



TO ASSESS THE EFFECTS OF HYPERVENTILATION ON PATTERN REVERSAL VISUAL EVOKE POTENTIAL IN HEALTHY SUBJECTS

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ABSTRACT **Introduction:** Visual evoked potential is affected by various physiological parameters like hyperventilation, changes in the pH, and electrolyte imbalances. These parameters are supposed to cause changes in the electrical conductivity of nerve fibers. The present study aims to record the electrical changes with hyperventilation. **Methods:** The study was conducted in the hospital on 50 healthy volunteers, of age group 18-70 years at the Neurophysiology lab of Gandhi medical college. The cases were enrolled as per inclusion and exclusion criteria. All the variables were grouped as per mathematic transformation of them into nominal /ordinal/interval/and ratio /percentage variables. Further point estimates with dispersion measures were calculated with the help of MS- Excel. All the data were analyzed using IBM SPSS v 22 software. **Results:** The mean age of the volunteers enrolled in the study was 38.8 years. The average latency was found to be decreased after hyperventilation in both males and females. The average value found is described in the figure as follows: Before hv- female avg latency 104 male avg latency 107. After hv – female avg latency 102 male avg latency 10. Similarly, Before the HV – the female amplitude of 14.02; the male amplitude was 16.11, and After the HV- the female amplitude was 14.04; the male amplitude 4.4. **Conclusion:** As hyperventilation affects the conduction and generation of evoked potentials across the neuron, so does hyperventilation also affect the generation of VEP across different neurons. Other physiological factors that affect the VEP include pupillary size, gender, age, and drugs, as well as factors that affect the conduction of impulses through the neurons.

KEYWORDS : Visual evoked potentials, Hyperventilation, Visual pathway

INTRODUCTION:

Hyperventilation, alkalosis, and hypocalcemia have been shown to significantly improve neurological deficits such as visual impairment, nystagmus, and ocular paresis in patients with central nervous system demyelination. [1]It has been suggested on theoretical grounds that this improvement is the result of changes in nerve fiber excitability and enhanced conduction in demyelinated nerve fibers. [2, 3]The effects of hyperventilation may be mediated by a number of factors. Both the reduction in pCO₂ and the rise in extracellular pH which accompanies hyperventilation are known to enhance neural excitability in peripheral nerve fibers. [4, 5]In the present study, we recorded pattern-reversal visual evoked potentials (VEPs) before and after hyperventilation in healthy subjects and known visual pathway involvement to determine whether there is any evidence that this procedure improves conduction in the visual pathway.

MATERIAL & METHOD:

This a hospital-based observational study, carried out in the neurophysiology lab of the Department of Physiology Gandhi Medical College Bhopal and associate Hamidia Hospital Bhopal. The study was carried out on 50 apparently healthy volunteers aged 18 to 70 years during the period of October 2019 to March 2020. Those people who had Diabetes, Hypertension, Multiple sclerosis, or any other demyelinating disease which may lead to neuropathy, a history of head injury, cerebrovascular accident, epilepsy, idiopathic Bell's palsy, significant ocular disorders, a patient suffering from cardiovascular illness or cardiac autonomic neuronal dysfunction, history of smoking, alcoholism, chronic drug intake were excluded. All the information about the procedure (in their native language and in English) of the test and plausible adverse effects were provided to the patients in detail (handouts of the test to be performed) before the test.

Statistical Analysis Plan- All the variables will be grouped as per mathematic transformation of them into nominal /ordinal/interval/and ratio /percentage variables. Further point estimates with dispersion measures will be calculated with the help of MS- Excel. All the data were analyzed using IBM SPSS software. Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at a 5% level of significance. Chi-square/Fisher Exact test has been used to find the significance of study parameters on a categorical scale between two or more groups. Student t test and ANOVA were used to compare the mean of quantitative variables. The null hypothesis of discrepant results was declined when the p-value was less \leq than 0.05.

RESULTS:

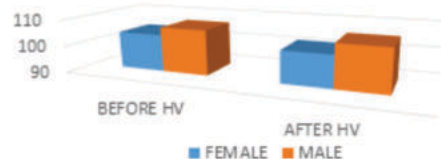
The mean age of the volunteers enrolled in the study was 38.8 years. The study's youngest and oldest fellows were 18 and 80 years old. The following table shows the age-wise distribution pattern.



Graph 1- Age Wise Distribution Of Subjects Involved In The Study

- In the study maximum number of subjects involved in the study are of 30-40 age group
- The male-to-female ratio in the study was 1.27:1.

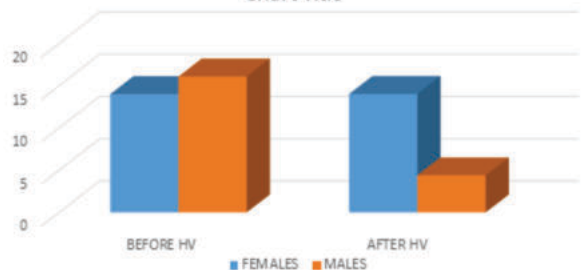
COMPARISON OF LATENCY BETWEEN FEMALE AND MALE SUBJECTS



Graph 2- Comparison Of Change In Latency In Female And Male Subjects

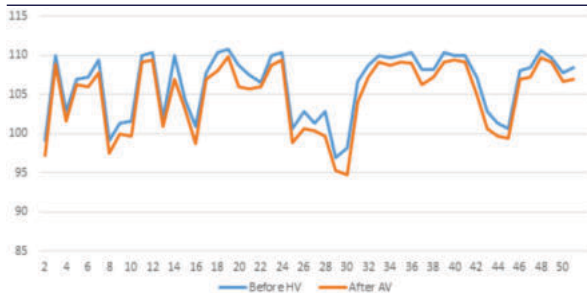
The average latency was found to be decreased after hyperventilation in both males and females. The average value found is described in the figure as follows: Before hv- female avg latency 104 male avg latency 107. After hv – female avg latency 102 male avg latency 10.

Chart Title



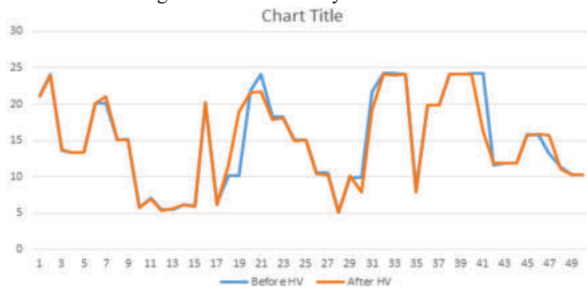
Graph 3- Comparison Of Change In Amplitude Between Female And Male Subjects

Before HV – female amplitude 14.02 ; male amplitude 16.11. After HV- female amplitude 14.04 ; male amplitude 4.4



Graph 4- Comparison Of Effect Of Hyperventilation On Latency [both Eyes] Of The Subjects

Before ventilation the highest value of latency is 110.6. After ventilation the highest value of latency is 109.8



Graph 5- Comparison Of Effect Of Hyperventilation On Amplitude [both Eyes] Of The Subjects

Before hyperventilation highest value of amplitude is 24.2. After hyperventilation highest value of amplitude is 24.07

DISCUSSION:

VEP has been shown to be a very sensitive diagnostic tool though it is a non-specific one. VEPs are used to quantify the functional integrity of the visual pathway, i.e. the integrity of the optic nerves, pathways to the visual cortex of the brain, and occipital cortex. Any anomaly that affects the visual pathways or visual cortex in the brain can affect the VEP. When properly performed, VEP can contribute in providing important information on the visual pathways in patients with diseases like optic neuritis, multiple sclerosis, compressive lesions of the optic nerve and optic chiasm, and also in neurodegenerative diseases not primarily involving the visual pathways [6-8]. VEP is more sensitive in diagnosing abnormalities in the anterior visual pathway, i.e. before the optic chiasm. Every disease has its own characteristic findings on VEP for example significant prolongation of P100 latency, with relative preservation of amplitude is seen in demyelinating diseases like Multiple sclerosis.

Our study was conducted on 50 healthy volunteers with standard protocol. Many studies were conducted in the past for the assessment of visual evoked potential and its clinical applications in various metabolic and structural disorders of the brain and the visual pathway. Hyperventilation is one of the commonest maneuvers to elicit changes in the measured evoked potential. Similar studies were conducted earlier on healthy subjects to assess the effect of hyperventilation on VEP. [9-13]

In our study, the mean age of the group is 38.8 years. This is similar to that found in many other studies. There are many studies mentioned in the literature that had made a comparison between some pathological conditions and normal healthy individuals. [14-23] Apart from this, there are some studies that had enrolled individuals of age more than 40 years [16], and also some had enrolled the pediatric population [24, 25] and those the age of 17-21 years. [15]

Age is an important factor in visual electrophysiology. There were many studies in the literature reporting faster VEP amplitude and peak times before the second decade of life and progressive increased latencies after the seventh decade of life. Our results had shown the same pattern but due to less number of cases, the findings are not statistically significant. [26] The sex ratio in our study was found to be 1.27:1. There were many studies that compared and analyzed the difference in latency and amplitude in males and females. A similar study on medical students was conducted by Sharma R et al with an equal ratio of males and females in Patiala. [16] In our study, we found

that the values of latency and amplitude in females were smaller than that of males. Similar results were found in many other studies that were conducted in different parts of the world and in different eras. [17,18] Many studies were done to explain this and the explanation is based on the findings of functional MRI such as larger brain size, a higher percentage of white matter, and a lower percentage of gray matter in men in relation to women. [27] In a study, it was postulated that gender-based effects on VEP were attributed to differences in the central processing of patterned stimuli, possibly by a heightened sensitivity in older females. [28] The exact cause of this gender difference in VEP parameters is not clear but it may be related to anatomical or endocrinal differences [29]. In a study conducted by Marsh MS et al., [30] compared the differences in the pattern VEP between pregnant and non-pregnant women, it was observed that the mean P100 latencies for all responses were shorter in the pregnant women. The difference in blood levels of sex steroids may be the likely cause of differences in P100 latencies between pregnant and non-pregnant women. They postulated that this endocrine difference may also account for the gender difference in VEP latency. Similarly, Kaneda Y et al., postulated that the sex differences in VEP may be attributed to genetically determined sex differences in neuroendocrinological systems. [31] In another study, women presented higher P100 amplitude in relation to men. Similar findings were obtained in our results that the VEP latencies are comparable between both genders. The probable explanation for this finding is the influence of hormones that seemed to contribute to higher amplitude in women. [32] The mean values of latencies, before hyperventilation among the females and males, were 104ms and 107ms while it was decreased to 102ms and 106ms respectively after hyperventilation. This is in accordance with the results of many studies conducted in the past. [31-34] In our study, the mean latency (in milliseconds) of the P100 wave in normal female subjects was 88.31 ± 8.799 and 88.788 ± 8.984 in the left and right eye respectively. The mean latency (in milliseconds) of P100 wave in normal male subjects was 93.214 ± 10.656 and 93.41 ± 10.628 in the left and right eye respectively. In a study done by Shibasaki H and Kuroiwa Y, the mean peak latency of N70, P100 and N145 waves in normal subjects were 67.8 ± 4.04 , 92.5 ± 4.44 and 136.0 ± 12.11 respectively. In a previous Indian study of Visual Evoked Potentials in young adults, Tandon OP and Sharma KN reported P100 latency of 95.37 ± 6.85 msec for males and 91.07 ± 49 msec for females. [14,16] The difference in the values in this study and in past literature may be due to the difference in the recording instruments and their calibration which differs from institute to institute, therefore there is need for each institute to have its own parameters according to the device. Our results showed that the latencies of N70, P100 and N155 waves were significantly longer in males as compared to females. The amplitude of P100 wave was higher in females in both left and right eye as compared to males. Our results were in agreement with the results of previous studies [33-35] which showed shorter latencies and higher amplitude in females. On the contrary, some studies showed no significant gender difference in VEP latencies. [14,16,32] The probable explanation to this finding is based on the fact that hyperventilation leads to reduction in pCO₂ and increases alkalinity of the extracellular compartment. Also, it lead to secondary reduction in the levels of serum-ionized calcium, thereby enhancing the axonal excitability and increasing the safety factor for transmission.

The average height of the subjects included in our study was 157 cm. After seeking various studies conducted in the past, we found that Kothari et al. performed Pattern reversal visual evoked potential (PRVEP) recording from normal subjects in accordance with the standard directive of the International System of Electroencephalogram electrode placements and found a positive correlation between the VEP latencies and increasing height and hence concluded that it is influenced by the height of the individual. In our study, we were unable to establish such a relationship.

Eye dominance had an influence on the VEP. In the literature, it has been shown that information perceived by the dominant eye strongly activates the ipsilateral visual cortex, Schintu S et al. hypothesized that eye dominance may modulate visuospatial attention bias. [35] Many studies were conducted in the past that suggested that the mean latency of the P100 peak was significantly shorter with stimulation of the dominant eye. [36] It was observed that there were disparities in the values of latencies and amplitudes between the dominant and the non-dominant eyes, suggesting electrophysiological evidence of lateralization in the nervous system. The results of our study are in accordance with those of many other studies. [38]

CONCLUSION:

The study was conducted on healthy volunteers. VEP measures the time that it takes for visual stimulus to travel from the eye to the occipital cortex. It gives us an idea of whether the nerve pathway is abnormal in any way, this means that it takes a longer time for electrical signals to be conducted from the eyes, resulting in an abnormal VEP. Many physiological factors affect the VEP like pupillary size, gender, age, and drugs and it also gets affected by the factors affecting the conduction of impulses through the neurons, as hyperventilation affects the conduction and generation of evoked potential across the neuron, so hyperventilation also affects the generation of VEP across different neurons.

REFERENCES:

- Davis FA, Becker FO, Michael JA, Sorensen E. Effect of intravenous sodium bicarbonate, disodium editate (Na₂EDTA), and hyperventilation on visual and oculomotor signs in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1970;33:723-32.
- Davis FA, Schauf CL. The pathophysiology of multiple sclerosis: a theoretical model. In: Klawans HL, ed. *Models of Neurological Diseases*. Amsterdam: Excerpta Medica 1974:83-107.
- Rogart RB, Ritchie JM. Pathophysiology of conduction in demyelinated nerve fibers. In: Morell P, ed. *Myelin*. New York: Plenum Press 1977:353-82.
- Lorente de No R. A study of nerve physiology. *Stud. Rockefeller Inst Med Res* 1947, part 1, vol 1.
- Tasaki I, Singer I, Takenaka T. Effects of internal and external ionic environment on excitability of squid giant axon. A macromolecular approach. *J Gen Physiol* 1964;48: 1095-123.
- Cohen SN, Syndulko K, Tourtellotte WW. Clinical applications of visual evoked potentials in neurology. *Bull Los Angeles Neurol Soc*. 1982;47:13-29.
- Carter JL. In: *Clinical Neurophysiology*, ed. Daube JR and Rubin DL. 3rd ed. Oxford University Press; 2009. Visual Evoked Potentials; pp. 311-22.
- Odom JV, Bach M, Brigell M, Holder GE, McCulloch DL, Tormene AP, et al. ISCEV standard for clinical visual evoked potentials (2009 update) *Doc Ophthalmol*. 2010;120:205-14.
- Tandon OP, Sharma KN. Visual evoked potential in young adults: a normative study. *Indian J Physiol Pharmacol*. 1989 Oct-Dec;33(4):247-9.
- Ekayanti MS, Mahama CN, Ngantung DJ. Normative values of visual evoked potential in adults. *Indian J Ophthalmol*. 2021 Sep;69(9):2328-2332.
- Sharma R, Joshi S, Singh KD, Kumar A. Visual Evoked Potentials: Normative Values and Gender Differences. *J Clin Diagn Res*. 2015 Jul;9(7):CC12-5
- Tello C, De Moraes CG, Prata TS, Derr P, Patel J, Siegfried J, Liebmann JM, Ritch R. Repeatability of short-duration transient visual evoked potentials in normal subjects. *Doc Ophthalmol*. 2010 Jun;120(3):219-28.
- Trevino RC, Majcher CE, Henry AM, Rodriguez M, Sponzel WE. Visual evoked potential repeatability using the Diopsys NOVA LX fixed protocol in normal older adults. *Clin Ophthalmol*. 2018 Sep 7;12:1713-1729.
- Streletz LJ, Bae SH, Roeshman RM, Schatz NJ, Savino PJ. Visual evoked potentials in occipital lobe lesions. *Arch Neurol*. 1981 Feb;38(2):80-5.
- Kuroiwa Y, Celesia GG. Visual evoked potentials with hemifield pattern stimulation. Their use in the diagnosis of retrochiasmatic lesions. *Arch Neurol*. 1981 Feb;38(2):86-90.
- Tandon OP, Sharma KN. Visual evoked potential in young adults: a normative study. *Indian J Physiol Pharmacol*. 1989 Oct-Dec;33(4):247-9.
- Ekayanti MS, Mahama CN, Ngantung DJ. Normative values of visual evoked potential in adults. *Indian J Ophthalmol*. 2021 Sep;69(9):2328-2332.
- Sharma R, Joshi S, Singh KD, Kumar A. Visual Evoked Potentials: Normative Values and Gender Differences. *J Clin Diagn Res*. 2015 Jul;9(7):CC12-5
- Gregori B, Pro S, Bombelli F, La Riccia M, Accornero N. Vep latency: sex and head size. *Clin Neurophysiol*. 2006 May;117(5):1154-7.
- Dotto PF, Berezovsky A, Sacai PY, Rocha DM, Salomão SR. Gender-based normative values for pattern-reversal and flash visually evoked potentials under binocular and monocular stimulation in healthy adults. *Doc Ophthalmol*. 2017 Aug;135(1):53-67.
- Kothari R, Singh S, Bokariya P, Singh R. Association of Height With Pattern Reversal Visual Evoked Potentials. *Asia Pac J Ophthalmol (Phila)*. 2013 May-Jun;2(3):221-6.
- Atilla H, Tekeli O, Ornek K, Batioglu F, Elhan AH, Eryilmaz T. Pattern electroretinography and visual evoked potentials in optic nerve diseases. *J Clin Neurosci*. 2006 Jan;13(1):55-9.
- Lesiakowski P, Lubiński W, Zwierko T. Evoked potentials in diagnosis of visual dysfunction in amateur boxers. *Phys Sportsmed*. 2018 Nov;46(4):449-459.
- Taylor MJ, McCulloch DL. Visual evoked potentials in infants and children. *J Clin Neurophysiol*. 1992 Jul;9(3):357-72.
- Frank Y, Kurtzberg D, Kreuzer JA, Vaughan HG Jr. Flash and pattern-reversal visual evoked potential abnormalities in infants and children with cerebral blindness. *Dev Med Child Neurol*. 1992 Apr;34(4):305-15.
- Kuba M, Kremla ek, Langrova J, Kubova Z, Szanyi J, Frantis ek V (2012) Aging effect in pattern, motion and cognitive visual evoked potentials. *Vis Res* 62:9-1.
- Knickmeyer RC, Wang J, Zhu H, Geng X, Woolson S, Hemer RM, Konneker T, Styner M, Gilmore JH (2014) Impact of sex and gonadal steroids on neonatal brain structure. *Cereb Corte* 24:2721-2731.
- La Marche JA, Dobson WR, Cohn NB, Dustman RE (1986) Amplitudes of visually evoked potentials to patterned stimuli: age and sex comparisons. *Electroencephal Clin Neurophysiol* 65:81-85.
- Gastone G. *Celesia. Visual Evoked Response in evoked potential*; 6ed. Philadelphia: WB Saunders; 1998.
- Cohen SN, Syndulko K, Tourtellotte WW. Clinical applications of visual evoked potentials in neurology. *Bull Los Angeles Neurol Soc*. 1982;47:13-29.
- Marsh MS, Smith S. Differences in the pattern visual evoked potential between pregnant and non-pregnant women. *Electroencephalogr Clin Neurophysiol*. 1994;92(2):102-6.
- Mitchell KW, Howe JW, Spencer SR (1987) Visual evoked potentials in the older population: age and gender effects. *Clin Phys Physiol Meas* 8:317-32
- Rieke Oelkers, Konrad Grosser, Eberhard Lang, Gerd Geisslinger, Gerd Kobal, Kay Brune, Jörn Löttsch, Visual evoked potentials in migraine patients: alterations depend on pattern spatial frequency, *Brain*, Volume 122, Issue 6, June 1999, Pages 1147-1155.
- Vijayalakshmi TN, Jayaraman RM, Bhanu, Anandan H. Evaluation of Visual Evoked Potential in Migraine Individuals. *Int J Sci Stud* 2016;4(4):46-50.
- Schintu S, Chaumillon R, Guillaume A, Salemm R, Reilly KT, Pisella L, Farnè A. Eye dominance modulates visuospatial attention. *Neuropsychologia*. 2020 Apr;141:107314.
- Hull BM, Drasdo N. The influence of age on the pattern-reversal electroretinogram. *Ophthalmic Physiol Opt*. 1990 Jan;10(1):49-53.
- Seyal M, Sato S, White BG, Porter RJ. Visual evoked potentials and eye dominance.

- Electroencephalogr Clin Neurophysiol. 1981 Nov;52 (5):424-8.
38. Kamis U, Gunduz K, Okudan N, Gokbel H, Bodur S, Tan U. Relationship between eye dominance and pattern electroretinograms in normal human subjects. *Int J Neurosci*. 2005 Feb;115(2):185-92.