

A study of pattern VEP in amblyopic children during the course of their therapy

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Abstract

Purpose: To find out the usefulness of Pattern VEP in monitoring the progress of Therapy in amblyopic children and also to ascertain the role of Pattern VEP (obtained at the time of initial diagnosis) in estimating the expected visual outcome after therapy. **Materials and Method:** This was a prospective interventional study conducted at Upgraded Department of Ophthalmology, SMS Medical College and Hospital, Jaipur. 50 children <15 years of age with anisometropic/strabismic/mixed/isoametropic amblyopia fulfilling the inclusion criteria were included in the study. The diagnosed cases underwent Amblyopia therapy. Follow up was done every 4 weekly interval for compliance to therapy and improvement in visual acuity. VEP was recorded at 1month, 3 months and 6 months. **Results :** In the present study, maximum number of patients belonged to 3-6 years of age (51.1%). They were followed by 33.3 % children of 7-10 years and the rest of 15.6% children in 11-15 years age group. At the time of initial diagnosis, majority of patients (31.1%) had P100 latency between 110 and 119 followed by 22.2% patients in 100-109 range. A decrease in P 100 latency was evident in our study. At initial VEP study the maximum patients had a P100 latency between 110 and 119 but after 6 months of therapy 37.8 % patients had P100 latency <100. At 3rd month only 2 patients had P100 latency >130 and at 6th month only 1 had >130 P100 latency. Corresponding to decrease in P100 latency there was increase in P 100 Amplitude of the affected eye after therapy. **Conclusions:** This study found that in amblyopic children, Pattern VEP showed characteristic changes of “Prolongation of P100 latency” and “Reduction of P 100 amplitude” (p<0.5) during the course of therapy. A gradual increase in visual acuity was also seen along with characteristic pattern VEP changes. Thus, pVEP can serve as an objective test for diagnosis and monitoring of children under amblyopia therapy. The present study also concluded that values of P100 latency obtained at the time of initial diagnosis can be used to estimate the expected visual outcome after therapy.

Keywords: Amblyopia therapy; Pattern VEP; P100 Latency; P100 Amplitude; Visual acuity.

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INTRODUCTION

Amblyopia is defined as a decrease of visual acuity in one eye caused by abnormal binocular interaction occurring in one or both eyes as a result of pattern vision deprivation during visual immaturity, for which no cause can be detected during the physical examination of the eye and

which in appropriate cases, is reversible by therapeutic measures¹. Amblyopia is primarily a cortical phenomenon, caused by unequal competitive input from the two eyes into area 17 of the primary visual cortex. However, additional structural and functional abnormalities have also been observed in the lateral geniculate body of animals and humans.¹ The Snellen's letter chart, a minimum resolvable acuity measurement, is the most common clinical method of acuity assessment.¹² Since this measurement utilizes complex symbols and requires a subjective response from the patient, it involves processing by the visual pathway through to the frontal cortex.¹³⁻¹⁵ Little is known about the affects of amblyopia on the higher cortical centres, however, several of these areas do appear to have abnormal processing.¹⁶⁻¹⁷ The defects associated with amblyopia may be greater in the higher cortical centres because these areas mature later than the primary visual cortex which allows the

amblyogenic factors that are present more time to alter neural function. Thus, Snellen acuity, which is a function of higher cortical processing, may not yield the best estimate of visual potential in amblyopia.³ A form of grating acuity, laser interferometry, has been used to predict amblyopes' post-therapy acuity.²⁰ However, interferometry has not become an accepted clinical test. One reason may be that interferometry is a subjective test and the patient responses can be somewhat variable, especially in young children.³ An objective test which assesses the striate cortex, such as visual evoked potentials (VEPs), may overcome this objection.²³⁻²⁵ Pattern VEPs (pVEP) have been used to identify amblyopes and monitor their acuity and progress during amblyopia therapy.³ In preverbal and preschool children who are unable to undergo conventional vision testing, pattern visual evoked potential (pVEP) can be used as a primary technique for electrophysiologically detecting amblyopia in suspected patients and monitoring of patients undergoing occlusion therapy for amblyopia patients. The pVEP response has been shown to increase in amplitude during amblyopia therapy along with the improvement in visual acuity.^{23,26,27} It has been reported that pattern reversal visual-evoked response acuity correlates with the best-corrected Snellen's acuity in normal subjects.²⁸⁻²⁹ Increases in the amplitude on pattern visual evoked potential (pVEP) appear to reflect vision improvement during amblyopia treatment.⁴ Recent reports have indicated that the pVEP can be used as a predictor of the outcome of amblyopia therapy.²⁴ Patients with moderate increases in the P100 latency before therapy had poorer therapy outcomes.²⁴ Acuties determined with the pVEP in normal subjects display a good correlation with acuties measured psychophysically, however, the procedure is time consuming.³⁰⁻³⁶ The present study was undertaken to primarily assess the usefulness of Pattern VEP in following the progress of therapy in amblyopic children and also to investigate whether P100 latency

could predict visual outcomes in amblyopic children including not only strabismic but also anisometric or Isometric amblyopia.

MATERIALS AND METHODS

This was a prospective interventional study conducted at Upgraded Department of Ophthalmology, SMS Medical College and Hospital, Jaipur. 50 children <15 years of age with anisometric/strabismic/mixed/isoametric amblyopia fulfilling the inclusion criteria were included in the study. Amblyopia due to congenital cataract, congenital severe ptosis, corneal opacity or any other stimulus deprivation associated causes; children with paralytic/restrictive Squint; children with eccentric fixation or any severe sensory deprivation (ARC); children < 3 year of age (as they are not cooperative for pattern VEP) were excluded from the study. All children underwent a detailed examination to identify amblyopia and its type. Snellen's visual acuity chart was used for this purpose.

Follow up was done every 4 weekly interval for compliance to therapy and improvement in visual acuity. VEP was recorded at 1month, 3 month and 6 month (Visual acuity/Cover Uncover test/Pattern VEP). All the data was recorded on a standard Proforma and the results were duly tabulated.

OBSERVATIONS AND RESULTS

Children of age group 3 to 15 years presenting to the Eye OPD with complaints of diminution of vision, inward or outward deviation of eyes and difficulty in reading, were investigated for presence of amblyopia. On the basis of previously defined criteria for amblyopia 50 patients were taken in the study. 5 patients did not report for follow ups after their first VEP. These patients were excluded from our study and data was analyzed for the remaining 45 patients.

Table 1: Age distribution of patients

Sr. No.	Age Group (years)	No. of patients	Percentage
1	3 – 6	23	51.1
2	7 – 10	15	33.3
3	11 – 15	7	15.6

Patients were distributed into three age groups, with the maximum number of patients belonging to 3-6 years of age (51.1%). They were followed by 33.3 % children of 7-10 years and the rest of 15.6% children in 11-15 years age group.

Table 2: Distribution of patients on basis of initial VEP

Sr. No.	Category	Initial P100 Latency	No. of patients	Percentage
1	A	<100	9	20
2	B	100 – 109	10	22.2
3	C	110 – 119	14	31.1
4	D	120 – 129	8	17.8
5	E	≥ 130	4	8.9

On the basis of initial P100 latency obtained on VEP, patients were divided into 5 categories. Majority of patients (31.1%) had P100 latency between 110 and 119

and were categorized into group C. Next to it were patients in group B (22.2% patients), followed by groups A, D and E respectively.

Table 3: Improvement in P 100 Latency of patients during study

Sr. No.	P100 Latency of patients	0 month		3 month		6 month	
		No.	%	No.	%	No.	%
1	<100	9	20	11	24.4	17	37.8
2	100 – 109	10	22.2	14	31.1	9	20
3	110 – 119	14	31.1	9	20	12	26.7
4	120 – 129	8	17.8	9	20	6	13.3
5	≥ 130	4	8.9	2	4.4	1	2.2

A decrease in P 100 latency was evident in our study. At initial VEP study the maximum patients had a P100 latency between 110 and 119 but after 6 months of

therapy 37.8 % patients had P100 latency <100. At 3rd month only 2 patients had P100 latency >130 and at 6th month only 1 had >130 P100 latency.

Table 4: Improvement in P100 Amplitude of patients during study

Sr. No.	P 100 Amplitude of patients	0 month		3 month		6 month	
		No.	%	No.	%	No.	%
1	<3	9	20	0	-	0	-
2	3 – 5.99	18	40	10	22.2	1	2.2
3	6 – 8.99	14	31.1	22	48.9	11	24.4
4	9 – 11.99	4	8.9	13	28.9	26	57.8
5	≥ 12	0	-	0	-	7	15.6

Corresponding to decrease in P100 latency there was increase in P 100 Amplitude of the affected eye after therapy. Initially more than half of the children (91.1%)

had amplitude of less than 6. On the other hand at 6 month only 1 patient had amplitude of less than 6 with majority of patients (57.8%) between 9 and 11.99.

Table 5: Visual acuity of patients in different categories

Sr. No	Category(n)	Visual Acuity in Log MAR								
		NC	0-0.3 (6/6-6/12)	>0.3-0.6 (6/12P-6/24)	>0.6-1 (6/24 P-6/60)	>1 (>6/60)				
1	A (9)	1	0	-	5	55.6%	3	33.3%	0	-
2	B (10)	0	0	-	8	80%	2	20%	0	-
3	C (14)	1	0	-	5	35.7%	6	42.8%	2	14.3%
4	D (8)	0	0	-	1	12.5%	6	75%	1	12.5%
5	E (4)	0	0	-	1	25%	1	25%	2	50%

Visual acuity of patients was converted into log MAR and the obtained acuities were divided into 4 groups. Three patients were non cooperative and there visual acuity could not be obtained. None of the patient in each group had an initial acuity between 0 and 0.3 (6/6 – 6/12). Majority of A and B category patients had visual acuity

ranging from >0.3 to 0.6, 55.6% and 80% patients respectively. On the other hand in category C and D, 42.8% and 75% of children respectively had a visual acuity between >0.6 and 1. In category E half of the patients had acuity of greater than 1.

Table 6: Visual acuity of patients after 3 months of therapy

Sr. No	Category(n=no. of patients)	Visual Acuity in Log MAR								
		NC	0-0.3 (6/6-6/12)	>0.3-0.6 (6/12P-6/24)	>0.6-1 (6/24 P-6/60)	>1 (>6/60)				
1	A (9)	1	4	44.4%	4	44.4%	0	-	0	-
2	B (10)	0	5	50%	5	50%	0	-	0	-
3	C (14)	1	5	35.7%	6	42.8%	2	14.3%	0	-
4	D (8)	0	0	-	6	75%	2	25%	0	-
5	E (4)	0	0	-	2	50%	1	25%	1	25%

None of the patients in category A and B had visual acuity worse than 6/24 i.e.>0.6 after 3 months of therapy. Category C patients also showed improvement with nearly half of the patients (42.8%) having vision between 6/12 P and 6/24.

Table 7: Visual acuity of patients after 6 months of therapy

Sr. No	Category(n=no. of patients)	Visual Acuity in Log MAR									
		NC	0-0.3 (6/6-6/12)		>0.3-0.6 (6/12P-6/24)		>0.6-1 (6/24 P-6/60)		>1 (>6/60)		
1	A (9)	1	7	77.8%	1	11.1%	0	-	0	-	
2	B (10)	0	9	90%	1	10%	0	-	0	-	
3	C (14)	1	7	50%	5	35.7%	1	7.1%	0	-	
4	D (8)	0	1	12.5%	6	75%	2	12.5%	0	-	
5	E (4)	0	0	-	2	50%	1	25%	1	25%	

After 6 months of therapy majority of patients in category A, B and C had a vision of 6/12 or better. Category D and E also reported improvement in visual acuity with 75% and 50% patient in each group respectively having vision

between 6/12P and 6/24. Only one patient belonging to group E had a vision worse than 6/60 after completion of 6 months of therapy.

Table 8: Interocular latency difference of patients during the study

Sr. No.	Interocular P 100 Latency	0 month		3 month		6 month	
		No.	%	No.	%	No.	%
1	<5	20	44.4	21	46.7	25	55.6
2	5 – 9.9	6	13.3	8	17.8	4	8.9
3	10 – 14.9	6	13.3	5	11.1	7	15.6
4	15 – 19.9	4	8.9	4	8.9	4	8.9
5	≥ 20	9	20	7	15.6	5	11.1

A gradual decrease in interocular latency difference was seen in our study. At initial VEP less than half of the patients (44.4%) had interocular P100 latency difference

of <5, with 9 patients (20%) recording ≥ 20 interocular latency. After 6 months of therapy more than half of the patients (55.6%) had latency difference of <5.

Table 9: Interocular amplitude difference of patients during the study

Sr. No.	Interocular P 100 Latency	0 month		3 month		6 month	
		No.	%	No.	%	No.	%
1	<2	14	31.1	12	26.7	22	48.9
2	2 – 3.99	10	22.2	17	42.5	15	33.3
3	4 – 5.99	7	15.6	10	22.2	8	17.8
4	6 – 7.99	7	15.6	5	11.1	0	-
5	≥ 8	7	15.6	1	2.2	0	-

Similar decrease in Interocular P100 amplitude was also evident. Before initiation of therapy nearly 50% patients had Interocular P 100 amplitude difference of >4 but the VEP done at 6th month showed > 4 interocular P 100 amplitude difference in only 8 children (17.8%).

DISCUSSION

Visual loss due to amblyopia can be permanent if corrective measures are not taken in time. The burden of disability due to this problem can become massive when one takes into account the duration of life with visual disability. Amblyopia and associated strabismus can also result in devastating psychosocial and economic burdens. Therefore, follow up measures and proper treatment of the problem in either of the eyes is very important. In present study, on the basis of initial P100 latency obtained on VEP, patients were divided into 5 categories.

Majority of patients (31.1%) had P100 latency between 111 and 120 and were categorized into group C. Next to it were patients in group B (22.2% patients), followed by groups A, D and E respectively. However W Chung *et al*⁴ had majority patients (32%) in group B followed closely by group C with 26% cases. Majority of patients (19) presented with an initial visual acuity of 0.3-0.6 log MAR units similar to the findings of Sethi *et al* with 42% children in this category and lowest no.(8%) with visual acuity >6/60. Visual acuity of patients was converted into log MAR and the obtained acuities were divided into 4 groups. Three patients were non cooperative and their visual acuity could not be obtained. None of the patient in each group had an initial acuity between 0 and 0.3 (6/6 – 6/12). Majority of A and B category patients had visual acuity ranging from >0.3 to 0.6, (55.6% and 70% patients respectively). On the other hand in category C and D,(

42.8% and 75%) of children respectively had a visual acuity between >0.6 and 1. In category E half of the patients had acuity of greater than 1. Patients with normal VEP (category A and B) had more than 50% pts with visual acuity < 0.6 log MAR indicating mild to moderate amblyopia while patients with abnormal VEP with latency >130 had visual acuity >1 log MAR indicating severe amblyopia. This finding was in accordance with the fact that visual acuity at presentation depended upon severity of amblyopia and prolongation of P wave latency on pattern VEP can give a rough estimate of severity of amblyopia, which was similar to the findings of Friendly and Weiss *et al*⁸ who used P100 latency and amplitude in the diagnosis of amblyopia. However no statistically significant correlation was found between initial vision and initial P100 latency by Chung *et al*⁴ In children with isoametropic amblyopia more than half were in category A and B i.e their initial P100 latency was less than 110. On the contrary more than half of the strabismic, anisometropic and mixed amblyopes belonged to category C, D and E. Strabismic amblyopes had worst initial P100 latency with 25% children having latency ≥ 130 . However, in study by Chung *et al*⁴ majority of isoametropes (81%) were present in group 1 (grp A + B+ C) similar to the results of our study with 80% of isoametropes in grp 1 (A+B+C). In our study maximum pts in grp 2 (D+E) were of anisometropic amblyopia (41.6%) however study by Chung *et al*⁴ had maximum strabismic amblyopes (42.8%) in grp 2. In present study, a steady improvement in visual acuity was observed over 6 months because of continued refractive adaptation as well as additional effect of occlusion therapy on the amblyopic eye. Visual improvement was maximum for category A patients, in which there was a 3 Snellen's line improvement and was least for category E patients which was only 1.63 lines. Therefore mean visual improvement in group 1 of Chung *et al*⁴ i.e. group A+B+C of our study came out to be 2.75 lines and 1.91 lines for group 2(C+D) however according to findings of chung *et al* visual improvement in group 1 (A+B+C) was 3.69 ± 2.14 lines and group 2 (D+E) was 2.27 ± 2.21 lines. From this it can be inferred that in cases with normal or near normal visual evoked response latencies the prognosis is better but in cases where the latencies were clearly abnormal before the treatment, the prognosis is poor. This notion was also supported by Illiakis and Moschos⁶ *et al* in their study. A decrease in P 100 latency was evident in our study. At initial VEP study the maximum patients had a P100 latency between 110 and 119 but after 6 months of therapy maximum (37.8%) patients had P100 latency < 100 . The mean P100 latency during initial VEP was 112.2msec and after 6 months of therapy it was 110.3msec. Corresponding to decrease in P100 latency

there was increase in P 100 amplitude of the affected eye after therapy. Initially more than half of the children (91.1%) had amplitude of less than 6. On the other hand at 6 month only 1 patient had amplitude of less than 6 with majority of patients (57.8%) between 9 and 11.99. The mean P100 amplitude in initial VEP of amblyopic eye was $5.33 \mu\text{v}$ which increased to $10.18 \mu\text{v}$ after 6 months of therapy. A similar trend of decrease in P100 latency with improvement in visual acuity is seen by Dutta *et al*⁹ in their study. Similarly in study of Petrinovic *et al*¹⁰ P100 latency was prolonged and P100 amplitude was suppressed in patients of amblyopia and during course of treatment a decrease in P100 latency ($p > 0.05$) and increase P100 amplitude ($p < 0.05$) is seen with improvement in visual acuity. Similarly prolonged P latency and reduced P100 amplitude was also used as a diagnostic criteria for amblyopia Friendly and Weiss *et al*¹¹. In the study by Oner and Coskun¹² *et al* the difference for P100 wave latencies was similar before and after the occlusion therapy there was a step by step improvement in P100 amplitude at each visit and the difference was statistically significant when compared with the baseline value. P100 amplitude increased from initial 5.9 ± 0.6 to 6.6 ± 0.6 ($p < 0.01$) and P latency decreased from 102.6 ± 3.2 to 99.4 ± 3.3 ($p > 0.05$) A gradual decrease in interocular latency difference was seen in our study. At initial VEP less than half of the patients (44.4%) had interocular P100 latency difference of < 5 , with 9 patients (20%) recording ≥ 20 interocular latency. After 6 months of therapy more than half of the patients (55.6%) had latency difference of < 5 . Similar decrease in interocular P100 amplitude was also evident. Before initiation of therapy nearly 50% patients had Interocular P 100 amplitude difference of > 4 but the VEP done at 6th month showed > 4 interocular P 100 amplitude difference in only 8 children (17.8%). Similarly in study by Samuel Sokol¹³ analysis of the interocular latencies for the amblyopic children showed a small but significant latency difference ($p < 0.05$) for P100; latency for the amblyopic eye was slightly longer (mean difference = 4 ms). Again in study by Arden and Barnard¹⁴ they found that the VER amplitudes measured varied greatly, more so in these children than in the adults and measurements of voltage were therefore not useful. However, the relative amplitude of response in the two eyes is a much more reliable index, as previously shown, and should not exceed 10 per cent. Similarly in study by Friendly and Weiss¹¹ this interocular amplitude difference in VEP was taken as a diagnostic criteria in unilateral amblyopia. They took normalized P100 amplitude (P100amp of amblyope eye/P100amp of normal eye) cut off as 1 and any value < 1 was diagnostic of amblyopia. Therefore based upon this prolonged P latency and normalized P100

amp/interocular amplitude ratio can be used in the diagnosis of amblyopia in preverbal children. On initial visual assessment it was observed best initial visual acuity was seen amongst patients of isoametropic amblyopia, 60% patients had visual acuity in range of $>0.3 - 0.6$ log MAR. Poorest visual acuity (>1 log MAR) was seen in anisometropic amblyopes, similar to study by Woldeyes and Girma⁷ best visual acuity at initial presentation was seen among isoametropes with 58.3% with V/A 6/18-6/36. However in findings of Sethi *et al*² best visual acuity at initial presentation was seen among patients with strabismic amblyopia with 25.5% pts in range of $>0.3-0.6$ log MAR and poorest among isoametropic amblyopia. At 3rd month follow up improvement in visual acuity was seen in all types of amblyopic patients with best improvement shown by isoametropic amblyopes. Subsequent visual assessment at 6th month demonstrated a similar trend of improvement in visual acuity. Best visual acuity at 6 months as well as best improvement in visual acuity was seen in isoametropes as 73.3% of isoametropic patients (11) finally had visual acuity of less than 0.3 ($< 6/12$) after therapy with a mean visual acuity of 0.24 log units and a decrease of 0.41 log units (maximum) in a period of 6 months. This was followed by mixed amblyopes and anisometropic amblyopes both showing a mean improvement of 0.40 log units in visual acuity. However mixed amblyopes had better visual status at 6 months than anisometropes with a mean of 0.32 log MAR and half of the patients having a final vision of less than 0.3 log MAR. However the amount of improvement was same for two. Minimal improvement was seen among patients with strabismic amblyopia with a mean decrease of 0.32 log units in 6 months and almost 50% patients with a visual acuity poorer than 6/12 at end of 6th month. At the completion of 6 months of therapy only 1 patient with isoametropic amblyopia had a log MAR vision of >1 , probably due to poor compliance. According to Kenneth Wright³⁸ bilateral amblyopia has a better visual outcome than unilateral amblyopia which is similar to what is seen in our study. However in study by Rutstein and Corllis¹⁵ best improvement in visual acuity was seen among strabismic amblyopes of 0.36 log units next being anisometropic with 0.33 log units and least in isoametropic group with 0.14 log units. In other study by Levartovsky and Oliver¹⁵ on unilateral amblyopia mixed type of amblyopes showed a maximum improvement of 0.24 log units (from 0.37 to 0.13 log units), anisometropes showed 0.16 and strabismic showed a minimum of 0.05 log units improvement in visual acuity (difference not significant). In another study on unilateral amblyopia by Arikan and Yaman *et al*¹⁷ maximal improvement was shown by strabismic-

anisometropic amblyopia with a mean visual acuity improvement of 0.46 log MAR units followed by strabismic amblyopia with 0.38 log units and minimal with anisometropic amblyopes with 0.35 log units. A similar trend was seen among unilateral amblyopes in the study of Stewart and Fielder *et al*⁸ where maximum improvement of 0.46 ± 0.32 log units was seen in mixed amblyopes and minimum of 0.28 ± 0.2 log units amongst anisometropes. The difference was however not statistically significant ($p=0.03$) The mean P 100 latency was maximum for isoametropic amblyopes, 115.69 with a standard deviation of 11.5. Minimum average P 100 latency was 108.35 (standard deviation of 10.46) for anisometropic amblyopes. In a study by Heravian and Daneshvar *et al*¹⁸ on unilateral amblyopia they found mean P100 latency in strabismic amblyopes to be 115.5 ± 10.2 msec and p100 amplitude equals to $17.1 \pm 25.1 \mu v$ while patients with anisometropic amblyopia had mean P100 latency of 109.6 ± 9.5 msec and amplitude equals to $10.8 \pm 6.8 \mu v$. In another study on unilateral amblyopia by Goyal and associates¹⁹

CONCLUSION

This study found that in amblyopic children, Pattern VEP showed characteristic changes of “Prolongation of P100 latency” and “Reduction of P 100 amplitude” ($p < 0.5$) during the course of therapy. A gradual increase in visual acuity was also seen along with characteristic pattern VEP changes. Thus, pVEP can serve as an objective test in children for diagnosis and monitoring of children under amblyopia therapy. The present study also concluded that since pVEP specifically assesses the location affected by amblyopia (i.e. visual cortex), the values of P100 latency obtained at time of initial diagnosis can be used to estimate the expected visual outcome after therapy.

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