



## Case study

## Cognitive impairments in patients with first episode psychosis: The relationship between neurophysiological and neuropsychological assessments



Isabel Morales-Muñoz<sup>a,\*</sup>, Rosa Jurado-Barba<sup>b,c,d,f</sup>, Sara Fernández-Guinea<sup>f</sup>, María José Álvarez-Alonso<sup>b,c</sup>, Roberto Rodríguez-Jiménez<sup>c,d,e</sup>, Miguel Angel Jiménez-Arriero<sup>c,d,e</sup>, Gabriel Rubio<sup>c,e</sup>

<sup>a</sup> Neuroscience Center, University of Helsinki, Helsinki, Finland

<sup>b</sup> Laboratory of Clinical Psychophysiology, Department of Psychiatry, Hospital 12 de Octubre, Madrid, Spain

<sup>c</sup> Department of Psychiatry, Hospital 12 de Octubre, Madrid, Spain

<sup>d</sup> Centro de Investigación Biomédica en Red de Salud Mental, CIBERSAM, Madrid, Spain

<sup>e</sup> Department of Psychiatry, Complutense University of Madrid, Madrid, Spain

<sup>f</sup> Department of Basic Psychology II (Cognitive Processes), Complutense University of Madrid, Madrid, Spain

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## ABSTRACT

Cognitive deficits in schizophrenia have been widely reported. Neurophysiological and neuropsychological assessments have been conducted to study these impairments. Event-related potentials (ERPs) are relevant markers of cognitive deficits in schizophrenia, and reductions in specific ERP components have been found. The MATRICS Consensus Cognitive Battery (MCCB) was developed to obtain a consensus battery for the assessment of cognitive deficits in schizophrenia. Here, we aimed to study modulations of several ERP components in first episode psychosis (FEP). We also examined neuropsychological deficits using the MCCB, and correlations between ERP and MCCB impairments. Thirty-eight FEP patients were compared to thirty-eight healthy controls. The following ERP components were examined: P1, N1, MMN, P2, early-P3 and late-P3. We used an auditory three-stimulus oddball paradigm, with standard (60%), target (20%) and distractor (20%) stimuli. FEP patients showed significantly lower amplitudes of P2, early-P3 and late-P3 components. FEP patients also showed significant deficits in all the MCCB cognitive domains. Finally, correlational analyses found strong associations between amplitudes of P2, early-P3 and late-P3 components and MCCB tests for attention and speed of processing. These findings indicate that deficits in late auditory ERP components are present in FEP, whereas early components are preserved. These reductions in late ERP components were related to attentional deficits in FEP as assessed by MCCB. These findings indicate that MCCB is a valid battery for studying cognitive impairments in the initial stages of schizophrenia, and highlight the utility of converging neurophysiological and neuropsychological measures to examine attentional impairments in schizophrenia.

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## 1. Introduction

Schizophrenia is a complex neuropsychiatric disease with a strong neurocognitive component [1,2]. However, the neuropathology of this disease still remains uncertain, as well as the specific cognitive deficits underlying different forms of functional impairment [3]. One of the reasons for these uncertainties could be found in the characteristics of the samples of patients. The majority of studies of neurocognition in schizophrenia have been conducted with

heterogeneous samples of chronic patients with schizophrenia [4]. Fortunately, over the last 20 years there is a growing interest in performing studies with patients experiencing first episode psychosis (FEP), in order to potentially minimize the confounding variables associated with the course of schizophrenia [2].

Event-related potentials (ERPs) are changes in the brain's electrophysiological activity, which typically occur in response to stimuli [5], and are important neurophysiological biomarkers in schizophrenia research. The P3 component (also called P300) is a positive deflection of the electroencephalogram that is elicited about 300 ms after an attended unusual or task-relevant stimulus. When a participant is instructed to respond to an infrequently presented target stimulus in a single-stimulus or a two-stimulus

\* Corresponding author at: Neuroscience Center, University of Helsinki, Viikinkaari 4, FI-00014, Finland.

E-mail address: [isabel.moralesm8@gmail.com](mailto:isabel.moralesm8@gmail.com) (I. Morales-Muñoz).

oddball discrimination task, the P3 component, sometimes known as P3b, is elicited with maximum amplitude over parietal brain areas [6]. In the absence of task instructions, an infrequent or a physically deviant distracter can also elicit a P3 component, known as P3a that is characterized by fronto-central amplitude maximum and relatively short peak latency [7]. P3a and P3b, components have been found to be reduced in schizophrenia [8]. Reduced mismatch negativity (MMN) to deviant auditory stimuli has also been found in schizophrenia [9], as well as decreased P1 [10], N1 and P2 amplitudes [11] to both auditory and visual stimuli.

Cognitive deficits are core features of schizophrenia [12]. Deficits have been found across a wide range of cognitive domains, such as in attention, executive function, spatial ability, verbal learning and memory. A better understanding of the specific cognitive impairments is of critical importance for developing treatments for the improvement of these deficits associated with schizophrenia [13]. The MATRICS Consensus Cognitive Battery (MCCB) was developed to obtain a consensus cognitive battery for use in clinical trials in schizophrenia [14]. Seven separable cognitive factors have been identified and replicated across studies and represent the fundamental dimensions of cognitive deficit in schizophrenia: speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory that are incorporated in the MCCB, reasoning and problem solving, and social cognition [15].

In this study, we investigated the relationship between abnormalities in specific ERP components and test scores in the cognitive domains regarding processing speed and attention/vigilance from the MCCB. We hypothesized that reductions in ERP amplitudes would be related to diminished performance in the cognitive domains that are mostly impaired in schizophrenia.

## 2. Methods

### 2.1. Participants

Thirty-eight patients diagnosed with FEP were recruited from the Psychiatry Service of the Hospital 12 de Octubre in Madrid. FEP patients were defined as those subjects presenting for the first time to health services with psychotic symptoms. Diagnoses were made according to the Diagnostic and Statistical Manual of Mental Disorders (4th edition) using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). Exclusion criteria were history of brain damage, organic diseases of the Central Nervous System, or mental retardation. All patients were on antipsychotic medication prior to the assessment. Symptoms were assessed with the Positive and Negative Syndrome Scale-PANSS [16]. Prior to their inclusion in this study, the average period of psychotic symptomatology lasted six months. The control group ( $n = 38$ ) consisted of psychiatrically, medically, and neurologically healthy volunteers who were not receiving any psychiatric medication and had no first- or second-degree relatives with psychosis. Demographic and clinical data are summarized in Table 1.

All subjects had normal hearing. The neurophysiological and neuropsychological assessments were conducted in two separate sessions. The interval between the two sessions was less than one month.

The study was approved by the ethics commission of the Hospital 12 de Octubre. All subjects gave written informed consent prior to participation in the study.

### 2.2. Neurophysiological assessment

The electrophysiological recordings were performed at the Laboratory of Clinical Psychophysiology of the Hospital 12 de Octubre.

**Table 1**  
Sociodemographic and clinical variables (mean  $\pm$  standard deviation).

Variables	Patients with FEP ( $n = 38$ )	Controls ( $n = 38$ )	<i>P</i>
Age	26.7 $\pm$ 2.39	30.3 $\pm$ 0.95	0.10
Gender			
Female/Male	7/31	23/15	<0.001
Years of education	10.92 $\pm$ 2.33	11.58 $\pm$ 2.67	0.258
Tobacco consumption			
Yes/No	13/25	29/9	<0.001
Antipsychotic			
Typical/Atypical/Both	1/26/1	0/0/0	<0.001
PANSS			
Positive	18.61 (5.92)		
Negative	15.61(9.09)		
General	38.52(6.45)		
Psychopathology			
Total	72.35(17.55)		

FEP = first episode psychosis, PANSS = Positive and Negative Symptom Scale.

After being fitted with a cap for EEG recording, subjects were seated comfortably in a light and sound-attenuated room. In a three-stimulus oddball paradigm, stimuli were 80-dB tones, presented binaurally through earphones, with a pseudorandom 1–1.5 s inter-stimulus interval. Of the tones 60% were standards of 1000 Hz, 20% targets of 2000 Hz and 20% distractors of 500 Hz presented in a random sequence. The duration of all the tones was of 50 ms. Subjects were instructed to mentally count the number of targets. A total of 600 tones were presented in a single session.

EEG data were collected from 16 scalp sites according to the 10–20 International system using Brainvision Recorder (Brainproducts; [www.brainproducts.com](http://www.brainproducts.com)), referenced to Cz during recording. Vertical electro-oculogram (VEOG) was monitored for eye-blink artifact using two additional electrodes above and below the right eye. Electrode resistance was kept below 5 k $\Omega$  at all electrode sites. The EEG was recorded with a band-pass filter of 0.5–70 Hz, with a sampling rate of 250 Hz. Data were imported and analyzed in ERPLABv2.0. Scalp channels were re-referenced to the average of O1 and O2 (O1 + O2/2) for data analysis. Automated artifact rejection was performed prior to averaging to discard trials with eye movements, blinks or amplifier blocking. Signals were averaged in 590 ms epochs with a 250 ms pre-stimulus baseline and digitally filtered with a Butterworth infinite impulse response with a low-pass filter of 30 Hz (3 dB attenuation at 45.1 Hz). Epochs were averaged separately for standard, target and distractor tones. Measurement windows for ERPs of interest were established on the basis of inspection of the waveforms, and the most representative electrodes for each component were chosen for statistical analysis. P1 was measured as the mean amplitude between 50 and 70 ms (at C3, C4, F7, F8), N1 between 90 and 120 ms (at C3, C4, Fz), MMN between 140 and 180 ms (at T3, T4, F7, F8), P2 between 180 and 240 ms (at C3, C4, Fz), early P3 between 250 and 350 ms (at P3, P4, Pz, FP1, FP2, F7, F8, Fz) and late P3 between 350 and 450 ms (at P3, P4, Pz, FP1, FP2, F7, F8, Fz). Amplitudes in the early and late P3 intervals were measured separately as posterior positive (P3, P4, Pz) and anterior negative (FP1, FP2, F7, F8, Fz) deflections.

### 2.3. Neuropsychological assessment

The neuropsychological evaluation was performed using the MCCB. This battery covers 7 cognitive domains in 10 tests (see Table 2). The tests were administered in the same order as in other studies [17,18]. Nevertheless, we only used for this study those MCCB subtests related to the two following cognitive domains: processing speed and attention/vigilance, as these are the two domains that are more related to the ERP components of this study.

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