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A STUDY OF P300 - EVENT RELATED EVOKED POTENTIAL IN THE PATIENTS OF MAJOR DEPRESSION

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Abstract : Many studies involving various electrophysiological parameters have been conducted in psychiatric disorders like schizophrenia and dementia to assess their cognitive dysfunctions. Not much reports are available in major depression. The present study was conducted in 20 patients of major depression to evaluate their cognitive functions in terms of P300. P300 or P3 wave of auditory event related evoked potentials (ERPs) is usually seen around 300 msec of presenting of target stimulus, if the subject is responding to it. Auditory ERPs were recorded using the standard 'odd ball' paradigm. The latencies of various compnents of ERPs N1, N2, P1, P2, and P3 were recorded and compared with those of 20 normal age and sex matched controls. The latency of P300 was found to be significantly delayed in cases of major depression as compared to that of controls. Other waves were also delayed in cases of depression but the difference was not statistically significant. Our results suggest that P300 latency is longer in the patients of major depression disorders which could be due to constitutive altered 'cognitive neuronal pool' or a neurotransmitter/neuropeptide imbalance. Further studies involving larger populations are required to elucidate the diagnostic and predictive role of latency of P300 in the cases of depression.

Key words : depression, event related evoked potential, P300 latency, cognition

INTRODUCTION

Event related evoked potential (ERP) is an endogenous potential which represents the cognitive functions of the brain. There are several studies showing the presence of abnormal ERPs in cognitively impaired patients e.g. Alzheimers, Schizophrenia, Dementia, and the mentally retarded. A lot of variability exists in the results obtained in the ERPs recorded in various psychiatric disorders. For example, there are many reports of P_{300} abnormalities in schizophrenia (1, 2, 3), stating that these patients have smaller P3 amplitudes than their controls. Shagess et al (4) also reported that depressed patients had smaller P_{300} than controls and that the depressed patients' P_{300} amplitudes usually fell between the Schizophrenics and that of

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controls. Two studies (2, 5) report that schizophrenics had delayed P_{300} latency.

Amidst so much of variability in the P_{300} latency and amplitude in psychiatric disorders, this study was undertaken to assess P_{300} changes in patients of major depression using auditory event related potentials.

METHODS

The present study was carried out in the Department of Physiology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi.

20 patients of major depression, in the age group of 35.55 ± 11.28 years, were taken from the Psychiatric O.P.D. of Guru Teg Bahadur Hospital. The diagnosis was made on the basis of the DSM IV criterion for major depression. A detailed medical, neurological, psychiatric and personal history was taken. Patients suffering from hypertension, diabetes mellitus or any other major medical disorder were excluded from the study. Similarly smokers or patients suffering from any type of addiction were not included in the study. The duration of illness for which the person suffered from the disease was on an average between eight to ten years. The severity of symptoms of depression was also classified on the basis of scale given in the DSM IV criterion for major depression. A detailed treatment history was also recorded taking into consideration the types of drugs the patient was on and how compliant he was. The history of E.C.T. was also looked for. Most of our patients belonged to lower middle class stratum of the society and were well aware of their illness and symptoms. All of them were literate with a fairly good I.Q. level, though a formal I.Q. evaluation was not done. They were age and sex matched with twenty healthy control subjects (age 34.15 ± 10.87 years), belonging to the paramedical staff of the college, were taken as controls.

Recording of P_{300}

The technique of recording auditory event related evoked potentials using 'odd ball' paradigm is a standard one which has already been used in our own department for various cognitive studies (6, 7, 8) including the one reporting the nomative data (9).

Evoked responses were picked up from the scalp by using Ag/AgCl disc electrodes, mounted on Cz, Pz, A1, A2 positions as per 10-20 international System of electrode placement.

The SMP-4100 system was used for measuring ERP along with MEB 5200 Evoked potential recorder (Nihon Kohden, Japan). With the help of shielded headphones (Elagra Dr 531) attached to it, two differently pitched tones were delivered binaurally with a relatively long inter-stimulus interval. The frequent non-target stimulus had a frequency and target of 2 K Hz. The stimulus rate was 0.5 Hz and stimulus sequence was random.

Subject was well informed about the testing procedure. He was made to relax, feel comfortable and sit on a chair in a sound-proof and air-conditioned room. Electrode recording sites on the scalp were

thoroughly cleaned with spirit and skin-pure. Electrolyte paste (Elefix) was applied on the recording surface of disc electrodes. Electrodes were positioned and fixed with sticking tape. These electrodes were then connected to an impedance meter and skin to electrode transition impedance monitored and kept below 5K Ohms. The montages used were as follows :

Active electrode (-) : Vertex (Cz), Midline parietal (Pz)

Reference Electrode (+) : Both ears connected (A1 + A2)

Grounding Electrode : Forehead (Fpz)

After the electrodes were connected, the subject was prepared and equipment switched on. The monitor display was checked to ensure that the incoming signals did not exceed 50-60% of display dimension; if they did, the whole procedure of preparation of subject and measurement was redone. The subject was asked to respond by pressing a button each time the rare stimulus was presented. For this event, the response obtained was amplified, averaged (32 counts) into a computer and displayed on the CRT screen of the Evoked Potential recorder. The graph was obtained on the heat sensitive paper and also on the X-Y plotter of the machine.

The long latency Event Related Potential responses in the auditory 'odd-ball' paradigm stimulus consist of up going negative and down going positive waves P1, N1, N2, P3. The latencies of these various waves along with amplitude of P300 were recorded with the help of cursors. The alues of these latencies and P3 amplitude of the patients were compared with that of the controls.

RESULTS

Table I shows the values of latencies of various negative and positive waves of ERPs. Of these, initial components i.e. P1, N1, P2 are supposed to be stimulus related and latter N2, P3 are event related.

The latencies of N2, P2 though are higher in patients but the latency of the P300 component of event related potential was significantly more in the patients of major depression as compared to that of controls ($P < 0.05$). The representative tracings of ERP of a control and a case of depression are shown in Fig 1. However, no significant difference was found in the P300 amplitude of the patients and that of the controls.

TABLE I : Showing values of ERPs in control and patients of depression.

ERP Parameter	*Control*	*Patients*	*P value*
N1 Latency (msec.)	122.60 ±38.27	119.40 ±19.80	N.S.
N2 Latency (msec.)	224.40 ±37.40	243.70 ±35.05	N.S.
P1 Latency (msec.)	74.30 ±31.60	80.80 ±25.23	N.S.
P2 Latency (msec.)	185.90 ±34.59	195.20 ±430.11	N.S.
P3 Latency (msec.)	329.10 ±34.84	360.40 ±38.81	0.001
P3 Amplitude (uV.)	13.20 ±4.96	13.84 ±4.82	N.S.

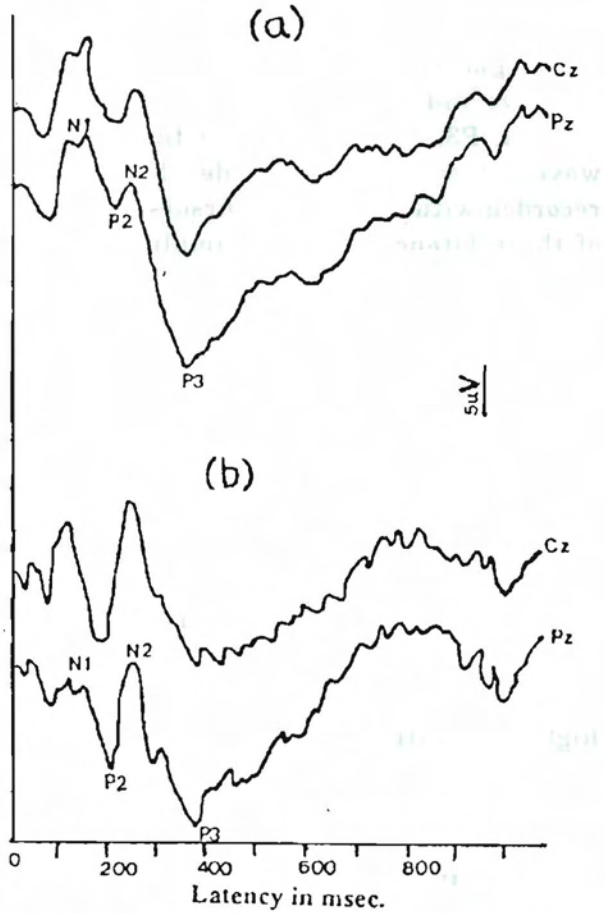

Fig. 1 : Graph showing ERP recordings (a) Control and (b) Patient of depression.

DISCUSSION

Our study showed a significant increase in the latency of the P300 component of the ERPs in the patients of major depression. In electrophysiological terms the interval between a stimulus and the peak of P300 depends on the latency of the endogenous event which in turn depends on the time required to recognize and evaluate its relevance and subjective probability. A slower reaction time can be attributed to various reasons like:

(a) A patient of major depression was less prepared for the stimulus,

(b) He had a greater difficulty in discriminating between different stimuli,

(c) He is less confident about his decisions,

(d) His decision time is longer, or

(e) His response execution time is longer

Since P300 depends on the contexual evaluation of the stimulus, all the above factors could be contributing towards a delayed P300.

The P_{300} component of ERP vocabulary, elucidates aspects of human information processing programmes. There are a multitude of neural elements which determine the meaning of an ERP. They happen to have a property of being simultaneously activated at certain clinical points in the information processing activity of the cortex. Thus ERPs map out the so called COGNITIVE SPACE which consists of interalia of the decisions, expectations, plans, strategies, associations and memories. A delayed P_{300} wave could be a reflection of an altered cognitive space in the patients of major depression. Whether this altered cognitive function is costitutive of the pathology of depression disorder, or, it is genetically inherent in the patients of depression or people who are prone to develop affective depressive mood disorder, are a few questions which when answered could give us a better understanding of role of ERPs in depression disorders.

A delayed appearance of the P_{300} compnent of ERP could also be a reflection of an altered neurochemical profile in a patient of major depression, which is very basic and well propounded in the pathophysiology of depression. The catecholamine (10) and indolamine (11) deficiency hypothesis was the first major hypothesis of the pathophysiology of depression. The cholinergic hypothesis (12) states that excess cholinergic activity is involved in depression. Various neuropeptides such as CRH, ACTH, VIP, TRH, VIP, CCK, beta-endorphin, substance P, oxytocin, neuropeptide Y, somatostatin, galanin and many other neuropeptides are co-localized and co-released with the classical neurotransmitters like NA, 5-HT, DA and Ach. Studies on the role of these neuropeptides in the pathogenesis of depression are available, which indicate that these neurochemicals either directly, or to some extent, indirectly through their interaction with the classical neurotransmitter system are involved in the pathogenesis of depressive illness (13, 14, 15, 16, 17). And since interactions of some of these very transmitters and neuropeptides may also generate N2 and P3 compnents of ERPs and result in gene expression for depression, it provides a broader and heterogeneous platform for elucidation of exact pathogenesis of depression.

All the patients in our study were on antidepressant medication, and, their case histories varied in severity and duration. Inspite of the heterogenity in duration, severity, treatment compliance, individual response to treatment and other occult factors our group of patients of major depression showed a delay in electro-physiological parameter of cognitive function that is P_{300}. Thus we could hypothesize that a delayed P300 component is an elctro-physiological feature of depressive illness. Though its sensitivity and specificity in making a diagnosis or predicting an individual's probability of developing major depression requires further research involving larger population sizes.

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