Journal of Affective Disorders 201 (2016) 101–111

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

P600 alteration of syntactic language processing in patients with bipolar mania: Comparison to schizophrenic patients and healthy subjects

Chang Woo Lee [a,1], Sung Hwa Kim [b,1], Miseon Shim [c], Vin Ryu [d], Ra Yeon Ha [e], Su Jin Lee [f], Hyun-Sang Cho [f,g,*]

[a] Department of Psychiatry, Jin Hospital, Bucheon, Republic of Korea
[b] Department of Psychiatry, Hallym University College of Medicine, Hwaseong, Republic of Korea
[c] Department of Biomedical Engineering, Hanyang University, Seoul, Republic of Korea
[d] Department of Psychiatry, Seoul National Hospital, Seoul, Republic of Korea
[e] Department of Psychiatry, Seoul Bukbu Hospital, Seoul, Republic of Korea
[f] Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea
[g] Department of Psychiatry, Yonsei University College of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Received 25 November 2015
Received in revised form
5 April 2016
Accepted 9 May 2016
Available online 10 May 2016

Keywords:
Bipolar mania
Schizophrenia
P600
Event-related potential
Syntactic processing

ABSTRACT

Background: Disturbances in thought, speech, and linguistic processing are frequently observed in bipolar manic patients, but the underlying neurophysiological mechanisms are not well understood. P600 is a distinct, positive event-related potential component elicited by syntactic violations. Using the P600 ERP, we examined neural processing of syntactic language comprehension in patients with bipolar mania compared to patients with schizophrenia and healthy people.

Method: P600s were recorded from 21 manic patients with bipolar disorder, 26 patients with schizophrenia, and 29 healthy subjects during the presentation of 120 auditory sentences with syntactic violations or non-violations. Subjects were asked to judge whether each sentence was correct or incorrect.

Results: Patients with mania and schizophrenia had significantly smaller P600 amplitudes associated with syntactic violations compared with healthy subjects. There was no difference in P600 amplitude between patient groups. For behavioral performance, patients with schizophrenia had significantly less accurate rates and longer reaction times compared with healthy subjects, whereas manic patients exhibited no significant differences in accuracy and only showed increased reaction times in comparison with healthy subjects.

Limitations: Psychotropic drug usage and small sample size.

Conclusion: Patients with bipolar mania have reduced P600 amplitude, comparable to patients with schizophrenia. Our findings may represent the first neurophysiological evidence of abnormal syntactic linguistic processing in bipolar mania.

1. Background

Studies have found that patients with mania and schizophrenia exhibit more communicational and grammatical errors in language processing or pattern compared with healthy individuals (Docherty et al., 1996; Harvey and Brault, 1986). Although quantitative differences in formal thought or language pathology may not exist between manic and schizophrenic patients, qualitative differences exist (Goodwin and Jamison, 2007). For example, in a recent investigation of linguistic ability in Italian speakers with bipolar disorder and schizophrenia, patients with schizophrenia had more pervasive linguistic deficits than those with bipolar disorder, although there were several similarities in the grammatical errors in syntactic (i.e., the way in which words are combined grammatically to make meaningful phrases or sentences) (Kircher et al., 2005) comprehension between the two groups (Perlini et al., 2012). While there is some descriptive understanding of language comprehension in manic patients, neural investigation into manic languages has been scarce. Few studies report the electrophysiological characteristics of linguistic processing especially in manic patients.

Electrophysiological tools for detecting event-related potentials (ERPs) hold great promise for examining the neural processes of

* Corresponding author at: Department of Psychiatry, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea.
E-mail address: chs0225@yuhs.ac (H.-S. Cho).
[1] These authors contributed equally to this study as first authors.

http://dx.doi.org/10.1016/j.jad.2016.05.008
0165-0327/

language comprehension at resolutions in the order of milliseconds (Ainsworth-Darnell et al., 1998). The best studied ERPs associated with language comprehension are the N400 and the P600 (Luck, 2014). N400 is a negative-going wave with peak amplitudes approximately 400 ms in response to violations of semantic expectancies (e.g., "I had lunch with several old shirts") (Luck, 2014). Osterhout and Holcomb have reported that syntactic violations (e. g., "John forced the man was lying") elicit the appearance of a distinct component of ERPs called P600 (Osterhout, 1997; Osterhout and Holcomb, 1992). More recent studies have reported that syntactic processes are associated with not only P600 but also an early left anterior negativity (ELAN), which is observed between 100 and 200 ms (Friederici, 2004). Unlike P600, an ELAN is particularly associated with the violation of phrase structure; thus, it might reflect first-pass parsing processes to build the initial structure of the sentence (Friederici, 2004). P600 is a large-amplitude, late-emerging, centro-parietal positive wave, occurring around 600–1000 ms (Friederici, 2002; Osterhout and Holcomb, 1995). It is thought to reflect a second-pass attempt to understand a sentence (Kuperberg, 2007). The P600 has been linked to various syntactic violations, including violations of verb-noun number agreement (e.g., "The spoiled child throw the toy on the ground") (Hagoort et al., 1993), gender agreement (e.g., "The woman congratulated himself") (Gunter et al., 2000), subjacency (e.g., "What was a picture of printed by the newspaper? ") (Neville et al., 1991), and phrase structure (e. g., "John discovered Bob's of pictures the suspect") (Friederici and Meyer, 2004; Neville et al., 1991). The P600 is also associated with grammatically correct, but temporally ambiguous structures in garden path sentences (e.g., "The broker persuaded to sell the stock was sent to jail") (Osterhout and Holcomb, 1992), and with difficulties in the integration of sentences (i.e., "who" questions relative to "whether" ones) (Friederici, 2004). Thus, the P600 is widely considered to be an indicator of syntactic operations involving structural repair, reanalysis, and integration (Friederici, 2002; Gouvea et al., 2010). In addition to language-related syntactic processing, the functional interpretations of P600 are still debated in terms of the general processing of context updating (Osterhout, 1999), the interaction of syntactic and prosodic information (Eckstein and Friederici, 2005), and non-specific sentence integration (Kaan et al., 2000) including sentence wrap-up processes associated with final words (Cowles et al., 2007; Kuperberg et al., 2006a).

The majority of ERP studies on sentence processes have been conducted in the visual modality (Osterhout et al., 2004). When controlling of visual presentation rate to the normal reading speed, there was a similar P600 effect for the visual and the auditory modalities (Hagoort and Brown, 2000). However, it is difficult to match the on-line characteristics of normal sentence processing when using visual presentation (Hagoort and Brown, 2000; Kerkhofs et al., 2008). Thus, we decided to use auditory presentation as it could provide a natural rate more easily than visual presentation.

Many studies have focused on the linguistic characteristics of patients with schizophrenia and their neural underpinnings. Patients with schizophrenia exhibit deficits in both the comprehension (Bagner et al., 2003) and production (Tavano et al., 2008) of syntactically complex sentences. Such deficits of syntactic comprehension are related to the working memory capacity for reading and/or listening (Bagner et al., 2003; Condray et al., 1996). Using ERPs, schizophrenic patients have abnormally diminished P600 amplitudes associated with morphosyntactic violations (e.g., "For breakfast, the boys would eats toast and jam") (Kuperberg et al., 2006b). In patients with schizophrenia, the P600 elicited by syntactic violations of phrase structure does not differ from that elicited by non-violations; however, healthy subjects have more positive amplitudes of the P600 component in the syntactic violations versus non-violations (Ruchsow et al., 2003). This absence of the P600 syntactic mismatch effect in syntactic violations suggests that patients with schizophrenia fail to incur later integration processing (Ruchsow et al., 2003). In bipolar disorder, only one recent study has examined the late positive complex (LPC, ranging from 450 to 800 ms), in which manic patients were required to judge congruency between the final word of a sentence and sentence context (Cermolacce et al., 2014). The results showed preserved amplitudes of LPC and N400 in manic patients.

A previous study explored P600 in mania (Cermolacce et al., 2014), but they used semantic stimuli. We think that observing P600 elicited by syntactic violation is important, because syntactic P600 is assumed to be independent of the task and seems to be more robust than semantic P600 (Schacht et al., 2010, 2014). We hypothesized that because patients with bipolar mania and schizophrenia share considerable deficits in syntactic performance at clinical and behavioral levels, manic patients would show reduced P600 responses comparable to patients with schizophrenia when applying a more sensitive method, elicited by syntactic violation. Therefore, we hypothesized that both patient groups would have attenuated P600 amplitudes when compared to healthy controls. We also investigated the relationship between P600 amplitude and clinical characteristics, measured via BPRS and YMRS.

2. Methods

2.1. Subjects

Subjects in two patient groups (bipolar mania, n=21; schizophrenia, n=26) were diagnosed by two psychiatrists based on clinical interviews and criteria described in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) (American Psychiatric Association, 2000). Diagnoses of bipolar I disorder and schizophrenia were confirmed using the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) by two qualified psychiatrists (C.W.L and S.H.K). Subjects were recruited from outpatient and inpatient units at Severance Mental Health Hospital in the Yonsei University Health System. Patients with schizoaffective disorder, severe personality disorder, recent substance abuse, a history of head trauma, or other Axis I disorders were excluded. Twenty-nine healthy control subjects were recruited from the local community via website advertisements. Control subjects were screened using the MINI by psychiatrists (C.W.L and S.H.K) to exclude those with neurological and major psychiatric disease. This study was approved by the Institutional Review Board of Severance Mental Health Hospital and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all subjects.

Intelligence quotient (IQ) was assessed using a short form of the Korean Wechsler Adult Intelligence Scale (K-WAIS), comprised of three sub-tests on "information", "digit span", and "picture completion". Mood status of the bipolar patients was measured by the Young's Mania Rating Scale (YMRS) (Young et al., 1978) and the Montgomery-Åsberg Depression Rating Scale (MADRS) (Asberg et al., 1978). The Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) was used to evaluate general psychopathology in patients with bipolar disorder and schizophrenia. The BPRS was divided into five subscales according to previous study (Shafer, 2005), including affect, positive symptoms, negative symptoms, resistance, and activation.

Demographical data and the clinical characteristics of the two patient groups and the control group are summarized in Table 1. The symptom severity ratings of the bipolar patients (YMRS, Mean=14.5, SD=6.0) and schizophrenic patients (BPRS, Mean=24.5, SD=13.4) indicated that they were mildly ill (Leucht