

Auditory Event-Related Potential (P300) in Patients with Schizophrenia

Zahraa Tariq Hasson, Ali Fuad Al-Hashimi, Uday Khalid Al Qaisy¹

Departments of Physiology, ¹Psychiatry, College of Medicine, Al-Nahrain University, Baghdad, Iraq

Abstract

Background: Schizophrenia is a psychiatric disorder characterized by multiple symptoms such as positive symptoms, negative symptoms, and cognitive symptoms. Cognitive deficit can be detected with specific neurophysiological tests. Among these tests are the measurements of auditory P300 event-related potential which is a neurophysiological method that allows the examination of cognitive functioning of the human brain. **Objective:** The aim of this article is to assess cognitive deficits in chronic schizophrenia patients by studying the amplitude and latency of P300 potential and to compare findings with those from control subjects. **Materials and Methods:** The present study was a case-control study extended from January 2020 to May 2020. Forty subjects were enrolled in this study: 20 patients aged 20–50 years comprising 11 males and 9 females diagnosed with schizophrenia and 20 apparently healthy volunteers comprising 11 males and 9 females were analyzed. **Results:** The results of the current study revealed that a highly significant difference was found in the years of education between patients and controls (P -value <0.001) with no significant difference to be noticed regarding age or gender. When analyzing the P300 component with an unpaired t -test, the patient group showed delayed latency and smaller P300 amplitude than the control group ($P<0.001$). **Conclusion:** The present study concludes that P300 indices could be valuable biomarkers to assess changes in cognitive functioning of patients with schizophrenia.

Keywords: Cognition, P300, schizophrenia

INTRODUCTION

Schizophrenia is a complex illness that is characterized by significant impairment of social, psychological, and cognitive functioning.^[1] Cognitive deficits are one of the most important features in schizophrenia with significant consequences on patients' psychosocial functioning, which are present before the beginning of psychotic symptomatology.^[2]

The auditory P300 event-related brain potential is an index of endogenous cognitive processes. It is a positive voltage deflection in the event-related potential occurring approximately 300 ms after stimulus onset. It reflects a variety of cognitive processes such as decision-making, novelty processing, attention, memory update, and other cognitive activities that elicited by a change in the sensory environment. It is perhaps the most studied of the event-related potentials and usually elicited in most research settings by auditory and visual modalities.^[3] The P300 amplitude is thought to reflect attentional resource

allocation, phasic attentional shifts, and working memory updating of stimulus context, whereas P300 latency is thought to reflect processing speed or efficiency during stimulus evaluation.^[4]

Elevated amplitudes and shorter latencies of P300 components are related to higher attention with increased consciousness. Cognitive processing by ERPs can be influenced by factors such as age, gender, education, reading habits, cognitive performance, the presence of depressive symptoms, and level of social and cultural interaction.^[5,6] Several studies had revealed decreased P300 amplitude and longer latency in schizophrenic patients

Address for correspondence: Dr. Zahraa Tariq Hasson,
Department of Physiology, College of Medicine,
Al-Nahrain University, Baghdad, Iraq.
E-mail: Dr.zahraa.tariq83@gmail.com

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when compared with healthy controls.^[3,7-9] However, conflicting results concerning P300 latency in patients with schizophrenia were noticed in the literature.

Wang *et al.*^[10] assessed unmedicated first episode schizophrenia patients and demonstrated a reduction in P300 amplitude with normal P300 latency when compared with unaffected controls. Winterer *et al.*^[11] studied frontal and temporo-parietal P300 latencies and found no difference concerning temporo-parietal P300 latency between schizophrenia patients and control group, whereas they found prolonged frontal P300 latency in same patients compared with controls. The aim of the present study is to investigate the cognitive impairment in chronic medicated schizophrenia patients by studying the P300 amplitude and latency and to compare findings with those from healthy control subjects.

MATERIALS AND METHODS

Subjects

The present study was a case-control study conducted in the Neurophysiology Unit at Al-Imamain Al-Kadhimain Medical City and the Psychiatric Clinic at the Medical Consultation Office of Al-Nahrain University, College of Medicine, Baghdad, Iraq for the period extended from January 2020 to May 2020. All the selected subjects were enlightened about the electrophysiological and psychoanalytical examination, and an informed consent for participation in the study was provided. The study was approved by the Institute Review Board of the College of Medicine, Al-Nahrain University.

The study included 20 chronic medicated schizophrenic patients diagnosed clinically as per Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM V-TR) criteria, aged 20–50 years, who were collected and referred from Psychiatric Clinic in Al-Imamain Al-Kadhimain Medical City hospital by a psychiatrist. Those will be compared with 20 age- and sex-matched healthy controls with no history of any medical, psychiatric, or organic disease.

The following instrument was used for all patients and control subjects:

1. The EMG/EP machine

Cadwell EMG/EP machine (made in USA) serial no. VND301, product no. CE658A, manufactured: June, 2013.

2. The electrodes (paired surface disc recording electrodes and grounding electrode).

3. Stimulator (headphones) was connected to the back of the Sierra Wave base unit by cable.

Event-related potential (P300)

Subjects were asked to lie down on a couch with a head rest. Single channel record was done by using surface

electrode on the vertex (Cz) as an active electrode, over the left mastoid process as a reference electrode (A1) and over the forehead as a ground electrode (G). The electrode impedances were kept $<5 \text{ k}\Omega$ (k_{ohm}). Auditory stimuli were presented binaurally by calibrated headphones. Within an odd-ball paradigm, the frequent stimulus (1000 Hz) occurs in 80% and the rare stimulus (3000 Hz) occurs in 20% of the total number of presentations. Both stimuli were presented at an intensity equal to 65 dB. Subjects were instructed to close their eyes and to be mentally attentive to count the number of the rare stimuli [Figure 1]. P300 responses were identified, with subsequent measurement of their latencies and amplitudes [Figure 2].

Statistical analysis

This is a case-control study, most of data were continuous and expressed as mean $\pm$ standard deviation, and comparison of these data was done by using unpaired Student's *t*-test. Sex was expressed as frequency and percentage, and comparison of these data was done using Fisher's exact test. *P*-value less than 0.05 was considered as significant. Pearson's correlation was studied between different parameters in the current study. The software programs used were Microsoft Excel 2019 and SPSS (Statistical Package for Social Sciences) version 23 (Property of IBM Corp., Copyright IBM Corporation and Licenses 1989, 2015).

RESULTS

Demographic characteristics

Forty subjects were enrolled in this study: 20 patients diagnosed with schizophrenia and 20 apparently healthy volunteers were analyzed. The mean age of patients was 35.1 ± 10.28 years, comprising 11 males and 9 females, with duration of disease being 8.91 ± 5.47 years, compared with mean age of 35.15 ± 9.28 years of apparently healthy volunteers, comprising 11 males and 9 females and years of education being 14.6 ± 2.6 years [Table 1].



Figure 1: Site of electrodes on the scalp of the patients

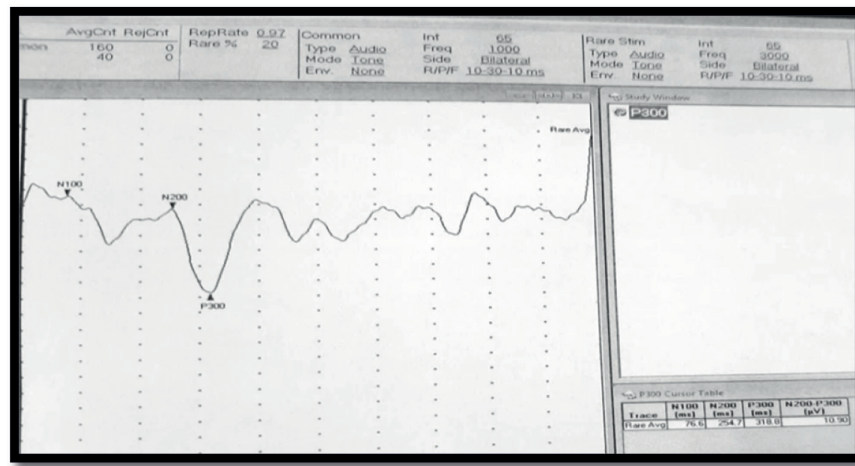


Figure 2: Photograph shows the amplitude and latency of P300

Table 1: Comparison of age, sex, duration of education, duration of disease, and duration of treatment between patients and controls

Parameters	Patients, <i>n</i> = 20, mean ± SD	Controls, <i>n</i> = 20, mean ± SD	<i>P</i> -value
Age (years)	35.1 ± 10.28	35.15 ± 9.28	0.987*
Sex*			
Female	9 (45.0)	9 (45.0)	1.000**
Male	11 (55.0)	11 (55.0)	
Education (years)	6.15 ± 5.55	14.6 ± 2.6	<0.001
Disease (years)	8.91 ± 5.47		
Treatment (years)	6.8 ± 5.5		

*Unpaired *t*-test; **Fisher's exact test

A highly significant difference was found in the years of education between patients and controls (*P*-value < 0.001) with no significant difference to be noticed regarding age or gender (*P*-value = 0.987, 1.000, respectively).

The event-related potential (P300) parameters (amplitude and latency) were analyzed by the unpaired *t*-test. The mean latency of P300 for patients was highly significantly prolonged when compared with that of the control group (457.13 ± 141.85 and 313.93 ± 20.99 ms, respectively, *P* < 0.001). In contrast, the mean P300 amplitude was highly significantly decreased in patients when compared with controls (5.64 ± 2.25 and 11.46 ± 3.2 μ V, respectively, *P* < 0.001) [Table 2].

P300 latency revealed a significant positive correlation with duration of treatment ($r=0.477$, *P* < 0.034) [Table 3]. No other significant correlations were recorded.

DISCUSSION AND CONCLUSION

In the current study, no significant difference was noticed regarding gender and age between the two studied groups; however, highly significant difference was found in the years of education between patients and controls. This can be explained that most schizophrenic patients had their first onset in early adulthood; then, recurrent hospitalizations would deprive the patient from

completing his or her educational life. It had been stated that schizophrenia is often associated with recurrent hospitalizations, poor social functioning, low education, and high-unemployment rates. Evidence highlights that not completing primary school and receiving low school marks were associated with a higher risk of schizophrenia.^[12,13]

P300 represents a family of related potentials related to different aspects of working memory processing. Analysis of event-related potentials (P300) in the current study revealed significantly lower amplitude and prolonged latency in schizophrenic patients compared with controls. These findings were in agreement with the outcome of other studies that revealed decreased P300 amplitude and longer latency in schizophrenic patients when compared with healthy controls.^[3,7-9]

Clinically, schizophrenia patients often present attention, verbal memory, and working memory dysfunctions. Previous studies suggested that aberrations of P300 amplitude in schizophrenia patients were indicators of these dysfunctions, which might be further related to structural and functional changes in the schizophrenia patient's temporal lobe and parietal lobe.^[14,15] P300 represents a complex summation of activity from the interaction of multiple brain regions, including the

temporal, frontal, and parietal lobes, where lesions to the gray and white matter of the frontal and temporo-parietal junction resulted in P300 amplitude abnormalities.^[16,17] Huang *et al.*^[18] found that in an odd-ball paradigm, discrimination between target and standard stimuli is thought to activate frontal lobe activity which engages the required attention effort through task performance. In contrast, auditory P300 latency represents the timing of cognitive processing, and a shorter P300 latency indicates increased cognitive processing efficiency, which would result in increased P300 amplitude.^[7]

On the contrary, Wang *et al.*^[10] demonstrated a reduction in P300 amplitude with a normal P300 latency in unmedicated first episode schizophrenia patients when compared with unaffected controls. However, in the current work, only chronic medicated schizophrenic patients were included which denotes a progressive affection of speed of information processing and might explain the latency differences between both studies. Winterer *et al.*^[11] studied frontal and temporo-parietal P300 latencies in schizophrenia patients and control group; they found no difference concerning temporo-parietal P300 latency whereas prolonged frontal P300 latency when compared with controls. Conversely, in the current study, P300 parameters were evaluated in the central brain area (CZ) not in the frontal (Fz) or parietal area (Pz). In the current study, a significant positive correlation between duration of treatment and P300 latency was found, which means that prolonged antipsychotic treatment could compromise the efficiency of P300 performance. Data from literature were conflicting concerning the relationship between P300 parameters and duration of treatment. A study focussed on the differences between treated schizophrenics and drug-naive ones revealed that the P300 latency was prolonged in previously treated schizophrenics compared with

neuroleptic-naive schizophrenics and normal controls, demonstrating a positive correlation with duration of treatment.^[19]

A meta-analysis by Jeon and Polich^[20] that included 104 cross-sectional studies found no significant differences in P300 latency or amplitude between subgroups of schizophrenic patients who were and were not medicated. While in the meta-analysis by Bramon *et al.*^[21] that included 46 cross-sectional studies comparing medicated and non-medicated patients, they found a significant increase in P300 amplitude but not in P300 latency with duration of medication. A meta-analysis of follow-up treatment studies of schizophrenia in China has found a small but significant increase in P300 amplitude and a significant decrease in P300 latency with the duration of antipsychotic treatment. They claimed that P300 indices, particularly P300 amplitude, could be valuable biomarkers to monitor changes in cognitive functioning among patients with schizophrenia who receive treatment with antipsychotic medications.^[22] A recent study by Hassan *et al.*^[9] that included 1-year follow-up revealed that psychotropic medications could bring a partial recovery in P300 amplitude in previously unmedicated schizophrenic patients but not in P300 latency.

However, discrepancy in results concerning relation between duration of treatment and P300 parameters could be explained by different types of antipsychotics used in the treatment between different studies with different durations of treatment and patient's compliance.

From the above, it can be concluded that diminished P300 amplitude and prolonged latency in schizophrenic patients compared with control subjects most likely represent impaired processing of external information due to a decline in working memory or attentional ability,

Table 2: Comparison of P300 amplitude and latency between patients and controls by unpaired *t*-test

P300	Patients, <i>n</i> = 20, mean±SD	Control, <i>n</i> = 20, mean±SD	<i>P</i> -value
Amplitude (μV)	5.64±2.25	11.46±3.2	<0.001
Latency (ms)	457.13±141.85	313.93±20.99	<0.001

Table 3: Correlation between P300 amplitude and latency with other parameters in patients

Parameter		P300	
		Amplitude (μV)	Latency (ms)
Age (years)	<i>r</i>	-0.122	0.143
	<i>P</i>	0.609	0.548
Duration of education (years)	<i>r</i>	0.014	-0.079
	<i>P</i>	0.952	0.741
Duration of disease (years)	<i>r</i>	-0.220	0.218
	<i>P</i>	0.351	0.356
Duration of treatment (years)	<i>r</i>	-0.419	0.477
	<i>P</i>	0.066	0.034

which may explain impaired cognitive performance of schizophrenic patients and confirms the previous observation that P300 presents as a biological vulnerability marker for schizophrenia.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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