



Computerized evaluation of deambulatory pattern before and after visual rehabilitation treatment performed with biofeedback in visually impaired patients suffering from macular degeneration

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Abstract

Aims: The aim of this study was double: the primary endpoint was to evaluate the efficacy of visual rehabilitation of visually impaired patients with macular degeneration (AMD). The secondary endpoint was to assess the effect of rehabilitation treatment on the ambulatory pattern using a computerized evaluation of walking, focusing the attention on space-time parameters that are influenced in patients with visual impairment.

Methods: 10 patients with AMD were enrolled, 6 males and 4 females, and examined 15 eyes, at Department of Sense Organs, Faculty of Medicine and Dentistry Sapienza University of Rome, Italy.

Visual rehabilitation was carried out with the use of a microperimeter MPI using the examination of biofeedback. Patients are asked to move their eyes in coordination with an audible feedback that alerts the patient when he is setting properly the fixation target previously selected. All patients were subjected to 10 sessions lasting 15 minutes each for each eye, 1 time per week. The best corrected visual acuity (BCVA) was assessed by far with the ETDRS optotype IN LOG MAR, and by close to 25 cm by adding + 4 ball (addition to near) to the BCVA. For each eye the PB (print body) on the distance of 25 cm was measured; Its fixation stability for 30 seconds was examined by microperimeter. Gait Analysis was performed with system ELITE BTS SpA (Milan, Italy).

Results: At the end of the rehabilitation treatment with biofeedback it was found a marked improvement in BCVA. The BCVA before the rehabilitation treatment was ETDRS 12 LETTERS = 0.86 logMAR. At the end of the visual rehabilitation 16 LETTERS = 0.78 logMAR. The near visual acuity presented a decrease of the printer body measurement (PB) and a statistically significant improvement in the fixation stability.

Analysis of the spatial and temporal parameters of gait cycle, aimed at assessing the global aspects of gait (speed, rhythm, symmetry, fluidity, dynamic balance) showed no significant changes after the treatment, indicating that the previously structured locomotor pattern was not modified.

Conclusions: The results obtained by the visual rehabilitation with Biofeedback show a pronounced and statistically significant improvement in visual performance. In fact, the absolute values of retinal sensitivity before and after the visual rehabilitation cycle with biofeedback showed a marked improvement of the specific retinal sensitivity and consequently an improvement of the vision efficiency. Further studies are needed to better understand the "correlation" between low-vision and walking.

Keywords: Biofeedback; visual rehabilitation; AMD; best corrected visual acuity; microperimeter MPI; Gait Analysis

Introduction

The increase in life expectancy in many countries and the increase in quality of life has led scientific community to engage in studies to increase the visual performance in visually impaired subjects Friedman et al (2004) [1] estimated that 1.75 million individuals in the US suffer from macular diseases and that about 15% of these are aged more than 90 years. In addition, the World Health Organization (WHO) estimated that 8 million people are visually impaired due to age related macular degeneration (AMD). AMD is set to become the most frequent cause of low vision in old age, with around 30% of people over 75 affected. The currently etiology is still debated [2]. Numerous therapies have been taken into account to limit AMD development [3]. In particular, the visual rehabilitation in low vision patients with AMD has allowed to maintain a visual functional residual greater than 1/10 [4].

Rehabilitation treatment makes use of resources designed to specialize the vicarious macula or preferential retinal location (PRL) to replace the damaged one [5]. In the past years, several techniques of visual rehabilitation using biofeedback have been proposed, from simpler systems like accomotrack or IBIS, to more complex systems such as the visual path-finder [6]. Recently, the introduction of new technologies developed with the device MP1 (microperimeter), led to better knowledge of the cognitive process of rehabilitation and a better diagnostic approach for follow up of patients with AMD [7]. An efficient PRL needs to maintain a stable image in a visual area (Schuchard 2005) [8]. Biofeedback (BF), synonymous with "biological feedback", consists of a self-regulating technique, used in medicine and in psychology, to gain control of functions of an organ (visual, tactile) or involuntary psychic reactions, with the aid of sophisticated devices that make perceptible the variations of these functions [9]. These devices, through an acoustic, visual or tactile detection system, directly and faithfully show the slightest variation in functions of the organ investigated, so that the subject may be aware of and exert voluntary control over it [10].

Initially, the possibility of voluntary control of accommodation in the use of biofeedback in ophthalmology has been studied in NASA pilots at the end of the 60s, in the US, by the Stanford Research Institute [11]. The feedback control was based on signal processing in sound stimulus: refractive change resulted in a change in the frequency of the sound recognizable by the subject. The results obtained from Randle3 (1970) [12], about the possibility of learning the tune voluntary control of accommodation have been encouraging. This was reported by numerous ophthalmological studies, as demonstrated by Nakao (1999) [13].

Mezawa (1990) [14] found positive responses in patients with congenital nystagmus after treatment with acoustic biofeedback. The studied parameters included the foveation time, the amplitude and frequency shown after completion of the training. In all patients it was found subjective improvement of their vision when they suppressed their nystagmus. Mezawa (1990) and Giorgi (2005) in 110 patients (179 eyes) with decreased visual acuity for different causes has undergone visual rehabilitation with IBIS (improved biofeedback integrated system) resulting in improved visual acuity in 130 eyes of 179 (72 , 62%).

The perception of sound increases the patient's conscious attention Buia C.8 (2006) [15], where it facilitates the visual lock on the fixation target and stay on the same target on the retina. The likely mechanism facilitates the transmission of stimuli between intraretinal neurons, as best between the retina and the brain. Vingolo E.M.9 (2006) [16] reports that 10 minutes of training with micro perimeter MP1 biofeedback per session for 10 sessions in patients with AMD showed a marked and statistically significant improvement in visual performance.

The aim of this study was double: the primary endpoint was to evaluate the efficacy of visual rehabilitation of visually impaired patients with macular degeneration. After a cycle of training orthotic sessions, a BIOFEEDBACK method through the use of microperimeter MP1 was used to increase the fixation stability of the new PRL (macula vicarious) to replace the damaged one. This method helps the patient to reorganize his oculomotor system and increase the permanence of images on the retina, thus promoting whole visual function.

The secondary endpoint was to assess the effect of rehabilitation treatment on the ambulatory pattern using a computerized evaluation of walking, focusing the attention on space-time parameters that are influenced in patients with visual impairment.

Materials and Methods

10 patients with AMD were enrolled, 6 males and 4 females, and examined 15 eyes, at Department of Sense Organs, Faculty of Medicine and Dentistry Sapienza University of Rome, Italy. the age of patients ranged from 55 to 79 years. Informed consent was obtained from patient. The study adhered to the tenets of the Declaration of Helsinki for research involving human subjects.

All patients underwent comprehensive examination of the anterior and posterior segment of the bulb, evaluation of the IOP and instrumental examinations of the retinal morphology, optical coherence OCT and microperimetry.

The best corrected visual acuity (BCVA) was assessed by far with the ETDRS optotype IN LOG MAR, and by close to 25 cm by adding + 4 ball (addition to near) to the BCVA. For each eye the PB (print body) on the distance of 25 cm was measured; It fixation stability for 30 seconds was examined by microperimeter.

Microperimetry and fixation of the macular area performed with MP1 made use of a software with automatic correction of eye movement. We evaluated the fixation behavior, the position and the stability of PRL. Visual rehabilitation was carried out with the use of a microperimeter MP1 using the examination of biofeedback. Patients are asked to move their eyes in coordination with an audible feedback that alerts the patient when he is setting properly the fixation target previously selected. All patients were subjected to 10 sessions lasting 15 minutes each for each eye, 1 time per week.

The Microperimeter MP-1 integrates into a single instrument subjective data of computerized perimetry and the objective data of retinal images, obtaining accurate, repeatable and fully automatic measurements of retinal and macular functions [17].

Laboratory equipment GAIT ANALYSIS

The system designed for this study, system ELITE BTS SpA (Milan, Italy) [18], is installed in the Laboratory of Gait Analysis in the Department of Sciences of Locomotor Apparatus, Medical Chair of Physical and Rehabilitation at the "Sapienza "University of Rome.

This system has been conceived for the study of Movement Analysis, which provides for the acquisition of the kinematic data, dynamic and synchronized electromyography ,and it allows to visualize in three dimensions the gait of the subject.

Results

Gait Analysis Data

Gait analysis data are reported in **Table 1**.

Rehabilitation Data with Biofeedback

Statistical rehabilitation data are shown in **Table 2**. At the end of the rehabilitation treatment with biofeedback it was found a marked improvement in BCVA. The near visual acuity presented a decrease of the printer body measurement (PB) and a statistically significant improvement in the fixation stability.

Visual acuity by near

For the near visual acuity, the PB value decreased from 22 to 14 (**Fig. 1**)

Visual acuity by far

The BCVA before the rehabilitation treatment was ETDRS 12 LETTERS = 0.86 logMAR. At the end of the visual rehabilitation 16 LETTERS = 0.78 logMAR (**Fig. 2**)

Fixation Behavior

In fixation tests the difference between the averages before and after the rehabilitation treatment is statistically significant ($p = 0.022$). This is the most significant parameter statistically (**Figs. 3, 4**).

Table 1. Gait analysis data

| Pre | Stride leng dx | Stride length sx | Step width dx | Step width sx | Stance duration dx% | Stance duration sx% | Double support time dx | Double support time sx | Mean sp | cadency |
|-------------|-------------------|------------------------|-------------------|------------------|---------------------------|---------------------------|------------------------------|------------------------------|----------------|-----------------|
| 1 | 0,984 | 0,899 | 0,122 | 0,148 | 67,4 | 66,7 | 0,256 | 0,2 | 0,73 | 92,346 |
| 2 | 1,094 | 1,059 | 0,119 | 0,109 | 61,7 | 63,6 | 0,19 | 0,14 | 0,933 | 103,815 |
| 3 | 1,06 | 1,093 | 0,115 | 0,14 | 62,8 | 59,8 | 0,123 | 0,157 | 0,856 | 95,452 |
| 4 | 1,176 | 1,172 | 0,168 | 0,18 | 58,6 | 58,4 | 0,107 | 0,113 | 0,979 | 100,084 |
| 5 | 1,144 | 1,142 | 0,169 | 0,21 | 58,5 | 59 | 0,088 | 0,074 | 1,154 | 121,33 |
| 6 | 0,927 | 0,951 | 0,124 | 0,129 | 56,7 | 60,9 | 0,09 | 0,088 | 0,725 | 92,774 |
| 7 | 0,91 | 0,872 | 0,094 | 0,123 | 64,4 | 65,1 | 0,243 | 0,173 | 0,676 | 90,707 |
| 8 | 1,345 | 1,306 | 0,136 | 0,131 | 58,4 | 57,9 | 0,09 | 0,077 | 1,349 | 122,062 |
| 9 | 0,88 | 0,88 | 0,16 | 0,131 | 63,1 | 64 | 0,172 | 0,125 | 0,51 | 110,1 |
| 10 | 0,862 | 0,862 | 0,146 | 0,153 | 61,6 | 59,7 | 0,11 | 0,14 | 0,712 | 99,021 |
| mean | 1,0382 | 1,0236 | 0,1353 | 0,1454 | 61,32 | 61,51 | 0,1469 | 0,1287 | 0,8624 | 102,7691 |
| post | | | | | | | | | | |
| 1 | 0,937 | 0,816 | 0,111 | 0,129 | 70,6 | 61,1 | 0,195 | 0,285 | 0,63 | 74,929 |
| 2 | 1,108 | 1,095 | 0,104 | 0,099 | 60,9 | 65 | 0,18 | 0,155 | 0,927 | 100,939 |
| 3 | 1,11 | 1,05 | 0,14 | 0,116 | 64,6 | 62,1 | 0,13 | 0,135 | 0,68 | 105,9 |
| 4 | 1,149 | 1,18 | 0,203 | 0,167 | 58,7 | 60,2 | 0,09 | 0,1 | 1,031 | 106,165 |
| 5 | 1,15 | 1,08 | 0,21 | 0,179 | 60,9 | 66,6 | 0,137 | 0,124 | 0,81 | 118,8 |
| 6 | 0,981 | 1,002 | 0,115 | 0,107 | 59,1 | 55 | 0,09 | 0,088 | 0,822 | 99,514 |
| 7 | 0,958 | 0,91 | 0,092 | 0,115 | 64,3 | 66,4 | 0,2 | 0,2 | 0,667 | 85,754 |
| 8 | 1,063 | 1,03 | 0,115 | 0,12 | 62,2 | 62,2 | 0,195 | 0,14 | 0,835 | 95,611 |
| 9 | 0,826 | 0,852 | 0,144 | 0,16 | 59,8 | 63,3 | 0,15 | 0,14 | 0,694 | 99,18 |
| 10 | 0,5 | 0,391 | 0,159 | 0,143 | 60,8 | 59,6 | 0,112 | 0,13 | 0,823 | 108,746 |
| mean | 0,9782 | 0,9406 | 0,1393 | 0,1335 | 62,19 | 62,15 | 0,1479 | 0,1497 | 0,7919 | 82,86437 |
| P | 0,22216 | 0,14822 | 0,59214789 | 0,0452311 | 0,2451312 | 0,63307632 | 0,947868374 | 0,092637327 | 0,33556 | 0,426948 |

Table 2. Statistical rehabilitation data

| Analysis | Visual acuity by far pre | Visual acuity by far post | Visual acuity by near pre | Visual acuity by near post | Fixation pre | Fixation post |
|------------------------------|--------------------------------|---------------------------------|---------------------------------|-------------------------------------|-----------------|------------------|
| Number | 15 | 15 | 15 | 15 | 15 | 15 |
| Mean | 12,47 | 15,67 | 21,47 | 15,07 | 55,60 | 80,00 |
| Standard Dev. | 10,10 | 11,29 | 15,15 | 8,36 | 33,23 | 20,42 |
| T | 0,8183 | | 1,4323 | | 2,4228 | |
| Degrees of freedom | 28 | | 28 | | 28 | |
| P (level of significance) | 0,420072 | | 0,163118 | | 0,022122 | |

Figure 1. Visual acuity by near

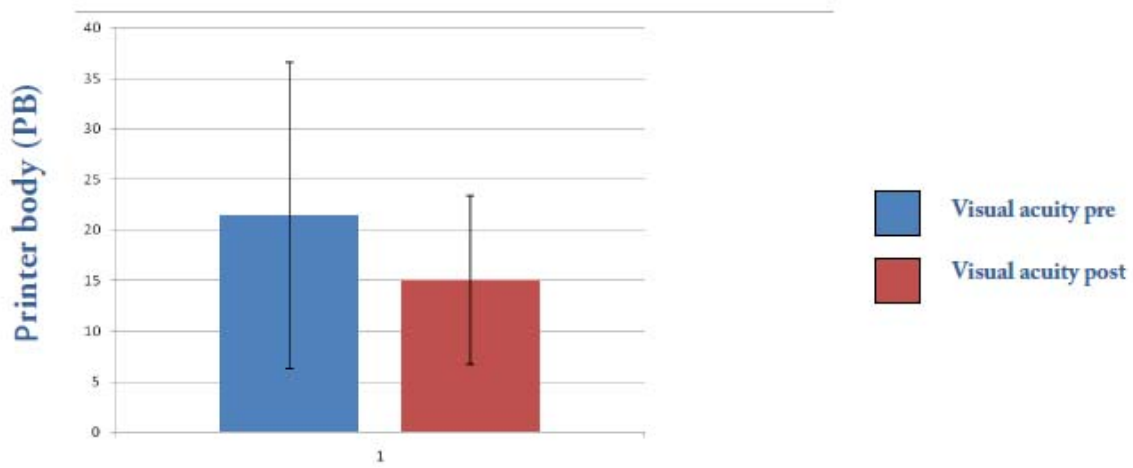


Figure 2. Visual acuity by far (4 meters)

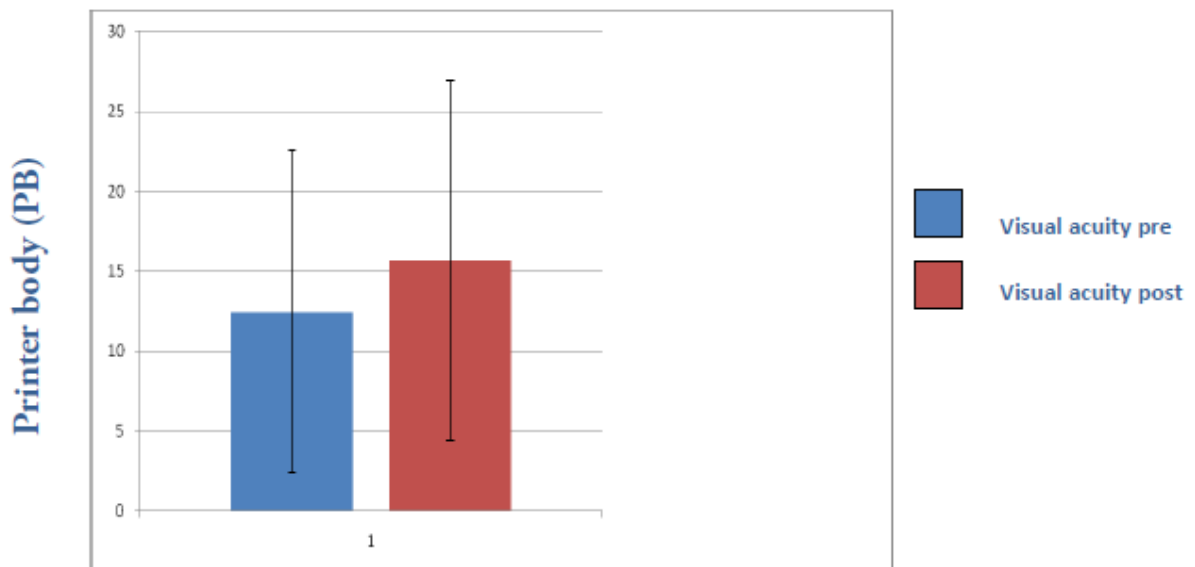


Figure 3. Microperimetry: ellipse concentration of fixation

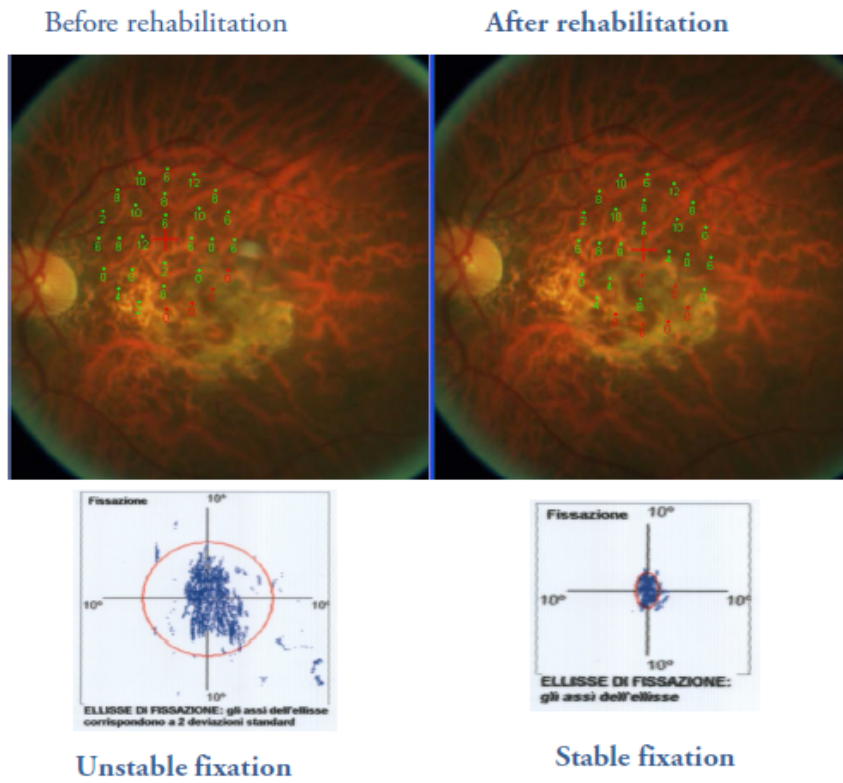
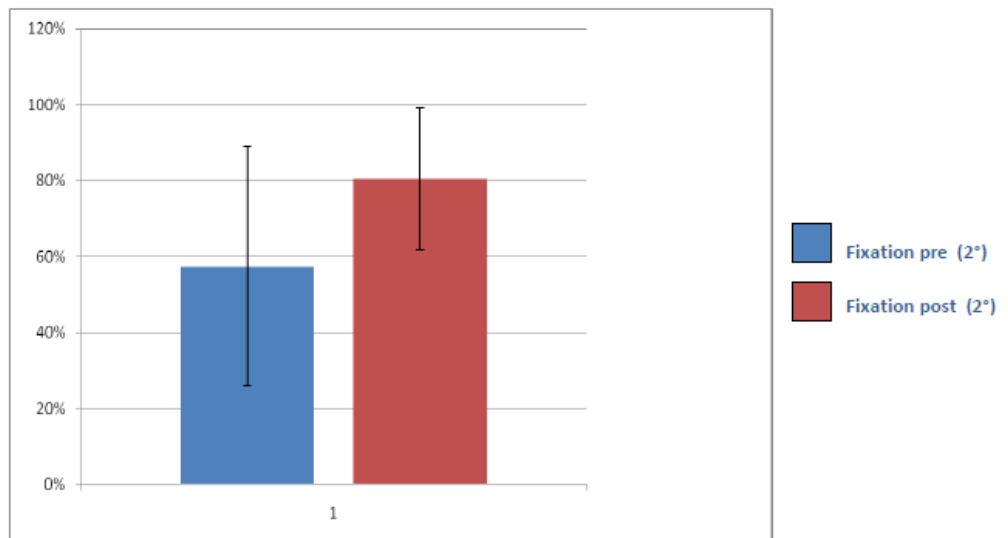


Figure 4. Fixation Behavior (%)



Discussion

Probably more than in any other field of medicine, clinical practice in ophthalmology has been enhanced by technological innovation and in particular by the recent progresses occurred in electro-optical field [19].

Surely the application of biofeedback in ophthalmology is an aspect of this reality. As already pointed out, biofeedback can be defined as "A technique capable of increasing the ability of an individual in the voluntary control of physiological functions through the use of devices that make perceptible variations of the same function" [20].

While the results concerning the application of biofeedback in the treatment of blepharospasm, strabismus, nystagmus are still controversial, those obtained by this technique of visual rehabilitation in patients suffering from retinal diseases, particularly macular and nerve optical diseases, are interesting [21-24].

It is well known that the majority of diseases involving the retina and optic nerve determine a reduction of visual acuity often associated with campimetric deficits. The resulting visual deficits are in most cases irreversible.

Because of these therapeutic limitations, biofeedback has been also developed in ophthalmology with the aim to improve the visual discomfort in low vision patients [25].

Microperimetry is an important instrumental examination that allows assessment of the sensitivity of retinal points in different diseases of the retina, to determine the position of total or relative scotoma, and to evaluate the location and stability of the PRL [26]. Microperimetry has also become an indispensable method in visual rehabilitation, and to follow the evolution of the eye retinal function [27].

It is assumed, by the results emerging in patients with macular degeneration who learn to perceive the visual stimulus no longer on the damaged foveolar cells, but on the healthy ones from the surrounding areas, that learning the use of eccentric fixation is the most plausible mechanism to explain the visual improvement in patients treated with biofeedback.

Conclusions

Analysis of the spatial and temporal parameters of gait cycle, aimed at assessing the global aspects of gait (speed, rhythm, symmetry, fluidity, dynamic balance) showed:

- average speed of the lower path compared to the reference range, for the simultaneous presence of a reduced rate and reduced step length;
- symmetry of the spatial (step length) and temporal

(duration of support) parameters;

- slight widening of the supporting base and slight extension of the bipedal support phase.

These elements suggest a gait strategy well organized from the space-time point of view, with slight deviations from normality attributable to a compensatory strategy for low vision, with a tendency to preferentially use mechanically stable configurations (bipedal support, enlarged basis) [28]. The post-treatment evaluation does not show significant changes, indicating that the previously structured locomotor pattern has not been modified.

The results obtained by the visual rehabilitation show a pronounced and statistically significant improvement in visual performance. The experimental data obtained in our population were interesting; In fact, the absolute values of retinal sensitivity before and after the visual rehabilitation cycle with biofeedback showed a marked improvement of the specific retinal sensitivity and consequently an improvement of the vision efficiency.

Because degenerative diseases are prevalent in old age, certainly the increase in life expectancy will lead to greater incidence of these diseases with great social importance. It is therefore understandable that the visual rehabilitation of these patients should be considered of extreme importance.

Further studies are needed to better understand the "correlation" between low-vision and walking, thanks to the collaboration between different professionals involved in the rehabilitation process. It is just because of such collaboration that the psychophysiological, and therefore clinical, mechanisms of the patients involved can be better understood.

References

1. Friedman DS, O' Colmain BJ, Munoz B, et al. Eye Diseases Prevalence Research Group. Prevalence of age-related macular degeneration in the United States. *Arch Ophthalmol* 2004; 122:564-72.
2. La Torre G, Pacella E, Saulle R et al. The synergistic effect of exposure to alcohol, tobacco smoke and other risk factors for age-related macular degeneration. *Eur J Epidemiol.* 2013 May;28(5):445-6. doi: 10.1007/s10654-013-9798-7.
3. Giustolisi R, Pacella F, Mastrangelo O et al. Verteporfin photodynamic therapy combined with intravitreal ranibizumab in neovascular age-related macular degeneration: 24-month follow-up. *Senses Sci* 2014; 1 (3):113-118 doi: 10.14616/sands-2014-3-113118.

4. Querques G, Capuano V, Frascio P et al. Emerging therapeutic options in age-related macular degeneration. *Ophthalmic Res.* 2015;53(4):194-9.
5. Giorgi D, Contestabile MT, Pacella E et al. An instrument for biofeedback applied to vision. *Appl Psychophysiol Biofeedback.* 2005 Dec;30(4):389-95.
6. Vingolo EM, Salvatore S, Domanico D et al. Visual rehabilitation in patients with myopic maculopathy: our experience. *Can J Ophthalmol.* 2013 Oct;48(5):438-42.
7. Verboschi F, Domanico D, Nebbioso M et al. New trends in visual rehabilitation with MP-1 microperimeter biofeedback: optic neural dysfunction. *Funct Neurol.* 2013 Oct-Dec;28(4):285-91.
8. Schuchard RA. Preferred retinal loci and macular scotoma characteristics in patients with age-related macular degeneration. *Can J Ophthalmology* 2005; 40: 303-312.
9. Vingolo EM, Salvatore S, Limoli PG. MP-1 biofeedback: luminous pattern stimulus versus acoustic biofeedback in age related macular degeneration (AMD). *Appl Psychophysiol Biofeedback.* 2013 Mar;38(1):11-6.
10. Pacella E, Pacella F, Mazzeo F et al. Effectiveness of vision rehabilitation treatment through MP-1 microperimeter in patients with visual loss due to macular disease. *Clin Ter.* 2012 Nov;163(6):e423-8.
11. Battaglia-Mayer A, Ferrari-Toniolo S, Visco-Comandini F. Timing and communication of parietal cortex for visuomotor control. *Curr Opin Neurobiol.* 2015.
12. Randle Rj. Volitional control of visual accommodation. Advisory group for aerospace research and development. Conference proceedings 82, Garmisch-Partenkrchen, Germany, 1980.
13. Nakao M, Nomura S, Shimosawa T, Fujita T, Kuboki T. Blood pressure biofeedback treatment, organ damage and sympathetic activity in mild hypertension. *Psychother Psychosom.* 1999;68(6):341-7.
14. Mezawa M, Ishikawa S, Ukai K. Changes in waveform of congenital nystagmus associated biofeedback treatment. *Br J Ophthalmol.* 1990 Aug;74(8):472-6.
15. Buia C, Tiesinga P. Attentional modulation of firing rate and synchrony in a model cortical network. *J Comput Neurosci.* 2006; 20:247-64.
16. Vingolo EM, Salvatore S, Limoli PG. MP-1 biofeedback: luminous pattern stimulus versus acoustic biofeedback in age related macular degeneration (AMD). *Appl Psychophysiol Biofeedback.* 2013 Mar;38(1):11-6.
17. Vingolo EM, Cavarretta S, Domanico D et al. Microperimetric biofeedback in AMD patients. *Appl Psychophysiol Biofeedback.* 2007.
18. Kim SJ, Ogilvie M, Shimabukuro N et al. Effects of Visual Feedback Distortion on Gait Adaptation: Comparison of Implicit Visual Distortion Versus Conscious Modulation on Retention of Motor Learning. *IEEE Trans Biomed Eng.* 2015 Sep;62(9):2244-50.
19. Fujii GY, De Juan E Jr, Sunness J, Humayun MS, Pieramici DJ, Chang TS. Patient selection for macular translocation surgery using the scanning laser ophthalmoscope. *Ophthalmology* 2002; 109:1737-44.
20. Amore FM, Paliotta S, Silvestri V ET ALL. Biofeedback stimulation in patients with age-related macular degeneration: comparison between 2 different methods. *Can J Ophthalmol.* 2013.
21. Verdina T, Giacomelli G, Sodi A et al. Biofeedback rehabilitation of eccentric fixation in patients with Stargardt disease. *Eur J Ophthalmol.* 2013 Sep-Oct;23(5):723-31.
22. Grenga PL, Trabucco P, Meduri A et al. Microperimetric biofeedback in a patient with oculocutaneous albinism. *Can J Ophthalmol.* 2013 Oct;48(5):e105-7.
23. Jarc-Vidmar M, Popovic P, Hawlina M. Mapping of central visual function by microperimetry and autofluorescence in patients with Best's vitelliform dystrophy. *Eye (Lond).* 2006 Jun;20(6):688-96.
24. Bianchi E, Scarinci F, Ripandelli G et al. Retinal pigment epithelium, age-related macular degeneration and neurotrophic keratouveitis. *International journal of molecular medicine, vol. 1,* 2012 p. 232-242, 2012.
25. Tarita-Nistor L, González EG, Markowitz SN, Steinbach MJ. Plasticity of fixation in patients with central vision loss. *Vis Neurosci.* 2009 Nov;26(5-6):487-94.
26. Crossland MD, Dunbar HM, Rubin GS. Fixation stability measurement using the MP1 microperimeter. *Retina.* 2009 May;29(5):651-6.
27. Tarita-Nistor L, González EG, Markowitz SN, Steinbach MJ. Fixation characteristics of patients with macular degeneration recorded with the mp-1 microperimeter. *Retina.* 2008 Jan;28(1):125-33.
28. Radvay X, Duhoux S, Koenig-Supiot F, Vital-Durand F. Balance training and visual rehabilitation of age-related macular degeneration patients. *J Vestib Res.* 2007;17(4):183-93.