



## Brief report

# Behavioral measures and event-related potentials reveal different aspects of sentence processing and comprehension in patients with major depression

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Received 3 July 2007; received in revised form 7 May 2008; accepted 7 May 2008

## Abstract

**Background:** We used the method of event-related potentials (ERPs) during standard semantic judgment task to explore the functional relationship between the deficit in semantic comprehension in women with depression and the potential dysfunction of brain processes mediating language comprehension.

**Method:** Eleven patients with major depression and 13 healthy participants were required to read congruous and incongruous sentences and to judge if they made sense. Accuracy and reaction times for semantic judgment were analyzed conjointly with the latency and the peak amplitudes of N100, P200, N400 and LPC components which were recorded at the final word of correctly judged sentences.

**Results:** Patients were less accurate in semantic judgment in comparison to healthy participants. They exhibited slower reaction times and prolonged latency of the N400 and the LPC. A congruity effect was observed in both groups in P200, N400 and LPC interval. The peak amplitude of the ERP components did not differ between patients and healthy participants. In patients lower accuracy was correlated with more prolonged N400 latency and more negative N400 amplitude for congruous sentence endings. Age correlated with prolonged latency and amplitude reduction of the LPC component.

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*Limitations:* Small number of participants, exclusively female patients.

*Conclusions:* Combined analyses of behavior and ERP measures of semantic processes in depression showed that semantic impairments, motor slowness and a delay in the timing of neural processes which mediate language comprehension might be functionally related and may be influenced by the age of the patients.

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*Keywords:* Major depression; Language; Semantic processing; Sentence comprehension; ERPs; N100; P200; N400; LPC

## 1. Introduction

The study of deficits of language comprehension in patients with major depression and its relation to the underlying neuropathophysiology is of crucial importance to our understanding of the etiology, manifestation and treatment of depression (Austin et al., 2001).

In the present study we used the method of event-related potentials (ERPs) during standard semantic judgment task to explore the functional relationship between the deficit in semantic comprehension in women with major depression and the potential dysfunction of brain processes, which mediate language comprehension.

It is well established that the amplitude of the N400—a negative potential peaking at around 400 ms after the onset of a content word—is sensitive to sentence congruity. Kutas and Hillyard (1980) first observed more negative N400 amplitude to words that were semantically incongruous *versus* congruous with their preceding sentence context, such as to word “socks”, in the sentence, “He spread the warm bread with socks”. By using the N400 sentence congruity paradigm Deldin et al. (2005) showed that patients with severe and acute depression and those with dysthymia exhibited normal sentence processing as indexed by the N400 amplitude during passive sentence reading tasks. This latter result may indicate that the neural generators of the N400 components, mainly located in the temporal cortex and in some portions of the frontal cortex in the left and the right hemisphere (Halgren et al., 2002; Maess et al., 2006), are not impaired in depression. However, several studies have demonstrated that at resting individuals with major depression exhibit abnormal blood flow in a number of brain regions involved in language processing, including prefrontal and temporal cortex (eg. Drevets et al., 1992).

Furthermore, semantic deficits in patients with depression are particularly evident when patients are asked to make decisions on the basis of what they have read or been told. These deficits also appear in standard neuropsychological testing on nearly all tests of verbal abilities (Golinkoff and Sweeney, 1989; Lafont et al., 1998; Fossati et al., 1999; Henry and Crawford, 2005)

including sentence (Braff and Beck, 1974; Braff et al., 1983; Iakimova et al., 2006) and text comprehension (Henderson, 1987), especially when greater cognitive effort or greater depth of processing is required (e.g., Cohen et al., 1982).

Since task instructions and decisions requirements modulate the neural dynamics of language comprehension (see Kuperberg, 2007), we explored whether semantic impairments and potential N400 abnormalities in patients with depression may be particularly evident when patients are required to make an explicit judgment about the sentence congruity. In such judgment tasks, the N400 elicited by incongruous words is followed by a late positive component (LPC) (see Curran et al., 1993) which reflects an extensive integrative semantic reanalysis (see Kuperberg, 2007) and efficient decision-making strategies (Coulson and Kutas, 2001). The neural sources of the LPC engage extensively the prefrontal cortex circuit (Friederici et al., 2003; Kuperberg, 2007). Given that patients with depression exhibit several dysfunctions of frontal lobes (e.g., Drevets et al., 1992), we expected that impaired semantic judgments about the congruity of the sentences, would be related with more abnormalities in ERP components (e.g. N400 and LPC) which underlie language comprehension in patients with depression.

## 2. Methods

### 2.1. Subjects

Eleven right-handed patients whose symptoms met the DSM IV criteria for major depression (APA, 1994) were recruited from the psychiatric unit of Versailles Hospital. Clinical symptoms were evaluated by the Hamilton Depression Rating Scale (HDRS, Hamilton 1967) and the Salpêtrière Retardation Rating Scale (Widlöcher, 1983; Dantchev and Widlocher, 1998). All patients were taking stable doses of antidepressants, and four patients were also taking anxiolytics.

Thirteen right-handed healthy participants without history of psychiatric disorders (evaluated by the M.I.N.I. DSM IV, Lecrubier et al., 1997) were recruited from the local community. Healthy participants were matched with

the patients on demographic factors: age, education, vocabulary skills (Binois and Pichot, 1959) (see Table 1) and were paid 30.50 Euros (~37 US dollars) for participating. All participants were native French speakers between the ages of 18 and 54 without history of: neurological impairments, epilepsy, alcoholism, or regular drug use. Patients had not undergone electroconvulsive therapy during the preceding 6 months. All participants gave a written, informed consent.

## 2.2. Materials

Three hundred twenty French sentences were used to construct two counterbalanced experimental lists in which 160 sentences ended with a congruous and moderately expected final words (mean cloze probability=0.47%) and 160 sentences ended with an incongruous final words (e.g. congruous: “He’s putting the dominos back in their box”; incongruous: “The road is lit by a lion”). The following characteristics were controlled and did not differ across conditions: sentence length ( $7\pm 2$  words), length ( $5\pm 3$  letters) and frequency of use of the final word (19,722; Brulex, Content et al., 1990).

## 2.3. Procedure

Participants were seated at ~80 cm in front of a computer screen. Sentences were presented visually in four successive blocks. The final word of each sentence was always presented alone at the forth block. Each block was displayed for 200 ms followed by a white screen which was displayed for 350 ms. The next sentence appeared 2200 ms after the end of the preceding one. The participants were instructed to silently read each sentence and to judge whether it made sense or not. They had to respond after the last word of the sentence by pressing a button with their right

hand (left button: “yes” response; the right button: “no” response). A training phase was conducted before the task.

## 2.4. ERP recording and data analysis

Electroencephalogram was recorded with a REEGA 2000 with twelve Ag/AgCl electrodes (10–20 system; Jasper, 1958): F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, T3, T4, Oz. The vertical and horizontal electro-oculogram was recorded with four additional electrodes. Reference electrodes were connected to the ear lobes. All impedances were kept below 1.8 k $\Omega$ . The data were sampled on 512 Hz for 1800 ms beginning 200 ms prior to the onset of the last word in each sentence and digitally filtered offline at a bandwidth of 0.80–12 Hz. Within-subject average of ERP waveforms were computed for each site and sentence-ending type. Single trials exceeding  $\pm 100$   $\mu$ V and those in which incorrect or omitted responses occurred were not included in the average. The data were analyzed by calculating the peak amplitude and latency of the ERP amplitude over four intervals: 0–100 ms (N100), 100–200 ms (P200), 200–450 ms (N400), and 450–700 ms (LPC). The peak amplitude and latency of each ERP component were determined as the data point with the largest positive (P200 and LPC) or negative (N100 and N400) voltage in each time interval.

## 2.5. Statistical analysis

The mean percentage of correct judgments (% CR) and the mean reaction times (RT) for correct judgments were analyzed using two separate repeated measures ANOVAs with “group” “condition” analysis. The peak amplitudes and latencies of each ERP components were analyzed using separate repeated-measures ANOVAs: group condition (i.e., congruous *versus* incongruous) electrode location (frontal, central, parietal) and electrode site (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4). Significant interactions were analyzed with Tukey’s HSD post hoc test. Greenhouse–Geisser corrections were used for all ANOVAs.

Reports on results are restricted to effects involving the effect of “group”, “condition” and their subsequent interactions. The impact of socio-demographical and clinical variables on both ERP and behavioural results were assessed with Pearson correlations.

## 3. Results

### 3.1. Behavioral data

Congruous sentences were judged less accurately than incongruous sentences [condition: ( $F(1.22)=6.41$ ;  $p<.02$ );

Table 1  
Clinical and demographic characteristics (mean $\pm$ SD) of patients and controls

	Patients (n=11)	Controls (n=13)	$p^1$
Age	32 ( $\pm 10.52$ )	31 ( $\pm 9.62$ )	$p<.65$
Education (yrs)	13 ( $\pm 3.27$ )	13 ( $\pm 2.78$ )	$P<.99$
Vocabulary	24 ( $\pm 5.56$ )	27 ( $\pm 3.65$ )	$P<.19$
Previous EDM episodes	2.5 ( $\pm 1.2$ )		
Sex	11 women	10 women	
HDRS 21 items (total score) <sup>2</sup>	25.45 ( $\pm 4.25$ )		
SRRS (total score) <sup>3</sup>	20.54 ( $\pm 5.24$ )		

<sup>1</sup>Patients *versus* Controls.

<sup>2</sup>Hamilton Depression Rating Scale, French adaptation (J.D. Guelfi).

<sup>3</sup>Salpêtrière Retardation rating Scale (SRRS).

mean % CR ( $\pm$ SD): congruous=84,7 ( $\pm$ 9.03) versus incongruous=91.12% ( $\pm$ 13.04)]. Patients were less accurate and had longer reaction time compared to control participants [group effects: accuracy ( $F(1,22)=17.71$ ;  $p<.0004$ ); patients=81.59 ( $\pm$ 16.5) versus controls=94.23 ( $\pm$ 3.4); reaction time ( $F(1,22)=32.57$ ;  $p<.0001$ ); patients=983 ms ( $\pm$ 121) versus controls=718 ms ( $\pm$ 70.5)]. There was no significant interaction between group and sentence type.

### 3.2. Psychophysiological data

#### 3.2.1. Peak amplitude (cf. Fig. 1a and b)

The peak amplitude of the N100 did not differ as a function of the sentence congruity in contrast to the peak amplitude of the other components: In the P200 interval, incongruous sentence endings were associated with more positive peak amplitude than congruous sentence endings over the frontal locations (incongruous=0.83  $\mu$ V versus congruous=0.31  $\mu$ V; “condition” “location” ( $F(2,44)=9.97$ ;  $p<.0002$ ,  $\epsilon=0.28$ ). In the N400 interval, incongruous sentence endings (-1.82  $\mu$ V) were associated with more negative peak amplitude than congruous ones (0.69  $\mu$ V) (condition: ( $F(1,22)=16.91$ ;  $p<.00004$ ,  $\epsilon=1$ )). In the LPC interval, incongruous sentence endings (3.71  $\mu$ V) were associated with more positive peak amplitude than congruous ones (1.77  $\mu$ V) (condition: ( $F(1,22)=12.11$ ;  $p<.002$ ,  $\epsilon=1$ )] (Fig. 1a and b).

Patients exhibited a trend of reduction of the peak amplitude of the N100 component (patients: -0.62  $\mu$ V versus controls: -1.54  $\mu$ V;  $F(1,22)=2.98$ ;  $p=0.09$ ). No other group (P200:  $p=0.11$ ; N400:  $p=0.13$ ; LPC:  $p=0.59$ ), group condition (N100:  $p=0.82$ ; P200:  $p=0.99$ ; N400:  $p=0.70$ ; LPC:  $p=0.66$ ) effects and its subsequent interactions were significant.

#### 3.2.2. Peak latencies measures

The peak latency of the N100 and the P200 did not differ between the two groups. In contrast, patients had a delayed peak of latency of the N400 (patients: 376 ms versus controls: 306 ms) and the LPC (patients: 640 ms versus controls: 520 ms) in comparison to healthy participants.

#### 3.2.3. Correlations

Significant correlations were shown only in patients with depression: Greater age was correlated with a reduced peak amplitude and prolonged latency of the LPC component (peak amplitude: Fz:  $p=.05$ ; Cz:  $p=.06$ ; Pz=.09; peak latency: Fz:  $p=0.02$ ; Cz:  $p=.002$ ; Pz=.004). The percentage of correct semantic

judgments to congruous sentences was correlated with more positive N400 peak amplitude for congruous sentence endings (Fz:  $p=0.02$ ; Cz:  $p=.001$ ; Pz=.001). Slower reaction time for semantic judgments was correlated with reduced LPC amplitude (congruous: Fz:  $p=0.02$ ; Cz:  $p=.03$ ; Pz=.07; incongruous: Fz:  $p=0.002$ ; Cz:  $p=.001$ ; Pz=.002).

## 4. Discussion

Patients with major depression exhibited slower and less accurate sentence comprehension in comparison to healthy participants, consistently with the results from other studies (Braff and Beck, 1974; Braff et al., 1983; Henderson, 1987; Georgieff et al., 1998; Besche et al., 1997; Besche-Richard et al., 2002). The latency of the N400 and the LPC components were also delayed in patients. These results provide evidence that motor slowness may be functionally related to slower timing of neural processes which mediate semantic comprehension. In patients, correctly judged sentences were associated with normal amplitude of the N400 and the LPC components. Incongruous sentence endings elicited larger N400 and LPC amplitudes than congruous ones, consistent with the classical congruity effect (Kutas and Hillyard, 1980). An early congruity effect was observed on the P200 amplitude over frontal electrodes. This effect indicates that prior to final word identification listeners/readers compare incomplete visual information with an expectation derived from the semantic context (Van Petten et al., 1999; Rugg, 1983). Such expectation-based strategy of contextual integration was observed in both patients and controls. Our results replicate those of Deldin et al. (2005) which demonstrated normal N400 amplitude in patients with depression and patients with dysthymic disorder and extended these results on other ERP components (e.g. the P200, the LPC) and on a new explicit semantic judgment task. From these results it would be tempting to conclude that the neural processes which mediate language comprehension are not impaired in patients with depression. However, such conclusion appears to be premature as far as the correlations between ERP and behavior measures are considered. Correlation analysis showed that reduced accuracy of semantic judgments of congruous sentences were associated to enhanced N400 amplitude for these sentence endings and that longer reaction times were associated with reduced LPC amplitude for incongruous sentence endings. These results indicate that more severe semantic impairments (i.e. in terms of accuracy and motor slowness of semantic judgments), might be associated with more

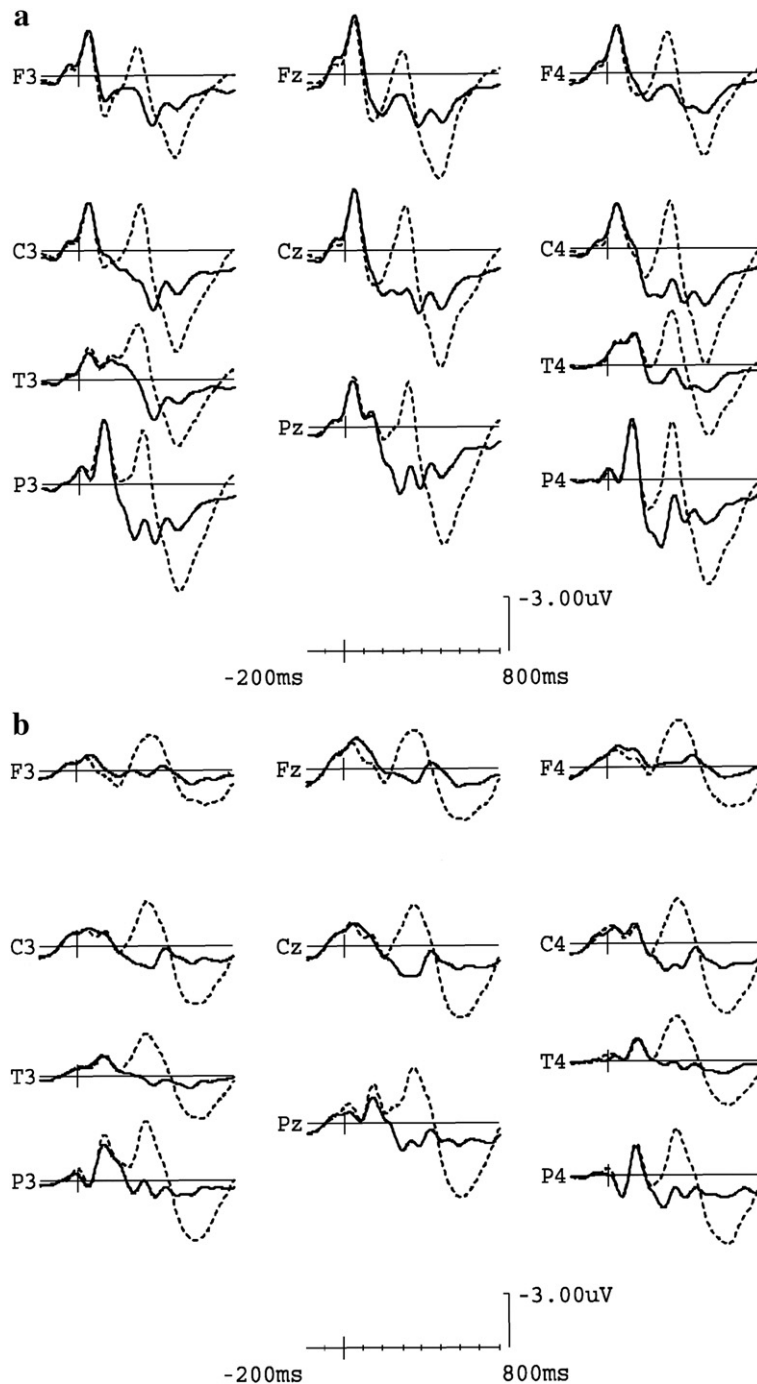


Fig. 1. a. Average ERP waveforms of controls ( $n=13$ ) during processing of correctly judged incongruous (dotted line) and congruous (solid line) sentence endings. b. Average ERP waveforms for patients ( $n=11$ ) during processing of the correctly judged incongruous (dotted line) and congruous (solid line) sentence endings.

abnormalities in the underlying brain processes. Moreover, the patients' age was positively correlated with reduced amplitude and latency delay of the LPC component. This result convey evidence that the stage

of semantic reanalysis and complex integration, which is reflected by the LPC and mediated by the prefrontal cortex (Friederici et al., 2003; Kuperberg, 2007), might be more impaired in aged in comparison of younger patients.



Despite the several limitations of the present study (small number of patients, exclusively women; visual identification of the ERP components), the results indicate that combined analyses of behavior and brain measures of semantic processes may be particularly interesting for studying the impact of the patients' heterogeneity on the cognitive and neural mechanisms associated with depression. Such research may be also useful to explore the neurocognitive mechanisms of cognitive distortions which are commonly cited as one of the major causes for the depression (e.g., Beck et al., 1979). Psychotherapies with patients with depression always involve language comprehension and have high cognitive demands. Behavior and ERP measures of semantic processes might be potentially used to identify patients who may be expected to exhibit positive response on psychotherapies (see Deldin and Chiu, 2005).

#### Role of the funding sources

Findings for the study were provided by the Psychiatric Unit of Versailles's Hospital (Service de Psychiatrie, CH de Versailles, 177 route de Versailles, 78157 Le Chesnay Cedex).

The Psychiatric Unit of Versailles's Hospital had no further role of the study design; in the collection analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

#### Conflict of interest

We confirm that this article is not under simultaneous consideration by any other publication and had never been submitted or published in other journal before. There are no conflicts of interests. All data and images are original. All authors have read and approved the paper.

#### Acknowledgments

We would like to thank Dr. Paul Kretchmer and his colleagues from the San Francisco Edit for the English proofs of the manuscript. Thanks to Dr. Margarita Anastassova for the helpful comments of the article.

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