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P300 IN PATIENTS WITH ALCOHOL DEPENDENCE

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ABSTRACT **Objective:** To study the change in amplitude and latency of P300 in patients with alcohol dependence as compared to the normal controls. Scalp recorded P300, the long latency event-related potential (ERP) occurring in response to stimulus is primarily originated from sub-cortical structures, has been reported to be an indicator of neuronal structure change. **Aim:** This study aimed to evaluate cognition in patients of alcohol dependence with two weeks abstinence using (Event Related Potential) P300 auditory paradigm. **Methods:** Forty four male patients (mean} ±SD age: 43.61} ±7.38} range: 20-60) with alcohol dependence diagnosed to ICD-10 criteria and 44 male healthy control (mean} ±SD age: 42.64} ±8.33} range: 20-60) were included in the study. Auditory ERP's were recorded by odd ball two sound discrimination task procedures after two weeks abstinence. **Results:** Compared with healthy subjects (n = 44), patients had prolonged latencies (P = 0.003) decreased amplitude (P = 0.701) of P300 component of ERPs. We found that the patients had significantly longer P300 latency. P300 amplitude was not significantly different from those of the controls. **Conclusion:** We concluded that our finding of delay P300 latency and decrease in amplitude may indicate neuronal structure impairment due to alcohol in patients with alcohol dependence. Our results indicated cognitive impairment in patients with alcohol dependence. This is important to determine prognosis and managing patients.

KEYWORDS : alcohol dependence, cognitive functions, event related potential.

INTRODUCTION

Today alcohol abuse and dependence are most common substance related disorders. In India, it is estimated that 75 million people are alcohol users.[1] Fifty to 80% of individuals with alcohol use disorders experiences mild to severe neurocognitive impairment, mainly affecting executive functions, episodic memory, and visuospatial capacities related to multiple brain lesions.[2]

P300 is a component of event related potential and named so as it occur about 300 m sec after the stimulus. Event-related potentials ERPs recorded from the human scalp can provide important information about how the human brain normally processes information. ERPs are very small voltages generated in the brain structures as reaction to specific stimuli.[3] The P300 wave is a positive deflection in the human ERP. Typical peak latency in young adult subjects making a simple discrimination is 300 ms. It can be obtained in an "oddball" paradigm when a subject detects an occasional "target" stimulus in a regular train of standard stimuli.[4] They are believed to reflect activity of complex neuronal networks responsible for new stimuli detection and discriminative behaviour of individuals e.g. important stimulus versus unimportant.[5]

In previous studies it was also shown that alcoholics had significantly delayed P300 latencies.

Maes M. et al. (2001)[6] and Kim H S.et al. (2004),[7] found significantly longer latencies in alcoholic patients compared to the controls.

The present study was planned to evaluate the cognitive functions using event related potentials P300 and in patients of alcohol dependence with two weeks abstinence (recently detoxified alcoholic individuals)[8] and compared the findings with that of the normal healthy controls.

MATERIALS AND METHODS

This study was conducted by the Department of Physiology in associations with Departments of Psychiatry and Neurology, Indira Gandhi Medical College (IGMC) Shimla, which is one of the tertiary care centers of Himachal Pradesh and also has coverage of majority of population of this state.

Sociodemographic profile: The mean age of the two groups was 43.61years (SD±7.38) for the patients of study group and 42.64 years (SD±8.33) for the normal healthy control group. Among forty four patients thirteen were matriculate (29.5%). Fourteen patients (31.86%) were educated above tenth standard, where as fifteen (34.1%) patients were less then tenth standard. Only two patients were illiterate. Controls included in study had same level of education as that of the experimental group.

Study subjects: Forty Four patients of alcohol dependence syndrome of study group diagnosed as per ICD-10 criteria were recruited during the third week of their treatment (detoxification) in Department of Psychiatry, IGMC and Hospital Shimla. Twenty eight patients of alcohol dependence were brought by family members or relatives and sixteen had come themselves for seeking treatment. They had all abstained from alcohol for at least two weeks. For the normal Control group, 44 normal healthy subjects were selected from amongst the volunteers and attendants of Psychiatric and Neurological patients with the Psychiatry or Neurology Departments. A written informed consent was obtained from all subjects before their participation. The study was approved by ethical committee of IGMC Shimla.

Selection of subjects: a). Study group: Subjects who fulfilled the following inclusion and exclusion criteria were included in the study. Inclusion Criteria: Male patients of alcohol dependence between age group 20-60 years, abstinent from alcohol for at least 2 weeks who fulfilled ICD-10 criteria for diagnosis of alcohol dependence syndrome. Exclusion criteria: Patients with hearing loss, significant liver disease, clinical evidence of Wernicke-Korsakoff syndrome, significant history of head trauma or brain surgery and history of anticholinergic drug scopolamine and drug dependence other than nicotine or caffeine. b). Control group: The control group included forty four normal healthy male subjects. Selection of subjects was made who fulfilled the following criteria: Inclusion criteria: Normal healthy male subjects between 20-60 years of age. Exclusion criteria: Subjects with hearing impairment as determined by the standard protocol for P300 studies in the Department of Neurology, IGMC Shimla, not having any serious medical problem or psychiatric illness on anamnestic recall, significant history of head trauma or brain surgery and history of anticholinergic drug scopolamine of drug dependence other then nicotine or caffeine

ASSESSMENT TOOLS

ALCOHOL USE EVALUATION WAS DONE USING: 1). Alcohol Use Disorder Identification Test (AUDIT) Questionnaire.[9] 2). CAGE

Questionnaire.[10] The patients of alcohol dependence with two weeks abstinence were assessed on structured interview schedules AUDIT (Alcohol Use Disorder Identification Test) and CAGE (Cut Down, Annoyed, Guilty and Eye opener) Questionnaire.

P300 COGNITIVE FUNCTION TEST: Recording of P300 was done using twelve channels Nihon kohden machine, MEB 2300 by an auditory 'odd ball' paradigm in all the subjects. It has an in built facility to rejects artifacts. The stimuli were presented through earphones which have supra-aural ear cushions. The auditory stimuli consisting of common and rare types. The subjects were first explained about the odd ball procedure for recording P300. The areas of electrodes placement were cleaned with cotton dipped in rectified spirit. Rubbing was done till the surface appeared red, indicating high vascularity. Clean silver Surface recording electrodes on which bentonite paste was put, were placed at F_z, C_z, and P_z and referenced to link mastoid $A_1 + A_2$. Ground electrode was placed at Fp_z. Additional infra orbital electrodes $X_1 + X_2$ were placed to monitor eye movements and to remove the contaminated response wave form from averaging. The impedance of all electrodes was maintained at less than 5 kilo ohms during the whole recording procedure. After impedance matching earphones were placed without dislodging of the electrodes. Sound were delivered binaurally through the head phones. Target infrequent high-pitch tones of 2000 Hz (20% rare) randomly presented in a series of non target low-pitch tones of 1000 Hz (80% frequent). The latency and amplitude of P300 was measured.

DATA ANALYSIS
Calculations were done with statistical software SPSS window, version 20. Data were presented as mean ± standard deviation. Student's *t*-test was used for comparison of means. Correlation between score of cognitive testing P300 and clinical characteristics were assessed using Pearson's test.

RESULTS
P300 LATENCY AND AMPLITUDE IN PATIENTS OF ALCOHOL DEPENDENCE AND NORMAL CONTROL GROUP
The mean P300 latency of alcoholic patients was 371.00±43.77 msec. and those of the normal controls 344.64±39.04 msec. There was a significant difference in the mean latency of two groups (p=0.003*). Statistically no significant difference was found in P300 amplitude in two groups (patients of alcohol dependence7.26±4.027 μv and normal controls 6.1±4.42 μv was compared (p=0.701) (Table-1).

Table-1 P300 latency and amplitude in patients of alcohol dependence and normal control group

Variable		Patients (n=44) mean±SD	Normal Controls (n=44) mean±SD	Significance P
P300	Latency msec	371+-43.77	344.64+-39.04	0.003*
	Amplitude μv	7.26+-4.02	7.61+-4.42	0.701

DISCUSSION
Alcohol dependence is a chronic disease resulting in disturbances of various cognitive functions. Parson et al. when examined patients of alcohol addiction, found reduced blood flow rates, glucose metabolism disturbances in prefrontal cortex, in structure of the limbic system and cerebellum as well as decreased number or size of neurons, glia hypertrophy in the hippocampus and in the frontal cortex with reduced number of neural connections in these brain structures.[11]

Even mild-to-moderate drinking can adversely affect cognitive functioning (i.e., mental activities that involve acquiring, storing, retrieving, and using information).In our study all the subjects were male between 20-60 years of age. This reflects that female drinking is less in the region and is still currently unacceptable. It is also possible that less number of females utilize de-addiction services in general hospital setting due to socio-cultural issues of a society in which female drinking is still a taboo.

The relationship between drinking and cognitive function may be confounded by various other factors including family history, head trauma and diet. Maintenance of lasting abstinence is associated with cognitive recovery in these patients, but some impairment may persist and interfere with the good conduct and the efficacy of management.[12]

The patients of alcohol dependence with two weeks abstinence were assessed on structured interview schedules AUDIT (Alcohol Use

Disorder Identification Test) and CAGE (cut down, annoyed, guilty and eye opener). These are the instruments for screening of alcohol use disorder. These instruments are highly sensitive, easy to administer and are brief. Both these test have been validated for use in clinical and epidemiological settings. The information was also obtained from the family members of patients to corroborate the findings.

In the present study the cognitive functions assessed by P300 of event related potential in the patients of alcohol dependence with two weeks abstinence were compared with normal healthy controls. Analysis of independent sample test for P300 revealed a significant group difference for P300 latency.

The P300 latency of patients of alcohol dependence was found significantly delayed. Moreover, alcoholic individuals displayed reduced amplitude of event related potential P300 but there was statistically no significant difference the two groups. The latency and amplitude of P300 wave in the present study for the control group and study group are shown in table[1].

P300 abnormalities have been reported in alcoholism in several studies. Basically, P300 amplitude is reduced and P300 latency is prolonged.13,14,15 The present study also shows similar results.

In our study the cognitive functions assessed by P300 in patients of alcohol dependence with two weeks abstinence were significantly different from that of normal healthy controls, indicating that alcohol dependence has contributed to cognitive dysfunctions.

CONCLUSION
P300 latency in patients with alcohol dependence was significantly different from that in normal controls. P300 latency was longer in patients with alcohol dependence as compared to normal controls. There was no significant difference in P300 amplitude between the patient group and normal control group. Such results indicate impairment in cognitive functions in patients with alcohol dependence.

LIMITATIONS OF THE STUDY
Though conducted with a relatively sound methodology, this study nonetheless has few limitations. The study did not include women. Assessment was made, when the patients abstinent for two weeks. Greater delay between starting sobriety and assessment would reduce the bias of prolonged withdrawal symptoms. This study has shown that cognitive impairment is especially prolonged in early abstinence and might recover with longer duration of abstinence. More analytical studies, especially of longitudinal design, are required to establish the association of different Sociodemographic variables with alcohol consumption and consistency of different patterns of consumers.

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