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Auditory P300 event related potentials in acute and transient psychosis—Comparison with schizophrenia

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ABSTRACT

Background: Limited biological research data are available on acute and transient psychotic disorder (ATPD) vis-à-vis schizophrenia. P300 event related potentials (ERP) have been extensively studied as an important neurophysiological parameter in schizophrenia. However, no P300 ERP studies comparing the two disorders are available. We compared auditory P300 ERP in patients remitted from ATPD with schizophrenia in remission and biologically unrelated healthy controls.

Methods: In this case-control study design, 25 subjects remitted from ATPD were age-/gender-matched with healthy controls and patients with schizophrenia in remission. Clinical assessment and auditory P300 ERP (amplitude and latencies at central and parietal sites, reaction time) were recorded. The ERP parameters were compared across the three groups.

Results: All three groups showed significant differences in P300 amplitudes and latencies at central and parietal sites. Schizophrenia group differed significantly ($p < 0.001$) from the ATPD group in all the P300 parameters. The ATPD group was found to have lower Pz latency ($p < 0.05$) and lower mean reaction time ($p < 0.001$) as compared to healthy controls.

Conclusion: The results suggest that P300 could easily distinguish between ATPD and schizophrenia in remission, thus neurophysiologically differentiating the two disorders. Lower P300 latency and reaction time, which indicate hyper-arousability, distinguished ATPD from normal controls, with implications for a better understanding of ATPD.

1. Introduction

The status of Acute Transient Psychotic disorders (ATPD) as a distinct nosological entity continues to be debated, especially in comparison with schizophrenia. Although it does fulfill most of the earlier mentioned validating criteria (Robins and Guze, 1970), a huge lacuna still exists within the purview of laboratory research. Though family studies (Das et al., 1999; Singh et al., 2004) have tried to point out some genetic differences between ATPD and schizophrenia, few researchers have attempted to further examine this difference. ICD-10 (WHO, 1992) had mentioned that "Systematic clinical information that would provide definitive guidance on the classification of acute psychotic disorders is not yet available" in the description of ATPD.

The P300 event-related brain potential is an index of endogenous cognitive processes, typically elicited by infrequent sensory stimuli that are either task relevant or novel. It is associated with brain activity related to the engagement of attention especially orienting and involuntary shifts to changes in the environment. It is usually elicited by the "oddball" paradigm and amplitude and latency are measured at different positions (frontal, parietal and central). The P3a component of P300 is produced when a demanding stimulus commands frontal lobe attention (Allen et al., 2009) and P3b component is produced when attention resources are allocated for the memory updating in the temporo-parietal association cortex (Michie et al., 2002).

There are several studies across the world on P300 in patients with schizophrenia during different stages of illness. Reduced amplitude and/or delayed latency of P300 has been a robust finding in individuals with schizophrenia irrespective of neuroleptic medication status and phase of illness (Bramon et al., 2004; Jeon and Polich, 2003; Mathalon et al., 2000; Rao et al., 1995). P300 has many a times been proposed to be an endophenotype of schizophrenia. However, studies on P300 are lacking in ATPD. In a PubMed search, we could find only two published studies in patients with cycloid psychosis (now clubbed under ATPD) which

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had reported normal P300 latency but significantly higher amplitudes (Strik et al., 1996, 1993). Moreover, none of these existing studies have specifically used the ICD-10 diagnostic criteria for ATPD. To the best of our knowledge, there has been no P300 study conducted so far that attempts to compare ATPD diagnosed as per ICD-10 with schizophrenia.

In this study we attempted to study auditory P300 event related potentials (ERP) parameters in patients with ATPD in remission and compared it with patients with schizophrenia in remission and with biologically unrelated healthy controls. In addition, we also tried to study the differences in clinical variables such as age, gender, symptomatology, time of presentation and premorbid personality between the patients diagnosed with ATPD and those with schizophrenia.

2. Methods

A case control design was followed in which every patient of ATPD in remission was matched for age and gender with healthy controls and with age and gender for schizophrenia patients in remission. Patients were recruited over a period of one and half years (from January 2013 to June 2014). Twenty five patients each in the two disorders groups (ATPD and schizophrenia) and 25 healthy control subjects (with no mental disorder and biologically unrelated to the patients) were recruited by purposive sampling and one time cross-sectional assessment was done in all the subjects. The study was approved by the Institutional Ethics Board (Postgraduate Institute of Medical Education and Research, Chandigarh, India) and the methods used followed the broad definition of the Declaration of Helsinki. Written informed consent was obtained from all subjects prior to testing.

2.1. Subjects

All the patients were recruited from Outpatient Department of Psychiatry, Postgraduate Institute of Medical Education and Research, Chandigarh, India. Patients diagnosed as having ATPD and schizophrenia in remission by a consultant psychiatrist were approached. After obtaining informed consent from the patients and their accompanying caregivers, the patients were re-assessed on ICD-10 criteria to confirm the diagnosis. All the patients then underwent a comprehensive psychiatric, neurologic and medical evaluation. Psychiatric evaluation included assessment and rating of psychopathology on Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962) for the ATPD and schizophrenia group. We specifically chose BPRS scale as it has shown greater reliability in picking up affective symptoms inaddition to other symptoms of psychosis (positive, negative, disorganization etc.) keeping in mind that subjects with ATPD had more of an affective polymorphic symptomatology and most of the earlier studies on ATPD had used BPRS for assessing psychopatholgy (Agarwal and Sitholey, 2006; Bunevicius et al., 2014; Khanna et al., 1997; Strik et al., 1993). Additionally, BPRS had also shown good interrater reliability and consistency in assessing psychopathology in schizophrenia too (Andersen et al., 1989; Leucht et al., 2005).

All the patients in the ATPD group were in complete remission for at least 3 months after the onset of symptoms. Remission in the schizophrenia group was determined by using the defined criteria for remission of the Remission in Schizophrenia Working Group, 2005 (Andreasen et al., 2005). Current medications in all the patients were noted and the antipsychotic doses were converted to chlorpromazine equivalents (Woods, 2003).

Source of healthy controls was any healthy volunteer (in age group of 18–50 years) who consented for the study or was done by asking the index subjects to bring controls i.e. friend/spouse who after proper written and informed consent, were assessed in detail by using the Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998) to rule out psychiatric illness. None of the healthy controls had any personal or family history of any psychiatric or neurological illness. All the participants in the study were right handed.

Uncooperativeness, history of epilepsy, head trauma with loss of consciousness, medical diseases like uncontrolled diabetes mellitus and hypertension, history suggestive of intellectual disability or pervasive developmental disorders, substance dependence (excluding nicotine) and hearing impairment were exclusion criteria for all groups. Additionally, those subjects who had received Electroconvulsive therapy (ECT) in the past or those who had extrapyramidal symptoms (EPS) during the assessment were excluded from the study.

P300 data was successfully collected from 25 patients with ATPD, 25 patients with schizophrenia and 25 unrelated healthy controls.

2.2. Electrophysiological recordings

The auditory P300 ERP was recorded using Nicolet Viking Select system. EEG activity was recorded from the scalp with the help of 38 electrodes placed according to the 10/20 international system. Linked earlobes were used as the reference, the forehead as ground. The machine records the ERP tracing at the central (Cz) and parietal (Pz) sites and has an inbuilt facility to reject artifacts. Testing was done using auditory 'oddball' paradigm in which two types of sound were presented to the subject through a headphone. One masking noise that was continuous was of 40 dB and the other being an intermittent louder target noise produced at 55 dB randomly. The subject was directed to recognize the second type of noise and press a button given in his preferential hand each time he heard it. A preset count of 100 was made with a rejection level of 3 divisions. A total of 500 stimuli at a frequency of 0.3–1 Hz were presented with a 15% oddball stimulus. The standard tone was delivered at 1000 Hz and the 'oddball' tone at frequency of 2000 Hz. The data were bandpass filtered in range of 0.2 Hz–2 KHz. Data were digitalized with 12 bits of resolution at the rate of 256 samples per sec. Accepted target tones, for which a correct response had been recorded were averaged. The P300 waveform was located by identifying peaks within the time window of 250–420 ms post stimulus. The amplitude was measured in microvolts corresponding to the absolute value of the electrical potential attained from the trough of the proceeding, opposite waveform (peak to peak). Latency was measured in milliseconds from point of stimulus to attainment of peak voltage. The reaction time which is the time taken both cognitively to process and physically to respond to the stimulus is also an essential parameter of P300 (See Fig. 1). Reaction time in milliseconds was displayed as an average in the machine.

2.3. Analysis

The Statistical Package for Social Sciences (SPSS) version 21.0 for Windows was used. Descriptive analysis was carried out using mean and standard deviation with range for continuous variables and in terms of frequency and percentages for discontinuous socio-demographic and clinical variables. The three groups were compared using appropriate parametric and non-parametric tests such as unpaired student *t*-test, Fisher's exact test, Chi-square test and ANOVA wherever applicable. The findings of P300 parameters (mean amplitude, mean latency at Cz and Pz sites and reaction time) in the three groups were initially assessed for normality of distribution using Kolmogorov-Smirnov test, and then were compared using one way ANOVA followed by post-hoc analysis using Scheffe test.