Neurophysiological and neuropsychological assessment of recent-onset schizophrenia
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Citation for published version (APA):

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The P300 event-related potential and subjective experience in schizophrenia

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In editorial processing, Schizophrenia Bulletin
Abstract

The purpose of the study was to investigate the relationship of the P300 with subjective experiences in recent-onset schizophrenic patients. In 31 young patients with schizophrenia we assessed the P300 at the midline frontal, central and parietal electrode site and subjective experiences with a self-assessment scale (subjective well-being under neuroleptics scale). Reduced score on the mental functioning and self-control factors of the subjective experience questionnaire was related to prolonged P300 latency at all electrode sites. Our results suggest that young patients are aware of their information processing deficits and that the assessment of subjective experience in patients with schizophrenia is a valid method for gaining insight into the schizophrenic disease process.
Introduction

Event-related potentials (ERPs) are studied in schizophrenia to gain insight into information processing abnormalities that may constitute a core deficit of this disease (Braff 1993; Ford et al. 1999). ERPs are derived from the electroencephalogram and reflect brain activity in response to sensory stimuli. In the auditory P300 paradigm, rare high-pitched relevant tones are presented randomly amidst standard, low-pitched tones. The P300 is the positive ERP component that occurs at approximately 300 msec after presentation of a relevant tone. Amplitude reduction of the P300 is the most replicable biological abnormality in schizophrenic patients (Ford 1999). P300 latency prolongation has also frequently been reported in schizophrenia (Pfefferbaum et al. 1984; Nieman et al. in press).

The P300 has been investigated widely in schizophrenia, as well as other biological markers like disturbed eye movements (Hutton et al. 1998; Nieman et al. 2000). The main symptoms of schizophrenia entail subjectively experienced alterations in perception, emotion and cognition. Relating biological markers like the P300 to subjective experience in schizophrenia may validate the assessment of subjective experience. Data on the relationship between subjective experiences of schizophrenic patients and biological markers are scarce. Jin et al. (1998) studied P50 ERP suppression in schizophrenic patients in relationship with subjective experience of sensory gating deficits. They found that those patients who endorsed experiences of sensory inundation had normal levels of P50 suppression whereas patients who tended to endorse fewer complaints of perceptual anomalies had P50 suppression deficits. Light and Braff (2000) commented on this paradoxical finding by stating that the results of Jin et al. (1998) may be explained by the limits on self-report in schizophrenic patients. They argued that schizophrenia patients often have both diminished insight and limited self awareness of their deficits. The aim of the present study was to investigate the relationship of the P300 with subjective experiences in recent-onset schizophrenic patients.
Method

Subjects
Thirty one young recent-onset schizophrenic patients (four women) were assessed with the P300 and the Subjective Well-being under Neuroleptics scale (SWN), mean age was 21 years (2.9, SD). All patients attended the adolescent psychiatric clinic of the Academic Medical Center for inpatient and outpatient treatments and they all satisfied the DSM IV (APA, 1994) criteria for the diagnosis of schizophrenia or schizoaffective disorder (n=4). The diagnosis at admission was made in a clinical consensus meeting of three experienced psychiatrists, a research psychologist and two residents with the use of all possible information, such as medical records, interviews with patients and parents. Exclusion criteria were mental retardation, epilepsy, endocrine disease, diagnosis of a primary alcohol- or drug related psychosis, hearing disorders and known neuropsychological impairment due to factors other than schizophrenia such as closed head injury.

Event-related Potential Recording
Full details of P300 recording have been reported in a previous publication (Nieman et al. in press) and are therefore only briefly described here. Target stimuli with a frequency of 2000 Hz and standard, nontarget stimuli with a frequency of 1000 Hz were presented binaurally through headphones at an intensity of 75 dB above hearing threshold. In the session, lasting about 15 minutes, 60 targets were presented randomly amidst 465 nontargets. The subjects were instructed to count the targets and respond to them with a button press. The total number of counted targets was asked at the end of the session. To familiarize the subjects with the task, three practice trials were presented.

Ag-AgCl disc electrodes were attached to the midline frontal (Fz), central (Cz) and parietal (Pz) sites according to the international 10-20 system with a reference electrode on linked ears and a ground electrode on the forehead. The electro-oculogram (EOG) was recorded from an electrode located laterally at the supraorbital ridge of the right eye referenced to an electrode located laterally below the left eye. Trials with eye movement artifacts were excluded from analysis. The subjects were seated in a comfortable chair with eyes open. Sixty trials were entered into the P300 measures. The P300 was recorded in patients when they had been on the same medication for six weeks, when they were no longer in an acute, psychotic phase of the disease.
Subjective Experience Assessment
The subjective experiences of the patients were assessed with the SWN (Naber et al. 1995; De Haan et al. 2000). The SWN is a self-rating scale that assesses the subjective experience in the past 7 days. Analyses based on a study in 216 patients with schizophrenia indicate good practicability, and reliability (Naber et al. 1994, 1995; De Haan et al. in press). In the Dutch translation of the SWN the possible relationship between subjective experiences and neuroleptics was not mentioned.

The scale consisted of 38 items, divided in 12 singular and 26 dual items. The dual items consisted of 13 positive and 13 negative formulated items. For example, 'I feel indifferent towards my family, friends and colleagues' and 'I have intense contact with my family, friends and colleagues'. Patients were asked to mark the applying response on a 6-point Likert scale ranging from 1 'not at all' to 6 'very'. Naber et al. (1994, 1995) found five factors, each consisting of about seven statements including dual items: Emotional regulation e.g. 'My feelings and experiences are flat, nothing touches me' and 'I have a stable and well-balanced emotional life'. Items of the mental functioning factor are shown in the table. Social integration e.g. 'I feel alone and lost' and 'I feel very inhibited in talking to people and making contact'. Items of the self-control factor are shown in the table. Physical functioning including statements such as 'I feel full of energy and life' and 'I feel without strength and exhausted'. Subjective experience was assessed in the same week as the P300.

Table: All items of the mental functioning and self-control factors of the SWN

<table>
<thead>
<tr>
<th>SWN Mental functioning factor</th>
<th>SWN Self-control factor</th>
</tr>
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<tbody>
<tr>
<td>My thoughts are jumpy and not aimed; I experience difficulty in organized thinking</td>
<td>My thoughts always evolve around the same topics, I can not break free</td>
</tr>
<tr>
<td>My thinking is difficult and slow</td>
<td>My thoughts and feelings are strange to me</td>
</tr>
<tr>
<td>I can realize my thoughts and ideas</td>
<td>I feel powerless and have no control over myself</td>
</tr>
<tr>
<td>I have few ideas and little imagination</td>
<td>My feelings and behavior are not appropriate in situations</td>
</tr>
</tbody>
</table>
Statistical Analysis.
Correlations between the five factors of the SWN and P300 latency and amplitude at the three electrode locations were examined with Pearson correlation coefficients. Using a Bonferroni correction, only two-tailed p values smaller than 0.03 were considered significant. Patients were categorized in two mental functioning categories, divided by the mean of the score on this factor of the whole patient group. The data were analyzed with a statistical computer program (SPSS 10 for Windows, Chicago, IL).

Results

Reduced score on the mental functioning factor of the SWN, implying worse mental functioning, was related to increased P300 latency at all electrode sites (Fz $r = -0.56$, $p < 0.001$; Cz $r = -0.62$, $p < 0.0001$; Pz $r = -0.51$, $p < 0.004$). Figure 6.1 represents the grand average ERPs in the patient groups with a high and a low score on the mental functioning factor of the SWN.

Figure 6.1: Grand average ERPs elicited by infrequent target stimuli in the patient groups with poorer and better mental functioning. The black lines represents the grand average ERPs in the patient group with poorer mental functioning ($n = 15$) and the grey lines represent the grand average ERPs in the patient group with better mental functioning ($n = 16$) as assessed with the SWN. The arrow indicates stimulus presentation. $\mu V = $ microvolt.
Figure 6.2 depicts the scatterplot of the correlation between P300 latency at the central electrode site and the score on the mental functioning factor of the SWN.

![Figure 6.2: Scatterplot of the relationship between P300 latency and the mental functioning factor score. Patients who indicated on the SWN that they experienced difficulty with thinking showed delayed P300 latencies whereas patients who indicated they experienced no difficulty with mental functioning displayed less delayed P300 latencies. Cz = central electrode site.](image)

Furthermore, there was a relationship between reduced score on the self-control factor of the SWN and increased P300 latency (Fz $r = -0.39$, $p < 0.03$; Cz $r = -0.44$, $p < 0.01$; Pz $r = -0.46$, $p < 0.01$). There were no significant relationships between the SWN and P300 amplitude. Relationships of the P300 with the emotional regulation, social integration and physical functioning factors of the SWN were also not significant. Partial correlation analyses, controlling for medication, intelligence, sex and age showed that these variables were not underlying factors in the relationship between P300 latency and subjectively experienced mental functioning/self-control.

**Discussion**

We found a strong relationship between increased P300 latency at all electrode sites and reduced subjectively experienced mental functioning and self-control in recent-onset schizophrenic patients. These findings suggest that information processing deficits start early in schizophrenia and that young patients are aware of these deficits. Furthermore, our results provide support for the validity of the assessment of subjective experience with the SWN in patients with schizophrenia. The self-control factor...
included several items about self-control of thought processes. This overlap may explain our result that both the mental functioning and the self-control factor of the SWN were related to P300 latency.

The discrepancy of our results and the results reported by Jin et al. (1998), who did not find a relationship between P50 abnormalities and worse subjective experience, may be associated with the fact that P50 suppression is an involuntary, automatic process, taking place early in the information processing process whereas the P300 reflects later cognitive processes.

In a study of Møller and Husby (2000), subjective experiences of patients in a prodromal phase of schizophrenia were explored to increase understanding of the schizophrenic disease process. The authors took a phenomenological stand and deduced core dimensions of experience and behavior from extensive interviews held with the patients. For example, they argued for 'extreme preoccupation by and withdrawal to overvalued ideas (e.g. preoccupation with religious mysticism/philosophy)' as a core dimension. The phenomenological approach of Møller and Husby is supported by our finding that the subjective experiences of schizophrenic patients are closely correlated with an objective biological marker like the P300.

In future studies, different aspects of subjective experience of schizophrenic patients may be investigated on their relationship with biological markers to gain more insight into the schizophrenic disease process and its biological substrate.

Acknowledgment

This study was funded by grant 28-1241/2 from the 'Dutch Health Research and Development Council. The authors thank Prof. Dr. BPR Gersons, Dr. LJ Bour and T. Boeree for their contributions to this study.

References


Chapter 6


