



Original Research Article

Effect of smoking on visual evoked potential

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ABSTRACT

Introduction: The relationship of smoking with visual evoked potential is debated. Cigarette smoke contains cytotoxic compounds which directly or indirectly cause damage to neuronal cells. Smokers develop elevated carboxyhaemoglobin levels which might impair function of central nervous system by affecting oxygen transport and its utilization leading to perceptual-motor delay in smokers.

Objectives: To record the visual evoked potential in smokers and non-smokers aged 20-40 years and to compare between two groups for any changes in P100.

Materials and Methods: Age matched 100 male smokers and 100 male non smokers in the age group of 20-40 years were studied for visual evoked potential. Smoking in terms of pack years was noted. Data was statistically analyzed.

Results: Visual evoked potential was affected in smokers with prolongation of latency and decrease in amplitude of P100 in both the eyes than non smokers, with is statistically highly significant. There is a significant positive correlation between smoking history expressed in pack-years and latency of P100 in smokers group.

Conclusion: Smoking causes degeneration in optic nerve shown by increased latency of P100 which increases as the number of pack-years increase.

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1. Introduction

Tobacco smoking is the most important preventable cause of death and disease among adults. World Health Organization estimates that worldwide 5 million deaths are caused prematurely by smoking every year.¹ In India, over 6, 00,000 people in the age group of 25-69 years die due to smoking every year.² Currently in India there are about 120 million people who either smoke cigarette or bidi.³ Current percentage of male tobacco smokers are 24.3% in India and 23.2% in Karnataka according to Global Adult Tobacco Survey 2010.⁴

Deaths among smokers are mainly from tuberculosis, respiratory, vascular and neoplastic disease. Smoking is associated with a reduction in median survival of 8

years for women and 6 years for men.⁵ Cigarette smoke contains numerous human carcinogens like nicotine, tar, carbon monoxide, nitrosamines, and polynuclear aromatic hydrocarbons.⁶

Smoking affects almost every system in the human body. Smokers have increased risk of multiple cancers, heart diseases, strokes and emphysema.⁷ Smoking is also associated with many eye diseases like tobacco-toxic optic neuropathy, thyroid ophthalmopathy, cataract, strabismus and colour vision defects as shown by various studies.⁸ Chronic cigarette smoking appears to be associated with deficiencies in executive functions, cognitive flexibility, general intellectual abilities, learning and/or memory processing speed, and working memory.⁹ As smoking affects visual system as found by many studies, we have taken up this study to know the association of ill effects of smoking with neurophysiological test like visual evoked

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potential.

Studies have shown that VEP in smokers with Chronic Obstructive Pulmonary Disease have significantly prolonged latency, decreased amplitude of P₁₀₀ in both the eyes as compared with healthy volunteers which shows that there is degeneration in quality of sight because visual receptors are sensitive to hypoxemia.¹⁰

The present study is aimed to evaluate the changes in latency and amplitude of P100 in smokers. The hypothesis being tested is that “there is effect of smoking on visual evoked potential and visual reaction time in Davangere population”

2. Objectives

1. To record the visual evoked potential in non-smokers and smokers aged 20-40 years
2. To evaluate whether there are any significant changes in latency and amplitude of P₁₀₀ waves recorded in smokers when compared to non-smokers.

3. Review

Prem Prakash Gupta et al., in their cross-sectional study assessed 40 stable COPD patients with no visual impairment who were smokers and 40 age-matched healthy volunteers who were non smokers. Subjects were assessed for any visual evoked potentials abnormalities using electrophysiological tests, spirometric indices and Mini Mental State Examination. They observed significantly prolonged latency and decreased amplitude of P100 in both eyes of subjects in study group when compared with healthy volunteers. They concluded that prolonged latency suggested nerve demyelination, whereas significant decrease in amplitude suggests axonal involvement. Various factors like chronic hypoxemia, tobacco smoke, malnutrition have been suggested for VEP abnormalities.¹⁰

Friedman J et al, in their study auditory and visual evoked potentials were recorded in 10 heavy smokers. Recordings were made during periods of tobacco deprivation, normal smoking, and immediately after smoking. Tobacco smoking increased the amplitude of the late waves of visual evoked potentials. There was a decrease of the amplitude after 12 hour of abstinence from smoking when compared to the amplitude in a normal smoking period.¹¹

J.F. Golding, studied the effect of cigarette smoking on resting EEG, visual evoked potentials and photic driving on 30 young healthy male and female habitual cigarette smokers and found out that there was no significant effects of smoking on VEP amplitudes or latencies. They suggested that smoking may produce both increase and decrease in evoked potential amplitude depending on a number of factors nicotine dose, nature of task and personality.¹²

Shafa MA et al, in their cross-sectional case-control study on 30 subjects with both chronic cigarette smoking

and opium smoking was compared with subjects with only chronic cigarette smoking. Pattern reversal visual evoked potentials (PRVEP) were recorded. They concluded that chronic cigarette smoking and opium-dependence together significantly increased the amplitude of VEP compared with chronic cigarette smoking alone which may be due to stimulatory effects of both substances on visual nervous system.¹³

4. Materials and Methods

4.1. Source of data

The present study was carried out on 100 smoking and non-smoking male population from residential areas of Davangere in the age group of 20-40 years. The subjects selected as study and controls were age matched. Smokers were divided into three groups depending on their smoking history in terms of pack-years. Female subjects were excluded from the study because many use smokeless form of tobacco and acceptance rate is very low.

4.2. Study group

100 male smokers from Davangere in the age group of 20-40 years.

4.3. Control group

100 normal healthy males' non smokers from Davangere in the age group of 20-40 years.

4.4. Inclusion criteria

4.4.1. Study group

1. Male smokers aged between 20-40 years as study group.
2. Subjects with normal vision 6/6 with or without correction.
3. Subjects who have given written consent

4.4.2. Control group

1. Male non-smokers aged between 20-40 years as control group.
2. Healthy subjects from residential area as evaluated by general physical, systemic and ophthalmological examination.
3. Subjects with normal vision 6/6 with or without correction
4. Subjects who have given written consent.

4.5. Exclusion criteria

1. Age below 20 years and above 40 years.
2. History of alcohol consumption.
3. Subjects with history of diabetes mellitus and hypertension.

4. Subjects having cataract, anisocoria, extreme pupil size, colour vision defect and optic neuritis.
5. Subjects with systemic illness.

4.6. Protocol

All subjects were given a questionnaire to answer. This questionnaire includes: Socio- Demographic data, Smoking history in detail. Written consent was obtained from the subjects after explaining the procedure. A general physical and systemic examination was conducted on all the subjects. A thorough eye check up was done; visual acuity and colour vision were tested. Taking into consideration the predetermined inclusion and exclusion criteria, subjects were selected and assigned into case or control groups. VEP was recorded using RMS EMG EP MARK II machine.

4.7. Methods

The smoking history of each subject of the test group was expressed in terms of pack-years. Pack-years of smoking is defined as the number of packs (one pack is equal to 20 cigarettes) smoked per day multiplied by the duration of smoking (in years). Subjects were instructed to refrain from smoking one hour before the tests.

Electrophysiological studies for the evaluation of VEP was carried out using RMS EMG EP MARK II supplied by Recorders And Medicare Systems (Pvt) Limited. Procedure for VEP recording as recommended by the International Federation of Clinical Neurophysiology (IFCN) Committee was followed with stimulus configuration consisting of the transient pattern reversal method in which a black and white checker board was generated (full field) and displayed on VEP monitor (color 14") by an electronic pattern generator inbuilt in Evoked Potential Recorder (RMS EMG EP MARK II).

After screening into study or control group according to inclusion and exclusion criteria subjects were instructed to come to Research Laboratory with their hair washed without applying oil. Study was conducted in Research laboratory, Department of Physiology, SS Institute of Medical Sciences and Research Centre, Davangere. Research Laboratory is a noise proof room with equipments.

4.8. Subject preparation

1. Subjects were briefed about the procedure to alleviate their apprehension and assure full relaxation during testing procedure.
2. Subject was seated comfortably in a quiet darkened room at a distance of 100 centimeters from a computer screen.

4.9. Electrode placement

1. After thorough vigorous cleaning, the electrodes are attached to the surface of scalp with conducting jelly or electrode paste (RMS recording paste), which is rubbed lightly into the area with cotton swab to ensure goo, stable electrical connection.
2. Electrodes were fixed as per 10-20 International system which was originally devised for EEG recording. This system specifies the position of scalp electrodes as percentage of distances between the nasion and theinion over the vertex.
 - a. The active electrode was placed on the scalp over the visual cortex at Oz i.e, 10% of the whole distance from nasion to occipital protuberance or 3-5cm above the occipital protuberance (inion).
 - b. Reference electrode was placed at Fz i.e, 12 cm above nasion or 30% from nasion.
 - c. Ground electrode was placed at Cz i.e vertex

1. Skin resistance is kept as low as $5K\Omega$ and these electrodes were connected to electrode box by connecting wires
2. Subject was instructed to fix gaze and concentrate on a small red rectangle present at the centre of screen with one eye while the other eye was covered with a patch.
3. Stimulus given was black and white checker board pattern of size 8x8.
4. Low pass filter was set at 2Hz, High pass filter was set at 100Hz
5. Amplification was between 20,000-1,00,000
6. The rate of pattern reversal was 1.71 Hz and an average of 300 responses was recorded from both right and left eye separately.
7. Mean luminance of the central field was 100cd/m^2 and background luminance was $20\text{-}40\text{cd/m}^2$
8. Two trials were obtained to ensure reproducibility of the VEP pattern.
9. Latency and amplitude of P100 wave was recorded in both the groups.

4.10. Statistical analysis

Student's unpaired 'T' test has been used to find out the significance of homogeneity of study characteristics between two groups of subjects. Simultaneous comparison of all 3 groups of cases is carried out by oneway ANOVA test which was followed by Tukey's post hoc test for pairwise comparison. Spearman's coefficient of correlation test was applied to find the correlation among 3 groups of cases with respect to pack years. Differences were considered significant at $p < 0.05$ level. The data has been analyzed by using SPSS 18 (Trial Version) USA, Chicago. Microsoft word and Excel have been used to generate graphs, tables etc.

5. Results

5.1. Study design

Case-control study with 100 male smokers and matched controls of 100 male non smokers is taken to study the effect of smoking on VEP.

The age distribution of subjects included in the study is shown in Table 1. The study groups are age matched as the p value is 0.06.

Table 2 show the comparison of latency of P100 waves of VEP between smokers and non smokers in both right eye and left eye. These tables depict that there is highly significant difference in latency of both groups.

Table 3 show the comparison of amplitude of P100 waves of VEP between smokers and non smokers in both right eye and left eye. These tables depict that there is highly significant difference in amplitude of both groups.

Table 4 shows Comparison of latency between smokers with relation to pack years in right eye and left eye, shows that latency of left eye is affected in smokers. On comparison of different groups latency of subjects in group II (2-5 pack years) are most affected and value is statistically significant.

Table 5 shows Comparison of amplitude between smokers with relation to pack years in right eye and left eye, shows that amplitude of right eye is affected in smokers. On comparison of different groups amplitude of subjects in group II (2-5 pack years) are most affected and value is statistically significant.

Table 6 shows Spearman's correlation of pack years with latency and amplitude of VEP of smokers. There is positive correlation for latency of both eyes with a significant P value.

6. Discussion

Cigarette smoking affects almost every system in the human body and it is accepted as a risk factor for various cancers, heart diseases, strokes, emphysema and many eye diseases as shown by various studies. This study was taken up to study the effects of cigarette smoking on vision through electrophysiological technique like VEP and by measuring visual reaction time. In this study the male subjects selected were age matched, in the age group of 20-40 years since with increasing age smokers tend to develop COPD and polyneuropathy which affects the visual evoked potentials. This study was taken up to study changes in VEP before clinical signs and symptoms related to vision appear in smokers.

VEP was compared in smokers and non smokers. History of smoking in terms of pack years was noted to compare among smokers.

Analysis of this study showed that VEP was affected in smokers with prolongation of latency and decrease in amplitude of P100 in both the eyes when compared to non

smokers, which indicates that the difference is statistically highly significant. An increase in VEP latency clinically means degeneration in the quality of sight. Since VEP is a sensitive tool to detect subclinical visual impairment.

Study by Rose FC, on smokers with optic neuritis found that there was high incidence of colour vision defects in smokers when compared with non smokers. Vascular effects of smoking may be due to a direct effect of nicotine which could act either by depressing retinal ganglion cell function, block transmission in demyelinating nerve fibers, blocking synaptic transmission at lateral geniculate body or depressing receptor cells in striate cortex.¹⁴

Cigarette smoke contains many cytotoxic compounds like carbonmonoxide, free radicals etc which directly or indirectly cause damage to neuronal cells, promote oxidative damage. Smoking is also associated with deficiencies in auditory-verbal learning or memory, general intellectual abilities, visual search speeds, processing speed and executive functions.¹⁵

The delayed response to visual stimuli in smokers might be due to various patho-physiological changes probably like atherosclerosis of arteries and arterioles supplying cerebral hemisphere. This may be the result of tobacco smoking which leads to abnormal increase in total blood triglycerides, enhanced blood coagulability due to increased fibrinogen. There is reduction in small airways function with low levels of PaO₂ and PaCO₂ which might lead to decreased cerebral blood flow. Smokers develop elevated carboxyhaemoglobin levels which might impair function of central nervous system by affecting oxygen transport and its utilization leading to cognitive dysfunction and perceptual-motor delay in smokers.¹⁶

Prolonged latency and reduced amplitude of P300 secondary to cigarette smoking was found in a study by Mostafa S, this effect was explained by hypoxia resulting from COPD associated with chronic smoking and due to nicotine which is main toxic substance in cigarette smoking.¹⁵

Though there are different opinions regarding effects of smoking on VEP, studies suggest that immediately after smoking reaction time becomes faster than baseline¹⁷ and there is increased amplitude, decreased latency of P100^{12,13,18} produced due to the stimulant effect of nicotine on CNS.

7. Limitations of this study

The present study is a case-control study where the subjects were randomly selected from the population. The sample size is very small. A large population based study is required to conclude the results. The VEP abnormalities are nonspecific and are not characteristic of any specific etiology.

Table 1: Age distribution of subjects studied

Age (Years)	Cases	Controls	Total No.	Total %
20-24	7	14	21	10.5
25-29	30	32	62	31
30-34	34	31	65	32.5
35-40	29	23	52	26
Total	100	100	200	100
Mean+/-SD	31.5+/- 5.1	30.16+/-5.04		

*Student's unpaired t test, Samples are age matched with P= 0.06

Table 2: Comparison of latency between smokers and non smokers in both right eye and left eye

Visual Evoked Potential	Cases Mean + SD	Controls Mean + SD	Mean Difference	P Value, significance
Latency (msec) Right eye	112.13 + 4.39	107.69 + 3.78	4.44	<0.001 HS
Latency (msec) Left eye	111.83 + 4.46	107.57 + 3.69	4.26	<0.001 HS

* Student's unpaired t test, HS – Highly significant

Table 3: Comparison of amplitude between smokers and non smokers in both right eye and left eye

Visual Evoked Potential	Cases Mean + SD	Controls Mean + SD	Mean Difference	P Value, significance
Amplitude (uV) Right eye	3.51 + 1.61	6.41 + 2.08	2.90	<0.001 HS
Amplitude (uV) Left eye	3.62 + 1.58	6.70 + 2.07	3.08	<0.001 HS

* Student's unpaired t test, HS – Highly significant

Table 4: Comparison of latency between smokers with relation to pack years in right eye and left eye

Pack years	<2 (n=56)	2-5 (n=35)	>5 (n=9)	P* Value	Significant pairs**
Visual evoked potential	Mean + SD	Mean + SD	Mean + SD		
Latency msec, Right eye	111.29 + 4.43	113.57 + 4.31	111.81 + 3.21	0.051	
Latency msec, Left eye	110.45 + 4.43	113.98 + 4.02	112.04 + 3.01	0.001S	I&II

* One way ANOVA test, S- Significant

** Tukey's post hoc test

Table 5: Comparison of amplitude between smokers with relation to pack years in right eye and left eye

Pack years	<2 (n=56) I	2-5 (n=35) II	>5 (n=9) III	P Value	Significant pairs
Visual evoked potential	Mean + SD	Mean + SD	Mean + SD		
Amplitude (uV) , Right eye	3.54 + 1.69	3.17 + 1.37	4.66 + 1.55	0.04	II & III
Amplitude (uV), Left eye	3.64 + 1.75	3.42 + 1.39	4.26 + 0.91	0.36	

*One way ANOVA test ** Tukey's post hoc test

Table 6: Spearman's correlation of pack years with latency and amplitude of VEP of smokers

Visual Evoked Potential		P value
Latency msec, Right eye	0.24	0.01 S
Amplitude (uV), Left eye	-0.084	0.40 NS
Latency msec, Right eye	0.31	0.002 S
Amplitude (uV), Left eye	-0.103	0.30 NS

S- Significant

8. Conclusion

In this study the visual evoked potential on male smokers and non smokers were studied. The data was statistically analyzed which revealed that smokers had Increased latency & Decreased amplitude of P100 waves of VEP in both eyes. There exists a significant positive correlation between smoking history expressed in pack-years and latency of P100 in smokers group.

9. Source of funding

None.

10. Conflict of interest

None.

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