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N400 anomalies in schizophrenia are correlated with the severity of formal thought disorder

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Abstract

We explored the link between N400 anomalies and clinical profile in schizophrenia patients. N400 was recorded in 50 schizophrenia patients and 40 healthy controls during a lexical decision task with semantic priming. Comparison between controls and schizophrenia patients showed the classical anomalies reported for N400 in schizophrenia patients: greater amplitude for related words and lack of N400 effect. Analyses of the correlations between N400 effect and various symptoms of schizophrenia (formal thought disorder, positive symptoms, negative symptoms, overall symptoms, mean neuroleptic dose) or socioeducational data (age, vocabulary level, number of years of study) revealed that only the correlation with formal thought disorder was significant: the higher the scores for formal thought disorder, the lower the N400 effect observed.

Keywords: Schizophrenia; Thought disorder; N400; Language; Context processing

1. Introduction

Formal thought disorder, or disorganized speech, is one of the central signs of schizophrenia (Andreasen, 2003; Kircher et al., 2003; Kumar and Debruille, 2004). The importance of this disorder has led to intensive efforts to identify the cognitive dysfunctions involved. Although schizophrenia patients display impairment in all aspects of language (De Lisi, 2001), their deficit is generally thought to be due to an anomaly in semantic context processing (Hardy-Baylé et al., 2003; Kerns and Berenbaum, 2003).

Over the last fifteen years or so, a number of studies based on event-related potentials (ERP) have used the N400 paradigm to investigate language processing in schizophrenia. The N400 is a negative component of the ERP with a peak latency almost 400 ms after stimulus presentation that has been associated with language functions (Kutas and Hillyard, 1980). The N400 is elicited in sentence-pro-

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cessing studies and in lexical decision tasks in which context is reduced to the level of the word. The amplitude of the N400 component has been demonstrated to be larger for words preceded by semantically unrelated context than for words preceded by related context at centroparietal scalp sites, and at lateral sites over the right hemisphere than over the left hemisphere (Bentin et al., 1985; Chwilla et al., 1995; Holcomb, 1988). The modulation of N400 amplitude by semantic relatedness is referred to as the N400 effect. It is widely thought that the N400 effect reflects contextual integration processes (Kutas and Federmeier, 2000).

Various studies of N400 in schizophrenia patients have revealed anomalies in this ERP component: a) decreases in the N400 effect and/or increases in amplitude in response to words related to the context (Adams et al., 1993; Grillon et al., 1991; Hokama et al., 2003; Kostova et al., 2003a; Matsuoka et al., 1999; Mitchell et al., 1991; Nestor et al., 1997; Niznikiewicz et al., 1997; Ohta et al., 1999; Olichney et al., 1997; Strandburg et al., 1997), indicating an ineffective use of context and b) a delayed latency, which has been reported in most studies and indicates a generally slowing of information processing.

The N400 paradigm appears to be a useful means of identifying the cognitive anomaly underlying language disorders in schizophrenia patients (Kumar and Debruille, 2004). However, many questions remain unanswered, particularly as concerns the clinical characteristics of patients with N400 anomalies. Not all schizophrenia patients display N400 anomalies and even the earliest studies in this area reported that some schizophrenia patients had N400 amplitude anomalies, others had delayed latencies and still others had normal N400 responses (Grillon et al., 1991). The variability of N400 anomalies demonstrates the importance of defining the clinical characteristics of study groups very precisely. We need to know which patients have decreased N400 effects and which have normal N400 effects. Few studies have dealt with this issue. Some studies have reported decreases in N400 effects only in schizophrenia patients with an early age-at-onset and long duration of illness (Olichney et al., 1997); others have observed a correlation with formal thought disorder (Andrews et al., 1993) or with formal thought disorder and mean neuroleptic dose (Salisbury et al., 2000). The main purpose of our study was to explore the link between N400 anomalies and clinical profile in schizophrenia patients.

2. Materials and methods

2.1. Subjects

Fifty subjects (36 men, 14 women) meeting DSM-IV schizophrenia diagnosis criteria (American Psychiatric Association, 1994) participated in this study. Diagnosis was made by an experienced independent clinician. Patients were recruited during hospitalization (Psychiatric Department, Versailles Hospital) or during outpatient follow-up. All patients had stable symptoms and were on neuroleptic treatment. Psychotic symptoms were evaluated using the Positive and Negative Syndrome Scale, PANSS (Kay et al., 1987). Formal thought disorder was evaluated using the Thought, Language and Communication disorders scale, TLC (Andreasen, 1979). The control group consisted of 40 healthy subjects (19 men, 21 women) matched with the schizophrenia patients for age, socioeducational level (number of years of study) and vocabulary level (Binois and Pichot, 1959). Table 1 summarizes the clinical and socioeducational characteristics of all the participants.

The exclusion criteria for participation as a patient or control were: age less than 20 years or over

Table 1
Socioeducational and clinical characteristics of the participants

	Controls $n=40$	Schizophrenia patients $n=50$	F	p
Age	28.92 ± 8.71	31.59 ± 8.91	1.99	0.16
Years of study	12.95 ± 2.58	12.31 ± 3.18	1.04	0.31
Vocabulary[a]	26.44 ± 4.42	24.67 ± 6.67	2.02	0.16
TLC[b]		13.16 ± 6.60		
PANSS[c] total score		82.75 ± 18.77		
PANSS positive scale		21.08 ± 6.50		
PANSS negative scale		22.28 ± 5.46		
Neuroleptics[d]		656.63 ± 283.48		

Note: means ± standard deviations.
[a] Vocabulary: Binois–Pichot test.
[b] TLC: Thought, Language and Communication Disorders.
[c] PANSS: Positive and Negative Syndrome Scale.
[d] Neuroleptic dose (chlorpromazine equivalent).