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Research Article

Effects of Smoking on Pattern Visual Evoked Potentials

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Abstract

Aim: The aim of the study is to get a better understanding of the side effects of smoking by evaluating the effect of recently elevated smoking rate on Visual Evoked Potentials (VEP) and to determine whether it is necessary to use different normals when evaluating the VEP measurements of smoking patients.

Material and Methods: The patients who have applied to our ophthalmology and neurology outpatient clinics during 2021-2022 are included to the study. Detailed ophthalmologic examination of the patients as well as their VEP test is completed followed by a dilated fundus examination assessment. The patients with normal results are included to the study. The smoking rate is calculated on pack/year basis. Pattern VEP (PVEP) recording is performed based on Keypoint (Dantec, Denmark) and International Society for Clinical Electrophysiology of Vision (ISCEV) criteria. Data obtained through the study are analyzed by SPSS 21.0 version software. Countable variables with normal distribution between two independent groups are analyzed with Independent Sample T test whereas variables without normal distribution are analyzed with Mann Whitney U test. Chi-square test is used for comparing categorical variables.

Results: 71 patients were included to the study where 33 of them were placed in smoking group and 38 in non-smoking group (control group). Smoking group had a yearly cigarette package consumption of 5.20±8.93 (0.2-40). VEP latency and amplitude changes were compared and according to the obtained results; there was P100 latency prolongation in between left and right eye of the patients in the control group and smoking group but it did not have any statistical significance (p=0.910 and p=0.697 respectively). There was no statistically significant difference in either left nor right eye in terms of smoking and P100 and N70 latencies (p=0.707, p=0.838, p=0.717 and p=0.621 respectively). Similarly, there was no significant correlation between yearly package consumption and P100 and N70 latencies and amplitudes of left and right eyes (p=0.503, p=0.410, p=0.776 and p=0.940 respectively).

Conclusion: No significant effect of smoking is found on VEP values thus leading us to believe that the same normal intervals can be used in the evaluation of VEP results of both smoking and non-smoking patients.

Keywords: Smoking, VEP (Visual Evoked Potential), nicotine

INTRODUCTION

The side effects of smoking, a habit which has become even more popular after the 20th century, have begun to be understood over the years. Cigarettes contain nicotine and carbon monoxide which cause not only cholinergic neurotransmitter effect due to cholinergic agonist but also changes in the electrical activity of peripheric and central nerve system due to demyelination in the body. Receptors in the eyes and on the visual pathways are affected by this neuropathy. However, the tests run in the ophthalmology and neurology clinics might be insufficient to diagnose the early changes of the neuropathy. This is where the Visual Evoked Potential (VEP) test plays an important role (1-4).

VEP test is an important ocular electrophysiological visual measurement which is based on the occipital field recording of electroencephalographic signals generated in the brain by visual stimulus received through the eye. VEP test enables us to obtain quantitate data on visual pathways from retina to brain by means of optic disc hence supporting the clinical diagnosis of unexplained vision loss, optic nerve damage and neurological diseases (5). VEP allows the assessment of all visual pathways especially starting from the field of vision obtained from the eye to the visual cortex placed in the occipital lobe.

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Furthermore, the fibers coming from central retina to visual cortex are located close to surface in the occipital cortex whereas fibers coming from peripheral retina are located much deeper in the calcarine sulcus, hence the effect of stimulus received from the peripheral retina is much less on the signals during the VEP measurements (6).

Clinic VEP use has somewhat decreased in the recent years due to advanced magnetic resonance imaging (MRI) technology. Although MRI has the advantage of showing all anatomic intracranial changes in detail, VEP still is better in terms of showing functional changes (5,6). VEP remains to be the superior method especially in terms of determining functional disorders in pre chiasma anterior vision nerve transmission or in other words, in the optic nerves (5). Recording of the visually stimulated potentials are done according to the protocol suggested and lately updated in 2016 by ISCEV (International Society for Clinical Electrophysiology of Vision) (7,8).

In our current study, we wanted to evaluate the effect of smoking on pattern VEP which is a very important electrophysiological test. Based on this information, we also aimed to understand whether different normal values should be used for smoking and non-smoking patients while evaluating VEP results.

MATERIAL AND METHOD

This study is conducted by the Ophthalmology and Neurology outpatient clinics of our hospital. Both smoking and non-smoking patients have been included to our study. The study was performed in accordance with the principles of Declaration of Helsinki and approved by the institutional (Ethics committee of Duzce University-181/2022). Furthermore, informed consent forms were signed and submitted by each patient prior to each procedure related to the protocols and goals of the study. Only the patients with no systemic disease nor alcohol consumption and are within the age of 18-65 are included to the study.

Based on the exclusion criteria; patients with neurological diseases or diseases that might affect the optic disc such as multiple sclerosis, papilledema, optic neuritis, etc. as well as patients with alcohol and addictive substance history, patients with high intraocular pressure and glaucoma results or systemic diseases such as diabetes or high blood pressure, patients who have undergone eye surgery for any given reason or have amblyopia, diplopia, cataract, myopia or hyperopia of over 3D, astigmatism of over 1D or anisocoria and pupil size of under 3 mm are not included to the study.

Best corrected visual acuity, eye movement, pupil reflexes, slit lamp biomicroscopy, intraocular pressure measurement with goldmann applanation tonometry and dilated fundus examinations were performed on the patients. VEP test was performed before the dilated fundus evaluation considering that there might be changes in the VEP test after the dilation. All VEP tests were performed by a single experienced neurologist and all measurements were taken in between the hours of 9:00-11:00 to avoid the effect of any diurnal change.

Two groups, namely smoking and non-smoking, were created for our study and smoking rate was calculated on pack/year basis.

VEP measurements were obtained by using Keypoint (Dantec, Denmark) device and 16-inch screen. In order to perform the Pattern VEP (PVEP) recording, active electrode was placed 2 cm above the protuberantia occipitalis externa of occipital bone whereas reference electrode was placed on vertex and ground electrode was placed on the hairline border of the forehead. Electrical potentials emerged in the bilateral occipital cortex of the patient were recorded while he/she was in a dark room, staring at the fixation point located in the middle of moving chessboardlike designs on the screen placed 1 meter away. The recording was done with one eye, while the other one is closed and the process was repeated similarly for both eyes. There were 12x16 number of 2-inch squares on the screen and all the small squares were of the same size. Contrast was 99% according to Michelson constant. Sweep rate was set to 30 ms/D and 5uV/D, sensitivity to 30 uV/D and filter to 1 Hz-200 Hz. 250 stimuli were given during recording for the averaging and the average of measurements were calculated automatically. The staring of the patient at the fixation point was supervised closely by an experienced electrophysiology technician. The measurements of the patients wearing glasses were evaluated together with their glasses. Detailed information and standardization criteria related to visual stimuli respond recording were published by ISCEV. We complied with the ISCEV criteria in recordings of our study (8).

Obtained data was evaluated with the SPSS 21.0 (IBM Corp.; Armonk, NY, USA) software. Categorical variables were indicated by numbers and percentages whereas countable variables were indicated by average±SD. Countable variables with normal distribution between two independent groups were analyzed with Independent Sample T test whereas variables without normal distribution were analyzed with Mann Whitney U test. Chi-square test was used when comparing categorical variables. When the correlation between two countable independent variable was analyzed, Pearson correlation analysis was used for data with normal distribution and Spearman correlation analysis for data without normal distribution. $p<0.05$ was taken to be significant.

RESULTS

Demographic data of the participants in the study are given in Table 1. 71 patients participated to the study where 33 of them were in smoking group and 38 in non-smoking group (control group). Furthermore, the age average of the groups was similar; 36.30±9.36 in smoking group and 36.39±6.78 in control group. Similarly, the gender distribution between two groups was similar; 13(39.4)/20(60.6) M/F in smoking group and 15(39.5)/23(60.5) M/F in control group. Smoking rate in the smoking group was found to be 5.20±8.93 (0.2-40) pack/year.

Table 1. Comparison of demographic data between groups

(n)	Smoking (33)	Nonsmoking (38)	P
Age (range)	36.30±9.36 (21-57)	36.39±6.78 (22-49)	0.962*
Gender M (%) / F (%)	13(39.4) /20(60.6)	15(39.5) /23(60.5)	0.995#
Pack/year (Range)	5.20±8.93 (0.2-40)	0	

M: Male, F: Female, *Independent Sample T test # Chi-square test

VEP latency and amplitude changes were compared throughout the study and the obtained data were evaluated as a table (Table 2). According to these findings; no significant difference was found between the smoking and control groups in terms of the P100 and N70 latencies of both right and left eye (p=0.697, p=0.419 right eye respectively and p=0.910, p=0.542 left eye respectively). Similarly, there was no statistically significant difference between the smoking and control groups in terms of N70 latency of both right and left eye (p=0.572 and p=0.419 respectively).

Table 2. Comparison of VEP measurements between groups

	Smoking (33)	Nonsmoking (38)	P
L P100 ms	107.23±5.38	107.07±6.12	0.910
R P100 ms	106.81±5.28	106.23±7.08	0.697
L N70 ms	76.45±5.49	77.34±7.44	0.572
R N70 ms	77.53±4.89	76.16±8.60	0.419
L P100 uV	-7.43±4.26	-6.95±3.34	0.600
R P100 uV	-7.97±3.85	-7.69±2.95	0.729
L N70 uV	1.56±2.11	2.16±2.70	0.304
R N70 uV	1.71±2.34	2.44±2.99	0.266

L: Left, R: Right

Although the N70 amplitudes of both right and left eyes of non-smoking patients were found to be high, there was no statistically significant difference (p=0.266 and p=0.304 respectively). There was no statistically significant difference between both groups in terms of P100 amplitude of both right and left eye (p=0.729 and p=0.600 respectively).

Based on the analysis of latency and amplitude differences in P100 and N70 values of right and left eyes, no statistically significant difference was found between two groups (Table 3).

Table 3. Comparison of VEP measurements between groups

	Smoking (33)	Nonsmoking (38)	P
L/R dif. P100 ms	1.84±2.07	2.21±1.81	0.420
L/R dif. N70 ms	5.18±4.27	3.63±3.72	0.106
L/R dif. N70 uV	0.99±0.77	1.24±1.02	0.254
L/R dif. P100 u V	1.28±1.06	1.20±0.93	0.756

L: Left, R: Right, Dif: Difference

The correlation analysis between the measured VEP parameters and smoking pack/year rates are shown in Table 4. Based on this analysis, there was no statistically significant correlation between the pack/year consumption and P100 and N70 latencies for both right and left eye (p=0.707, p=0.838, p=0.717 and p=0.621 respectively). Similarly, there was no statistically significant correlation between the pack/year consumption and P100 and N70 latencies for both right and left eye (p=0.503, p=0.410, p=776 and p=0.940 respectively).

Table 4. Comparison of the smoking amount and VEP values

	L P100 ms	R P100 ms	L N70 ms	R N70 ms	L/R dif. P100 ms	L/R dif. N70 ms
Pack / year	0.707	0.838	0.717	0.621	0.153	0.083
	L N70 uV	R N70 uV	L P100 uV	R P100 uV	L/R dif. N70 uV	L/R dif. P100 uV
Pack / year	0.503	0.410	0.776	0.940	0.122	0.659

L: Left, R: Right, Dif: Difference

DISCUSSION

As a result of this study, we found that there was no significant difference in the VEP tests of smoking and non-smoking healthy people.

It is a known fact that smoking causes vasoconstriction and the rate of vasoconstriction varies according to the smoking amount. Consequently, the veins in the brain also change, causing differences in the VEP values. It may lead to differences in both latencies and amplitudes of VEP (9,10).

Review of literature shows that there is no final consensus on the effects of smoking on VEP amplitudes and latencies. In two studies done by Friedman J et al. as well as other studies done by Hall RA et al. and Woodson PP et al., an increase in the VEP amplitudes was detected (11-14). Furthermore, Knott VJ et al. stated a decrease in amplitudes as a result of their study (15). In their study, Durukan AH et al. stated a decrease in amplitudes after an acute smoking period (1). In our study, the effect of acute smoking was not evaluated and no difference was found in amplitudes between chronic smokers and nonsmokers. In their studies, Pritchard et al., Woodson et al. and Conrin et al. found a decrease in P100 latencies (2,14,16). Hetzler et al. analyzed various latencies and found a general prolongation in latencies (4). Pandey et al. found no statistically significant difference in between latencies. Likewise, we did not find any significant difference between smoking and non-smoking groups in terms of P100 latency in our study. Smoking has various effects on the human body therefore we found diverse results in the literature related to VEP. Previous studies show that chronic smoking has effect on ocular blood flow. In their study, Robinson et al. reported an increase in the blood flow of macula after smoking (17). Furthermore, smoking is found to be decreasing the choroid blood flow in the study done by Kocak et al. and further found to be increasing the blood flow around the optic disc head in the study done by Tamaki et al (18,19).

However, this theory is not always sufficient to justify the

unexpected findings in the audio and visual modalities of some of the studies (1,15). Therefore, a more reliable approach might be considering other accompanying factors besides plain smoking, such as smoking history/ duration, life style, etc., when evaluating the effect of smoking on VEP altitudes or similar measurements (1,20-22). Combining these results would also enable us to get a better understanding about the smoking habit which might have various underlying reasons like psychological urge, stimuli requirement, concentration tool, stress management, mood stabilizer, even referring to Pomerleau hypothesis when heavy smoking is involved (1,12, 23,24).

In their study made with patients whose ocular blood flow in 3 retrobulbar veins were measured, Kurysheva et al. found statistically significant correlation between P100 amplitudes and ocular blood flow as a result of their VEP evaluations (25). There are studies which show that smoking causes not only demyelination in the optic disc retrobulbar area but also increase in reactive oxygen molecules due to decreased ocular blood flow and changes in pVEP due to generated free radicals and disrupted neuro transmitter balance. Therefore, it is possible to determine the changes with pVEP before neuropathy emerges.

The limiting factors of our study are relatively limited number of participating patients and being single-centered. Another limitation of our study is that only chronic smokers were included, and the effect of acute smoking was not evaluated. On the other hand, the previous studies related to effects of smoking on VEP have been mostly done 2-3 decades ago. Therefore, it gives our study the strength of being one of the recent studies done on the effects of smoking on VEP, especially after the current developments of VEP.

CONCLUSION

VEP test, with an ever-increasing importance, is a non-invasive measurement method which is being frequently used in neuro-ophthalmologic evaluations. On the other hand, the increase in smoking rates appears as a severe public health issues. When the multi-organ effects of smoking are considered; it is evident that it should be treated seriously in terms of its effects both on visual and brain activities. Furthermore, it is very important not only to acknowledge the normal values while evaluating the VEP results but factors effecting the normal values should be well known as well. The increasing importance of the VEP test and the fact that there is no conducted study related to the elevating smoking in the last decade despite the developments lead us to the idea of addressing this subject. There was no significant difference between the VEP parameters of smoking and non-smoking groups in our study which enables us to conclude that the same VEP normal values can be used for both smoking and non-smoking individuals. However, even though we have not found any significant results in our study, there are contrary findings in the limited literature reviews. We believe that additional studies should be conducted on a wider scale and multi-centered basis with a larger group of patients.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *The study was performed in accordance with the principles of Declaration of Helsinki and approved by the institutional (Ethics committee of Düzce University - 181/2022).*

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