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## Assessing the Effect of Opium Dependence on Visual Evoked Potential (VEP) in Men

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<b>Background:</b>	<b>Abstract</b> Opium-dependence having different effects on the nervous system is a common problem, especially in the Middle East and Iran. The aim of this study is evaluating the effects of opium-dependence on visual evoked potential (VEP) in men.
<b>Methods:</b>	Thirty subjects with both chronic cigarette smoking and opium-dependence (group 1) and 30 subjects with only chronic cigarette smoking (group 2) were included in this cross-sectional case-control study and after urinary tests of opium, the pattern reversal visual evoked potentials (PRVEP) were recorded in the standard condition and variables such as N75, P100, N135 and amplitude were obtained and then analyzed with SPSS <sub>16</sub> . P value < 0.05 was assumed significant statistically.
<b>Findings:</b>	The mean of N75 ( $70.426 \pm 22.028$ ), P100 ( $115.457 \pm 29.176$ ) and N135 ( $165.402 \pm 66.712$ ) was not significantly different between the two groups. The mean of the amplitude of VEP in group 1 ( $6.856 \pm 3.248$ ) was significantly higher than group 2 ( $4.933 \pm 2.50$ ) ( $P < 0.05$ ).
<b>Conclusion:</b>	Our study showed that chronic cigarette smoking and opium dependence have no significant effect on the late components of the VEP (N75, P100 and N135), but chronic cigarette smoking and opium-dependence together significantly increase the amplitude of VEP compared with chronic cigarette smoking alone, probably due to the chronic stimulatory effects of concomitant use of these two substances on the eyes and the visual nervous system.
<b>Key words:</b>	<b>Opium, Cigarette, Visual evoked potential</b>

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## Introduction

Opioid dependence is a set of physiologic, behavioral, cognitive signs representing frequent and continuous use of opioid drugs in spite of its remarkable complications.<sup>1</sup> Although abuse of other drugs is increasing, opium abuse is decreasing. Nevertheless, in some societies such as Iran opium abuse is still the most significant.<sup>2,3</sup> In some areas, especially in Asia and the Middle East there are some beliefs that opium has a preventive effect on cardiovascular diseases, hypertension and diabetes mellitus.<sup>4</sup> These beliefs probably are the main reason for the prevalence of opium addiction in these societies.<sup>5</sup>

Medical complications of opioid abuse in the nervous system are globus pallidus and spinal cord grey matter degeneration in autopsy, transverse myelitis, amblyopia, plexitis, peripheral neuropathy, Parkinsonism syndrome, cognitive and personality changes, pathologic changes in the muscles and peripheral nerve degeneration.<sup>1</sup>

The Visual Evoked Potential (VEP) record is very useful in assessing visual function. VEP is a noninvasive technique and has an excellent time analysis about 1/1000 second. Therefore, VEP allows studying dynamic changes in the nervous system. Pattern Reversal Visual Evoked Potential (PRVEP) is the most sensitive electrophysiological test for assessing optic nerve dysfunction.<sup>6</sup> PRVEP has two major elements (i.e. N75, P100), both produced in the occipital lobe.<sup>6</sup> This study aimed to assess the effect of opium dependence on VEP; therefore assessment of the optic nerve in men.

## Methods

In this case-control study, one hundred twenty eight cases were included. Regarding the high prevalence of concurrent smoking and opium dependency, specific inclusion criteria was considered for the case group and thirty 25- to 48-year-old men referred to the addiction cessation, psychiatric and neurologic clinics were recruited according to the following criteria: 1) Opium consumption by the smoking method which is diagnosed by psychiatrists with the SCID diagnostic tool according to DSM-IV criteria, 2) Daily opium consumption of 2 to 4 grams for 5-10 years duration, 3) Smoking pattern of 50-100 packs/year, 4) Positive opiate urine test detected by the rapid immunochromatographic test,

5) Confirmation of the mentioned test is carried out by columnar liquid-solid chromatography test and thin layer chromatography (TLC).

In the control group, thirty men referred to the addiction cessation, psychiatric and neurologic clinics without a history of recent or frequent opium abuse and a negative urine opium test (detected by the rapid immunochromatographic test) were matched with the case group subjects in term of age, social status, smoking habit and cigarette brand. Demographic data and written consent was obtained.

The exclusion criteria were as follow:

- 1) Glaucoma, retinopathy, maculopathy, current or past uncorrected refractive errors,
- 2) Neurological disorders affecting VEP such as anterior ischemic optic neuropathy (AION), stroke, multiple sclerosis (MS), optic nerve neuritis history, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), polyarteritis nodosa and other vasculitis,
- 3) Other opioid abuse such as cocaine, methadone, heroin, alcohol,
- 4) Ethambutol, sodium valproate, carbamazepine consumption over 1 month,
- 5) History of eye trauma leading to decreasing vision,
- 6) Past abnormal VEP,
- 7) Occupational eye trauma such as welding,
- 8) Diabetes, blood sugar level less than 60 mg/dl and more than 140 mg/dl,
- 9) History of idiopathic intracranial hypertension (IIH), migraine,
- 10) Opium and cigarette consumption in the last 3 hours and existing cigarette and opium withdrawal signs.

VEP for each subject was recorded at a distance of 70 cm, with EMG-NCS-EP set, model Axon 4000s, manufactured by Negarandishegan (an Iranian factory). It was with reversal checkerboard full-field pattern. Each part was 14 × 10 mm, 80% contrast, 1 Hz frequency and the average transparency in the field center was about 100 cd/m<sup>2</sup> with Oz-Fz montage.

The reference electrode was placed in the midline, 6 cm above the nasion (according to Fz, 10-20 system), the active electrode being placed 2 cm above occipital pole in Oz, and finally the ground electrode placed in the right mastoid bone. VEP was recorded with 200 consecutive monocular simulations. It was recorded twice, once from each eye and then the waves were superimposed for each eye.

In order to prevent bias in this study, a physician who knew VEP, but was blinded to the study did the signing VEP in term of variables (i.e. amplitude, N75, P100 and N135).

The average of each variable (i.e. amplitude, N75, P100 and N135) for both subjects' eyes was recorded and data analysis was performed by SPSS software (version 16). Student's t-test was used for comparing means and a p value less than 0.05 was considered significant statistically. Urine test for addiction and blood glucose test was carried out in the reference laboratory of Kerman University of Medical Sciences. The ethical committee of neuroscience research center in Kerman University of Medical Sciences approved this study (Ethical code: EC\KNRC\89-1:/89).

## Results

The sample had a mean (SD) age of 32.4 (5.12) years, and 32.5 (5.04) years in the case and control group, respectively. There was no significant difference between the mean N75 in the two groups. In addition, there was no significant difference between P100 values and N135 values in the two groups. Table 1 shows that the mean of VEP amplitude was significantly greater in the case group compared with the control group ( $P < 0.05$ ). Therefore, results indicated that VEP amplitude (including summation of N75 and P100 amplitudes) in men with concomitant opium dependence and chronic cigarette smoking was greater than men who are only chronic cigarette smokers (Table 1).

## Discussion

Based on our findings, there was no significant

difference in VEP-related latent elements (including N75, P100, and N135) among the three groups. Bauer et al's study suggested that there was no difference in PSVEP between healthy people and people with a past history of opioid dependence, but an obvious latency in N75 and P100 (related to PSVEP) was observed in people who were using methadone.<sup>7</sup> It seems that this difference between our findings and Bauer's study is related to the different effect of methadone and opium-related alkaloids on the optic nerve or visual centers in the occipital lobe.

McGlone et al, in a study to assess the effect of methadone on VEP, concluded that the VEP wave was non-recordable in neonates who were exposed with methadone during pregnancy.<sup>8</sup> The difference between our findings and McGlone's study is probably due to the following reasons. Firstly, methadone, like many other substances and drugs, has a remarkable effect on the development of fetal visual and nervous systems resulting in VEP changes in the fetus, but in the current study our sample were adults who had mature and well-developed visual and nervous systems. Secondly, the substances in these two studies were different. Bauer et al reported obvious latency in P100 in subjects who had a past history of cocaine consumption<sup>9</sup> which is different from our findings. As Bauer mentioned, it seems that it is due to the vasoconstrictor effect of cocaine on the retina and occipital perfusion. This effect has not been proved for opium and is not considerable.

**Table 1.** Comparison of N75 latency, P100 latency, N135 latency and amplitude of visual evoked potentials (VEP) between "men with concomitant opium-dependence and chronic cigarette smoking" and "men with only chronic cigarette smoking"

Variables	Groups	No.	Mean	Std. Deviation	P Value
N75	Cigarette and Opium	30	71.7433	12.5055	0.688
	Only Cigarette	30	70.2583	13.0257	
P100	Cigarette and Opium	30	114.9863	18.0459	0.583
	Only Cigarette	30	113.7633	13.1741	
N135	Cigarette and Opium	30	162.6533	27.4678	0.683
	Only Cigarette	30	169.7367	42.8553	
Amplitude	Cigarette and Opium	30	6.8567	3.2484	0.018
	Only Cigarette	30	4.9333	2.5060	

Our findings indicate that VEP amplitude in the form of peak-to-peak (summation of P100 and N75 amplitude) in men with concomitant opium dependency and chronic cigarette smoking was significantly greater than men who were only chronic cigarette smoking. Kuroda et al showed that morphine leads to significant increase in the amplitude of early and late components of VEP (including P1-N1, N1-P2, P3-N3 and N3-P4) in rats.<sup>10</sup> It is concurrent with our findings. Regarding this fact that codeine, betaine and especially morphine are the most important alkaloids in opium, and considering our findings and Kuroda's study, it seems that this finding results from the simulative effect of morphine and other opium alkaloids on the visual nervous system. Common causes of amplitude changes are refractive errors and pupil size. Therefore, if we consider opium-related pupil stenosis relationship to the decrease in VEP amplitude, we can see the simulative effects of concomitant opium dependency and chronic cigarette smoking on the visual nervous system more

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obviously. But for more confidence it is necessary to assess the effect of concomitant opium dependency and chronic cigarette smoking on eye refractive index and visual nervous system via careful tests (i.e. as PET scan, assessing eye refractive index).

In summary, our study suggests that concomitant opium dependency and chronic cigarette smoking lead to significant VEP amplitude increase in comparison with only chronic cigarette smoking. Therefore, more assessment for identifying the effects of concomitant and/or separate opium dependence and chronic cigarette smoking on eye refractive index, other eye functions and visual nervous system is required.

**Conflict of interest:** The Authors have no conflict of interest.

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## بررسی تأثیرات وابستگی به تریاک بر پتانسیل برانگیخته بینایی (VEP) در مردان

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### چکیده

یکی از مشکلات شایع به خصوص در ایران و کشورهای خاورمیانه، وابستگی به تریاک است که اثرات مختلفی بر سیستم عصبی می‌گذارد. این پژوهش با هدف بررسی تأثیرات وابستگی مزمن به تریاک، بر پتانسیل برانگیخته بینایی VEP یا Visual evoked potential در مردان، انجام شد.

در این پژوهش مورد-شاهدی، تعداد ۶۰ نفر انتخاب شدند که از این تعداد ۳۰ نفر فقط به سیگار و ۳۰ نفر دیگر به صورت همزمان به تریاک و سیگار وابسته بودند. سپس آزمایش‌های ادراری تریاک، در شرایط استاندارد با آزمون PSVEP بررسی گردید و متغیرهای  $N_{135}$ ،  $P_{100}$ ،  $N_{75}$  و  $P_{100}$  Amplitude اندازه‌گیری و در نهایت توسط برنامه آماری SPSS ۱۶ آنالیز و مقایسه شد.  $P < 0/05$  از نظر آماری معنی‌دار تلقی شد.

میانگین دو گروه در  $N_{75}$  برابر  $22/028 \pm 70/426$ ، میانگین  $P_{100}$  در دو گروه  $29/176 \pm 115/457$  و میانگین دو گروه در  $N_{135}$  به میزان  $66/712 \pm 165/402$  بود که در هیچ کدام تفاوت معنی‌داری دیده نشد. میانگین Amplitude موج VEP در گروه مورد نظر  $3/248 \pm 6/856$  به صورت معنی‌داری بیشتر از گروه شاهد  $2/50 \pm 4/93$  بود ( $P < 0/05$ ).

نتایج نشان داد که وابستگی مزمن به تریاک در افراد سیگاری، هیچ تأثیری بر اجزای تأخیری پتانسیل برانگیخته بینایی ندارد، اما در وابستگی مزمن همزمان به سیگار و تریاک، Amplitude موج VEP به طور مشخص از افراد وابسته به سیگار تنها بیشتر است. علت این امر را می‌توان به اثرات تحریکی سوء مصرف مزمن و همزمان این دو ماده بر روی چشم و یا سیستم عصبی بینایی نسبت داد.

تریاک، پتانسیل برانگیخته بینایی (VEP)، سیگار.

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