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Assessment of Visual Evoked Potentials during pregnancy

Physiology

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ABSTRACT

Visual changes in pregnancy are common and knowledge of these ocular changes can help to differentiate the physiological changes from ocular manifestation of systemic and eye diseases in a pregnant woman. Visual evoked potentials (VEPs) provide a sensitive indication of abnormal conduction in the visual pathway. This cross sectional study was conducted in the Neurophysiology Unit of the Department of Physiology of a rural medical college. We performed VEP investigation on 60 pregnant females, 20 in each of the three trimesters clinically confirmed by the obstetrician of a tertiary care rural hospital. The mean N70, P100 and N155 latencies (in msec) and mean P100 amplitude for all the three trimesters of pregnancy have been established in this study. This study aimed to lay down the baseline data of VEPs in pregnancy sits use can be further optimised for visual disorders concerned with the pregnancy.

KEYWORDS:

P100 latency, P100 amplitude, N70 Latency, N155 Latency, pregnancy

INTRODUCTION

During pregnancy, the systemic physiology of a female gets drastically altered. The symptoms of nausea, vomiting, dietary cravings and avertions during normal pregnancy have been attributed to changes in hormonal profile and in central nervous system (1). Visual changes in pregnancy are common and knowledge of these ocular changes can help to differentiate the physiological changes from ocular manifestation of systemic disease and diseases pertaining to the eye in a pregnant woman.

Ovarian steroids have pervasive effects throughout the central nervous system including the sensory information processing in the brain. Visual Evoked Potentials (VEPs) reflect electrical phenomena occurring during visual processing and therefore can be used both in research and in clinical practice to elucidate the function of the visual system. VEP is a simple, low cost, non-invasive technique used to assess the functional integrity of the visual pathways. It is a graphic illustration of the cerebral electrical potentials generated by the occipital cortex evoked by a defined visual stimulus (2).

There has not been much documentation of visual function and its electrophysiological correlates during pregnancy. Some changes in the visual sensitivities during menstrual cycle have been suggested, with the threshold being reduced during menstruation (3). However any detailed reports, particularly from this part of the country, regarding sensory changes especially visual perception in pregnancy are lacking. Only one Indian study (4) could be retrieved through literature search that reported changes in VEP responses to pattern reversal in a very small cohort of ten, only third trimester pregnant women when compared to the non pregnant females.

Therefore in an attempt to evaluate the effect of pregnancy on visual pathways, VEPs were recorded in parous state so that we could lay down the baseline normative data of VEP in all three trimesters of pregnancy that may serve the purpose for clinical implications in various pregnancy associated visual disorders.

METHODOLOGY:

Setting-
This study was conducted in the Neurophysiology Unit of the Department of Physiology, Mahatma Gandhi Institute of Medical Sciences, Sevagram.

Study population:
We performed VEP investigation on 60 pregnant females, 20 in each of the three trimesters clinically confirmed by the obstetrician of the Department of Obstetrics and Gynecology in a tertiary care rural hospital located in central India. The controls were 40 healthy non-pregnant female volunteers.

Study Design: This study was a hospital based cross sectional study.
Method:
VEP recordings were done in accordance to the standardized methodology of International Federation of Clinical Neurophysiology (IFCN) Committee Recommendations (5) and International Society for Clinical Electrophysiology of Vision (ISCEV) Guidelines (6) and montages were kept as per 10-20 International System of EEG Electrode placements (7).

The stimulus configuration for VEP recording was transient pattern reversal method in which a black and white checker board will be generated (full field) on a VEP Monitor by an Evoked Potential Recorder (RMS EMG EP MARK II). The recording was done monocularly for the left and right eyes separately with the subject wearing corrective glasses, if any during the test.

VEP Waveform
The usual PRVEP waveform is the initial negative peak (N70), followed by a large positive peak (P100) and followed by another negative peak (N155). Positive wave P100 is shown with downward polarity and negative waves are shown with upward polarity in the recording.

STUDY PARAMETERS
1) P100 latency: The time interval between the onset of a visual stimulus and the first maximum positive deflection or excursion of the VEP signal.

2) P100 Amplitude It is measured from the peak of N70 to the trough of P100.

3) N70 Latency: The time interval between the onset of a visual stimulus and first negative wave in VEP signal.

4) N155 latency: The time interval between the onset of a visual stimulus and second negative wave in VEP signal.

Ethics consideration:
The study was approved by Institutional ethics committee (IEC). We obtained written informed consent from the patients before their enrolment in this study.

Data Analysis:
All data was abstracted on a standardized data collection form. Data was analysed using SPSS software (version 21.0). Continuous variables were presented as mean ± standard deviation (SD) and compared using Student's t-test. P value <0.05 was regarded as being statistically significant.

RESULTS
A total of 60 pregnant females, 20 in each of the three trimesters and 40 controls were investigated for VEP. The mean ± SD values of the general characteristics including age, height, weight, pulse per min. and blood pressure of the pregnant and control females have been summarized in Table 1. The difference in the mean age as well as mean height of cases and controls was not statistically significant.

Table 1: Demographic information of the study subjects:

	First Trimester (n=20)	Second Trimester (n=20)	Third Trimester (n=20)	Controls (n=40)
Mean± SD age(yrs)	23.95 ±3.33	24.65 ±4.35	24.25 ± 2.43	24.48±3.87
Height (in cms)	155.10 ±5.01	153.55±5.44	156±4.03	150.21 ±5.85
Weight (in Kgs)	47±5.27	48.25±9.83	53.65±5.66	48.13 ±10.82
Pulse per min	75 ± 5	81±7	83±6	77±4
BP (mm Hg)	118/78	110/70	124/82	120/80

The normative values of VEP parameters of Left and Right eye in pregnant females in respective trimesters have been expressed as mean ± SD in Table 2 and Table 3. It is evident that as we proceed from first to the third trimester, there was shortening of N70, P100 and N155 latencies and a reduction in P100 amplitude.

Table 2: Normative profile of LE VEP parameters in Pregnancy

	N70 Latency (msec)	P100 Latency (msec)	N155 Latency (msec)	P100 Amplitude (μV)
First Trimester	71.26 ± 3.62	100.10 ± 4.47	141.64 ±9.86	8.42 ± 3.85
Second Trimester	69.57± 4.50	99.88 ± 1.71	139.40 ± 11.19	6.80 ± 2.50
Third Trimester	68.48 ± 5.64	97.55 ±4.70	138.64± 13.79	6.33 ± 1.89

Table 3: Normative profile of RE VEP parameters in Pregnancy

	N70 Latency (msec)	P100 Latency (msec)	N155 Latency (msec)	P100 Amplitude (μV)
First Trimester	71.49 ± 3.59	100.17 ± 2.86	141.66 ± 10.45	7.98 ± 3.35
Second Trimester	69.28 ± 5.51	99.02 ± 4.83	139.54 ± 10.0	7.18 ± 2.59
Third Trimester	68.36 ± 6.10	98.09 ± 4.30	138.48 ± 13.47	6.31 ± 1.79

The pregnant females in the three trimesters have been compared to controls as regards all VEP parameters in Left eyes in Table 4 and in the right eyes in Table 5.

Table 4: Comparison between Pregnant females & controls as regards Left eyes

S.No		N70 Latency (msec)	P100 Latency (msec)	N155 Latency (msec)	P100 Amplitude (μV)
1.	Controls	71.83 ± 3.75	101.50±4.72	144.81 ± 8.53	6.74±2.38
2.	First Trimester	71.26 ± 3.62	100.10 ± 3.47	141.64 ±9.86	8.42±3.85
	p value*	0.576	0.244	0.202	0.041
3.	Second Trimester	69.57± 4.50	99.88 ±1.71	139.40 ±11.19	6.80±2.50
	p value *	0.04	0.143	0.041	0.928
4.	Third Trimester	68.48 ± 3.64	97.55 ±4.70	138.64± 13.79	6.33±1.89
	p value *	0.001	0.003	0.036	0.410

Table 5: Comparison between Pregnant females & controls as regards Right eye

S.No.		N70 Latency (msec)	P100 Latency (msec)	N155 Latency (msec)	P100 Amplitude (μV)
1.	Controls	71.56 ± 4.65	101.89 ± 4.25	145.10 ± 8.38	6.11 ± 1.85
2.	First Trimester	71.49 ± 3.59	100.17± 2.86	141.66 ± 10.45	7.98 ± 3.35
	t test	0.953	0.108	0.173	0.007
3.	Second Trimester	69.28 ± 2.81	99.02 ± 4.83	139.44 ± 10.0	7.18 ± 2.59
	t test	0.04	0.021	0.025	0.070
4.	Third Trimester	68.36 ± 4.10	98.09 ± 4.30	138.48 ± 13.47	6.31 ± 1.79
	t test	0.01	0.001	0.02	0.691

DISCUSSION
A number of neurophysiology laboratories are fast emerging in our country and have included visual evoked potential study to their routine procedures as this method is non-invasive, cheap, highly objective investigation to test the visual function. The present work was carried out to evaluate the variations in the pattern reversal visual evoked potentials in the three trimesters of pregnancy. All the 100 subjects under study were thoroughly examined and subjected to VEP testing after a detailed history.

The attributes of VEP are affected by a number of factors like age, sex, height, body temperature etc. It is therefore customary and pertinent to base the values used to define the range of normal variation on data obtained from normal subjects using the local equipment. The present study was well controlled with regard to the physiological variables influencing PRVEP so as to obtain reproducible and reliable normative data of VEP in pregnancy before using it as a diagnostic tool for disorders in the same.

The VEP findings of the present study elucidate that the mean N70, P100 and N155 latencies were shorter in pregnant women of all the

three trimesters when compared to non-pregnant group. A diminution in P100 amplitude was observed during pregnancy as we proceed from first to the third trimester.

Our study corroborates very well with the Indian study by Tandon & Bhatia (1991). The mean age of their patients was 24.2±2.9 years while that of our pregnant females was 24.25 ± 2.43 years. The mean age of their group of non pregnant females was 21.3±4.5 years whereas that of our control group was 24.48 ± 3.87 years. In their study, the values of VEP parameters for the third trimester Pregnant females were 68.5 ± 5.0 msec, 95.7 ± 6.4 msec and127.2 ± 8.8 msec respectively for N70, P100 and N155 latencies. Similarly the values for the control females were 73.2±6.2, 104.5±2.10 and 143.5±21.0 respectively. The mean latencies of third trimester females in our study are comparable with them as they are 68.48 ± 3.64, 97.55 ±4.70, 138.64± 13.79 for left eye, 68.36 ± 4.10, 98.09 ± 4.30, 138.48 ± 13.47 for right eyes.

Our results are also in concordance with Marsh & Smith (1994) who have also reported mean P100 latencies for all responses shorter in the pregnant women, with statistically significant differences for the left eye whole field latency ($P < 0.05$) and the left eye right and left half field latencies ($P < 0.005$ and $P < 0.05$, respectively) and the right eye right half field latency ($P < 0.05$). Similar to our observations, the latencies in women in their pregnant group showed a negative correlation with gestation. These observed differences in PRVEP latencies in pregnant and non-pregnant women and the association between latency and gestation are likely to be due to differences in circulating sex steroids, and this effect might be the primary reason for latency differences between the sexes (8).

The significantly lower latency of waves as compared to the control group implies that neural excitation and conduction processes are better in optic nerve and pathways during pregnancy and the hormonal millieu of pregnancy sensitises the process of neural conduction in visual pathways. In support of this notion, the significant reduction of mean VEP latency in the proliferative phase when estrogen levels are higher had been attributed to the facilitating effects of estrogen on the neural transmission in the optic pathways in an earlier study (3) where the researchers discovered the latency of the P100, was shorter in the proliferative phase with a statistically significant difference ($p<0.0001$) as compared to that in luteal phase. This shortened time could be due to estrogen facilitating neural transmission by decreasing transmission time.

Chemical energy transduction from light to nerve signals takes a greater part of the total potential time than the time required for stimulation produced by electrical stimuli or by accelerated ions stimulation on neuronal pathways. Therefore the hypothesis that energy transduction in the retina of females in pregnant condition is more efficient than in control females, can be suggested for explaining the reduced latencies during pregnancy.

As stated earlier, estrogen causes a reduction in the visual transmission time by enhancing the sensitivity of receptors in the optic pathways to dopamine. It also does so by augmenting the effects of glutamate via L type voltage –gated calcium channels that are present in CNS and visual pathways (9,10). Estrogen also inhibits the synthesis of GABA by inhibiting glutamate decarboxylase enzyme. In contrast to estrogen, Progestrone & its metabolites antagonize the effect of estrogen (11,12). Another result that remains to be clarified is the decrease of VEPs amplitude in pregnant cases for which it can be recapitulated that 17â-estradiol was shown to exert inhibiting properties on neuronal firing rate of ovariectomized rats, and an interference has been described between estrogen and acetylcholine effects on several brain neurons (13,14), finally resulting in a lower amplitude of VEPs. So these studies have indicated the involvement of sex steroids in sensory perceptions, and sex steroids are known to interact with neurotransmitters in sensory pathways.

Conclusion

Pregnancy involves predictable increases in hormone levels, so this study examined how naturally occurring changes in endogenous levels of steroid hormones during pregnancy may affect VEPs. A reduction in PRVEP latencies and decrement of amplitude in pregnant females were observed. In a nutshell, this study aimed to focus at the utility of VEPs as an objective electrophysiological method of assessment of visual pathway in pregnant state so that its use can be further optimised for the constellation of visual disorders concerned with the pregnancy namely diabetic retinopathy, Central serous chorioretinopathy, pituitary adenomas and meningiomas, HELLP syndrome etc.

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