolar patients does not allow us to precisely characterize the nature of neurolinguistics disturbances because these remain intertwined with non-linguistic cognitive processes (Wang et al., 2011).

Little is known about language disturbances in BD at a neurophysiological level, in contrast with what is known about such disturbances in schizophrenia. Event-Related brain Potentials (ERPs) and, in particular, the N400 component have been extensively used to explore the time course of language comprehension among healthy participants (Kutas and Federmeier, 2011) and people with schizophrenia (Kuperberg et al., 2010). The N400 component is one of the most explored ERPs in neurolinguistics. This negativity is observed with both visual and auditory linguistic stimuli (Kutas and Hillyard, 1980). Importantly, the N400 component is classically elicited by words unexpected or incongruous given the preceding semantic context because its amplitude is inversely correlated to word expectancy or semantic congruity (Kutas and Federmeier, 2011). The semantic context can classically consist of either pairs of words (semantic priming) or complete sentences. While most N400 studies have been conducted in the visual modality, a few experiments have used connected speech (i.e., complete sentences auditorily presented) (Connolly et al., 1990; Connolly and Phillips, 1994). Interestingly, the N400 effect (i.e., the difference wave between the N400s obtained from semantically incongruous and congruous words) typically develops earlier in natural speech (Holcomb and Neville, 1990, 1991; Besson et al., 1997; Hagoort and Brown, 2000).

The N400 component is typically followed by a positive component. This Late Positive Complex (LPC) was first associated with syntactic processing (Osterhout and Holcomb, 1992; Hagoort et al., 1993), but the LPC also reflects non-specific and non-linguistic cognitive processes such as the updating of mental representations or wrap-ups effects (Coulson et al., 1998; Osterhout and Hagoort, 1999; Kaan et al., 2000; Kim and Osterhout, 2005; Kuperberg et al., 2007).

An extensive literature on ERPs has provided evidence of a disturbed semantic processing in schizophrenia with a reduced N400 effect. This reduction has been shown during automatic or controlled cognitive tasks and, particularly, among patients suffering from formal thought disorders (for reviews, see Kuperberg et al., 2010; Wang et al., 2011). N400 is classically interpreted as involving automatic cognitive processes during word-pair paradigms with short Stimulus Onset Asynchrony (SOA $<$ 500 ms). The N400 effect is also reduced in schizophrenia when whole sentences or pairs of words with longer SOA ($>$ 500 ms) are presented; such cases are associated with more controlled cognitive processes (Kreher et al., 2008; Kiang et al., 2008; Kuperberg et al., 2010; Ditman and Kuperberg, 2010). Although most studies focus on N400 amplitude, delayed N400 (Kuperberg et al., 2006; Niznikiewicz et al., 2010), LPC latencies (Iakimova et al., 2005), and reduced LPC amplitude (Ruchsow et al., 2003; Iakimova et al., 2005; Kuperberg et al., 2006) can be observed in schizophrenia.

Regarding mood disorders, only two studies have examined the N400 component among patients with major depression or dysthymia. The results failed to show N400 amplitude alterations using a visually presented sentence context (Deldin et al., 2006; Iakimova et al., 2009). Moreover, only one recent study explored the N400 component among patients with acute mania, in comparison with patients with schizophrenia and healthy controls (Ryu et al., 2012). The results revealed a larger N400 amplitude for congruous words and a consequently reduced N400 effect in patients with BD when compared to healthy controls. This study relied on visually presented word pairs with a short SOA (325 ms) and thus explored semantic priming in only automatic and non-ecological conditions.

To the best of our knowledge, there is no data about the N400 component or LPC among patients with BD in natural speech conditions. The aim of the present study was to examine N400 and LPC during speech comprehension among participants with BD during mania to validate one of two competing hypotheses. On the one hand, patients with BD may present altered N400 and LPC amplitudes (*alteration hypothesis*) because (1) phenomenological manifestations of thought disorders are typically observed in manic patients (Goodwin and Jamison, 2007), (2) altered semantic priming occurs in remitted patients with BD at a behavioral level (Andreou et al., 2013), and (3) alteration of automatic semantic processing is observed in manic patients (Ryu et al., 2012). On the other hand, one may expect preserved N400 and LPC amplitudes in BD during natural speech comprehension (*preservation hypothesis*), supporting previous results on the comprehension of read sentences among patients with other mood disorders such as major depression and dysthymia (Deldin et al., 2006; Iakimova et al., 2009).

2. Methods

2.1. Participants

A total of 38 participants, including 19 bipolar type I patients and 19 healthy comparison subjects, were enrolled in this study. In the BD group, both inpatients ($n=10$) and outpatients ($n=9$) were recruited from the Marseille University Department of Psychiatry while presenting a mild to severe manic episode. Diagnoses of type I Bipolar Disorder (BD) were performed according to the DSM IV-TR criteria (American Psychiatric Association, 2000) using the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998). For bipolar patients, exclusion criteria were schizoaffective disorder, substance use disorder or any other axis I diagnosis, history of neurological disorder or head injury, electroconvulsive therapy during the preceding six months, and impaired or non-French native language. Healthy Subjects (HS) were recruited from the same local community as the patients, either via an announcement in local newspapers or from technical staff of the hospital institution. They were selected for matched age and gender with the BD patients and were given a small payment for participating. The exclusion criteria for HS were neurological or axis I psychiatric disorders, impaired hearing or non-French native language. Absence of a psychiatric history was confirmed by the MINI structured interview (Sheehan et al., 1998). For both BD and