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Event-Related Potentials (ERPs) in Psychotic Disorders and in Schizophrenia. The importance of the technique in a penal process - A Systematic Review

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Abstract

Evoked event related potentials are, nowadays, an important technique to use when we have to distinguish a high risk for psychosis (CHR) from psychotic disorders (PS) or from healthy subjects. This is an important tool also in penal process when neuropsychologist has to determine if a subject, responsible of a crime, is affected by a psychotic disorder (to determine he is unable to understand and want and he need to be cured) or if he has a normal mental state and so he must be punished by criminal law. This review is very useful to understand the state of art after 60 years of use of this technique, comparing healthy subjects with subjects at high risk for psychosis and from psychotic patient.

1. Review with Final Considerations

Early psychosis refers to the early course of psychotic disorder, including the prodrome and the period up to five years from first entry into treatment for a psychotic episode (i.e., first episode psychosis, or FEP) [1,2]. Cognitive deficits in schizophrenia have been widely reported so that cognitive impairments have been consistently regarded as a fundamental characteristic of schizophrenia [3]. These impairments involve a wide range of domains, such as processing speed, memory, attention, and executive function [4]. These deficits seem to occur prior to the onset of the illness [5] and persist throughout disease progression, potentially exacerbating unfavourable functional outcomes and prolonging disabilities [6].

More recently, longitudinal studies with longer follow-up periods have described certain cognitive deficits as progressive. Fett et al. observed a decline in most cognitive variables in patients with schizophrenia over 20 years following first admission [7]. Cognitive decline after first admission was also found in another long-term longitudinal study in patients with psychotic

disorders [8]. Besides, Rodríguez-Sánchez et al. followed up a large cohort of FEP patients for 10 years. They identified a subgroup of patients exhibiting cognitive from the entire patient sample with a stable pattern of cognitive functions [9]. These differential cognitive trajectories were attributed to potentially different biotypes within the schizophrenia diagnosis.

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. Event-related potentials (ERPs) are relevant markers of cognitive deficits in schizophrenia, and reductions in specific ERP components have been found [10].

A study was conducted in 2016 [11]. Thirty-eight patients with first-episode psychosis (FEP) were compared to thirty-eight controls. A condition-test paradigm of event-related potentials (ERP), prepulse inhibition (PPI), and some specific tasks of the MATRICS Consensus Cognitive Battery (MCCB) were used (i.e., TMT, BACS-SC, and Fluency for processing speed and CPT-IP for attention and vigilance). The ERP components measured were P50, N1, and P2. The PPI intervals examined were 30, 60, and 120 msec. Regarding the MCCB, processing speed and attention/vigilance cognitive domains were selected. FEP patients showed significant deficits in N1 and P2 components, at 30 and 60 PPI levels and in all the MCCB subtests selected. *S*ignificant relationships in N1 with PPI-60, and with one MCCB subtest for processing speed were obtained. In addition, this same subtest showed significant association with P2. Therefore, sensory gating functioning is widely impaired since the very early stages of schizophrenia.

A recent study [12] examined the longitudinal cognitive function changes in early psychosis utilizing the MATRICS Consensus Cognitive Battery (MCCB). Embase, PubMed, and Scopus were systematically searched from their inception to September 26th 2023. The inclusion criteria were longitudinal studies that presented follow-up MCCB data for individuals experiencing first-episode psychosis (FEP) and those with ultra-high risk for psychosis (UHR). Twelve studies with 791 participants (566 FEP patients and 225 healthy controls) were subjected to analysis. Suitable UHR studies were absent. Over time, both FEP patients and healthy controls showed significant improvements in MCCB total scores. Furthermore, FEP patients demonstrated improvements across all MCCB domains, while healthy controls only showed augmentations in specific domains such as speed of processing, attention, working memory, and reasoning and problem-solving. Visuospatial learning improvements were significantly greater in FEP patients compared to healthy controls. Subgroup analyses suggested that neither diagnostic type nor follow-up duration influenced the magnitude of cognitive improvement in FEP patients, so **t**he magnitude of cognitive improvement for MCCB domains was not significantly different between FEP and healthy controls other than visuospatial learning. This underscores visuospatial learning as a potentially sensitive cognitive marker for early pathologic state changes in psychotic disorders.

Interesting studies were conducted about P300, a component of Event related Potentials [13]. The 1965 discovery of the P300 component of the electroencephalography (EEG)-based event-related potential (ERP), along with the subsequent identification of its alteration in people with schizophrenia, initiated over 50 years of P300 research in schizophrenia.

The P300 evoked potential is a robust neurophysiological marker of schizophrenia that is dampened in patients with schizophrenia and, less consistently, in those with affective psychoses and those at clinical high risk for psychosis (CHR). How it may differ between patients with psychotic disorders (PS) and CHR is less studied, especially in youth. This study compared P300 activity among children and adolescents, aged 5-18 years, at CHR (n=43), with PS (n=28), and healthy controls (HC; n=24). Participants engaged in an auditory event-related potential (ERP) task to elicit a P300 response and completed clinical interviews to verify symptoms and diagnoses. Linear regression analyses revealed a decrease in P300 amplitude with increased severity of psychotic symptoms. PS participants showed a diminished P300 response compared to those at CHR and HC, particularly among adolescents aged 13-18. This response was most evident at centroparietal and parietal locations in the right hemisphere. The findings suggest that high risk and psychotic symptomatology is linked to attenuated parietal P300 activity in youth as young as 13 years. Further exploration of the P300 as a biomarker for psychosis in very young patients could inform tailored, appropriate interventions at early stages of disease progression.

Another study was conducted by Hamilton [14]. Forty-three individuals meeting psychosis risk syndrome (PRS) criteria, 19 schizophrenia patients, and 43 healthy control (HC) participants completed baseline electroencephalography recording during separate auditory and visual oddball tasks. Two subcomponents of P300 were measured: P3b, elicited by infrequent target stimuli, and P3a, elicited by infrequent nontarget novel stimuli. Auditory and visual target P3b and novel P3a amplitudes were reduced in PRS and schizophrenia participants relative to HC participants. In addition, baseline auditory and visual target P3b, but not novel P3a, amplitudes were reduced in 15 PRS participants who later converted to psychosis, relative to 18 PRS non-converters who were followed for at least 22 months. Furthermore, target P3b amplitudes predicted time to psychosis onset among PRS participants. These results suggest that P300 amplitude deficits across auditory and visual modalities emerge early in the schizophrenia illness course and precede onset of full psychosis. Moreover, target P3b may represent an important neurophysiological vulnerability marker of the imminence of risk for psychosis. The most important result is the sequent. ANOVA results demonstrated that there was a main effect of Group on P300 amplitudes, as well as a significant Group × Lead interaction. Follow-up comparisons demonstrated that at Cz and Pz, but not Fz, P300 amplitudes were greater in HC relative to PRS (Cz:P=.001,d=0.71; Pz:P=.0003,d=0.79) and SZ (Cz:P=.006,d=0.85; Pz:P=.0002,d=1.16), whereas amplitudes were comparable between PRS and SZ (Ps>.05).

These results suggest the importance to consider Event Related Evoked Pontentials when we have to study the mental state of a patient in order to underly a probably PRS or SZ status, different from healty subjects.

This study must be considered in the penal process, when we have to determine the ability to understand and want in a subject responsible of a crime.

Another recent study, of Huang et al, underlies this conclusion [15].

Event-related potentials (ERPs) during oddball tasks and the behavioral performance on the Penn Conditional Exclusion Task (PCET) measure context-appropriate responding: P300 ERPs to oddball targets reflect detection of input changes and context updating in working memory, and PCET performance indexes detection, adherence, and maintenance of mental set changes.

More specifically, PCET variables quantify cognitive functions including inductive reasoning (set 1 completion), mental flexibility (perseverative errors), and working memory maintenance (regressive errors). Past research showed that both P300 ERPs and PCET performance are disrupted in psychosis. This study probed the possible neural correlates of 3 PCET abnormalities that occur in participants with psychosis via the overlapping cognitive demands of the two study paradigms. In a two-tiered analysis, psychosis (n=492) and healthy participants (n=244) were first divided based on completion of set 1 - which measures subjects' ability to use inductive reasoning to arrive at the correct set. Results showed that participants who failed set 1 produced lower parietal P300, independent of clinical status. In the second tier of analysis, a double dissociation was found among healthy set 1 completers: frontal P300 amplitudes were negatively associated with perseverative errors, and parietal P300 was negatively associated with regressive errors. In contrast, psychosis participants showed global P300 reductions regardless of PCET performance. From this Huang conclude that in psychosis, overall activations evoked by the oddball task are reduced while the cognitive functions required by PCET are still somewhat supported, showing some level of independence or compensatory physiology in psychosis between neural activities underlying the two tasks, as we can see in the following figure.

In this figure we can see the most elevate evoked potentials in Healthy sybjects (HS) compared with Psychotic patients.

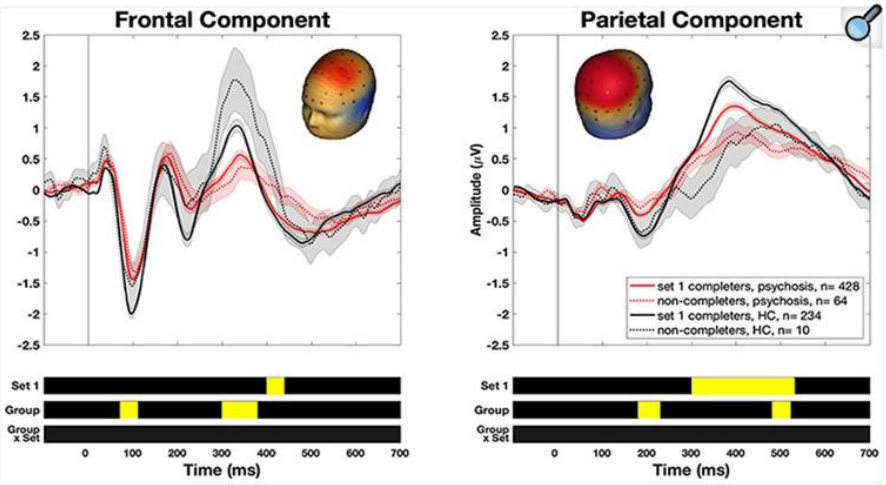

FIG. 1. **Amplitudes of frontal and parietal ERP components between set-1 completers and non-completers.**

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