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Low-Vision Rehabilitation by Means of MP-1 Biofeedback Examination in Patients with Different Macular Diseases: A Pilot Study

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Abstract Macular disease is one of the main causes of visual impairment. We studied the efficacy of low-vision rehabilitation by means of MP-1 biofeedback examination in patients with different macular disease. Five patients were enrolled (3 female and 2 male, mean age 53.8 years) and a total of 9 eyes was examined: 2 eyes with vitelliform dystrophy, 1 with a post-traumatic macular scar, 2 with Stargardt disease, 2 with myopic macular degeneration, 2 with cone dystrophy. All the patients underwent the following tests: visual acuity, reading speed, fixation test, MP-1 microperimetry. Low-vision rehabilitation, which lasted 10 weeks, consisted of 10 training sessions of 10 min for each eye, performed once a week using the MP-1 biofeedback examination. Statistical analysis was performed using Student's *t*-test. p values less than 0.05 were considered statistically significant. After training all patients displayed an improvement in visual acuity, fixation behaviour, retinal sensitivity and reading speed. Fixation behaviour within the 2° diameter circle improved and was statistically significant for reading speed ($p = 0.01$). Reading speed improved from a mean value of 64.3 to 92 words/min. Our results show that audio feedback can, by increasing attentional modulation, help the brain to fix the final preferred retinal locus. Audio feedback facilitates stimuli transmission between intraretinal neurons as well as between the retina and brain, which is where the highest level of stimuli processing occurs, thereby probably supporting a "remapping phenomenon".

Keywords Biofeedback · Low-vision rehabilitation · Macular disease · MP-1 microperimeter · Preferred retinal locus (PRL) · Scotoma

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Introduction

It has been estimated that 1.75 million individuals in the United States have macular disease (MD), and that nearly 15% of those over 90 years of age have visual impairment due to MD (Friedman et al. 2004). Furthermore, the World Health Organization (WHO) estimates that 8 million people are severely visually impaired because of age-related macular disease (AMD).

Macular diseases (e.g. AMD, Stargardt, cone-dystrophy, macular myopic degeneration, vitelliform dystrophy, post-traumatic macular scar) are characterised by the development of a central scotoma which, besides reducing reading speed, interferes with other visual functions: space perception, contrast sensitivity, stereopsis and fixation stability. This interference is due in part to the inability of these subjects to accurately track a target because of impaired ocular movement (Pidcoe and Wetzel 2006; McMahon et al. 1991). The degree of visual impairment in such subjects varies according to the age of the patients, the presence of other systemic pathologies, the environment in which they live, their education level and the psychological state with which they accept their condition.

As life expectancy increases in many countries, a growing concern over the quality of life of these people has led to studies aimed at investigating ways of improving their visual performance, but our inability to effectively

treat most macular degenerations is still high, leading to an increase in the number of low-vision patients.

Optical aids designed to improve low vision are generally uncomfortable for the patient, often resulting in a state of depression; moreover, the higher the magnification, the more restricted the field of vision becomes. It is for this reason that new biofeedback strategies aimed at improving retinal sensitivity and fixation stability have been proposed; the MP-1 microperimeter (Nidek Technologies, Italy) was designed to locate the new preferred retinal locus (PRL) more accurately, and consequently increase visual performance.

The MP-1 microperimeter uses cerebral plasticity and neurosensorial adaptation to the central scotoma of patients with macular diseases (MD) to improve their visual abilities and lay the basis for new, more manageable visual aids. Indeed, such patients often develop a new PRL, which can be defined as a discrete retinal area that contains more than 20% of the fixation points in a location that is considered unfavourable for reading (Crossland et al. 2005). Moreover, a sizeable proportion of patients use more than one PRL for a given task. It has been also found that some patients exhibit a re-referencing of the oculomotor system to the PRL, which leads them to say that they are looking straight ahead when they are fixating with the PRL (i.e. when the eye is not in the primary position). This phenomenon has been referred to as adaptive eccentric fixation or oculomotor re-referencing (Crossland et al. 2005).

The purpose of this study was to estimate the benefits of low-vision rehabilitation using the MP-1 biofeedback (BFD) examination to better define the PRL and increase its stability, thereby helping patients to re-reference their oculomotor system and improve their reading speed.

Methods

Participants

We randomly enrolled 5 patients (3 female and 2 male) who had come to Department of Ophthalmology of the A. Fiorini Hospital, at the "La Sapienza" University of Rome, with macular disease and an absolute central scotoma. As can be seen on Table 1, we examined 9 eyes: one eye with a post-traumatic macular scar (patient no 1); two eyes with vitelliform dystrophy (patient no 2), two eyes with myopic macular degeneration (patient no 3), two eyes with cone dystrophy (patient no 4); and two eyes with Stargardt disease (patient no 5).

Patients were diagnosed on the basis of a complete examination of the anterior and posterior segment, which included microperimetry, fluorescein angiography and ocular coherence tomography (OCT). Four eyes had an IOL implanted in the posterior chamber and had already undergone Nd-YAG laser capsulotomy. None of the patients displayed any glaucomatous or lens changes that may have affected visual acuity. All the patients read Italian as a first language, and none had a history of neurological or psychiatric disease, systemic hypertension, diabetes, or any other ocular pathology. The mean patient age was 53.8 years (range: 33–78 years). The time lapse

Table 1 Table of results

Patient number	Diagnosis	Scotoma size	Fixation location (PRL)		BCVA		Fixation Behaviour		Retinal sensitivity (dB)		Reading speed (words/min)	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	Post traumatic macular scar	<2°	Superior	Superior	0.3	0.2	32%	66%	16.2	16.9	174	206
2 Right eye	Vitelliform dystrophy	<4°	To the left	Superior	0.2	0	67%	100%	13.5	17.3	166	174
2 Left eye	Vitelliform dystrophy	<4°	To the left	To the left	1.1	0.5	49%	100%	9.6	13.2	18	24
3 Right eye	Myopic macular degeneration	–	In ring	In ring	0.7	0.4	27%	52%	6	6.2	38	55
3 Left eye	Myopic macular degeneration	>10°	Superior	Superior	1.7	1.1	23%	56%	6.1	6.5	5	12
4 Right eye	Cone dystrophy	>10°	Upper right	Superior	0.5	0.4	20%	80%	7.1	7.8	12	22
4 Left eye	Cone dystrophy	>10°	Upper left	Superior	1.7	1.22	17%	66%	6.5	8.5	5	12
5 Right eye	Stargardt disease	<4°	Superior	Superior	0.6	0.6	38%	97%	14.4	16.3	108	219
5 Left eye	Stargardt disease	<4°	Superior	Superior	0.5	0.5	34%	98%	14.8	16.6	53	103
Mean					0.811	0.546	34%	79%	10.4	12.1	64.3	91.8
SD					0.564	0.391	0.1576	0.198	4.2	4.8	68	86.3
p values						0.011		1.250		0.005		0.04

Pre, baseline values; Post, values at the end of low-vision rehabilitation; BCVA, best distance spectacle corrected visual acuity expressed in logMAR; Fixation location (PRL), location of the PRL related to the retinal lesion; Fixation behaviour, fixation behaviour within the 2° diameter circle; Reading speed, (words/min) assessment was done with an add selected for age and a + 4.00 (1×) on the top of this; *SD* Standard Deviation; *p* values, $p < 0{,}05$ were considered statistically significant

since the onset of visual acuity deterioration ranged from 2 to 40 years, and none of the patients had previously received visual rehabilitation with MP-1 biofeedback (BFD). Informed consent to participate in the study was obtained from all the patients. The ethics committee of our institution approved the study protocol. All the procedures adhered to the tenets of the Declaration of Helsinki.

Assessment Measures

All the patients underwent the same low-vision rehabilitation protocol which consisted of: a 22-item questionnaire, the assessment of distance and near visual acuity, reading speed test (words/min), fixation test, microperimetry, 10 training sessions.

The 22-item questionnaire on daily living activities and patients' expectations from rehabilitation was designed to confirm the priority task and identify any other residual functional skills requiring rehabilitation.

Best distance spectacle corrected visual acuity (BCVA) was determined using the Early Treatment of Diabetic Retinopathy Study visual acuity chart, which was converted to logarithm of the minimum angle of resolution (logMAR) for statistical analyses; the assessment of near visual acuity was determined at 25 cm or nearer with an add selected for age and a + 4.00 reading lens on top of this.

For each eye reading speed was measured by reading of black letters (type: Times New Roman) on a white background at a distance of 25 cm or nearer corrected with an add selected for age and a + 4.00 reading lens on top of this. Subjects were instructed to read each sentence aloud as fast as possible without skipping words (character size was adapted to patients' visual acuity and expressed in electronic points). The sentences contained high-frequency, non-technical words and were declarative in nature. Uppercase letters were used at the beginning of sentences, but no punctuation characters were used.

The microperimetry and fixation test of the macular area were performed with the MP-1 microperimeter from Nidek Technologies (Padua, Italy); for the fixation test: a 2° or 1° single cross fixation target was used in all eyes before BFD; after training only 1° single cross was used, and the examination time was set at 30 s.

Microperimetry was performed using the automated programme, the threshold test of 4–2 strategy, and a 1° single cross fixation target; however, at the beginning of the study the size was enlarged to a 2° single cross fixation target when patient was not able to see the 1° single cross fixation target. After training only 1° single cross target was used for all patients. Retinal threshold sensitivity was measured in all eyes using the mire of Goldmann III (round shape with a white background) with stimulus intensity ranging from 0 to 20 dB. Stimulus presentation time was 200 ms. When a stimulus was not detected within 2 s, the next stimulus began. Pretest training was performed for both microperimetry and fixation test and 5 min visual adaptation was allowed before starting the test. We assessed each eye separately for fixation behaviour, location and stability of the PRL, scotoma size and density, and central light sensitivity.

The assessment of distant and near visual acuity, reading speed test, fixation and microperimetry tests were repeated at the end of low-vision rehabilitation (i.e. after 10 weeks). Microperimetry was repeated using the follow-up function, which automatically retests the retinal sensitivity in exactly the same locations and under the same conditions as in the previous microperimetry examination.

Apparatus

The microperimetry, fixation test and rehabilitation were performed with the MP-1 microperimeter from Nidek Technologies (Padua, Italy), using the software version available in June 2003 (version: MP1 SW 1.4.1. SP1) with automated correction for eye movements which combines fundus tracking microperimetry and colour fundus photography in a single instrument, thereby allowing direct fixation control and a precise delineation of the scotoma (Springer et al. 2005; Rohrschneider et al. 2002; Sawa et al. 2006). Briefly, the instrument has a 45° field of view and a liquid crystal display monitor. The background luminance of the instrument is 1.27 cd/m2, while the highest stimulus intensity is 127 cd/m2. Stimulus attenuation ranges from 0 to 20 dB with Goldmann-type size. For the fixation stability assessment, movements of the fundus are tracked during the examination while the patient gazes at the fixation target. The autotracking system calculates horizontal and vertical shifts relative to a reference frame and maps the patient's eye movements during the examination.

Intervention

The low-vision rehabilitation consisted of 10 training sessions of 10 min for each eye, performed once a week using the MP-1 biofeedback examination. The patients were asked to move their eyes according to an audio feedback which advised them whether they were getting closer to the desired final fixation position. All the procedures were followed on a monitor and the results stored in a computer and on diskettes.

Statistical analysis was performed using paired Student's *t*-test. *p* values less than 0.05 were considered statistically significant for all tests because of the preliminary nature of this study.

Results

Scotoma Size and Density

Scotoma density was defined as follows: a reduction in the differential light threshold was categorised (1) as an "absolute scotoma" when one or more stimuli were not seen with the brightest stimulus (0 dB), (2) as a "relative scotoma" when a circumscribed area of reduced differential light threshold could be found and (3) as a "general reduced differential light threshold" when the threshold values were reduced to the same threshold level in the whole area examined (Rohrschneider et al. 2002).

All the eyes examined but one were affected by an absolute scotoma; the remaining eye had a relative scotoma due to vitelliform dystrophy.

We divided the eyes examined into three groups according to the diameter of the central scotoma: *Group A*: diameter >10°: 3 eyes (1 with myopic degeneration, 2 with cone dystrophy); *Group B*: diameter <4°: 4 eyes (2 with Stargardt, 2 with vitelliform dystrophy); *Group C*: diameter <2°: 1 eye (traumatic macular scar). One eye with macular myopic dystrophy, with a healthy retinal area at the posterior pole surrounded by areas of corioretinal atrophy, was excluded from the classification.

Although the scotoma size of three eyes (traumatic macular scar, vitelliform dystrophy, myopic dystrophy) may have been increasing, no change was observed during the training.

Fixation Location

At the beginning of the study fixation location in our patients was the following: 6 PRLs were located in the superior hemiretinal field (4 in a central position, directly over the scotoma, 1 upper left and 1 upper right the scotoma), 2 PRLs were positioned to the left of the retinal lesion, 1 PRL was in the middle of the ring scotoma.

At the end of low-vision rehabilitation fixation location was as follows: 7 PRLs were located in the superior hemiretinal field (in a central position over the scotoma); 1 PRL remained to the left of the retinal lesion and 1 PRL stayed in the middle of the ring scotoma. For three eyes fixation location was changed, while in six eyes fixation behaviour of the existing PRL was reinforced.

For the selection of the PRL to be trained with biofeedback examination it was chosen an area of 2° diameter circle located, if possible, over the scotoma, with an appropriate retinal sensitivity to ensure the reinforcement of fixation behaviour and fluent reading.

It has been demonstrated that reading speed improves dramatically if a newly trained retinal locus (TRL) is established in an area that is more favourable for reading (Nilsson et al. 2003), so the new PRL was chosen by the ophthalmologist, who paid particular attention to the width of the retinal area (for fluent reading patients must be able to read at least four letters) and to its sensitivity. Moreover, all the new PRLs were positioned in the superior hemi-retinal field, which is considered to be more favourable for reading, regardless of their previous position.

Fixation Behaviour

The fixation points recorded were classified in three groups for the fixation analysis, termed "stable", "relatively unstable" and "unstable". Fixation was regarded as "stable" if more than 75% of the fixation points were inside the 2° diameter circle (about 700 microns), as "relatively unstable" if less than 75% were inside the 2° diameter circle but more than 75% were inside the 4° diameter circle, and as "unstable" if less than 75% of the fixation points were inside the 4° diameter circle (Fujii et al. 2002; Fig. 1).

At the beginning of low-vision rehabilitation the eyes examined were divided as follows: *Group 1*: stable fixation: 0 eyes; *Group 2*: relatively unstable fixation: 4 eyes; *Group 3*: unstable fixation: 5 eyes.

At the end of the visual rehabilitation the stability of fixation had improved: *Group 1*: stable fixation: 5 eyes; *Group 2*: relatively unstable fixation: 4 eyes; *Group 3*: unstable fixation: 0 eyes.

Fixation behaviour within the 2° diameter circle improved, though this result was not statistically significant ($p = 1.25$); by contrast, the improvement of fixation behaviour within the 2° diameter circle related to reading speed was statistically significant ($p = 0.01$).

Patients' Direction of Gaze

At the end of the visual protocol, the patients' direction of gaze was examined: 2 patients (one with cone dystrophy and the other with Stargardt disease) upward; 3 patients (one had a post-traumatic macular scar and a normal fellow eye, another had myopic macular degeneration in both eyes, with a small non-atrophic area at the posterior pole in one and extensive corioretinal atrophy occupying all the posterior pole in the other, while the third had vitelliform dystrophy in both eyes, with a larger atrophic area in one eye) maintained their primary gaze position, defined as the position of the eye when a patient is looking at a visual target that is straight ahead (Schuchard 2005).

All the patients displayed an improvement in visual acuity, fixation behaviour, retinal sensitivity and reading

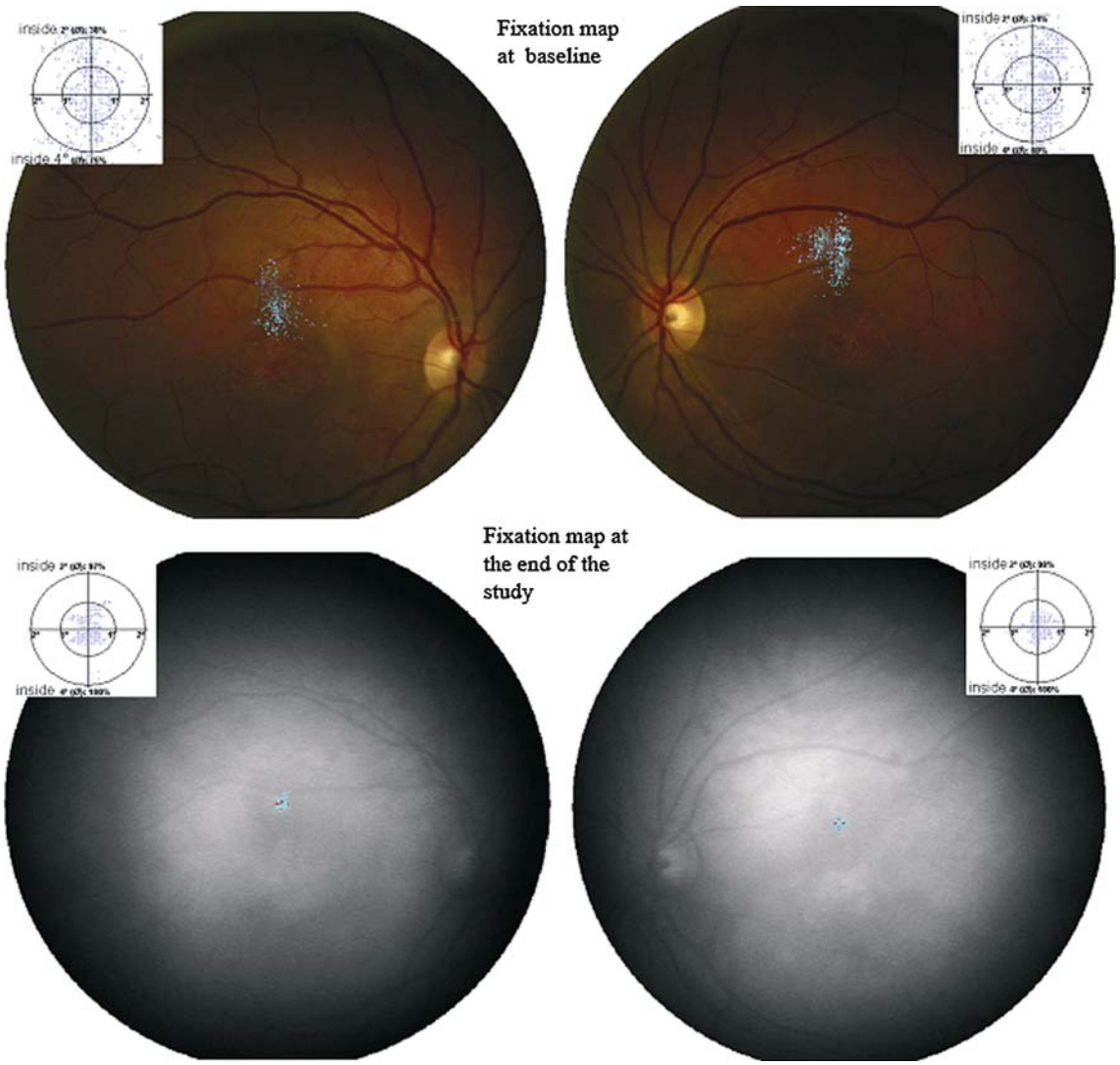

Fig. 1 Mp-1 images. The fixation map at baseline and the fixation map at the end of the study in patient number 5. For the selection of the PRL to be trained with biofeedback examination it was chosen an area of 2° diameter circle located, if possible, over the scotoma, with an appropriate retinal sensitivity to ensure the reinforcement of fixation behaviour and fluent reading (to read at least four letters). Fixation behaviour of the existing PRL was reinforced

speed, regardless of the size of the central scotoma, as shown in Table 1.

Visual Acuity

The mean best distance spectacle-corrected visual acuity (VA) was 0.81 ± 0.56 logMAR at the baseline assessment, and 0.54 ± 0.39 logMAR at the end of visual rehabilitation; this result was statistically significant ($p = 0.009$).

The mean character size value improved from 11.7 to 7.8; this result was statistically significant ($p = 0.03$). Improvement in distant visual acuity according to retinal sensitivity was statistically significant ($p = 0.0001$), while distant visual acuity related to fixation behaviour was not statistically significant ($p = 0.152$).

Reading Speed

Reading speed improved from a mean value of 64.3 words/min at the beginning of the study to 91.8 words/min at the end, and was accompanied by a decrease in the character size that could be read by the patient (from 11.7 to 7.8); this result was statistically significant ($p = 0.03$).

Subjective Changes

The first question patients were asked after the training period was: "did you benefit from the training?"; they were then asked: "did your reading improve after training?". The reply to these questions were in the form of "yes or no", all the patients replied yes.

Lastly, patients were asked to give examples from everyday life concerning changes after the training. As regards subjective changes, all the patients said their reading ability as well as independence had improved dramatically (they were able to read again some titles in the newspaper, or dial telephone numbers, or use the public transport after the training, etc.) and were very satisfied with the training.

Retinal Sensitivity

There was a considerable increase in the mean retinal sensitivity, as shown by a comparison of the microperimetry findings at the beginning and at the end of the study (see Table 1). This increase was statistically significant ($p = 0.005$). The increase in retinal sensitivity (retinal sensitivity was averaged over all points tested) was due to the fact that we trained patients to adopt a PRL ("retinal motor") with appropriate retinal sensitivity, to increase the number of correct fixation saccades and re-reference the oculomotor system, the other PRLs which showed low retinal sensitivity were automatically discarded, thus improving fixation behaviour.

Discussion

The aim of our study was to evaluate the efficacy of low-vision rehabilitation by means of MP-1 biofeedback examination in patients with different macular disease, and examine the relationship between PRL fixation stability and reading speed in patients with a central scotoma.

Macular diseases are ocular pathologies that affect the central retinal area, determining a reduction in visual acuity, contrast sensitivity, colour perception, ocular motility and altered stereopsis, and are accompanied by the appearance of scotomata in the visual fields and visual impairment.

It has been demonstrated a shift in the oculomotor reference from the fovea to a preferred eccentric retinal area is possible in patients with bilateral macular disease (Schuchard 2005; Alpeter et al. 2000).

Studies have described the use of multiple PRLs under different light conditions and for different tasks (Nilsson et al. 2003; Lei and Schuchard 1997; Steinman 1965; Crossland et al. 2004a, b). Patients are often unaware of how and when they use multiple PRLs (Crossland et al. 2005; Schuchard 2005; Fletcher and Schuchard 1997). The most basic eye movements made by the visual system are fixation, pursuit and saccadic movements. These tasks are believed to represent measurable parameters of the PRL quality for visual performance, i.e. to optimally function as a retinal locus for visual performance, the PRL needs to maintain the visual image in a discrete and stable retinal area, to track moving objects of interest in the visual field away from the PRL (saccadic movements) (Schuchard 2005).

These aspects of the PRL play an important role in the daily living activities of patients with maculopathies. The ability of the PRL to direct eye movements, whether it be saccadic ability (measured by the number and characteristics of saccades) or fixation stability, are far more closely correlated with reading speed and correct reading rate than either visual acuity or the presence of a scotoma (Schuchard 2005; Petre et al. 2000; Sunness et al. 1996; Cummings et al. 1985; Steinman et al. 1973; Whittaker et al. 1991). It is perhaps surprising that there is no correlation between scotoma size and fixation stability, as fixation is known to become less precise as eccentricity increases, and a larger scotoma will lead to a more eccentric PRL being used. Connection between visual acuity, central rentinal sensitivity and fixation stability has been demonstrated (Carpineto et al. 2007); a correlation between reading ability and fixation stability in patients with macular disease has been found (Crossland et al. 2004a, b).

Reading ability in patients with a central scotoma (whether dense or relative) is reduced. One of the objectives of visual rehabilitation with MP1 biofeedback is to allow low-vision patients to read again.

The new MP-1 microperimeter feedback examination allows the ophthalmologist to train the patient to fixate the target with the new PRL. Patients are asked to move their eyes according to an audio feedback which tells them whether they are getting closer to a fixation position chosen by the ophthalmologist. BFD training results allow a variety of optical aids to be used, such as prismatic lenses, spherical lenses, a high power optical magnifier and filters, because the patient performs better visually after training than before (Frennesson et al. 1995; Nilsson and Nilsson 1986; Romayananda et al. 1982).

Our results show that increased PRL fixation stability and retinal sensitivity improve reading speed and visual efficiency. Furthermore our experience with low-vision rehabilitation in patients with macular disease suggests that even if it is not possible in humans, at present time, to regenerate the affected retina, it could be possible to improve their residual vision, to restore a better visual performance and a much more positive psychological situation. All treated patients showed a good response after the treatment and asked us for new sessions.

Improvement trough BFD training in patients who suffer from macular disease which remain either stable or worsen, where the traditional treatment cannot offer further results, is of interest and well worthy of attention.

The reasons of this improvement are probably due to the fact that we trained a "retinal motor" PRL, with

appropriate retinal sensitivity, so as to increase the number of correct fixation saccades and re-reference the oculomotor system. The main drawback of our low-vision protocol using the MP-1 biofeeback examination is that the results obtained for both visual acuity and reading speed tended to lack constancy, but in our experience, five 10-min follow-up training sessions using the MP-1 BFD examination every 3 months are sufficient to maintain the visual performance achieved at the end of the protocol. Further studies are warranted to investigate the reasons underlying these results. The BFD effect is probably related to the brain's ability to perceive an efficient PRL for visual tasks. The audio feedback can, by increasing attentional modulation, help the brain fix the final PRL.

Sound perception increases the conscious attention of the patient, (Alpeter et al. 2000; Buia and Tiesinga 2006), thereby facilitating the lock-in of the visual target and increasing the permanence time of the target itself on the retina. This mechanism probably facilitates stimuli transmission between intraretinal neurons as well as between the retina and brain, where the highest degree of stimuli processing takes place, thereby supporting a "remapping phenomenon". Although cortical rearrangement, together with the resulting filling-in, may play an important role in the training of a PRL, this can happen for a variety of reasons, and further studies are needed to evaluate with specific evidence that a cortical remapping is responsible for it.

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