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Original Article

Is Fixation Preference a Potential Indicator of Macular Function in Children?

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Abstract

Objectives: Fixation preference testing is widely used to detect amblyopia, particularly in preverbal children. Pattern electroretinogram (pERG) is an electrophysiological test which is a sensitive indicator of macular function. The aim of this study was to investigate the relationship between fixation preference and macular function on pERG in children with strabismus.
Materials and Methods: The study included 11 children with strabismus. All underwent ophthalmological examination including fixation preference by binocular fixation pattern test, best corrected visual acuity (BCVA) assessment, and pERG.
Results: The mean age of the patients was 10.09±1.18 years. All patients had unilateral fixation. The mean BCVA was 0.85±0.17 in preferred and 0.48±0.19 in non-preferred eyes (p=0.003). The mean p50 amplitude was 6.07±2.06 μV in preferred and 5.29±2.20 μV in non-preferred eyes (p=0.203), and the mean N95 amplitude was 8.27±2.86 μV and 8.03±3.24 μV respectively (p=0.594). BCVA was correlated with p50 and N95 amplitudes in the non-preferred eyes (p=0.023 and p=0.014). Interocular BCVA difference was correlated with interocular P50 amplitude difference (r=0.688, p=0.019).
Conclusion: Although amblyopia is typically considered a cortical phenomenon, future larger studies are needed to investigate the relationship between fixation preference and macular electrophysiological function.
Keywords: ERG, fixation, macular function, pattern ERG, strabismus

Introduction

Visual acuity is a precise and established indicator of macular function. However, subjective evaluation of visual function is almost impossible in preverbal children. Vision can only be assessed qualitatively in this age group by fixation testing and tracking eye movements. Amblyopia, which can be considered a pediatric ophthalmological emergency, is defined as an interocular difference in visual acuity of 2 or more Snellen or logMAR lines.[1] Visual acuity measurement is imperative in amblyopia for diagnosis, follow-up, and assessment of treatment results. Thus, a valid evaluation of monocular visual acuity is always necessary in children.

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Clinical evaluation of fixation behavior can be used to estimate visual performance in children. The induced tropia test and binocular fixation pattern test have been introduced to assess equality of vision in preverbal children. Binocular fixation pattern assessment is a better option to estimate fixation preference in preverbal children with strabismus, whereas the induced tropia test with prisms can be used in children with a deviation of ≤10 prism diopters (PD) or without strabismus.[2,3,4] Fixation preference tests provide a qualitative measurement of vision. It is believed that children prefer to fixate with the healthy eye and there is no fixation preference in the absence of amblyopia.

Pattern electroretinogram (pERG) is a non-invasive clinical electrophysiological test which is mostly derived from macular ganglion cells.[5] The signal is very sensitive and can be affected by poor refraction or ocular surface and media problems that reduce the optical quality of the stimulus and retinal image.[5] P50 and N95 are the major components of pERG that reflect macular function.[5] pERG may also be combined with full-field ERG to differentiate macular and generalized retinal dysfunction, and with visual evoked potentials to differentiate macular and optic nerve dysfunction.[5]

The hypothesis of the present study was that fixation preference in a strabismic child may be associated with better ipsilateral macular function, thus suggesting a possible correlation between fixation preference and pERG signals, especially P50 amplitude. The purpose of the present study was to electrophysiologically evaluate macular function in children with strabismus and investigate its correlation with fixation preference.

Materials and Methods

A total of 11 children with horizontal strabismus were recruited for the study. The study was conducted in full accordance with the tenets of the Declaration of Helsinki and was carried out upon approval of the Institutional Ethics Committee (GO 17/561-23). Informed consent was obtained from the parents. All children under 15 years old who had heterotropia of more than 10 PD, were able to undergo monocular visual acuity assessment, and had reliable pERG recordings were included. Patients with other ocular morbidities and systemic diseases were excluded.

All children underwent a complete ophthalmological and orthoptic work-up including best corrected visual acuity (BCVA) in decimal at distance and fixation preference. The same experienced pediatric ophthalmologist (H.T.S.) tested the fixation preference in all children with binocular fixation pattern test. The evaluation of fixation was performed with appropriate spectacles on according to full cycloplegic refraction by having the patient fixate with both eyes open at the same time. An accommodative fixation target was shown. Then, the non-deviating eye is occluded to allow the deviating eye to fixate. After the removal of the occluder, if the non-preferred eye cannot hold the fixation, a fixation preference is suggested and noted as right or left. If there is spontaneous alternation between both eyes during fixation or each eye can hold the fixation through blinking or smooth pursuit, the fixation preference is categorized as free alternation. The fixation characteristic was noted as unilateral or free alternation. The grade of the fixation was not included in the analysis. Fusion was evaluated with Worth 4-Dot test and stereopsis with Titmus test.

All patients underwent pERG recorded with DTL electrodes placed in the fornix of the lower eyelid (Roland Consult, Germany). The pERG protocol incorporated the standards of the International Society for Clinical Electrophysiology of Vision (ISCEV).[6] Recordings were obtained from non-dilated eyes with appropriate refractive correction in place. According to the ISCEV guideline, the large positive component at 50 ms was defined as P50 and the following large negative component at 95 ms as N95.[6] Because external factors affecting optic quality may interfere with pERG recording, the best effort was made to position the electrodes appropriately to obtain stable and reliable pERG signals. Monocular stimulation was used during recording because of ocular misalignment.

Statistical Analysis

All statistical analyses were performed by using IBM SPSS Statistics 23.0 software (IBM Corp, Armonk, NY, USA). Descriptive statistics were expressed as mean ± standard deviation or median (minimum-maximum) for quantitative data according to the assumption of normal distribution, and frequency (percentages) for qualitative data. The Wilcoxon signed-rank test was used to compare two related samples. Relationships between variables were evaluated using Spearman's rank correlation coefficient. A p value less than 0.05 was accepted as statistically significant.

Results

A total of 11 patients met the inclusion criteria. The mean age of the patients was 10.09±1.18 (9-12) years. In all patients, fixation was unilateral.

The mean BCVA was 0.85±0.17 in the preferred eye and 0.48±0.19 in the non-preferred eye (p=0.003). The mean amount of horizontal deviation (1 exo-deviations and 10 eso-deviations) was 21.36±9.51 (16-46) PD. The spherical equivalent refractive error was +3.07±2.09 (0.25-7.62) D for the preferred eyes and +4.09±2.18 (1.37-8.75) D for the non-preferred eyes (p=0.003).

The mean p50 amplitude was 6.07±2.06 µV in preferred and 5.29±2.20 µV in the non-preferred eyes (p=0.203), and the mean p50 implicit time was 48.36±1.05 ms and 48.63±4.59 ms, respectively (p=0.790). The mean N95 amplitude was 8.27±2.86 µV in the preferred and 8.03±3.24 µV in the non-preferred eyes (p=0.594), while the mean N95 implicit times were 86.92±7.69 and 90.78±10.13, respectively (p=0.328). For the preferred eyes, there was no correlation between BCVA and N95 and P50 amplitudes or implicit times, whereas BCVA was correlated with p50 and N95 amplitudes in the non-preferred eyes ($p=0.023$, $r=0.6734$ and $p=0.014$, $r=0.711$, respectively). Moreover, interocular difference in BCVA was found to be correlated with interocular difference in P50 amplitude ($r=0.688$, $p=0.019$).

Discussion

With an estimated prevalence of 1-5%, amblyopia is the most common cause of preventable and treatable monocular vision loss in children.[1] Thus, assessment of visual acuity is particularly essential for the detection and follow-up of children with strabismus and amblyopia. However, this may not be possible with uncooperative or disabled children. Assessment of fixing and following, consistent objection to occlusion, preferential looking techniques, and fixation preference tests are mainly used to evaluate visual performance in children. However, only preferential looking tests can quantify visual acuity, and evaluation of fixing and following may underestimate particularly severe amblyopia.[7]

The binocular fixation pattern test was first described by Knapp and Moore.[8] Fixation preference testing is widely used to roughly evaluate and compare the vision of both eyes. This is imperative when subjective and quantitative assessment of visual acuity is not applicable. The absence of a fixation preference is considered to be indicative for equal vision, whereas its presence is considered a sign of amblyopia in the non-preferred eye. Binocular fixation pattern evaluation is especially used in patients with a deviation of 10 PD or higher.[9] In contrast, induced tropia tests with various prism strengths are preferred to detect amblyopia as an alternative to binocular fixation pattern testing in patients without strabismus or with a deviation smaller than 10 PD.[10] The fixation preference test was found to be sensitive in patients with esotropia and those with an interocular visual acuity difference of more than 3 lines.[11] However, studies investigating the sensitivity, specificity, and positive and negative predictive values of the fixation preference test had inconsistent results and mainly suggest that this test should be used with caution and confirmed by other tests. Its reliability has been questioned many times in the literature.[2,4,10,11,12,13]

The fixation preference test was found to show a high level of interexaminer agreement in different types of strabismus cases despite having low reliability in detecting interocular differences in visual acuity.[14] Furthermore, in some studies the clinical value of the fixation pattern test was found to be poor in the identification of children with amblyopia.[13,15]

Procianoy and Procianoy[15] suggested that the binocular fixation preference test is particularly useful in cases with either strong fixation preference or free alternation but may have limited reliability at intermediate grades.

Şener et al.[12] compared standard fixation preference grades with interocular logMAR acuity difference found a correlation in amblyopic patients with large-angle strabismus and demonstrated that this test is fairly accurate to determine interocular vision difference.

Alharkan and Khan[16] investigated the reasons for misinterpretation of binocular fixation pattern testing and found that contralateral ocular dominance may interfere with the test results and cause a false prediction of amblyopia. Ocular dominance was not identified in the present study.

Electrophysiological tests complement ophthalmological examination, particularly when the etiology of the visual impairment is undetermined. Tests that reflect the function of particular retinal areas may be valuable tools to detect retinal dysfunction in the absence of or even prior to clinical signs. pERG is an electrophysiological test evoked by a pattern stimulus and requires central fixation.[6] It reflects mainly the function of the retinal ganglion cells, but for a normal response the integrity of photoreceptors, bipolar, horizontal and amacrine cells and Müller cells is needed.[17] However, electrophysiological function of the macula can be abnormal even if there is no evident anatomical change. The pERG signal is very sensitive and prone to noise caused by ocular surface irregularities, refractive errors, and stimulus/electrode-related problems.

pERG has been used to assess and monitor macular function in the literature. Machalińska et al.[18] investigated pERG data in patients with asymptomatic unilateral internal carotid artery stenosis along with full-field ERG, pattern visual evoked potentials, and optical coherence tomography (OCT) and found that both P50 and N95 amplitudes were significantly smaller compared to healthy controls.

Okada et al.[19] investigated structure-function correlation in patients with macular telengiectasia type 2 and found subnormal P50 amplitudes. Nowacka et al.[20] evaluated the structure and function of the macula in patients with diabetic macular edema with pERG in addition to other tests and did not find any significant change during follow-up after treatment. Mastropasqua et al.[21] compared pERG signal as a macular function parameter in patients with Stargardt disease with healthy controls and showed that both P50 and N95 amplitudes were significantly reduced and implicit times were significantly delayed in patients with Stargardt disease.

Lubiński et al.[22] investigated the value of pERG in the prediction of postoperative visual acuity in patients with epiretinal membrane and demonstrated improvement of pERG parameters postoperatively along with an increase in visual acuity and decrease in macular thickness on OCT. They suggested that pERG seems to be valuable to predict postoperative visual acuity.[22]

Parisi et al.[23] compared pERG values in anisometropic amblyopic patients with normal controls and found no significant difference.

de Souza Lima et al.[24] showed no difference in pERG between hypermetropic anisometropic amblyopic and strabismic amblyopic patients but found significant differences in P50 and N95 latencies between strabismic amblyopic and control subjects. There were no patients with anisometropia in the present study.

Hamurcu et al.[25] demonstrated that P50 and N95 amplitudes were significantly lower in eyes with anisometropic amblyopia.

Multifocal ERG has also been studied in amblyopia. Al-Haddad et al.[26] investigated multifocal ERG in patients with anisometropic and strabismic amblyopia and found lower amplitude in the central ring in amblyopic eyes that was also correlated with the severity of amblyopia.

Study Limitations

It is worth noting that the number of patients enrolled in the study was very limited, thus an inference regarding the relationship between electrophysiological macular function and fixation preference cannot be made. Furthermore, the significant difference in spherical equivalent values between preferred and non-preferred eyes might have influenced pERG values. The patient numbers in the fixation preference groups were too small to draw any other meaningful conclusion. However, the results of this study can be considered preliminary.

Conclusion

The results of this study provide a comprehensive assessment of macular function in children with strabismus and demonstrate a potential correlation between interocular differences in electrophysiological parameters and visual acuity. Therefore, further larger studies are needed to emphasize the relationship between fixation preference and electrophysiological and clinical macular function.

Ethics

Ethics Committee Approval: The study was conducted in full accordance with the tenets of the Declaration of Helsinki and was carried out upon approval of the Institutional Ethics Committee (GO 17/561-23).

Informed Consent: Obtained.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: H.T.Ş., A.A.B., Concept: H.T.Ş., A.A.B., Design: H.T.Ş., Data Collection or Processing: H.T.Ş., A.A.B., J.K., Analysis or Interpretation: H.T.Ş., J.K., Literature Search: H.T.Ş., Writing: H.T.Ş.

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References

1. Holmes JM, Clarke MP. Amblyopia. Lancet. 2006;367:1343-1351.
2. Burggraaf F, Verkaik-Rijneveld MC, Wubbels RJ, de Jongh E. Is the 15Δ Base in Prism Test Reliable for Detection of Amblyopia in Anisometropic Patients? Strabismus. 2017;25:160-165.
3. Wallace DK. Fixation preference tests for amblyopia: invaluable, useless, or somewhere in the middle?. J AAPOS. 2010;14:201-202.
4. Cotter SA, Tarczy-Hornoch K, Song E, Lin J, Borchert M, Azen SP, Varma R; Multi-Ethnic Pediatric Eye Disease Study Group. Fixation preference and visual acuity testing in a population based cohort of preschool children with amblyopia risk factors. Ophthalmology. 2009;116:145-153.
5. Robson AG, Nilsson J, Li S, Jalali S, Fulton AB, Tormene AP, Holder GE, Brodie SE. ISCEV guide to visual electrodiagnostic procedures. Doc Ophthalmol. 2018;136:1-26.
6. Bach M, Brigell MG, Hawlina M, Holder GE, Johnson MA, McCulloch DL, Meigen T, Viswanathan S. ISCEV standard for clinical pattern electroretinography (PERG): 2012 update. Doc Ophthalmol. 2013;126:1-7.
7. Wallace DK. Tests of fixation preference for amblyopia. Am Orthopt J. 2005;55:76-81.
8. Knapp P, Moore S. Diagnostic procedures in an orthoptic evaluation. Am Orthopt J. 1962;12:63-69.
9. Zipf RF. Binocular fixation pattern. Arch Ophthalmol. 1976;94:401-405.
10. Wright KW, Edelman PM, Walonker F, Yiu S. Reliability of fixation preference testing in diagnosing amblyopia. Arch Ophthalmol. 1986;104:549-553.
11. Attarzadeh A, Hoseinirad A, Farvardin M, Talebnejad MR, Alipour A. Reliability of fixation preference for detecting amblyopia in strabismic patients. J Ophthalmic Vis Res. 2009;4:160-163.
12. Şener EC, Mocan MC, Gedik S, Ergin A, Sanaç AS. The reliability of grading the fixation preference test for the assessment of interocular visual acuity differences in patients with strabismus. J AAPOS. 2002;6:191-194.
13. Friedman DS, Katz J, Repka MX, Giordano L, Ibironke J, Hawse P, Tielsch JM. Lack of concordance between fixation preference and HOTV optotype visual acuity in preschool children: the Baltimore Pediatric Eye Disease Study. Ophthalmology. 2008;115:1796-1799.
14. Erkan Turan K, Taylan Sekeroglu H, Karahan S, Sanac AS. Fixation preference test: reliability for the detection of amblyopia in patients with strabismus and interexaminer agreement. Int Ophthalmol. 2017;37:1305-1310.
15. Procianoy L, Procianoy E. The accuracy of binocular fixation preference for the diagnosis of strabismic amblyopia. J AAPOS. 2010;14:205-210.
16. AlHarkan DH, Khan AO. False amblyopia prediction in strabismic patients by fixation preference testing correlates with contralateral ocular dominance. J AAPOS. 2014;18:453-456.
17. Anders LM, Heinrich SP, Lagrèze WA, Joachimsen L. Little effect of 0.01% atropine eye drops as used in myopia prevention on the pattern electroretinogram. Doc Ophthalmol. 2019;138:85-95.
18. Machalińska A, Kowalska-Budek A, Kawa MP, Kazimierczak A, Safranow K, Kirkiewicz M, Wilk G, Lubiński W, Gutowski P, Machaliński B. Association between Asymptomatic Unilateral Internal Carotid Artery Stenosis and Electrophysiological Function of the Retina and Optic Nerve. J Ophthalmol. 2017;2017:4089262.
19. Okada M, Robson AG, Egan CA, Sallo FB, Esposti SD, Heeren TFC, Fruttiger M, Holder GE. Electrophysiological characterisation of macular telengiectasia type 2 and structure-function correlation. Retina. 2018;38(Suppl 1):33-42.
20. Nowacka B, Kirkiewicz M, Mozolewska-Piotrowska K, Lubiński W. The macular function and structure in patients with diabetic macular edema before and after ranibizumab treatment. Doc Ophthalmol. 2016;132:111-122.
21. Mastropasqua R, Toto L, Borrelli E, Di Antonio L, Mattei PA, Senatore A, Di Nicola M, Mariotti C. Optical coherence tomography angiography findings in Stargardt Disease. PLoS One. 2017;12:e0170343.
22. Lubiński W, Gosławski W, Krzystolik K, Mularczyk M, Kuprjanowicz L, Post M. Assessment of macular function, structure and predictive value of pattern electroretinogram parameters for postoperative visual acuity in patients with idiopathic epimacular membrane. Doc Ophthalmol. 2016;133:21-30.
23. Parisi V, Scarale ME, Balducci N, Fresina M, Campos EC. Electrophysiological detection of delayed postretinal neural conduction in human amblyopia. Invest Ophthalmol Vis Sci. 2010;51:5041-5048.

24. de Souza Lima LCS, Dantas AM, Herzog Neto G, Damasceno EF, Solari HP, Ventura MP. Comparative electrophysiological responses in anisometropic and strabismic amblyopic children. Clin Ophthalmol. 2017;11:1227-1231.
25. Hamurcu M, Çelik A, Sarıcaoğlu MS, Bulut AK. Electrophysiologic evaluation of amblyopia. Eye Care Vis. 2017;1:3-4.
26. Al-Haddad C, Bou Ghannam A, El Moussawi Z, Rachid E, Ismail K, Atallah M, Smeets L, Chahine H. Multifocal electroretinography in amblyopia. Graefes Arch Clin Exp Ophthalmol. 2020;258:683-691.