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Visual Evoked Potential in Normal and Amblyopic Children

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Abstract:
Background: *Amblyopia refers to a decrease in best-corrected visual acuity in an eye having no organic pathology. Amblyopia is primarily a cortical phenomenon, caused by unequal competitive inputs from the two eyes into primary visual cortex area 17, although additional structural and functional abnormalities have been observed in the lateral geniculate nucleus of amblyopic animals and human. It has been estimated to affect 1–3% of the population Amblyopia usually affects only one eye, but it is possible to be amblyopic in both eyes if both are similarly deprived of a good, clear visual image. Detecting the condition in early childhood increases the chance of successful treatment.*

I. Objective

1. Recording of VEP in normal individuals.
2. Recording of VEP in Ambylopia individuals.
3. Comparison of the results of the above two groups.

II. Materials and Methods

52 Amblyopic children in the age group of 4-12 years belonging to both sexes were studied. Age and sex matched control group of 52 normal children were also studied.(Due criteria were adopted for inclusion and exclusion)Pattern Visual Evoked Potential (PVEP) were recorded on Viking Select neuro diagnostic system.

III. Results

In PVEP , P_{100} latencies were longer and amplitudes were shorter in amblyopic group compared to normal group. The data was subjected to various statistical analysis using SPSS-21 software. The difference in latencies and amplitudes between two groups (amblyopic & normal) was statistically significant when the data was subjected to the independent samples T test.

IV. Conclusion

P_{100} latency of PVEP at the time of presentation was significantly related to visual acuity. So PVEP test may be useful in future to identify amblyopia long before the appearance of symptoms and to follow treatment progress in pediatric amblyopes.

Keywords- Visual Evoked Potential (VEP), Amblyopia

V. Background

The term amblyopia describes a condition in which there is reduced visual function in one, or infrequently both, eye(s), despite optimum optical correction and the absence of overt pathology of the visual system. There is an acquired defect in vision that is due to an abnormal visual experience during a sensitive period of visual development. The neural basis of amblyopia is the study of the effects of the abnormal environmental influences on the genetically programmed development of visual processing system. The prevalence of amblyopia in humans is thought to be around 1% to 3%. Human amblyopes are usually asymptomatic when viewing with both eyes open, as the vision in the fellow eye is generally normal. The motivation for research is not necessarily to find a treatment for this generally asymptomatic condition but rather the realization that amblyopia may provide valuable insight into the role of early experience on the structure and function of the human brain.[1]

Several studies have been performed with electrophysiological methods used in humans and in animal models, to investigate the retinal and visual system in amblyopia dysfunction. Reported findings regarding retinal function are contradictory. The function of the entire visual pathway, from photoreceptors to the visual cortex, can be evaluated by visual evoked potential (VEP) recordings and the presence of abnormal VEP responses has been observed in amblyopia.[2]

As the VEP readings assess the bioelectrical response of the visual cortex, the observations derived from previous studies do not suggest specific information on whether the reported VEP abnormalities may be selectively related to a retinal dysfunction, a postretinal dysfunction, or both. That postretinal structures, in particular the lateral geniculate nucleus (LGN), may be involved in amblyopia dysfunctional processes was first suggested by Hubel and Wiessel and later documented in several studies in which morphologic and functional changes of the LGN were detected.[3]

Understanding Evoked Potentials- An evoked potential (or "evoked response") is an electrical potential recorded from the nervous system of a human or other animal following presentation of a stimulus, as distinct from spontaneous potentials detected by electroencephalography (EEG) or electromyography (EMG). Evoked potential amplitudes tend to be low, ranging from less than a microvolt to several micro volts, compared to tens of micro volts for EEG, mill volts for EMG, and often close to a volt for ECG. To resolve these low-amplitude potentials against the background of ongoing EEG, ECG, EMG and other biological signals and ambient noise, signal averaging is usually required. The signal is time-locked to the stimulus and most of the noise occurs randomly, allowing the noise to be averaged out with averaging of repeated responses.[4]

Signals can be recorded from cerebral cortex, brain stem, spinal cord and peripheral nerves. Usually the term "evoked potential" is reserved for responses involving either recording from, or stimulation of, central nervous system structures. Sensory evoked potentials (SEP) are recorded from the central nervous system following stimulation of sense organs (for example, visual evoked potentials elicited by a flashing light or changing pattern on a monitor; auditory evoked potentials by a click or tone stimulus presented through earphones) or by tactile or somatosensory evoked potential (SSEP) elicited by tactile or electrical stimulation of a sensory or mixed nerve in the periphery. They have been widely used in clinical diagnostic medicine since the 1970s, and also in intraoperative neurophysiology monitoring (IONM), also known as surgical neurophysiology.

Neuroanatomical and Neurophysiological Abnormalities in Amblyopia

Foveal vision in amblyopia resembles peripheral vision in normals. This suggests that inappropriately large receptor fields (spatial summation) have developed in the foveal visual cortex. This hypothesis would explain the loss of contrast sensitivity at high spatial frequencies with preservation of low spatial frequencies. The phenomenon of spatial uncertainty, defects in judging line offset effects (vernier acuity) and the altered psyhovisual performance when tested with crowded targets.

Amblyogenic Mechanisms - Disuse versus Competition

Two amblyogenic mechanisms have been proposedand that these may be effective, individually or, in unison, in the various forms of amblyopia. [5,6] Disuse - A lack of adequate retinal stimulation during infancy, causing visual deprivation with arrest of development at a stage at which the interference began, or disuse atrophy of afferent connections that were already present at birth. This is not regarded as being a major factor in the development of strabismic amblyopia is now being disputed. Since the salient feature of strabismic amblyopia is not the lack of afference but the incompatibility of visual impressions received by both eyes.

Competition- This is based on the view that stimulation of corresponding retinal points with unequal images causes rivalry between the two eyes which is decided in favour of the fixating eye, the other eye becoming amblyopic. Binocular deprivation and strabismus experiments support that competition rather than disuse is the main cause of the observed changes. The right circumstances must exist, however, for the competition to occur, since cells in the normal visual cortex tend to be dominated by one eye or the other, and the dominant eye does not take over the cell completely. It appears that the incompatibility of the visual input received by the two eyes causes a decrease or even blockage of synaptic transmission of the afferent impulses originating from the nonfixing eye

VI. Materials And Methods

Subjects- 52 amblyopic patients of different etiologies were selected for the study. The patients who were not treated earlier for refractive error, amblyopia or ocular disease were considered for study. Clear media and normal fundus on ophthalmoscopic examination was a prerequisite for selection criteria.

The 52 patients, based on the etiologies are divided as:

Strabismic- 11
Anisometropic- 16
Isometropic- 25

1.Age group: 4-13 years
2.Sex distribution: Out of 52 patients 32 were female and 20 were male children.
3.Type of study: Prospective study
4.Inclusion criteria: All the children with amblyopia above three years of age were included in the study group.
5.Exclusion criteria: Children below three years

-Non co-operative children
-Toxic Amblyopia

6. Place of Study: Study was conducted in the Dept of Ophthalmology, Seven Hills Hospital, Visakhapatnam, Andhra Pradesh.

7. History: A full and detailed history regarding the onset of defective vision, squint, duration of symptoms, associated symptoms and previous treatment history was taken. Consent of the subjects and their parents were taken prior to the examination. Ethical committee approval was taken prior to the study.

8.Visual acuity: The base level visual acuity was tested with Snellen's visual acuity charts, Optotype charts for both distance and near, without and with correction of refractive error were estimated monocular and binocularly.

9.52 age and sex matched controls were taken as a comparative group, out of which 33 were males and 19 were females.

20. VEPs were recorded in both the groups.

VEP (VISUAL EVOKED POTENTIALS)

Equipment- Nicolet Viking Select Neuro-diagnostic system version 10.0 was used to record visually evoked potentials.

Stimulus type: Pattern reversal visual evoked potential Stimuli are delivered through the Nicolet 2015 Visual Stimulator monocularly and the pattern stimuli were displayed on a color monitor.

Parameters: Distance- 100 cm, Visual angle-0˚54', Frequence-1.1HZ, Filters-1-100 HZ,

Sweeps -100.

Recording Technique -The patient is made to sit at a distance of 100 cm from a TV monitor which displays the checkerboard pattern. The preferred stimulus for clinical investigation of the visual pathways is a shift (reversal) of a checkerboard pattern (usually black and white). The squares simply reverse without change in total light output (luminance) from the screen. Patient is asked to fix his/her vision at a point in the center of the pattern field and view it with a single eye. (Monocular testing) Light-tight opaque patch to be placed over the unstimulated eye. Care was taken to have the patient in a comfortable, well-supported position to minimize artifacts especially noise. A minimum of two recordings of each VEP condition were acquired, measured and displayed to confirm reproducibility of the data.

Reproducibility - reliability –

Various studies show that P100 component of PSVEP is more consistent and reliable and shows reproducibility better than any other wave components of various long latency EPs and is less affected by attention and concentration. However, the examiner must observe the gaze direction, whether it is directed towards the center, whether the eyes are close or open etc. as these effect the amplitude.

Latencies recordings are at N_{75}, P_{100} and at N_{145}.

Amplitudes recorded atN_{75}-P_{100} and N_{100} -P_{145}.

Analysis: Evaluation and interpretation of VEP changes were done in the two groups based on the data recorded.

Statistical analyses: Analyses were performed using SPSS version 21.0 (PASW Statistics) for Windows. (SPSS, Inc., Chicago, IL).The data of both amblyopic group and control group were subjected to the following statistical analysis- Descriptive Statistics and Independent Samples T- Test.

Descriptive Statistics in Amblyopia

	N	Range	Minimum	Maximum	Mean	Std. Deviation	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
Age	52	8.0	4.0	12.0	8.058	1.9844	.089	.330	-.441	.650
VEPN75REP	52	31	61	92	74.23	6.676	.701	.330	.324	.650
VEPP100REP	52	59	87	146	115.50	13.457	.217	.330	-.533	.650
VEPN145REP	52	57	133	190	151.69	12.298	1.484	.330	2.495	.650
N75P100REP	52	16	2	18	5.30	3.399	1.880	.330	3.904	.650
VEPN75LEP	52	73	42	115	74.44	10.357	.709	.330	4.788	.650
VEPP100LEP	52	56	85	141	115.06	11.770	.118	.330	-.015	.650
VEPN145LEP	52	74	126	200	153.88	13.886	1.452	.330	3.683	.650
VN75P100LEP	52	21	2	23	5.59	3.743	2.675	.330	9.270	.650
Valid N (listwise)	52									

(VEP- Visual evoked potential, N75- first negative wave at 75thmilli sec, P100- first positive at 100thmilli sec, N145 – second negative wave at 145thmilli seconds. RE- Right eye,LE- Left eye, P- Patient.

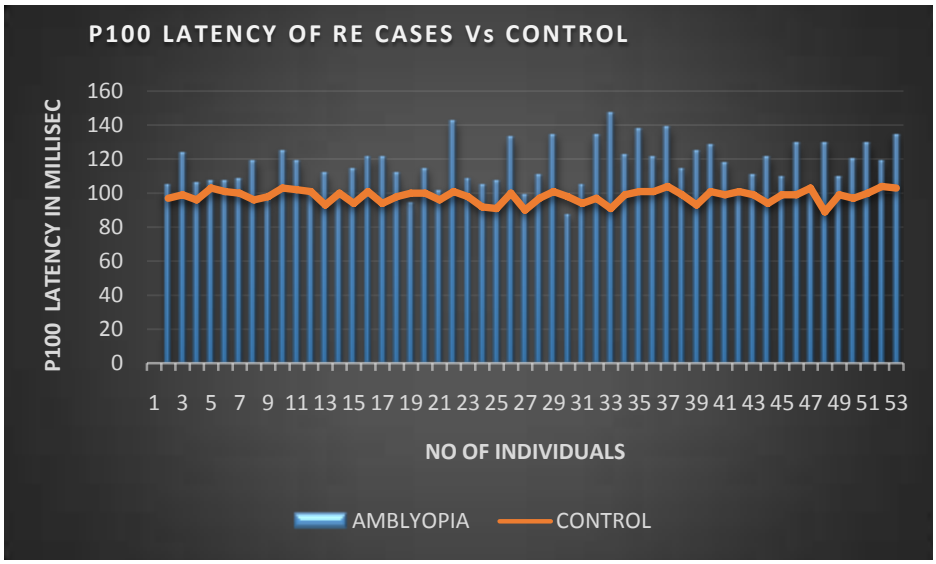
Descriptive Statistics Control

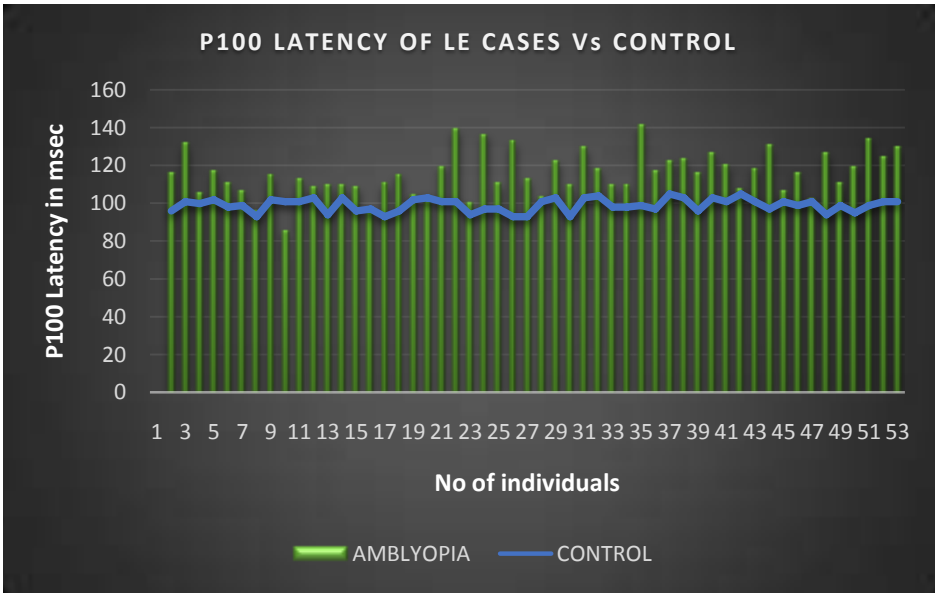
	N	Range	Minimum	Maximum	Mean	Std. Deviation	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
CAge	30	6.0	6.0	12.0	8.867	1.7167	-.130	.427	-.898	.833
VEPN75REC	52	29	58	87	71.65	6.312	-.067	.330	-.426	.650
VEPP100REC	52	15	89	104	98.19	3.726	-.706	.330	-.155	.650
VEPN145REC	52	46	104	150	137.62	7.217	-1.725	.330	8.131	.650
N75P100REC	52	17	1	18	11.82	3.367	-.998	.330	2.261	.650
VEPN75LEC	52	32	57	89	72.60	6.669	.054	.330	-.087	.650
VEPP100LEC	52	12	93	105	99.10	3.471	-.324	.330	-.954	.650
VEPN145LEC	52	20	130	150	138.83	5.684	.568	.330	-.667	.650
N75P100LEC	52	13	6	19	11.18	3.066	.847	.330	.796	.650
Valid N (listwise)	30									

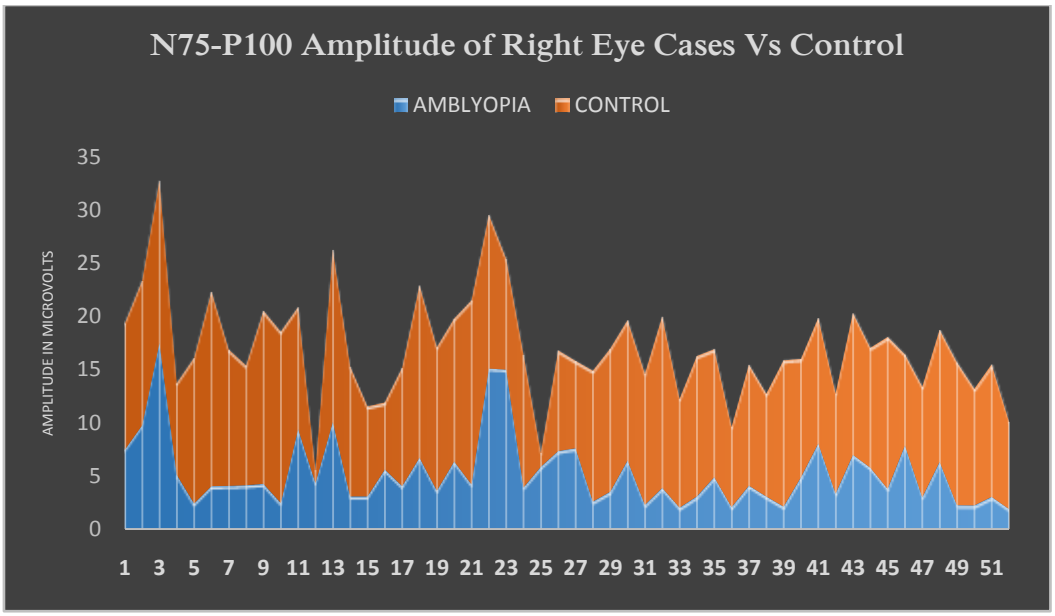
(VEP- Visual evoked potential, N75- first negative wave at 75thmilli sec, P100- first positive at 100thmilli sec, N145 – second negative wave at 145thmilli seconds. RE- Right eye,LE- Left eye, C- control)

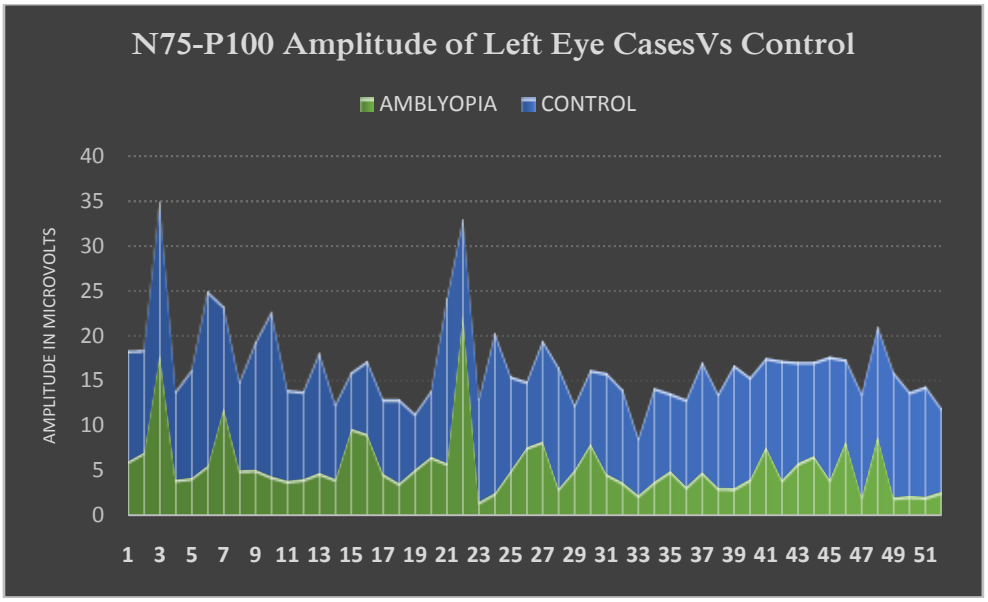
Sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	53	51.0	51.0	51.0
	Female	51	49.0	49.0	100.0
	Total	104	100.0	100.0	




P100 LATENCY OF LE CASES Vs CONTROL
P100 Latency in msec
160
140
120
100
80
60
40
20
0
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43 45 47 49 51 53
No of individuals
AMBLYOPIA
CONTROL


N75-P100 Amplitude of Right Eye Cases Vs Control
AMBLYOPIA
CONTROL
AMPLITUDE IN MICROVOLTS
35
30
25
20
15
10
5
0
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43 45 47 49 51



VII. Results

VEPs

1. The mean age of non-amblyopic group is 8.867+/-1.716 (33 males,19 females).The mean age of amblyopic group is 8.058+/-1.984 (20 males,32 females).
2. The mean value of latencies in milliseconds in right side in non-amblyopic group -N75 is 71.65+/-6.312, P100 is 98.19+/-3.726 and N145 is 137.62 +/-7.217 where as in amblyopics N75 is 74.23+/-6.676, P100 is 115.50+/-13.457 and N145 is 151.69 +/-12.298.
3. The mean value of amplitudes(in microvolts)for right side in non-amblyopics include N75-P100 is 11.82+/-3.367 where as in amblyopics N75-P100 is 5.30+/-3.399.
4. The mean value of latencies in milliseconds in left side in non-amblyopic group N75 is 72.60+/-6.669, P100 is 99.10+/-3.471 and N145 is 138.83+/-5.648,where as in amblyopics N75 is 74.44+/-10.357, P100 is 115,06+/-11.77 and N145 is 153.88+/-13.88.
5. The mean value of amplitudes(in microvolts)for left side in non-amblyopics include N75-P100 is 11.306+/-3.747,where as in amblyopics N75-P100 is 5.59+/-3.743.

Independent Samples T Test shows statistically significant variations in P100 latencies of right side (p=0.016) when amblyopes were compared with age matched controls.While similar analysis between left side P100 latencies was not statistically significant. The N75-P100 amplitude (in microvolts) was statistically significant (p=0.012) in right side when age matched amblyopes were compared with controls. The N75-P100 amplitude in the left eyes were not statistically significant,

VIII. Discussion

The response of visual cortex to patterned repetitive visual stimuli was tested in normal and amblyopic children, The VEP latencies and amplitudes were compared between normal and amblyopic children. A significant correlation was established in VEP P100 latencies and VEP N75-P100 amplitudes between normal and amblyopia groups. The P100 latency was significantly prolonged (statistically significant,$p<0.05$) and there was a significant decrease in N75-P100 amplitude($p<0.05$) in amblyopic group which is in accordance to previous studies.[7,8] There were no differences in other VEP parameters (N75, N145) between the two groups. In current study, the right eye of the amblyopic group showed more correlation than left. This may provide some information regarding specialization of functions in cerebral hemispheres. As all the patients examined happened to be right handed i.e left hemi sphere dominance (motor activities, speech etc.) it may be coupled with localization of some functions in left hemisphere related to cognitive process.[9]VEP P100is a long latency evoked potential. P-100 response of the visual evoked potential to pattern stimulation is a cortically originated wave either produced exclusively by area 17 or 18 or by a multiplicity of cortical neuronal pools.[10]Prolongation of P100 latency in our study, strongly suggest an abnormality at cortical level in amblyopia which is consistent with previous studies.[11,12] Also right sided P100 latencies more significant than left side suggesting, impairment of some cognitive function localized to left hemisphere based on impairment of processing of visual information

IX. Conclusion

VEP is a long latency evoked potential and P100 is a more reliable signal for processing information at cortical level. P100 latencies are prolonged and amplitudes are reduced in amblyopic group. P_{100} latency of PVEP at the time of presentation was significantly related to visual acuity. So PVEP test may be useful in future to identify amblyopia long before the appearance of symptoms and to follow treatment progress in pediatric amblyopes,[13,14]Further investigation is needed to determine whether these results are due to physiologic change(s) of amblyopia itself or to fixation in stability during the test.

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