Purpose: Low vision rehabilitation in advanced optic nerve damage was described previously in several reports demonstrating its positive effect in improving visual performances. Initially proposed simply as magnification system (optical and optoelectronics), in actual clinical practice new diagnostic and informatic tools helped the patient as active tasks for visual function recovery. Microperimetry allows to follow up the progression of the disease, to exactly localize position shape and deepness of the scotoma and finally to have a precise localization and evaluation of fixation. The goal of our study is to assess in a selected population of advanced glaucoma patients if microperimetric biofeedback may be able to restore partially some visual tasks.

Materials: Were selected 10 patients (18 eyes) with advanced primary open angle glaucoma that underwent to a rehabilitative protocol as follows: visual acuity evaluation, reading speed, microperimetry, fixation analysis (BCEA or Bivariate Contour Ellipse Area). Each patient scheduled 10 sessions of biofeedback for eye (10 minute each), recall of biofeedback schedule was reproposed at month 4-8-12. Statistical analysis was performed with double tailed T test student and Spearman to correlate reading speed and visual acuity with retinal sensitivity.

Results: Mean visual acuity at baseline was 0.98 ± 0,66 logMAR and at the end of scheduled protocol was 0,75 ± 0,60 logMAR; this value was statistically significant (p>0.05); reading speed was 31,4 ± 4,3 w/m at baseline and 55,6 ± 3,2 w/m at the end of training (p<0.05).

Conclusions: Biofeedback rehabilitative strategy was certainly useful for advanced glaucoma patients in terms of visual acuity and retinal sensitivity; it causes a very impressive change in visual expectance of the patients determining a better quality of life.
INTRODUCTION

Glaucoma is a chronic degenerative disease in which main clinical signs are optic nerve head damage with visual field alterations and high intraocular pressure. In late stage, when central portion of visual field has damaged, clinician looses one of the main parameters to evaluate disease progression and the patient experiences a very heavy loss in visual function that determines a limitation in common tasks and daily activities.

In our study, we attempt to reduce the impact of visual field alterations in patients with late phase glaucoma, with the goal of reducing visual difficulties, by the mean of newly designed biofeedback strategies with MAIA microperimeter (Centervue, Padua – Italy). This technique, presenting luminous stimulus, allows us to train fixation tasks, if necessary, or to select a new Preferential Retinal Location (PRL) in patients with loss of central fixation. Acoustic feedback indicates to the patient if Target Retinal Location (TRL) and fixation stability has reached. Biofeedback technique gives patient the knowledge of his fixation location and the frequency of sound indicates how far from the target zone is patient looking. In this study were evaluated best corrected visual acuity (BCVA), reading speed, fixation stability and localization with particular regard to the Behaviour Contour Ellipse Area (BCEA).

The aim of the study is to evaluate if, scheduling repeated sessions of microperimetric biofeedback, with MAIA, we may be able to improve visual performances of late stage glaucoma patients to obtain better quality of sight.
MATERIALS & METHODS

Were selected 10 patients affected by late stage primary open angle glaucoma: 7 male and 3 female mean age 65.12 years (between 59 and 71 yrs), a total of 18 eyes were examined, enrolled in UOC Oculistica Universitaria in the “A. Fiorini” Hospital Terracina Italy.

Inclusion criteria were: age included between 40 and 75 years, glaucoma diagnosis at least 10 years before the visit, cup disk ratio higher than 0.7 or asymmetry between eyes higher than 0.2, instruction level at least high school.

Exclusion criteria were primary glaucoma narrow angle, previously performed vitreoretinal surgical intervention, eye disease cornea, uveitis, vitreo-retinal diseases.

All patients underwent biomicroscopic examination of anterior and posterior segment, visual acuity evaluation, Goldmann applanation tonometry, gonioscopy (Goldmann lens), automated computerized perimetry (Humphrey HFA) threshold test 30-2, Optical Coherence Tomography (Heidelberg HRA, TMB module; Heidelberg-Germania) to evaluate retinal and RNFL layer thickness. Visual acuity in the worse eye was at baseline lower than 20/200, MD higher than -24 DB. At baseline was measured BCVA, for near and distance, data were evaluated as logMAR for statistical purpose. Near visual acuity was measured in CP on a randomized computerized text black on white mean difficulty for a common reader in Italian, MN-Read text in Italian was chosen for reading speed measurements. Each eye was tested singularly.

Microperimetry tested single point retinal sensitivity with MAIA microperimeter (CenterVue, Padua, Italia), 10-2 automatic program, 4-2 threshold strategy fixation point was single 1°. For highly impaired patients, which were not able to perceive this dimension, we increased progressively size (2°) and thickness. Goldmann III size white test on a white background was used, intensity varied from 0 dB and 36 dB, presentation time was 200 ms. On same Microperimetry we automatically evaluated fixation according Fujii classification and BCEA surface expressed in square degree to obtain a quite-normal distribution of values.

Rehabilitative protocol was scheduled as follows: session lasts 20 min once a week, for 10 weeks, Biofeedback training sessions were performed with MAIA microperimeter. These sessions were repeated at 4, 8 and 12 months. During each session, first step was fixation training toward foveal reflex with an acoustic feedback that allows to the patient knowing how they are looking; if fixation was efficient the sound was high, while when the gaze was far from the fixation point the sound became discontinuous and weaker: each session was monitored on line.

At the end of rehabilitative protocol (12 months) all patients were examined again: far and near BCVA, reading speed, microperimetry and fixation examination. Microperimetry was performed with follow-up strategy, in which each point was tested exactly in the same position and in the same illumination conditions of the previous examination (obtained through ROI localization on the retina).

Statistical analysis was performed with double tailed t-test Student, values p<0.05 were considered statistically significant. Spearman correlation was used to relate retinal sensitivity to BCVA and reading speed.
RESULTS

All patients completed the scheduled rehabilitative protocol. After that 13 eyes (72.22%) on 18 showed an improvement. Mean BCVA at baseline was 0.98 ± 0.66logMAR at the end was 0.75 ± 0.60 logMAR (p=0.32, not statistically significant).

Reading speed statistically progressed from a mean value of 31.4 ± 4.3 words/minute at baseline to 55.6 ± 3.2 w/min at the end of training (p=0.031). Also mean retinal sensitivity improved from 7.43 ± 8.28 dB to 8.33 ± 9.04 dB this values were statistically significant (p=0.022).

Fixation evaluation showed improvement both in terms of stability and in localization. Fuji mean values were P1=27% P2=77% at baseline and at P1=77% P2=93% after 12 months (p<0.05); these values were statistically significant. BCEA calculation presented a reduction in shape and size in a statistically significant way from 63% = 9.6 deg²; and 95% = 34.13 deg² to 63% = 4.03 deg²; and 95% = 17.03 deg² (p < 0.05).

Spearman correlation showed positive relationships between single point retinal sensitivity and visual acuity and reading speed (r=0.58).

1. Above, on the left: sensitivity map before the training; on the right: sensitivity map after the training. It can be observed an improvement of retinal sensitivity as well as fixation behavior after the visual rehabilitation. Below: Before: instable F.: P1:29%, P2:71%; after: relatively unstable F.: P1:70%, P2:88%.
DISCUSSION

Glaucoma is one of main causes of acquired blindness worldwide\(^49\). It is an asymptomatic disease especially in the early stage of its onset. Visual field deficit departs from the blind spot as Bjerrum scotoma and at a late phase of the disease resulting in a concentric reduction with foveal diminution in retinal sensitivity, which is so deep to determine functional damage that hampers common daily activities of the patient and to limit his autonomy\(^10\).

In our study, conducted on late stage glaucoma, patients tested biofeedback visual rehabilitation performed by MAIA strategy. The study population presented a statistically significant improvement of visual performances at the end of the rehabilitative protocol. Namely in reading speed and fixation stability, it was demonstrated the reduction of BCEA, meaning that fixations saccades oscillation was concentrated after the training.

In clinical practice, biofeedback training stabilizes, during several sessions, the PRL that becomes TRL, which is the new area of retina more useful to be finalized in better vision\(^4,17,18\). Our used standard procedure, overlapping fundus images, allowed to choose better function area clearly stressed out by the fixation cloud; this area must contains at least four consecutive letters to have a good reading speed (preferably localized in the upper retina and horizontally as near as possible to the fovea)\(^44\). As a consequence of biofeedback training and stimulation, new TRL determines improvement in near visual acuity and reading speed\(^11,12\).

These results confirm the utility of this technology in late stage of glaucoma. This system takes in advantage cerebral plasticity, passing towards a remodeling of ganglion cell synapses\(^2\). Moreover, neurosensorial adaptive tasks allow to override the lesions utilizing horizontal connections departed from other retinal eccentric regions; at the same time, the start of new fixation strategies overlay the optic nerve lesion, with the aim to obtain an improvement in visual abilities\(^2,14\). It is clear that visual rehabilitation is not only an intraocular rearrangement, but also involves brain’s upper level of neurosensorial connections.

For a long time, visual loss caused by retinal lesions or by cerebral damage was considered not reversible. Nevertheless, more studies on animals and humans in last ten years, demonstrated that there is a very high plasticity in the neural system that remains also in older patients. According to “neurosinaptic plasticity theory”, it is possible to stimulate formation of new synapses improving neurofunctional and neurovisual performances towards retinal or cortical training performed by different devices. In this way, via horizontal or amacrine cells would be possible to stimulate areas near to the lost fovea having better visual outcomes\(^41,42,56\).

In glaucoma patients, visual training determines better functioning and recruitment of undamaged areas leading to recovery of sharpness, contrast sensitivity and faster lock-in time in the visual saccades, either near damaged fibers or in immediately surrounding areas\(^40,46,47,48\).

Recent study conducted on glaucoma patients demonstrated that visual loss, even in advanced glaucoma, may be not permanent but it could be possible to reverse the retinal-cortical transmission via surviving ganglion cells situated in deeper retinal or cortical areas.
Iterative and repetitive stimulation are able to speed up intra fibers bioelectrical transmission requiring different scheduling depending from visual resources. Several studies are still required to investigate visual recovery in these clinical conditions with EEG and MRI\textsuperscript{31,53}.

Nevertheless positive results obtained in several studies, individual capabilities to maintain visual performance are still a chimera because most of the patients loose the achieved better performances after few months (4-6), so that recalling sessions need to be scheduled regularly to have a stable visual performance.

Finally, in this study microperimetry prove to be a good technical device. Eye-tracker allows a precise rendering of fixation spots, so that it is very easy to train a new PRL obtaining good functional results. More than 70\% of patients showed an improvement of functional visual tasks and they noted a real improvement in their quality of vision.

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