



P100 amplitude of pattern Visual Evoked Potential (P-VEP) in monitoring the effectiveness of occlusion therapy for Squint eyes

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ARTICLE INFO

Article history:

Received: 27 June 2011;

Received in revised form:

22 August 2011;

Accepted: 27 August 2011;

Keywords

P-VEP Signals,
P100 Amplitude,
Squint eye,
Visual acuity.

ABSTRACT

To evaluate the effectiveness and clinical significance of pattern visual evoked potential (P-VEP) as a predictor of occlusion therapy for patients with strabismic and amblyopia (squint eye). Methods: A total of 34 consecutive children with anisometropic squint were included in this study. All patients underwent a full initial ophthalmologic and orthoptic evaluation. P-VEP test was performed in all cases and binocular vision was tested and recorded. Part-time occlusion therapy was performed by using adhesive patches. Results: The mean ($\pm$ SEM) cycloplegic refractive error was $+5.6 \pm 0.6$ diopters (D) in the squint eyes and $+1.8 \pm 0.2$ D in the normal eye. The mean levels of best-corrected visual acuity were statistically differed between each measurement for occlusion therapy (for each, $p < 0.05$). The ratio of the patients with binocular vision increased after 6 months occlusion therapy and the difference was statistically significant ($p < 0.05$). In addition, P100 amplitude improved at each visit and the difference was significant when compared with baseline values (for each, $p < 0.05$). Conclusions: P100 amplitude of the P-VEP test parallels the improvement in subjective visual acuity in squint eyes under occlusion therapy. Therefore, this test may be useful in monitoring the visual acuity in the preverbal or non-verbal patched patients.

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Introduction

Functional squint is the most common cause of monocular visual impairment in children with an incidence of 1–5% in the general population [1, 2]. The most common treatment for unilateral squint is the occlusion of the dominant eye with an opaque patch to promote visual function in the squint eye [3, 4]. Squint is thought to be affecting primarily the function of the lateral geniculate nucleus and visual cortex. Therefore, it has been known that the conventional pattern visual evoked potential (P-VEP) is abnormal in squint. [5–8]. This study aimed to evaluate the effectiveness of P-VEP during the monitorization of visual acuity and to demonstrate whether this method was useful in such patients under occlusion therapy.

Patient and method

In this prospective study, we evaluated 34 consecutive children with squint under occlusion therapy aged between 4 and 11 years old. Inclusion criteria were as follows: (1) a difference in visual acuity of 2 lines or greater between two eyes; (2) cylindric or spheric difference of 1.5 D between two eyes; (3) the age over 3 years old (to avoid problems caused by patient in cooperation in smaller ages).

On the other hand, exclusion criteria were as follows: (1) any media opacities cataract, vitreous opacities, corneal opacities, etc.); (2) any ocular disease (the optic nerve and the retina, etc.) that may affect electroretinographic evaluation; (3) previous history of ocular surgery or therapy for management of squint.

All patients underwent a full initial ophthalmologic and orthoptic examination. Cycloplegic refraction was performed by instilling 2 drops of 1% cyclopentolate hydrochloride in each eye 5 min apart [9]. All refractive errors were corrected and best-corrected visual acuities were recorded. At the first visit,

refractive correction was given to anisometropic patients and was instructed to wear their eyeglasses regularly. P-VEP test was performed and binocular vision was tested with Worth's four-dot test and Bagolini striated glasses, which then were recorded at each visit. Occlusion therapy consisted of part-time occlusion using adhesive patches. The number of hours per day of occlusion varied depending on the child's age.

Recordings

P-VEP's were recorded with full-field black and white checkerboard pattern reversal. Recordings from the subject's scalp were obtained from an electrode placed 1 cm above theinion on the midline. A pair of ear clip cup electrodes filled with electrode paste were used for the reference and ground electrodes with an impedance of less than 5 kW. At least, 2 recordings of responses to 64 stimuli were recorded. Monocular viewing and natural pupils were used. The mean luminance of the stimulus was 46 cd/m².

Checks subtended 30° of visual angle and viewed at 0.5 m. Checks were 20'-sized with 90% contrast and 1.02 Hz frequency. Low and high frequency filters were respectively 1 and 100 Hz, and analysis time was 300 ms. Subjects were asked to relax and maintain fixation at the center of the stimulus pattern, and to refrain from blinking during the stimulus sequence. Refractive errors were corrected for the working distance used during the VEP test [10, 11]. All statistical analyses were performed by the statistical package.

Chi-square test was used to analyze the results of the Worth's four-dot test and Bagolini striated glasses tests whereas t-test was used to analyze the P-VEP parameters. A p value below 0.05 was considered to be statistically significant. The results were expressed as mean $\pm$ standard error of mean (SEM).

Result

In the present study, 19 boys and 15 girls with a mean age of 6.7 ± 0.2 years (range 4–11 years) were included. All patients were followed up at least for 6 months. The mean refractive error was $+5.6 \pm 0.6$ D in the squint eyes and $+1.8 \pm 0.2$ D in the normal eye. There were statistically significant differences between the visual acuity levels evaluated at baseline and at first, third and sixth months after the beginning of the occlusion therapy (for each, $p < 0.05$; Table 1).

Bagolini glasses

The results It is slightly dissociating test. This test is performed with the use of test striated glasses through which the patient sees light streak by each eye, viewing the light on the Maddox cross. Light streak is in the 45-degree meridian and another in the 135-degree meridian (see Figure. 1 a- d).

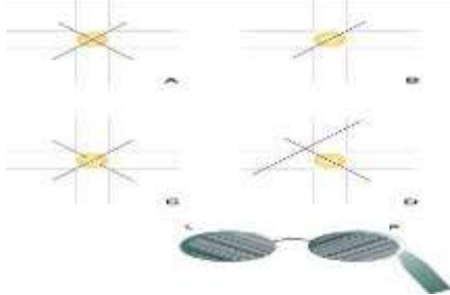


Figure 1 Bagolini glasses

Images of the light streaks images are interpreted as follows:

A. Two streaks crossing at the center of the light: normal retinal correspondence without strabismus or microstrabismus with the anomalous harmonious retinal correspondence. B. Two streaks are crossed but one is broken in the center: scotoma of the fixation point. C. Two streaks: one running centrally, and another shifted: squint with either normal or anomalous unharmonious retinal correspondence. D. One streak is visible: suppression of the deviating eye.



Figure 2 Fixation of Bagolini glasses

Worth four-dot test

This test is strongly dissociating the vision. Red-green glasses are worn which permeable for only colors adequate for each eye and enables to see red-green lights arranged into the cross (see Figure 3).



Figure 3 Worth four-dot test

Interpretation is dependent on the seen image:

- Visible four lights: normal binocular vision or micro strabismus of anomalous retinal correspondence.
- Visible only two red or green lights: suppression of one eye.
- Visible 5 lights: manifest squint with normal retinal correspondence or anomalous unharmonious correspondence (See Figure.4)

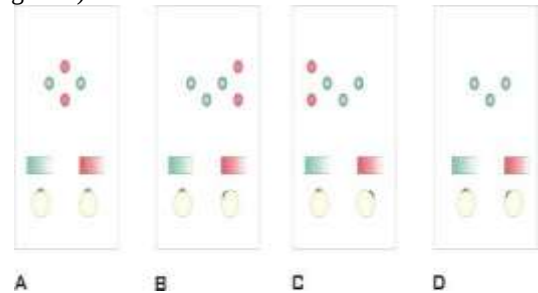


Figure 4 Possible Worth four-dot test. A-normal binocular vision, B-esotropia with uncross images C-exotropia with cross images, D-suppression one eye.

The results of binocular vision tests evaluated by Worth's four dot test and Bagolini striated glasses are shown in Table 2. The ratio of the patients with binocular vision that increased after 6-month occlusion therapy was increased.

The results of the P-VEP (see Figure 5) values are shown in Table 3. Although the difference for P100 wave latencies was similar before and after the occlusion therapy ($p > 0.05$), there was a step by step improvement in P100 amplitude at each visit and the difference was statistically significant (for each, $p < 0.01$) when compared with the baseline value (Figure 6 a–d). In addition, we found a positive correlation between P100 amplitude and the levels of visual acuity on snellen charts ($p = 0.003$, $r = 0.49$).

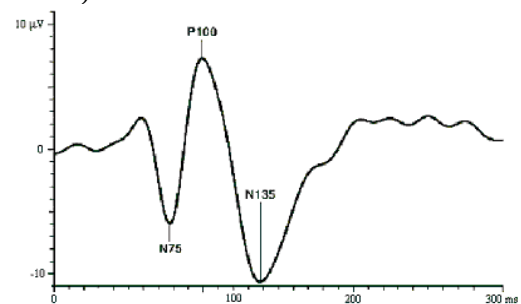


Figure 5 A VEP response. N75= negative peak 1; P100= positive peak 1 (P 100); N135= negative peak 2

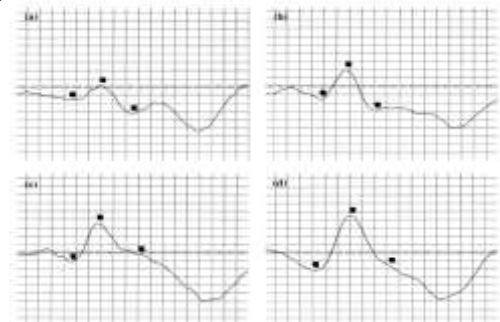


Figure 6 The layouts of P-VEP obtained; (a) pretreatment; (b) first month; (c) third month; and (d) sixth month after the beginning of the occlusion therapy. Note the improvement in P100 amplitudes step by step at each visit.

Discussion

Human squint is characterized by a decreased activation of the primary visual cortex, which is treated by both patching and atropine as an effective initial treatment [12–15]. Although the primary visual cortex is thought to be the most affected structure

in the visual pathway in squint, other abnormalities may occur earlier in the afferent visual system [16].

The binocular neurons of the primary cortex are involved in integrated visual functions, like simultaneous binocular vision, fusion and stereopsis. In case of eye misalignment, blurred image or the occlusion of the eye, the animal's binocular neurons disappear from the visual cortex and only monocular neurons remain [17]. Histologic examinations of the lateral geniculate nucleus have revealed cell shrinkage in the layers that receive stimuli from the squint eye [18].

It, however, remains unclear whether the retina is also affected during the process of squint. A class of retinal ganglion cells (the sustained or X cells) in the central retina is thought to provide the physiological basis of high visual acuity. Indeed, squint is thought to be associated with functional loss of these cells due to inappropriate stimulation of the fovea by blurred images during the critical period of development in squinting eyes, which have lost the ability to fix, or of penalized eyes [17].

The pattern electroretinogram (P-ERG), which is thought to originate from retinal ganglion cells, has been reported to be abnormal in squint with marked loss of visual acuity [16]. Some workers have reported in humans that squint has a reduced electroretinogram response to pattern stimuli [19]. However, some other investigators have observed no P-ERG deficit when the optical focus, fixation alignment, and the stability are individually optimized [20]. Similarly, reduced amplitudes of electro-oculogram have also been reported in squint eyes, suggesting the involvement of the retinal pigment epithelium in squint [21].

P-VEP is known to predominantly reflect the central retinal function. Therefore it is now used widely in clinical medicine, mostly by ophthalmologists.

Indeed it has been shown to be a sensitive detector of squint, particularly when small checks are used [22, 23]. Sokol et al. [24] reported that the sensitivity of the interocular method is 100% when the difference of acuity between eyes is 3 lines or greater. On the other hand, sensitivity falls to 50% for snellen acuity when the difference is 2 lines or fewer. Moreover, the latency of P-VEP is also abnormal in squint. However, because the effect is small, latency is not a sensitive marker of squint like amplitude [23]. Ohn et al. [25] reported that there was an agreement between the P-VEP acuity and the snellen acuity in patients with macular disease and squint. Consequently, P-VEP acuity can be used to detect snellen acuity in such patients.



Figure 7 P 100 Amplitude response on vision improvement

In the present study, we found that the latency of the P-VEP shortened during the course of occlusion therapy, though the differences were not significant. However, there was a step by step and significant increase in the amplitude of P100 wave at each visit. Furthermore, we found a positive correlation between P100 amplitude and snellen visual acuity. Therefore, this study demonstrated for the first time that P100 amplitude improved in squint eyes during the course of occlusion therapy. In addition

P-VEP amplitude increases in accordance with the improvement in visual acuity in amblyopic eyes. Therefore, we suggest that P100 amplitude of PVEP seems to be a useful method in monitoring the visual acuity in both preverbal and nonverbal children with squint under occlusion therapy.

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