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P50 gating in deficit and nondeficit schizophrenia

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ABSTRACT

Dysfunctional auditory sensory processing has generally been found in schizophrenia and it has been suggested that these deficits might be related to clinical and psychosocial variables. The present study included P50 recordings using a simple-paired click auditory evoked potential paradigm in sixty patients with deficit schizophrenia (DS), sixty patients with nondeficit schizophrenia (NDS), and sixty comparison subjects. The Schedule for the Deficit Syndrome was used to categorize patients as DS or NDS. The two patient groups did not differ in clinical variables, except for higher negative dimension and lower community outcome scores in DS than in NDS patients. There were no differences in P50 ratios between deficit and nondeficit subgroups; compared with normal subjects both groups of schizophrenia patients showed impaired P50 ratios ($p < 0.0001$). This ratio appears to be independent of positive and negative symptoms. However, impairment in P50 gating correlated with poorer community outcome. The data document the existence of early auditory sensory processing abnormalities in DS and NDS, and might suggest that common neuronal network abnormalities underlie both forms of schizophrenia. Deficient P50 gating may be associated with impaired functional outcome in schizophrenia.

1. Introduction

Middle latency auditory event-related potentials (MLAERPs) are a series of brain waves that are recorded at the scalp following auditory stimulation. MLAERPs decrease in amplitude when a second click is delivered about 500 ms after the first click (Boutros et al., 2004a). This inhibitory mechanism of the central nervous system has been named sensory gating. The early positive component of MLAERPs, occurring between 35 and 90 ms after the stimulus (P50), may reflect a preattentive stage of information processing, and has been widely evaluated in schizophrenia. Many studies have shown P50 gating deficits in schizophrenia patients (Adler et al., 1982; Boutros et al., 1991, 1993; Braff et al., 2007; Clementz et al., 1998; Clementz and Blumenfeld, 2001; Freedman et al., 1983; Judd et al., 1992; Sánchez-Morla et al., 2008). Nevertheless, some studies have failed to find any significant association between deficits in P50 gating and schizophrenia (Arnfred et al., 2003; Guterman and Josiassen, 1994; Kathmann and Engel, 1990), or found this association only in a subgroup of schizophrenia patients (Jin et al., 1998). Deficient P50 gating persists during stable periods and conventional antipsychotic medications do not remediate this deficit in schizophrenia patients (Freedman et al., 1987; Nagamoto et al., 1996), although the effects of new-generation antipsychotic medications with improvements in sensory gating

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deficits are inconclusive (Adler et al., 2004; Arango et al., 2003; Sánchez-Morla et al., 2009). Two meta-analyses (Bramon et al., 2004; de Wilde et al., 2007) support a high variability in effect size. These differences might be explained by differences in methodology and the lack of homogeneity of the samples (Patterson et al., 2008).

Some studies have reported that negative symptoms correlated with higher or more abnormal P50 ratios (Louchart-de La Chapelle et al., 2005; Ringel et al., 2004). Nevertheless, the majority of studies have failed to demonstrate a significant relationship between P50 sensory gating and negative symptoms (Adler et al., 1990; Arnfred and Chen, 2004; Light et al., 2000; Potter et al., 2006; Sánchez-Morla et al., 2008; Yee et al., 1998). The lack of homogeneity in the nature of the negative symptoms could explain the differences in data between studies (Buchanan, 2007). In fact, to our knowledge, the relationship between sensory gating and primary enduring negative symptoms has not been addressed.

Carpenter et al. (1985) provided a distinction between the primary and secondary negative symptoms of schizophrenia. Primary negative symptoms are idiopathic with enduring features and persist between periods of relapse. These authors (Carpenter et al., 1988, 1993; Kirkpatrick et al., 2001) proposed a subtype of schizophrenia characterized by primary and enduring negative symptoms named deficit schizophrenia (DS) which is distinct from other forms of schizophrenia (nondeficit schizophrenia, NDS). The deficit syndrome represents an attempt to find homogeneous clinical samples of patients diagnosed with schizophrenia. Comparisons of subtypes have long been an aspect of schizophrenia research. Hence, differences in psychopathologic (Galderisi et al., 2002), neurologic (Arango et al., 2000; Buchanan et al., 1990), neuropsychological (Brazo et al., 2002; Buchanan et al., 1994; Cohen et al., 2007), structural (Arango et al., 2008; Galderisi et al., 2008), metabolic (Kirkpatrick et al., 2009) and regional cerebral blood distribution abnormalities (Gonul et al., 2003; Vaiva et al., 2002) have been reported between deficit and nondeficit samples (for a review see Kirkpatrick et al., 2001). Also, it has been suggested that deficit and nondeficit schizophrenia differ with regard to defects in basic neurophysiological mechanisms. Neurophysiological studies have found that only schizophrenia patients with nondeficit forms or without pronounced negative symptoms show abnormalities in P3 components (Meisenzahl et al., 2004; Turetsky et al., 1998). More recently, Mucci et al. (2007) have reported the same results and suggest that schizophrenia patients with deficit forms have abnormalities of the early stages of attentional information processing, while patients with nondeficit schizophrenia have abnormalities of the late stages of information processing.

In the current study, the objective was to examine P50 auditory sensory gating, using a conditioning-test paradigm, in deficit schizophrenia patients and nondeficit schizophrenia patients in comparison with a control sample. We hypothesized that schizophrenia patients with the deficit syndrome would have more abnormalities of the early stages of attentional information processing than schizophrenia patients without the deficit syndrome. Moreover, we examined whether auditory sensory gating correlates with clinical symptoms or functional outcome in both groups of patients.

2. Methods

2.1. Patients

One hundred and twenty clinically stable outpatients with a diagnosis of schizophrenia according to the Structured Clinical Interview for DSM-IV (SCID-I) were recruited for the study. The clinical assessment was performed by two experienced clinical psychiatrists. Patients were recruited among those who were regularly attending the Severe Mental Disorder Program at Cuenca Hospital (Spain). They met the inclusion criterion of age between 18 and 55 years. The exclusion criteria were the following: 1) severe medical or neurological disease; 2) mental retardation; 3) drug abuse or dependence in the last 24 months; 4) previous electroconvulsive therapy, and 5) a history of brain trauma with loss of consciousness. All patients were clinically stable prior to enrolment in the study. They were considered clinically stabilized if during at least three months prior to assessment, there were no hospital admissions, the positive subscale score of the Positive and Negative Syndrome Scale (PANSS-P) did not change by more than 3 points, and there had been no changes in pharmacologic treatment. Patients meeting these criteria were then classified as having either DS or NDS after being interviewed by two trained psychiatrists using the Spanish version (Bernardo et al., 2007) of the Schedule for the Deficit Syndrome (SDS) (Kirkpatrick et al., 1989). Three hundred and two stabilized outpatients diagnosed with schizophrenia (DSM-IV) were evaluated with the SDS; eighty-two patients were classified as DS. Sixty randomly chosen patients with DS according to the SDS were included into the study. For each recruited patient with DS, an age- and sex-matched patient with NDS was recruited from the general group of patients with nondeficit schizophrenia.

2.2. Healthy controls

The control group was made up by sixty healthy volunteers, 18 to 55 years of age. All control subjects met the same exclusion criteria as patients and were given the SCID structured interview to rule out present or past psychiatric illness. Furthermore, subjects with first-degree relatives diagnosed with bipolar disorder, psychosis, or another psychiatric disorder were excluded in the screening interview. All subjects were from the same area and ethnic origin as the patient group.

2.3. Clinical evaluation

The patients' clinical status was determined using the Spanish version (Peralta and Cuesta, 1994) of the Positive and Negative Syndrome Scale (Kay et al., 1987) administered by two experienced psychiatrists on the research team (JSG and ESM). In addition, community outcome was assessed with the Spanish version (Rodríguez-Fornells et al., 1995) of the Quality of Life Scale (QLS) (Heinrichs et al., 1984). The QLS consists of 21 items scored from 0 to 6, with the highest scores reflecting normal functioning. The scale assesses four areas: interpersonal relations (household, friends, acquaintances, social activity, social network, social initiative, withdrawal, and sociosexual behavior), instrumental role