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Fixation patterns evaluation by means of MP-1 microperimeter in microstrabismic children treated for unilateral amblyopia

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PURPOSE. *The aim of the study was to evaluate the fixation patterns of microstrabismic children previously treated for unilateral amblyopia.*

METHODS. *Thirty-three children (mean age 7.3±1.5 years) were included in the study. Visual acuity (VA) was measured using the Early Treatment of Diabetic Retinopathy Study charts. Fixation was assessed by MP-1 microperimeter. Differences in position and stability of fixation between the fellow and the microstrabismic eyes were calculated by using the percentage of the preferred fixation points within central fixation and the percentage of the fixation points within target fixation, respectively. For statistical analysis Mann-Whitney test was used. To evaluate the influence of age and duration of anti-amblyopic treatment on microstrabismic eyes fixation, linear regression analysis was performed.*

RESULTS. *In the microstrabismic eyes VA was significantly reduced when compared to the fellow eyes (0.1236±0.0204 vs 0.0042±0.0032 logMAR; p<0.001). Position and stability of fixation were significantly better in the fellow eyes (93.21±0.65% vs 70.91±4.80%; p=0.002, and 89.88±0.94% vs 71.73±2.94%; p<0.001, respectively). A significant correlation was found between fixation stability and both the duration of anti-amblyopic treatment and pretreatment VA (p=0.024 and p=0.009, respectively) and between fixation centrality and pretreatment VA (p<0.001).*

CONCLUSIONS. *VA, centrality, and stability of fixation were significantly impaired in the microstrabismic eyes. Pretreatment VA was a risk factor for fixation impairment. The severity of fixation stability impairment was linked to the duration of anti-amblyopic treatment. (Eur J Ophthalmol 2007; 17: 885-90)*

KEY WORDS. *Fixation patterns, Microstrabismic children, Unilateral amblyopia*

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INTRODUCTION

Microstrabismus is characterized by a small angle of squint (either convergent or divergent) of less than 5 degrees and a harmonious anomalous correspondence (1, 2). In these patients, some degree of stereopsis and mild amblyopia are generally found (2). Nevertheless, when monocularly tested visual function and particularly reading performance may be relevantly impaired (2-4).

Diagnosis of amblyopia is based on reduced visual acuity (VA) (5), but other anomalies such as reduced contrast sensitivity (6, 7) and anomalous spatial sense frequently coexist (8, 9). Eccentric fixation is manifest in up to 80% of amblyopes (10, 11) and this, along with drift (12), contributes to the VA reduction. Amblyopia is more pronounced in cases with eccentric fixation (2).

The recently developed fundus-related MP-1 microperimeter allows for a fast, reliable microperimetric ex-

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amination of fixation and scotoma characteristics in patients with macular diseases (13-15), even when VA can be extremely poor, and fixation is unstable and eccentric.
An objective, repeatable examination of fixation may be a useful tool to study visual impairment in microstrabismic amblyopia. In the present study, children with microstrabismic amblyopia were tested in a standardized clinical setting considering the characteristics of amblyopic vision: VA was determined using Early Treatment of Diabetic Retinopathy Study (ETDRS) charts and fixation patterns were assessed using the MP-1 microperimeter, in order to evaluate some of the most relevant functional deficits.

PATIENTS AND METHODS

This prospective clinical study was performed at the Ophthalmology Clinic of the University "G. D'Annunzio" of Chieti-Pescara. The monocular VA and fixation patterns of 33 children previously treated for unilateral amblyopia due to primary microstrabismus (mean age: 7.3±1.5 years; range: 6–9 years) were evaluated. The study adhered to the tenets of the Declaration of Helsinki. Institutional Review Board (IRB) approval was obtained. Informed consent from the legally authorized representative was obtained prior to the testing session.
Children with unilateral microstrabismic amblyopia were included in the study population, under the condition that treatment was started before the age of 6 years when microstrabismic amblyopia had been initially diagnosed (mean age at therapy onset: 4.7±1.0 years). Amblyopia was defined as an interocular difference in best-corrected VA of at least two lines on an ETDRS chart (0.2 logMAR unit) (16). Microstrabismus was defined by a small angle of squint (either convergent or divergent; ≤5°) and the presence of a harmonious anomalous retinal correspondence (ARC) (2). Children with a larger angle of strabismus or a secondary microstrabismus following strabismus surgery were excluded.
The squint angle was measured by simultaneous prism and cover tests at near (0.3 meters) and far distance (4 meters). The presence of harmonious ARC was determined by means of both Bagolini striated lenses and synoptophore. Convergence and accommodation were also tested. Refractive errors were evaluated objectively by cycloplegic (cyclopentolate 1%) autorefractometry 1 week before the testing session and subjectively adjusted at the beginning of the testing session. All tests were performed with the child's optimal correction for far and near vision. VA was tested at a testing distance of 4 meters, using the ETDRS charts, and was recorded as the logarithm of the minimum angle of resolution (logMAR) for statistical analysis.
Anti-amblyopic treatment included correction of refractive error or accommodative disorder and occlusion therapy. In all children, treatment resulted in improved best-corrected VA (BCVA) of at least two lines over time. The duration of anti-amblyopic treatment ranged from 24 to 48 months (mean 32.48, SD ±7.85 months). At the end of anti-amblyopic treatment mean BCVA had improved from 0.3442 (SD ±0.349) to 0.1236 (SD ±0.0204) ($p<0.001$, Wilcoxon signed ranks test).
The demographic and clinical characteristics of the study population are given in Table I.
Fixation assessment was performed on all eyes by means of MP-1 microperimeter (Nidek Technologies Srl. Vigonza PD, Italy) using the software version available in 2003 (Version: MP1 SW 1.4.1. SP1), with automated correction

TABLE I - DEMOGRAPHIC CHARACTERISTICS OF THE STUDY POPULATION (N=33)

	Children with convergent microstrabismus (n=22)	Children with divergent microstrabismus (n=11)	Total (n=33)
Age, yr, mean ± SD	7.2±1.5	7.5±1.3	7.3±1.5
Females (%)	50	45.45	48.48
Children requiring refractive correction (%)	81.81	81.81	81.81
Myopia (%)	4.54	45.45	18.18
Hyperopia (%)	77.27	36.36	63.63
Anisometropia (interocular difference ≥1.50 D, %)	36.36	54.55	42.42
Patients with hypoaccommodation requiring near addition (%)	22.72	0	15.15
Prism Cover Test at far vision (Prism Diopters, Δ, mean ± SD)	4.0±1.2	–2.4±1.8	2.2±4.1
Prism Cover Test at near vision (Prism Diopters, Δ, mean ± SD)	7.0±2.5	–3.2±1.9	4.0±6.5

for eye movements. The infrared light was used for imaging, and the internal liquid crystal display was used for stimulus presentation.
MP-1 includes an automated tracking system to compensate in real time for any eye movement. At the
beginning of the examination, an infrared camera (resolution, 1 pixel [equivalent to 0.1°]) tracks a reference frame, and an area of interest is defined placing a cursor on a retinal landmark on the frozen image.
During examination, any eye movement is detected by image acquisition of 25 frames per second. The computer then calculates the shift between the reference image and the real-time fundus images with the stimulus position on the display corrected according to the actual location of the fundus. The MP1 device further enables the acquisition of color fundus photography at the end of the examination with an overlay of fixation points onto this color fundus image.
Mp-1 microperimeter acquires 750 fixation points within a 30-second time period.
For assessment of fixation, the fundus movements are tracked during examination while the patient gazes at the fixation target. The autotracking system calculates horizontal and vertical shifts relative to a reference frame and returns a map of the patient's eye movements during the examination. At the conclusion of testing, a scattergraph depiction of fixation is displayed. This is used to quantify the fixation pattern.
Children were instructed to fixate with their tested eye the center of the fixation target throughout the duration of the examination. For the purpose of this study, the fixation target was a 2° diameter ring.
The fixation pattern is graded based on two variables: fixation location (defined as the position of fixation with respect to the center of the foveal avascular zone) and fixation stability (defined as the ability of the eye to maintain fixation in the preferred retinal locus).

Fixation location

According to Fujii et al (17), in assessing the fixation location, the standard of central fixation is defined to approximate a 2-degree diameter (approximately 700-μm) circle centered on the fovea. Eyes with more than 50% of the preferred fixation points located within central fixation are classified as having predominantly central fixation. Eyes with more than 25% but less than 50% of the preferred fixation points located within central fixation are classified as having poor central fixation. Eyes with less than 25% of the preferred fixation points located within central fixation are classified as predominantly eccentric fixating. In situations where patients are unable to maintain foveal fixation even for a short duration, they are automatically classified as having predominantly eccentric fixation.

Fixation stability

Two terms have been suggested for evaluating stability of fixation: target fixation and extra-target fixation (17). Target fixation is defined as a 2-degree diameter circle positioned with respect to the gravitational center of all fixation points. Likewise, extra-target fixation is defined as a 4-degree diameter circle positioned with respect to the gravitational center of all fixation points. Eyes with more than 75% of the fixation points located within the target fixation are classified as stable. If less than 75% of the fixation points are located within the target fixation but more than 75% of the fixation points are within extra-target fixation the eye is classified as having relatively unstable fixation. If less than 75% of fixation points are located within the extra-target fixation, the pattern is described as being unstable fixation.

Statistical methods

The statistical package SPSS 10.0 for Windows (©1999 SPSS, Inc., Chicago, IL, USA) was used in the analysis of the data. Differences between sound and amblyopic eyes with respect to VA were analyzed for significance by Mann-Whitney test.
For the purpose of this study, differences between sound and amblyopic eyes with respect to the position of fixation were calculated by means of the percentage of the preferred fixation points located within central fixation and were analyzed for significance by Mann-Whitney test. Similarly, differences in stability of fixation between sound and amblyopic eyes were calculated by means of the percentage of the fixation points located within the target fixation and were analyzed for significance by Mann-Whitney test.
To evaluate the influence of pretreatment children's age, duration of anti-amblyopic treatment, and pre- and post-treatment BCVA on microstrabismic eyes fixation results, linear regression analysis was performed. The level of statistical significance was set at 0.05.

RESULTS

In the microstrabismic eyes, VA was significantly reduced when compared to the fellow eyes (p<0.001) (Tab. II).
Fixation patterns were impaired in the microstrabismic eyes (Tab. III). The percentage of the preferred fixation points located within central fixation was significantly higher in the fellow eyes (mean ± SD: 93.21±0.65; range: 87–98%) than in the microstrabismic eyes (mean ± SD: 70.91±4.80; range: 20–98%) (p=0.002). Similarly, the percentage of the fixation points located within the target fixation was significantly higher in the fellow eyes (mean ± SD: 89.88±0.94; range: 78–98%) than in the microstrabismic eyes (mean ± SD: 71.73±2.94; range: 35–99%) (p<0.001).
Nine out of the 10 (90%) children who achieved more than 75% of the fixation points located within the target fixation in their microstrabismic eye had underwent at least a 36-month duration anti-amblyopic treatment. Conversely, 4 out of 23 (17.4%) microstrabismic eyes having less than 75% of the fixation points located within the target fixation had been treated for at least 36 months.
When analyzing separately the results of the 10 children achieving a BCVA of logMAR 0.0 or better in their microstrabismic eyes, 5 microstrabismic eyes showed a relatively unstable fixation (Tab. IV). In this subgroup, significant

TABLE II - VISUAL PARAMETERS OF THE MICROSTRABISMIC AND THE FELLOW EYES OF THE STUDY POPULATION (N=33)

Variable	Microstrabismic eyes	Fellow eyes	p value*
Visual acuity (logMAR)	0.1236±0.0204	0.0042±0.0032	<0.001
Refractive error, spherical equivalent (D)	1.25±3.55	1.32±2.05	0.82

*Mann-Whitney test

TABLE III - PATTERNS OF FIXATION OF MICROSTRABISMIC AND FELLOW EYES OF THE STUDY POPULATION (N=33)

Variable	Microstrabismic eyes	Fellow eyes
Position of fixation		
Predominantly central	21 (63.63%)	33 (100%)
Poorly central	9 (27.27%)	0
Predominantly eccentric	3 (9.09%)	0
Stability of fixation		
Stable	10 (30.30%)	33 (100%)
Relatively unstable	20 (60.60%)	0
Unstable	3 (9.09%)	0

TABLE IV - PATTERNS OF FIXATION OF THE AMBLYOPIC AND THE FELLOW EYES IN CHILDREN ACHIEVING A BCVA OF LOGMAR 0.0 OR BETTER (N=10)

Variable	Microstrabismic eyes	Fellow eyes
Position of fixation		
Predominantly central	10 (100%)	10 (100%)
Poorly central	0	0
Predominantly eccentric	0	0
Stability of fixation		
Stable	5 (50%)	10 (100%)
Relatively unstable	5 (50%)	0
Unstable	0	0

differences were not found in relation to the percentage of the preferred fixation points located within central fixation (p=0.739) or to the percentage of the fixation points located within the target fixation (p=0.529).
Regression analysis demonstrated a statistically significant correlation between fixation stability and both the duration of anti-amblyopic treatment and the pretreatment BCVA (p=0.024 and p=0.009, respectively) and between fixation centrality and the pretreatment BCVA (p<0.001).

DISCUSSION

In the evaluation of visual function in children with amblyopia, vision tests considering the characteristics of amblyopic vision should be performed (18-20). Eccentric fixation has been described in up to 80% of amblyopes (9-11) and this, along with drift (12), contributes to the visual impairment. In their interesting study of reading acuity and speed in treated children with microstrabismic amblyopia, Stifter et al tested monocular fixation by direct ophthalmoscopy and found a stable or unstable central fixation in 75 to 79% of amblyopic eyes (4).
Fixation has received little attention in recent clinical amblyopia studies, but the presence of eccentric fixation (EF) in amblyopic eyes may be an important prognostic factor in the treatment of amblyopia and the ability to accurately diagnose and measure EF may be clinically important.
Fixation impairment in amblyopic patients could be analyzed by means of standardized testing procedures providing reproducible and comparable measurements, such as computerized fundus-related microperimetry.
The introduction of scanning laser ophthalmoscope (SLO) fundus-related microperimeter allowed analysis of fixation characteristics and retinal threshold of selected retinal areas, under direct fundus control (21-23). In a recent study by Johnson (24), SLO was used in the evaluation of macular scotomata in anisometropic or strabismic amblyopia.
The fully automatic fundus-related MP-1 microperimeter, recently introduced into clinical practice, uses a tracking system for constant evaluation of eye positioning, which does not depend on when the stimulus is presented, as it does for SLO (13). The MP-1 allows for a fast, reliable microperimetric examination of fixation and scotoma characteristics in patients with macular diseases (13-15), even when VA is extremely poor, and fixation is unstable and eccentric.
Fixation patterns can be evaluated either during microperimetry examination or during specific fixation assessment. When testing fixation in children the use of specific fixation assessment is preferred because, as a rule, the test lasts only 15 to 30 seconds.
In this study we compared VA and fixation patterns in healthy and microstrabismic eyes of 33 children previously treated for amblyopia due to primary microstrabismus. VA as measured by ETDRS tables was significantly lower in microstrabismic eyes when compared to fellow eyes. MP-1 fixation test was well tolerated by all children and allowed a fast classification of fixation abnormalities. Both centrality and stability of fixation were significantly impaired in the group of microstrabismic eyes. Eyes with a more central and stable fixation resulted in better VA than eyes with deterioration of stability and position of fixation. However, a stable fixation if associated with poorly central or predominantly eccentric position may be characterized by a reduced VA. These findings suggest that fixation pattern is likely reflective of foveal function.
Multivariate analysis showed a significant influence of pretreatment VA on both centrality and stability of fixation. These data suggest that pretreatment VA may be considered a risk factor for fixation impairment. Conversely, a correlation trend between VA at the end of treatment and fixation patterns exists, but is not statistically significant. In addition, even among the microstrabismic eyes with normal VA, fixation stability impairment is found in 50% of the eyes. Stability of fixation is significantly related to the duration of anti-amblyopic treatment. Nine out of 10 children who achieved more than 75% of the fixation points located within the target fixation and were thus classified as having a stable fixation in their microstrabismic eye had undergone at least a 36-month duration anti-amblyopic treatment. On the other hand, only 4 out of 23 eyes which resulted in an unstable fixation had been treated for at least 36 months. These findings may reflect an incomplete learning process following anti-amblyopia treatment.
In conclusion, since one of the major challenges facing clinical practice and research in amblyopia is obtaining valid, accurate, and reliable measures by which the visual function and the outcome of treatment can be quantified, our study suggests that the evaluation of the fixation patterns may be a valid method to obtain useful parameters for the follow-up and the outcome assessment of anti-amblyopic treatment. Further studies in-

volving a larger sample will be needed to establish if the persistence of fixation patterns impairment, especially fixation stability, also in presence of a complete VA recovery might be interpreted as a partially incomplete anti-amblyopic treatment.

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