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Original Article

Physiology Section

Visual Evoked Potential Response Among Drug Abusers- A Cross Sectional Study

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ABSTRACT

Introduction: There is important preclinical evidence that substance abuse may produce neurophysiological disturbances particularly in relation to altered neural synchronization in Visual Evoked Potentials (VEP).

Aim : The purpose of current study was to compare the latencies and amplitudes of different waveforms of VEP among different drug abusers and controls and also to identify early neurological damage so that proper counseling and timely intervention can be undertaken.

Materials and Methods: VEP was assessed by Data Acquisition and Analysis system in a sample of 58 drug abusers, all males, within age group of 15-45 years as well as in age matched 30 healthy controls. The peak latencies and peak to peak amplitudes of different waveforms were measured by applying one-way Anova test and unpaired t-test using SPSS version 16.

Results: In between drug abusers and controls, the difference in the duration of N_{75} and P_{100} waveform of VEP was found to be statistically highly significant ($p<0.001$) in both the eyes. Also the amplitude of wave P_{100} was found to be decreased among drug abusers in both eyes.

Conclusion: Chronic intoxication by different drugs has been extensively associated with amplitude reduction of P_{100} and prolonged latency of N_{75} and P_{100} reflecting an adverse effects of drug dependence on neural transmission within primary visual areas of brain.

Keywords: Amplitude, Latency, Visual stimulus

INTRODUCTION

Evoked potential has emerged as an important electro diagnostic technique. It measures electrical activity in brain in response to stimulation of sight, sound or touch. Drug addiction is a chronic, often relapsing brain disease because the abuse of drugs leads to changes in the structure and function of the brain [1]. It causes immediate and long-term problems. The most common types of drugs that people abuse fall into four categories: stimulants, depressants, hallucinogens and opioids. While the effect of each group of drugs is different, all of them are harmful to our body. It is unhealthy for the user's body, mind and social life [2].

It is estimated that 20 percent of Americans have used prescription drugs for non-medical reasons, which is prescription-drug abuse. Sedatives, tranquilizers and stimulants are used recreationally, a practice that has increased in recent years. Like prescription drugs, there are too many illegal drugs to go through the effects of each one, but, also like the prescription drugs, the abuse of any one of them, whether marijuana, LSD, or heroin, is unhealthy for the user's body, mind and social life [2]. The measurement of visual evoked potentials (VEP) has been considered a novel technique for assessing the neurological changes including subclinical state as a result of exposure to different drugs.

It is in this connection that the evoked potential study was done in drug abusers and the main objective of the present study was to detect subclinical abnormalities induced in visual pathways in a group of different drug abusers using VEP technique. Various researchers have done studies to evaluate the effects of different drugs on CNS using evoked potential studies.Chronic cigarette smoking and opium-dependence together significantly increase the amplitude of VEP as compared to chronic cigarette smoking alone. It may be probably due to the chronic stimulatory effects of these two substances on the visual system [3]. Decreased amplitude and increased latency of P_{100} component of averaged evoked potential has been reported in opiate abusers as compared to normal subjects which can be interpreted as a consequence of brain stem transmission disorders resulting from chronic intoxication [4,5]. The study on pattern shift VEP among 24 alcohol-dependent patients revealed statistically significant delays in P_{100}, and an increased number of clinical VEP abnormalities, among alcoholic patients in comparison to the control group [6].

MATERIALS AND METHODS

VEP were performed by using Data Acquisition and Analysis System, Medicaid Systems, Chandigarh, India in a sample of 58 different drug abusers and 30 controls. All the subjects were males in the age group of 15-45 yrs. The study was done at Guru Gobind Singh Medical College, Punjab during the period from June 2012 to March 2013. The patients were taken from Drug De-addiction Centre of this institute. Prior informed consent was obtained from each individual and the study was approved by the Institutional Ethics Committee. A self designed questionnaire (Proforma) was administered to all the subjects.

The substance abusers which were recruited for this study was alcoholics, opiate addicts e.g. heroin, morphine, tobacco chewers/ smokers, pharmaceutical drugs addicts like using cough syrups, pain killers, anti-emetics, etc. The subjects excluded from the study were the persons suffering from any type of post traumatic coma, neurological diseases (multiple sclerosis, optic neuritis, optic neuropathy etc.,), other psychiatric disorders, visual defects, etc. The patient was explained the test to ensure full cooperation. The usual glasses were allowed to put on during the test. The subjects were asked to discontinue any miotic or mydriatic drugs 12 hours before the test. Instructions were given to the subject not to sleep during the procedure and to fix the gaze at the centre of screen.

Equipment set up for VEP study was done as recommended by International Federation of Clinical Neurophysiology (IFCN) committee [7]. Two channels were used:

Channel 1: Oz – Fp_z Channel 2 : O_Z - A_1A_2 (linked ear)

The subjects were allowed to sit comfortably in a fully relaxed state. One eye was tested at a time. The skin at the point of placement of the electrodes was cleared with spirit. Using electrode paste or conducting jelly, the recording electrode was placed at occiput (o_z), the reference electrode at Fp_z or 12cm above the nasion. The ground electrode was placed at the vertex (C_z). The visual stimulus was delivered by LED goggles using red flash of light. To record flash visual evoked potentials, the low cut filter was set at 2 Hz and high cut filter at 200 Hz. Sweep speed was 50ms/div and sensitivity was set at 2μ v/div. About 200 epochs were averaged. The electrode impedance was kept below 5 kohms.

STATISTICAL ANALYSIS

The peak latency and peak to peak amplitudes of different waveforms (N_{75}, P_{100} and N_{145}) were measured and the data was compared between different drug abusers and controls and also in between the different groups of drug abusers and analyzed by applying unpaired t-test and one-way Anova test using the SPSS system (version 16.0 SPSS Inc., Chicago, IL, USA). The p-value <0.05 was considered to be statistically significant.

RESULTS

[Table/Fig-1] shows the comparison of the duration of different waveforms of VEP (N_{75}, P_{100}, N_{145}) of right eye between the drug abusers and controls. It was found that mean ± SD of latency of waveform N_{75} was 91.56 ± 15.63 among drug abusers while 70.76 ± 9.82 in controls and the difference between the two groups was found to be highly significant statistically (p<0.001). Also, mean ± SD of latency of waveform P_{100} was 129.45 ± 14.54 in drug abusers and 108.37 ± 25.46 among controls and the difference between the two groups was found to be highly significant statistically (p<0.001). Mean ± SD of waveform N_{145} was 165.13 ± 17.22 in drug abusers and 161.56 ± 37.55 in controls and the difference between the two groups was found to be statistically insignificant (p>0.05).

[Table/Fig-2] shows the comparison of the duration of different waveforms of VEP (N_{75}, P_{100}, N_{145}) of left eye between the drug abusers and controls. It was found that mean ± SD of N_{75} was 95.13 ± 22.97 in test subjects while 67.43 ± 7.80 in controls and the difference between the two groups was found to be highly significant statistically (p<0.001). Mean ± SD of P_{100} was 125.81 ± 16.95 among tests and 109.20 ± 15.33 among controls and the difference between the two groups was found to be highly significant statistically (p<0.001). Lastly mean ± SD of N_{145} was 160.60 ± 20.58 in abusers while 156.96 ± 43.92 in controls and the difference between the two groups was found to be statistically insignificant (p>0.05).

[Table/Fig-3] shows the comparison of amplitudes of P_{100} of VEP of both the eyes. In right eye, mean ± SD of amplitude was 5.87±3.97 in abusers while 7.72±2.05 among controls and the difference between the two groups was found to be significant statistically (p<0.05). And in left eye, it was 4.86±2.52 in test subjects and 9.68±5.01 in controls and the difference between the two groups was found to be highly significant statistically (p<0.001).

Eye	Wave	Drug abusers		Controls		T Value	p-value	Significance
		Mean	SD	Mean	SD			
Right	N_{75}	91.56	15.63	70.76	9.82	6.63	<0.001	HS
	P_{100}	129.45	14.54	108.37	25.46	4.95	<0.001	HS
	N_{145}	165.13	17.22	161.56	37.55	0.61	>0.05	NS

[Table/Fig-1]: Comparison of duration of waves (ms) of VEP of right eye between Drug Abusers (n=58) and Controls (n=30).
S= Significant (p<0.05), HS= Highly Significant (p<0.001), NS= Non Significant (p>0.05)

Eye	Wave	Drug abusers		Controls		T Value	p-value	Significance
		Mean	SD	Mean	SD			
Left	N_{75}	95.13	22.97	67.43	7.80	6.40	<0.001	HS
	P_{100}	125.81	16.95	109.20	15.33	4.43	<0.001	HS
	N_{145}	160.60	20.58	156.96	43.92	0.53	>0.05	NS

[Table/Fig-2]: Comparison of duration of waves (ms) of VEP of left eye between Drug Abus ers (n=58) and Controls (n=30).
S=p<0.05, HS=p<0.001, NS=>0.05)

Eye	Wave	Drug abusers		Controls		T Value	p-value	Significance
		Mean	SD	Mean	SD			
Right	Amp	5.87	3.97	7.72	2.05	2.38	<0.05	S
Left	Amp	4.86	2.52	9.68	5.01	5.84	<0.001	HS

[Table/Fig-3]: Comparison of Amplitude (μv) of w aveform (P_{100}) of VEP of right and left ey es between drug abusers (n=58) and controls (n=30).
(S=p<0.05, HS=p<0.001, NS=>0.05)

Eye	Wave	Mean ± SD				f Value	p-value	Signi-ficance
		Opiates (n=21)	Alcohol (n=11)	Pharma (n=14)	Tobacco (n=12)			
Right Eye	N_{75}	88.62± 14.80	92.91± 13.77	94.84± 15.68	83.83± 7.30	1.641	0.191	NS
	P_{100}	128.12± 13.65	129.09± 17.75	130.07± 12.07	126.58± 9.42	0.158	0.924	NS
	N_{145}	164.02± 19.46	161.32± 14.67	165.95± 12.61	164.58± 6.03	0.2	0.896	NS
	AMP	6.16± 4.30	3.90± 2.64	7.05± 4.47	6.13± 3.36	1.273	0.293	NS

[Table/Fig-4]: Comparison of duration of waves (ms) and amplitude (μv) of VEP of right eye between different groups of Drug Abusers (n=58) using one-way Anova Test.
(S=p<0 .05, HS=p<0.001, NS=> 0.05)

Eye	Wave	Mean ± SD				f Value	p-value	Signi-ficance
		Opiates (n=21)	Alcohol (n=11)	Pharma (n=14)	Tobacco (n=12)			
Left Eye	N_{75}	93.75± 32.00	93.93± 17.14	99.75± 27.83	79.33± 9.54	1.497	0.226	NS
	P_{100}	127.01± 18 .80	129 .23± 17.66	126.9 8± 15.08	112 .92 ± 10 .63	2.596	0.062	NS
	N_{145}	159.30± 24 .65	160.91± 17.03	159.4 0± 21.83	164± 6.25	0.163	0.921	NS
	AMP	5.02± 2 .81	4.1 7± 2 .80	5.3 4± 2.48	4.60± 0.75	0.549	0.651	NS

[Table/Fig-5]: Comparison of duration of waves (ms) and amplitude (μv) of VEP of left eye between different groups of Drug Abusers (n=58) using one-way Anova Test.
(S=p<0 .05, HS=p<0.001, NS=> 0.05)

In [Table/Fig-4] the latencies of different waveforms and amplitude were compared between different groups of drug abusers by applying one-way Anova technique and the difference in amplitude and latencies was found to be insignificant statistically (p>0.05) in all the waveforms of VEP of right eye.

In [Table/Fig-5], the latencies of different waveforms and amplitude were compared between different groups of drug abusers by applying one-way Anova technique and the difference in amplitude and latencies was found to be insignificant statistically (p>0.05) in all the waveforms of VEP of left eye.

DISCUSSION

Drug abusing is a big upcoming health problem prevalent in all societies. Unfortunately, across the globe and throughout time, drug abuse has manifested itself in one form or another, so it appears that drug-abusing affects both the psychological and physical well being of a person. The negative effects from drug abuse can have immediate and long-term consequences [8].

The recording of potential differences from scalp on giving visual stimuli is known as visual evoked potential and it shows a resultant response of cortical as well as subcortical areas. A normal VEP indicates the intactness of visual system. VEP is primarily a reflection of activity originating in the central visual field which is relayed to the surface of occipital lobe [9]. The P_{100} waveform of VEP is generated in primary visual area and visual association

areas (area 18 and 19) due to increased metabolism in these areas on giving stimulation [10].

So it is in this context that visual evoked potential study was done on a group of different drug abusers as VEP is considered to be a very useful technique for assessing the neurological damage done in optic nerve fibers. It is used to check the functional integrity of visual pathway.

This study compared the amplitudes and latencies of different waveforms (N_{75}, P_{100}, N_{145}) of VEP in a group of different drug abusers (n=58) with controls (n=30) and also in between the different groups of drug abusers.

In this study, the latencies of waves N_{45} and P_{100} of both the eyes was found to be prolonged in all the groups of drug abusers as compared to controls. It could be due to delay in conduction velocity associated with demyelination of optic nerve pathways because of chronic intoxication by different drugs. The latency of P_{100} depends upon the surviving fastest conducting fibers [11].

In this study, the amplitude of wave P_{100} of both eyes was also found decreased in different drug abusers. It could be due to axonal loss leading to conduction block of fibers in optic nerve pathway because of chronic and prolonged use of different drugs. But no difference was found in the amplitude and latencies of different waveforms of VEP of both the eyes in between the different groups of drug abusers. So it could be due to that all the drugs are affecting the visual pathway in the same way i.e. by damaging the myelin sheath of the nerve fibres, which is responsible for the fastest conduction in myelinated nerve fibres, leading to the prolongation of the duration of transmission of impulse across the optic nerve pathway. Similar findings were also reported by who found progressive bilateral and symmetric visual loss associated with optic neuropathy in alcoholics [12].

Kriss et al., also found gross VEP abnormalities on central field stimulation in 23 patients with tobacco-alcohol amblyopia [13]. Gross VEP abnormalities is in the form of loss of major positive components and its replacement by a negative wave N_{100} derived from paramacular areas of the field [14]. Chronic alcohol and tobacco smoking intake have been extensively associated to P_{100} amplitude reduction and prolonged latency [6,13,15-17]. Opioids (morphine, fentanyl) stimulates the retino-geniculate-cortex pathway and the thalamus-cortical circuit through the opioid receptors. Hence VEP is considered to be a useful tool for studying the side effects of different drugs on the visual system [18].

Decreased amplitude and increased latency of P_{100} component of averaged evoked potential has also been reported in opiates as compared to normal subjects which can be interpreted as a consequence of brain stem transmission disorders resulting from chronic intoxication [4,5,18,19]. Pharmacological drugs abusers (cough syrups, pain killers, antiemetics) also found increased latency of wave P_{100} [20]. Users showed similar results were shown by researches done on other drugs which includes amphetamine slowed reaction time and reduced early processing. Similarly, inhalant (volatile solvent) and N_2O abusers showed abnormal visual and auditory evoked potentials. N_2O damages the nervous system of chronic abusers. Evoked potentials showed abnormal VEPs with prolonged peak latencies of P_{100} [19-21]. Besides VEP, other evoked potential studies on a group of different drug abusers also showed the similar findings [22].

Therefore, our findings corroborate with the findings of above authors, thereby reiterating the fact that any type of drug abuse could damage the optic nerve pathways leading to long term effects on visual pathway.

LIMITATION

The limitations of the study is small sample size and also the effect of duration of exposure to different drugs on VEP can be studied between different drug abusers and be the area of future research.

CONCLUSION

In this study, the latencies of waves N_{45} and P_{100} of VEP was found increased and amplitude of waveform P_{100} was found to be decreased in both the eyes among all the groups of drug abusers because of brain stem transmission disorder in visual pathway due to chronic intoxication by different drugs. It could be due to defective myelination of optic nerve fibers and axonal loss leading to conduction block in visual pathway. It can therefore be assumed that VEP testing is a useful tool for evaluating effects of drugs on the visual system so that timely intervention and counseling can be done to prevent the adverse effects on the functional intactness and integrity of the visual pathway and also to motivate the drug abusers to go for de-addiction to prevent the permanent visual loss and to improve the quality of health care.

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PROFORMA

- Name Age Sex
- Address
- Occupation
- Type of substance abuse
- Family History of substance abuse
- Age at first substance abuse
- Frequency of substance abuse
- Quantity of substance abuse
- Total duration of substance abuse
- Time of last use
- History of any medical problem-i.e. any
  - Post traumatic coma
  - Visual defects
  - Other Psychiatric Disorders
  - Neuro logical diseases (Multiple Sclerosis, Optic neuritis, Optic neuropathy)
- History of any medication

RESULTS

VEP READINGS

Waves	N_{75} (msec.)	P_{100} (msec)	N_{175} (msec)	Amp. (mvolt)
Left Eye				
Right Eye				

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