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Pattern Visual Evoked Potential as a Predictor of Occlusion Therapy for Amblyopia

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Purpose: This study was conducted to investigate the role of the pattern visual evoked potential (pVEP) as a predictor of occlusion therapy for patients with strabismic, anisometropic, and isometropic amblyopia. The secondary aim was to compare the characteristics of pVEP between strabismic and anisometropic amblyopia.
Methods: This retrospective comparative case series included 120 patients who had received occlusion therapy or a glasses prescription for correction of strabismic, anisometropic, and isometropic amblyopia (20 patients had strabismic amblyopia, 41 patients had anisometropic amblyopia, and 59 patients had isometropic amblyopia). For each patient, the value of the P100 latency on pVEP at the time of the initial diagnosis of amblyopia was collected. Subsequently, the P100 latency was compared according to types of amblyopia. Fifty of 120 patients (7 patients with strabismic amblyopia, 21 patients with anisometropic amblyopia, and 22 patients with isometropic amblyopia) who were followed-up for longer than 6 months were divided into two groups based on the value of their P100 latency (Group 1, P100 latency 120 msec or less; Group 2, P100 latency longer than 120 msec.) The amount of visual improvement after occlusion therapy or glasses was compared between two study groups.
Results: The mean P100 latency was 119.7±25.2 msec in eyes with strabismic amblyopia and 111.9±17.8 msec in eyes with non-strabismic (anisometropic or isometropic) amblyopia (p=0.213). In Group 1, the mean visual improvement after occlusion therapy or glasses was 3.69±2.14 lines on Dr. Hahn's standard test chart; in Group 2, the mean improvement was 2.27±2.21 lines (p=0.023).
Conclusions: The P100 latency on pVEP at the time of initial diagnosis was significantly related to the visual improvement after occlusion therapy or glasses in patients with strabismic, anisometropic, and isometropic amblyopia. Therefore, it was presumed that patients with a delayed P100 latency might have less visual improvement after occlusion therapy or glasses. In addition, there was no apparent difference in P100 latency between patients with strabismic and non-strabismic (anisometropic or isometropic) amblyopia.

Key Words: Amblyopia, P100 latency, Visual evoked potential

When a patient is diagnosed with amblyopia, the latent potential of vision improvement is very important when deciding on therapy. Recently, various attempts have been made to assess which factors present at the time of diagnosis reflect the final visual outcome after amblyopia treatment.[1-6] It has been reported that pattern reversal visual-evoked response acuity correlates with the best-corrected Snellen acuity in normal subjects.[6,7] Increases in the amplitude on pattern visual evoked potential (pVEP) appear to reflect vision improvement during amblyopia treatment.[3]

Among patients with strabismic amblyopia, those with an eccentric fixation had a relatively delayed P100 latency and less vision improvement after 6 months of amblyopia treatment when compared with patients who had a central fixation.[1] However, there are only a limited number of reports about pVEP in patients with anisometropic amblyopia.[8]

To investigate whether P100 latency could predict visual outcomes in patients with functional amblyopia including not only strabismic but also anisometropic or isometropic amblyopia, patients were grouped by P100 latency on pVEP at the time of initial diagnosis, and visual improvement was compared after occlusion therapy between the two groups. Also, differences in P100 latency by type of amblyopia was sought.

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Subjects and Methods

Amblyopia was classified as strabismic, anisometropic, isometropic (high bilateral refractive errors), visual

Table 1. Potentially amblyopiogenic refractive errors warranting optical corrections in infants and young children

Isometropic	Diopters
Astigmatism	>2.50
Hyperopia	>4.50
Anisometropic	
Astigmatism	>1.50
Hyperopia	>1.50
Myopia	>3.00

deprivation, and organic according to the definitions proposed by the American Academy of Ophthalmology (Table 1).[9] When other compounding abnormalities with strabismus were present, unilateral hypermetropia greater than +4.50 diopters (D) with esotropia was classified as 'strabismic' and bilateral amblyopia with exotropia and hypermetropia greater than +4.50 D was classified as 'isometropia' according to the classification system established by von Noorden (Table 2).[10]

A total of 120 cases with strabismic, anisometropic, and isometropic amblyopia (20 patients with strabismic amblyopia, 41 patients with anisometropic amblyopia, and 59 patients with isometropic amblyopia) were included in this study from the patient database of our institution. Fifty of 120 cases (7 patients with strabismic amblyopia, 21 patients with anisometropic amblyopia, and 22 patients with isometropic amblyopia) complied with occlusion therapy or glasses correction and were followed-up for longer than 6 months. A retrospective, observational study was performed on patients with amblyopia who were younger than 14 years of age from March, 2001 to February, 2007.

Amblyopia was diagnosed when the difference in visual acuity between two eyes was greater than two lines on Dr. Hahn's standard test chart (unilateral amblyopia) or when the visual acuity of both eyes was less than the lower limit of age-matched visual acuity, namely, 20/50 for 3 year-olds and 20/30 for 5 year-olds (bilateral amblyopia).[9]

Patients with a history of any intraocular disease or surgery were excluded. Only patients who complied with the occlusion therapy or with glasses correction and follow-up for longer than 6 months were analyzed to investigate whether the initial P100 latency was related to the outcome of occlusion therapy.

In brief, the refractive errors of each patient were completely corrected by cycloplegic refraction and patients were asked to wear accurately-prescribed glasses. Patients with unilateral amblyopia received part-time occlusion therapy for 6 hours per day and were followed-up by their physician as needed. Visual acuity was checked at each visit. The pVEP was performed within 2 weeks after the initial visit. For pVEP, a NIC 2015 visual stimulator, NIC HGA 200 A amplifier, and NIC CA 1000 clinical averager (Nicolet, Co. USA) were used. From the patients' clinical records, values of P100 latency were collected.

For all 120 patients, the mean P100 latency was compared according to the types of amblyopia (strabismic amblyopia vs. non-strabismic amblyopia) and the dominance of eyes (dominant eye vs. non-dominant eye). We investigated the association between initial vision and initial P100 latency.

Fifty patients who complied with the occlusion therapy or glasses correction and who were followed-up for longer than 6 months were divided into two groups by their P100 latency. The patients who did not show a delayed P100 latency (120 msec or less) were placed in Group 1, and the others (delayed than 120 msec) were classified as Group 2. In the cases of bilateral amblyopia, the worst eye was selected for further analyses. Thirty-six patients (4 patients with strabismic amblyopia, 14 patients with anisometropic amblyopia, and 18 patients with isometropic amblyopia) were placed into Group 1, and 14 patients (3 patients with strabismic amblyopia, 7 patients with anisometropic amblyopia, and 4 patients with isometropic amblyopia) were assigned to Group 2.

The amount of visual improvement after occlusion therapy or glasses was compared between the two study groups (Group 1 vs. Group 2) for the 50 subjects followed-up for at least 6 months from the initiation of occlusion therapy or glasses.

For these 50 patients, we investigated the association between age at the time of treatment initiation and the amount of vision improvement after occlusion therapy.

For statistical analysis, a 2-tailed paired Student's t-test and correlation analysis using a Pearson correlation coefficient of SPSS 12.0 were used, and a P value of less than 0.05 was considered to be statistically significant.

Results

Out of a total of 120 cases, 20 had strabismic amblyopia, 41 had anisometropic amblyopia, and 59 had isometropic amblyopia. Unilateral amblyopia was present in 61 (50.83%) patients. The mean age was 7.56±2.37 (range, 2 to 13) years

Table 2. Causes of amblyopia and number of patients by diagnosis (Group A : at least 6 months follow-up)

Unilateral	No. of patients (Group A/Total)	Bilateral	No. of patients (Group A/Total)
Strabismic	7/20	Visual deprivation (Isometropic)	22/59
Anisometorpic	21/41		
Visual deprivation (blepharoptosis, hyphema)	Out of criteria		
Organic	Out of criteria		

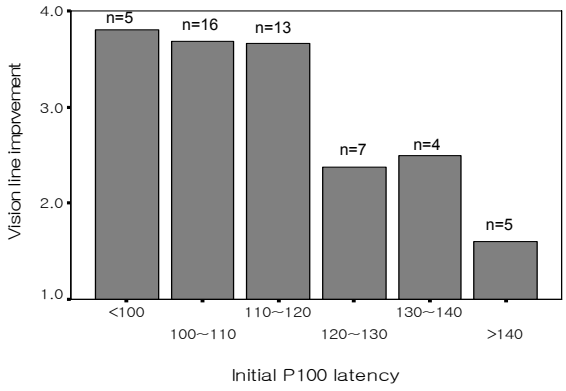

Fig. 1. Vision improvement according to initial P100 latency. In patients with a P100 latency shorter than 120 msec, the vision was improved by 3.69±2.14 lines on Dr. Hahn's standard test chart, and in patients with a P100 latency longer than 120 msec, the vision was improved by 2.27±2.21 lines (p=0.023).

old with 61 males and 59 females. The number of patients with at least 6 months of follow-up was 50 of 120 (41.67%). These patients had a mean follow-up of 3.01±1.69 (range, 0.5 to 6) years.

For all 120 patients, the mean P100 latency was 119.7±25.2 (range, 91.8 to 176.1) msec for strabismic amblyopia and 111.9±17.8 (range, 76.2 to 173.4) msec for non-strabismic (anisometropic or isometropic) amblyopia, but this difference was not statistically significant (p=0.213). For the 61 patients with unilateral amblyopia, when the amblyopic eye was compared to the unaffected eye, the P100 latency was delayed 8.45 msec in the strabismic amblyopic eye (p=0.577), and it was delayed by 0.66 msec in the anisometropic or isometropic amblyopic eye when compared to the non-amblyopic fellow eye, but these differences were not statistically significant (p=0.733). There was no statistically significant correlation between initial vision and initial P100 latency (r=-0.195, p=0.174).

For the 50 patients who were followed-up for longer than 6 months, the amount of visual improvement after occlusion therapy was plotted according to the initial P100 latency (Figure 1). In Group 1 (patients with 120 msec or less P100 latency), the patients' vision improved by 3.69±2.14 lines on Dr. Hahn's standard test chart; and in Group 2 (patients with P100 latency delay of more than 120 msec), vision improved by 2.27±2.21 lines (p=0.023). There was no statistically significant correlation between the age at the time of treatment initiation and the amount of visual improvement after occlusion therapy (r=0.038, p=0.794).

A comparison according to the types of amblyopia in each group was impossible due to a small sample size.

Discussion

Attempts to find markers other than visual accuity to predict the effect of treatment for amblyopia have been sought. Latent potentials have been proposed as a marker to determine the amount of anticipated vision improvement upon initiation of treatment.[1-6] Amblyopia is a type of developmental disorder that causes vision deterioration and is classified as strabismic, anisometropic, isometropic, stimulus deprivation, and organic-type. All types of amblyopia except organic-type are common causes of monocular amblyopia, and the prevalence of amblyopia is 1~5% in the general population.[11,12] Amblyopia is caused by the dysfunction of the lateral geniculate body and the visual cortex, and the pVEP test, which measures electrical changes in the visual cortex in response to a retinal stimulus by light, shows abnormal changes.[13-17] The pVEP is useful in the diagnosis of amblyopia and is used to follow changes in visual acuity during treatment. Generally, in amblyopia, the pVEP amplitude is decreased while the P100 latency is increased compared to normal eyes.[6,18-22]

To evaluate patients with amblyopia in whom it is difficult to determine visual acuity, a fixation test, optokinetic nystagmus, or VEP may be applied, and among these, VEP has the advantage of providing quantitative values.[6,7,23-27] The use of a sweep VEP technique and interocular amplitude method of pVEP allow the diagnosis of amblyopia with greater sensitivity.[2]

VEP could be applied not only to diagnose amblyopia, but also to monitor the effects of treatment and to allow prognosis of future treatment at the time of diagnosis.[7]

According to Wildberger,[18] VEP amplitude increases as visual acuity improves during treatment of amblyopia. According to Oner et al.[3] who reported on 34 cases of anisometropic amblyopia treated with occlusion therapy for 6 months, the level of visual improvement was proportional to the increase in the P100 amplitude thus proving the usefulness of pVEP for follow-up of amblyopia treatments.

Ridder et al.[2] have reported that the visual acuity predicted prior to amblyopia treatment by sweep VEP is closely related to the Snellen visual acuity after amblyopia treatment, and that sweep acuity is a good predictor of visual acuity after treatment.

According to Iliakis et al.[1] who investigated 60 cases of strabismic amblyopia, the P100 latency of patients with strabismus and eccentric fixation was greater than the P100 in those with strabismus and central fixation, and their prognosis was worse after occlusion therapy. Therefore, the P100 latency at the time of the initial diagnosis could be applied as a factor to predict the outcome of amblyopia treatment; however, the above study made comparisons between those with eccentric fixation and those with central fixation, so it is necessary to confirm whether these results could also be applied to other types of amblyopia including anisometropic amblyopia.[1]

In addition, during the process of the division of the patient groups, other standards (fixation pattern) other than P100 latency were included, so a selection bias may have been present. In the above experiments, the follow-up period

of occlusion therapy was 6 months, which is rather short to evaluate vision improvement after amblyopia treatment. To assess target vision after occlusion therapy more accurately, longer periods of follow-up after treatment are necessary.

We found no significant difference in the P100 latency pattern between strabismic amblyopia and non-strabismic (anisometropic or isometropic) amblyopia. The amblyopia patient group which included patients with strabismic, anisometropic, and isometropic amblyopia followed-up for longer than 6 months (average follow up period: 3.01 years) were classified according to the P100 latency at the time of the initial diagnosis, and the level of vision improvement after amblyopia treatment and the visual acuity at the final visit were compared. A linear correlation between initial P100 latency and vision improvement was not detected, but a longer P100 latency was related to a decrease in final visual acuity, and in cases with longer than 120 msec of P100 latency, a statistically significant reduction in final visual acuity was observed; however, in VEP testing, cases with a P100 latency shorter than 120 msec are more common, so in order to apply VEP as a predictor of amblyopia treatment, more studies with substantially larger numbers of subjects are required.

In patients with functional amblyopia, P100 latency showed similar values in eyes with strabismic amblyopia and non-strabismic (anisometropic or isometropic) amblyopia, and P100 latency on pVEP at the time of initial diagnosis was related to vision improvement after occlusion therapy. The initial P100 latency can therefore be used to predict outcomes after occlusion therapy for functional amblyopia.

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