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P50 inhibitory gating deficit is correlated with the negative symptomatology of schizophrenia

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Abstract

Abnormal sensory gating in schizophrenia has frequently been reported. The strength of central inhibitory pathways was measured using the P50 component of the auditory evoked potential in a conditioning–testing paradigm. The relationships between a relative decrease in P50 amplitude to repeated auditory stimuli and clinical symptoms remain controversial. Using the Positive and Negative Syndrome Scale, we studied the P50 auditory conditioning–testing paradigm in 81 schizophrenic subjects, categorized into subgroups with and without prominent negative symptoms, in comparison with 88 control subjects. We found increased ratios of testing stimuli to conditioning stimuli in both schizophrenic subgroups relative to findings in the control group. In addition, we found significantly increased mean latencies of the P50 responses to conditioning (C) and testing (T) stimuli and significantly increased T/C ratios in the subgroup with negative symptoms compared with the subgroup with non-negative symptoms.

Keywords: Sensory gating; Auditory evoked potentials; Schizophrenia; Negative symptoms; P50; Electrophysiology

1. Introduction

Disturbances in attention and information processing have been described in schizophrenia since Bleuler and Kraepelin. Moreover, these disturbances have been documented by clinical observations (McGhie and Chapman, 1961) and by both neuropsychological

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and electrophysiological data (Nuerchterlein and Dawson, 1984; for review, see Braff, 1993). Schizophrenic patients seem to be unable to filter out irrelevant noise when confronted by multiple, almost simultaneous auditory stimuli; in such situations, the patients' attention is drawn capriciously to many details that other persons would ignore, resulting in a flooding of sensory impressions in the patients. It has been proposed that this inability to filter sensory stimuli may result in more florid symptoms, such as hallucinations or delusions, or alternatively may increase negative symptoms (Venables, 1964).

Sensory gating has been conceptualized as the ability of the brain to screen out and filter irrelevant sensory stimuli. The strength of the central inhibitory pathways that underlie gating has been measured using decreased neuronal responsiveness to repeated stimuli (e.g. the relative decrease of the P50 component of mid-latency auditory evoked potentials to repeated identical auditory stimuli using a conditioning–testing paradigm). A great number of studies have reported abnormal P50 responses to this paradigm in schizophrenic patients, indicating diminished auditory gating mechanisms (Adler et al., 1982; for review, see Freedman et al., 1987a; Light and Braff, 1999).

Abnormal P50 responses have also been found in schizotypal subjects (Cadenhead et al., 2000) and in first degree relatives of schizophrenic patients (Siegel et al., 1984; Waldo et al., 1991). Recent evidence suggests that abnormal P50 responses may be a trait marker of a genetic defect in schizophrenia. This deficit has been linked to the alpha 7 subunit of the nicotinic receptor gene locus located on chromosome 15q14 (Freedman et al., 1997; Raux et al., 2002).

Few studies have examined the relationships between sensory gating impairments and clinical subtypes of schizophrenia. Non-paranoid patients have been characterized by significantly higher ratios of testing stimuli to conditioning stimuli (T/C ratios) than observed in paranoid patients or normal subjects (Boutros et al., 1991). However, other studies have failed to find any relationship between electrophysiological data and clinical symptomatology (Freedman et al., 1987b; Adler et al., 1990; Ward et al., 1996). The relationship between P50 suppression and clinical symptomatology remains to be more definitively characterized.

In this study, we used the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) to categorize our schizophrenic patients into subgroups with versus without prominent negative symptoms. The present study investigated differences between the two subgroups of patients and normal controls in inhibitory gating of evoked brain responses to repeated stimuli in an auditory conditioning–testing paradigm.

2. Methods

2.1. Subjects

Eighty-one patients [60 males, 21 females; mean age 38 ± 9.1 (SD) years] who satisfied DSM-IV criteria for schizophrenia, as determined by the French version of the Schedule for Affective Disorders and Schizophrenia-Lifetime version modified for the study of anxiety disorders (SADS-LA; Fyer et al., 1985; American Psychiatric Association, 1994), were recruited from our psychiatric hospital. Patients were required to be clinically stabilized for a minimum of 2 weeks with no change in neuroleptic dose at the time of their participation in the study. Four patients were receiving atypical neuroleptic medication: amisulpride in three cases (two of three were in the negative symptom subgroup) and risperidone in one (non-negative) case.

Eighty-eight normal controls [42 males, 46 females; mean age 29.5 ± 7.5 (SD) years] were recruited from the general population (through advertisements). Healthy subjects were screened with the Diagnostic Interview Schedule (Robins et al., 1981); they had no personal history of neurological or psychiatric disease and reported no family history of psychiatric illness (especially schizophrenia among first and second degree relatives). Controls were free of any psychotropic medication.

Subjects with deafness, neurological disease, and alcohol or substance abuse at the time of the study were excluded from participation. Daily rates of alcohol and substance consumption were assessed according to the subjects' statements. The study was approved by the ethics committee at our institution. All subjects gave written informed consent before participation. Table 1A presents demographic features of the subjects.