Visual rehabilitation with MP-1 biofeedback in advanced glaucoma: a cross-sectional study

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Abstract

PURPOSE: To evaluate the efficacy of visual rehabilitation with MP-1 Microperimeter biofeedback (NIDEK Technologies Srl, Padova, Italy) in advanced glaucoma to improve fixation stability, retinal sensitivity and reading speed.

METHODS: 16 patients (20 eyes) with advanced primary open angle glaucoma were submitted to rehabilitation protocol that consisted of: measurement of visual acuity; Reading Speed Test; Microperimetry with fixation study by BCEA (bivariate contour ellipse area) and retinal sensitivity. Rehabilitation protocol consisted of 10 training sessions, once a week, 10 minutes for each eye. Statistical analysis was performed
using the Student’s t-test, \( p \) values less than 0.05 were considered statistically significant.

**RESULTS:** at the end of rehabilitation protocol mean retinal sensitivity, BCEA and reading speed were improved; while BCVA had results no statistically significant.

**CONCLUSIONS:** Rehabilitation with MPI biofeedback is a useful means to improve the fixation stability of patients with advanced glaucoma, to stabilize PRL and to increase visual acuity improving the patient quality of life.

**Introduction**

Glaucoma is a complex disease that comprises a group of heterogeneous optic neuropathies characterized by a progressive degeneration of the optic nerve head and visual field defects.[1] It affects 70 million people and is the second leading cause of blindness worldwide. It is estimated that by the year 2020, this number would rise to around 79.6 million.[1] The prevalence of glaucoma varies widely across the different ethnic groups and is significantly higher in blacks (4.7%) than in the white population (1.3%).[2] POAG may be associated with or without an elevated IOP and has an adult onset (usually \( \geq 35 \) years) or juvenile onset (usually \(< 35 \) years).[3]

Glaucoma is characterized by irreversible damage to the retinal nerve fiber layer (RNFL) and ganglion cell layer with
corresponding typical visual field (VF) changes. [4] In the evaluation of glaucoma, RNFL thickness assessment is relevant, because thinning of the RNFL is directly correlated with loss of ganglion cells, which is assumed to be a primary site of glaucomatous damage.[5]

The management of patients with advanced glaucoma presents difficulties. Advanced glaucoma is considered to be enough loss of vision to produce significant symptoms and functional impairment that can include difficulty in performing visual tasks and tiring easily from those visual tasks. It is for these reasons that we thought to submit patients with advanced glaucoma to visual rehabilitation with MP-1 microperimeter (NIDEK Technologies Srl, Padova, Italy) biofeedback.

Through these methods, adopted in various branches of medicine, the patient learns in successive stages to appreciate the variations of a bodily function through a system that measures and converts these in acoustic and/or luminous signals; modify these signals and, therefore, the function connected to them; automatically control the function through practice even in the absence of the return signal.[6]

The purpose of this study is to evaluate the efficacy of visual rehabilitation with MP-1 biofeedback in patients with advanced glaucoma through the study of BCEA.

**Methods**

We have enrolled 16 patients (9 female and 7 male), who had come to Department of Ophthalmology A. Fiorini Hospital, “La Sapienza” University of Rome, with advanced open angle glaucoma and we have examined a total of 20 eyes, from January 2013 to March 2014. The mean patient age was 69 years old (range: 59–80 years old).

Were enrolled patients aged between 40 and 75 years, with diagnosis of glaucoma by at least 10 years, treated with hypotonic therapy. Patients with angle-closure and secondary glaucoma, previous corneal diseases, uveitis, vitreo-retinal interface diseases and retinal detachment were excluded.

The diagnosis of advanced glaucoma was based on a complete eye examination which included: biomicroscopic examination of
anterior and posterior segment, visual acuity, Goldmann applanation tonometry, gonioscopy with three mirror Goldmann lens, visual field (VF) examination by Octopus 30-2 static perimetry, Optical Coherence Tomography (OCT) Spectral Domain (Heidelberg HRA-2, TMB module Heidelberg, Germany) with RNFL study and pachimetry. Advanced glaucoma was defined as having either cup-to-disc ratio ≥ 0.7 or a cup-to-disc ratio asymmetry ≥ 0.2 between adjacent eyes, with a severely affected eye with best-corrected visual acuity below 20/200.

Institutional Review Board (IRB) approval and a written informed consent were obtained from all patients. All procedures adhered to the tenets of the Declaration of Helsinki.

All the patients underwent the same low-vision rehabilitation protocol which consisted of: the assessment of distance and near visual acuity, reading speed test (words/min), fixation test, microperimetry, 10 training sessions with MP-1 biofeedback with the study of BCEA.

Best distance spectacle corrected visual acuity (BCVA) was determined using Snellen chart, which was converted to logarithm of the minimum angle of resolution (logMAR) for statistical analyses; near visual acuity was determined at 30 cm with an appropriate addition.

The reading speed for each eye was measured by reading black letters on a white background (Times New Roman font) at 30 cm of distance with an appropriate addition.

Subjects were asked to read aloud as quickly as possible without skipping words (the size of the press corps has been adapted to the patient's visual acuity and was measured in electronic points). The sentences contained words that occur frequently in Italian and had no punctuation.

Microperimetry and fixation test were performed with MP-1 Microperimeter, NIDEK Technologies Srl, Padova, Italy, using the automated programme, the threshold test of 4–2 strategy, and a 2° single cross fixation target; however, at the beginning of the study the size was enlarged to a 3° single cross fixation target when patient was not able to see the 2° single cross fixation target. 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. Fixation stability was quantified by calculating a bivariate contour ellipse area (BCEA) encompassing 68% of fixation points based on collected fixation data by the MPI1 Microperimeter.

The rehabilitation protocol consisted of 10 training sessions of 10 minutes for each eye, performed once a week using the MPI1 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.

At the end of the rehabilitation, the assessment of distant and near visual acuity, reading speed test, fixation and microperimetry tests were repeated. Microperimetry was repeated with follow-up function, which automatically retests the retinal sensitivity in exactly the same locations and under the same conditions as in the previous examination.

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**

We have examined 16 patients (9 female and 7 male), for a total of 20 eyes, with advanced glaucoma from January 2013 to March 2014. The mean patient age was 69 years old (range: 59–80 years old). All participants completed the rehabilitation period. All patients had advanced glaucomatous visual field loss, with a mean deviation (MD) worse than -24 dB, having only a central or temporal island remaining in the VF gray scale, and clear evidence of glaucoma in the fellow eye (manifest as glaucomatous appearing discs and a glaucomatous VF).

Fixation stability, quantified by calculating a BCEA encompassing 68% of fixation points based on data collected by the MP-1 Microperimeter, became from $2.08 \pm 0.21 \text{deg}^2$ to $0.98 \pm 0.33 \text{deg}^2$ ($p=0.21$) and this result was statistically significant.
Mean retinal sensitivity became from $4.78 \pm 3.39$ dB to $8.87 \pm 5.44$ dB and this result was statistically significant ($p=0.035$).

The mean best corrected visual acuity (BCVA) was $0.76 \pm 0.32$ logMAR at the baseline assessment, and $0.84 \pm 0.60$ logMAR at the end of visual rehabilitation; this result was not statistically significant ($p=0.29$).

Reading speed improved from a mean value of $24.6 \pm 3.2$ words/minute at the beginning of the study to $48.9 \pm 2.5$ words/minute at the end of the training; this result was statistically significant ($p=0.037$).

**Discussion**

Glaucoma affects more than 60 million people worldwide; more than 10% are consequently legally blind in both eyes.[1]

The World Health Organization predicts that 44.7 million people will suffer from primary open-angle glaucoma (POAG).[7]

Abnormally high intraocular pressure (IOP) is related to the development of glaucoma.[8-9]

Comparative anatomy results suggest that the Schlemm’s canal, which connects the trabecular meshwork and collector canals, is a possible resistance point of aqueous humor outflow in primary open angle glaucomatous eyes.

Measurements of intraocular pressure and standard visual fields are the endpoints generally accepted by the FDA in evaluations of new therapies for glaucoma. Recently, we have seen that structural changes (e.g., in the optic disc measured by stereophotography) predict standard visual field outcomes.[10]

At the early stage of the disease, macular function is mostly spared. However, at the advanced stage, the scotoma threatens to the fixation area becomes particularly important.

At present, visual acuity testing, static and kinetic perimetry are used to monitor macular function of glaucoma patients. Visual acuity is a good indicator of foveal function, but it reveals only one aspect of macular function. Perimetry can show the functioning of individual retinal locations in the macula, but the number and location of the testing points might not be adequate to detect subtle changes around the fixation region and in advanced glaucoma reliable test results are difficult to obtain because of unstable fixation.
Advanced glaucoma is considered to be strong enough to produce significant loss of vision and functional impairment that create a hardship for patients. It’s for these reasons that we have tested the efficacy of MP-1 Microperimeter to improve the behaviour of fixation and to rehabilitate patients with advanced glaucoma. Takanori et al. investigated fixation behaviour in 39 eyes with advanced glaucoma using the MP-1 Microperimeter and they concluded that the MP-1 is able to illustrate the fixation patterns in glaucomatous eyes and that patterns are well correlated with retinal sensitivity.[11] Biofeedback applied to vision is still being studied both in its methodological and physiological aspects. Crossland et al. showed that the MP-1 Microperimeter uses cerebral plasticity and neurosensorial adaptation to the central scotoma of patients with macular diseases to improve their visual abilities and 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 and usually not the most profitable considering retinal sensitivity.[12] Contestabile, Vingolo, Giorgi, Mezawa et al. [6,13-15] have all proposed different visual rehabilitation techniques and instruments using biofeedback strategies starting from basic systems like Accomotrack Vision Trainer (which is a high-speed infrared optometer which records the vergence of light reflected from the retina at a rate of 40 Hz, than converts the signal into an auditory tone which increases in pitch and rate as accommodation decreases; the subject listens to the tone and thus receives immediate auditory feedback as to his/her accommodative status) or improved biofeedback integrated system (IBIS) devices, merging to more complex instruments as the fundus related MP-1 Microperimeter (NIDEK Technologies Srl, Padova, Italy). The MP-1 Microperimeter biofeedback examination allows the ophthalmologist to train the patient to fixate the target with a new PRL. Patients are asked to move their eyes according to an audio feedback which tells them whether they are getting closer to a
specific retinal region chosen by the ophthalmologist. Sound perception increases the conscious attention of the patient, thereby facilitating the lock-in of the visual target and increasing the permanence time of the fixation 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”.[16-17] Techniques of biofeedback have been performed in the treatment of ametropia (myopia, astigmatism, presbyopia), nystagmus and amblyopia.[15, 18-19] Various studies have demonstrated that a bivariate contour ellipse area (BCEA) can describe the locus of fixation in normal and affected individuals.[20-22] The area of this ellipse gives an indication of fixation stability, with larger areas corresponding to poorer fixation stability. The parameters of both measurements are now incorporated within the MP-1 test report. We have chosen to study fixation with BCEA because the Fujii classification has significant limitations: it does not make allowances for the typical elliptical nature of fixation distributions.[23] or for the multimodal fixation patterns frequently exhibited by people with macular disease.[24-26] It cannot differentiate between a subject who has good fixation within 2 discrete, yet spatially distant, retinal loci and one who has genuinely poor fixation, and it is very poorly related to any parameter of reading.

Studies have demonstrated the efficacy of low-vision rehabilitation by means of MP-1 biofeedback examination in patients with different macular disease and they demonstrated an improvement in visual acuity, fixation behaviour, retinal sensitivity and reading speed.[13] Some authors have evaluated the visual training biofeedback with Visual Pathfinder (LACE inc.) system in patients with high myopia and retinitis pigmentosa.[28-29] Various hypotheses regarding the mechanisms of visual function improvement after visual training techniques can be put forth. There could be improvement in ocular motor control and in 'searching capacity'.
Furthermore, learning to use eccentric fixation could be a mechanism contributing to amelioration [29]. In particular it is very important to note that visual function could be improved because patients undergoing training improve their ability to demonstrate their best visual acuity and other visual abilities.

Sabel et al. proposed the "residual vision activation theory" of how visual functions can be reactivated and restored.[30] The possibility and to what extent vision restoration can be achieved is a function of the amount of residual tissue and its activation state. Sustained improvements require repetitive stimulation which may take days or months.

Surely a certain role in the determination of the results could be due to subjective variables such as learning effect, motivation, level of attention, psycho-physical capacities, kind of environment and influence of the examiner. Connection between visual acuity, central retinal sensitivity and fixation stability has been demonstrated.[31]

In this study we wanted to demonstrate that it is possible to apply visual rehabilitation with MP-1 biofeedback also to patients with advanced glaucoma obtaining satisfactory results. In fact, an increased fixation stability and retinal sensitivity improve reading speed and visual efficiency. We also evaluate the utility of BCEA to assess visual function in advanced glaucoma. This bivariate contour ellipse area (BCEA) provides a precise continuous value for fixation stability, with smaller values corresponding to more stable fixation.[22] In the past decade, reports arising mostly from Germany have suggested that a specific pattern of visual stimulation directed to the border between the seeing and the blind field, Vision Restoration Therapy (VRT), can result in expansion of visual fields in those with brain or optic nerve injury.[32-33] Romano et al. demonstrated that visual restoration therapy (VRT) improves stimulus detection and results in a shift of the position of the border of the blind field as measured on suprathreshold visual field testing. These results support prior reports and support VRT as a useful rehabilitative intervention for a
The possibility and to what extent vision restoration can be achieved is a function of the amount of residual tissue and its activation state. Sustained improvements require repetitive stimulation which may take days or months.

Our experience with low-vision rehabilitation in patients with advanced glaucoma suggests that it could be possible to improve their residual vision, to restore a better visual performance and a much more positive psychological situation. These results confirm the usefulness of BCEA to achieve better analytical study and more accurate classification of the fixation pattern using microperimetry. It is important to highlight the strict correlation between BCEA fixation values with reading speed. In conclusion, the implementation of BCEA measurement in MP1 may result in a more accurate evaluation of the efficacy of visual rehabilitation and/ or medical or surgical treatment in patients with advanced glaucoma.

Would be desirable to perform studies with a larger number of patients to confirm the significance of the data.
Figure 1. MP-1 image of fixation at baseline (a) and after 10 training sessions (b) of one patient’s left eye submitted to rehabilitation protocol.

Figure 2. Interpolated image of microperimetry MP-1 before (a) and after (b) rehabilitation with the study of the BCEA.
References


