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Original Article

Short-Term Clinical Results of Preferred Retinal Locus Training

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Abstract

Objectives: This study evaluated acustic biofeedback training (BFT) using microperimetry in patients with foveal scars and an eligible retinal locus for better fixation.

Materials and Methods: A total of 29 eligible patients were enrolled in the study. The acustic BFT module in the MAIA (Macular Integrity Assessment, CenterVue®, Italy) microperimeter was used for training. To determine the treatment efficacy, the following variables were compared before and after testing: Best-corrected visual acuity (BCVA), values obtained in a full threshold 4-2 test using the MAIA microperimeter like average threshold, fixation stability via the P1, P2 and bivariate contour ellipse area (BCEA) 63% and 95%, contrast sensitivity (CSV 1000E Contrast Sensitivity Test), reading speed using the Minnesota Low-Vision Reading Test (MNREAD reading chart), and quality of life questionnaires (NEI-VFQ-25). In addition, changes in the fixation stability parameters were recorded during each session.

Results: The study group consisted of 29 patients with a mean age of 68.72 ±8.34 years. The median value for best-corrected VA was initially 0.8(0.2–1.6) logMAR and increased to 0.8(0.1–1.6) logMAR after eight weeks of PRL treatment (p=0.003). The fixation stability parameter P1 improved from a mean value of 21.28±3.08% to 32.69±3.69% (p = 0.001), and for P2 the mean value improved from 52.79±4.53% to 68.31±3.89% (p = 0.001). The mean BCEA 63% decreased from 16.11±2.27°C to 13.34±2.26°C (p = 0.127), and the BCEA 95% decreased from 45.87±6.72°C to 40.01±6.78°C (p = 0.247) after training. Reading speed with both eyes was 38.28±6.25 words per minute (wpm) before training and 45.34±7.35 wpm after training(p<0.001). Statistically significant improvement was observed in contrast sensitivity and quality of life questionnaire scores after training.

Conclusion: Beginning with the 5th session, the BFT for a new trained retinal locus improved average sensitivity, fixation stability, reading speed, contrast sensitivity, and quality of life in patients with macular scarring.

Keywords: Low vision rehabilitation, Microperimetry, Preferred retinal locus training

Introduction

Macular diseases affect a significant number of people worldwide. Most are over 60 years old and suffer from age-related macular degeneration (AMD). With increasing life expectancy, quality of life become an important concern and investigations aiming to improve or maintain the visual performance are increasing.[1]

The human brain contains maps of the retina on the surface of the occipital lobes which is called as “retinotopic map”. In patients with macular degeneration, the loss of foveal input leads to deprivation in the cortical regions responsive to foveal

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stimuli. Consequently cortical neurons located in the retinotopic position, corresponding to the scotoma, receive some degree of activity from the unimpaired neurons in the area surrounding the lesion. Over time, these weak connections are gradually reinforced. The system eventually evolves into a new stable state in which every neuron again receives the same amount of activity from the source layer. The brain's ability to adapt its function and structure to recover visual function is called neuroplastic capacity.[2,3] This reorganization of visual cortex has been shown by functional MRI studies in early childhood foveal vision loss.[4] However Baseler et al.[5] has demonstrated that large-scale remapping does occur in the adult brain. This raises concerns about peripheral reorganization in retina especially in macula.

As known some of the patients with foveal scar starts to use extrafoveal areas of the retina to compensate within six months. This is called as eccentric fixation and the eccentric region of the peripheral macula selected for fixation is called preferred retinal locus (PRL).[6] As demonstrated in the study by Shima et al.[6], PRL is not always the area with the highest retinal sensitivity or owns the ability to provide the best visual function and fixation stability. This finding offers a new concept of trained retinal locus (TRL) selected among the PRL used for fixation. To determine the TRL the locus closest to the fovea and with the highest retinal sensitivity is preferred to offer the best potential visual acuity.[6-8] However eyes with foveal scars were not able to stable fixation at these selected points and this decreased their quality of vision. To solve this problem these patients have been addressed in several rehabilitation strategies designed to increase fixation stability.[7,8] The biofeedback training technique (BFT) proposed by Nilsson et al.[8] and Fujii et al.[9] BFT, which uses a software module incorporated in a microperimeter, is one of these rehabilitation methods and appears to be the most promising one.

The BFT system uses audible and visible feedback signals to help patients identify and train the optimal retinal area and improve fixation and related tasks. Patients are asked to perform ocular movements in a specific direction, attempting to align a selected retinal locus with a visual target. This locus is either the PRL determined by the device software or a new locus determined by special criteria among patients' fixation points. The latter is called TRL. Biofeedback audio signals (beeping sounds) aid patients during the oculomotor task by increasing the auditory frequency as the target approaches the desired alignment.[10] This biological feedback enables the intercellular neurotransmitters to increase and establish cerebral links faster than the normal process.[7,11] Additionally, acoustic stimulation increases the patient's conscious attention and prolongs the time that the fixed image of the object is on the retina. It configures the relationship between neurons in the retina and brain. The theory of the phenomenon of remapping is based on this explanation.[10,12-14]

In the literature, few studies and cases reported promising outcomes of BFT. Even oculomotor exercises performed in BFT have been shown to improve fixation stability using either PRL or TRL. There is no consensus on the correct duration, number of training sessions, and or effect on patient quality of life.[2,10,15-18]

Our study aimed to assess the short-term efficacy of BFT on fixation stability. To better execute the effect, the intersessional variation of fixation parameters were also analyzed. Additionally, it is preliminary in evaluating the effect on contrast sensitivity and quality of life in addition to reading speed.

Materials and Methods

This study is based on non-comparative case series and enrolled subjects with macular scarring in both eyes at the Retina Unit, Faculty of Medicine, Department of Ophthalmology, xxx University. The study protocol was designed according to the Helsinki Ethics Declaration's principles and approved by the Ethics Committee for the Non-invasive Clinical Research of the Medical Faculty, xxx University. Among the patients with macular disease, those inactive for at least one year were included. Patients with any other ocular disease that might affect retinal sensitivity or hearing loss were excluded because it could hinder compliance with the training while receiving the device's audio signals. After explaining the purpose and possible consequences of the study, informed written consent was obtained from all subjects. All patients underwent a complete ophthalmological evaluation, including best-corrected visual acuity (VA) measurement with Snellen chart, biomicroscopic examination of the anterior segment and dilated fundus examination. The visual acuity values obtained on a decimal scale (Snellen) are converted to logMAR using the following established formula: logMAR = log10 (1/VA) for accurate statistical analysis.

Eligible patients underwent a full threshold 4-2 test using the MAIA (CenterVue®, Padova, Italy) microperimeter to evaluate localization and fixation stability in a 10-degree area consisting of 37 measurement points. Fixation stability was measured in two ways:

1. Calculating the percentage of fixation points located within a distance of one degree and two degrees, respectively (P1 and P2).[11] If more than 75% of the fixation points were located within P1, the fixation was classified as stable. If less than 75% of the fixation points were located within P1 but more than 75% of the fixation points were located within P2, the fixation was classified as relatively unstable. If less than 75% were located within P2, the fixation was classified as unstable.
2. Another parameter was the bivariate contour ellipse area (BCEA), assumed to be the most representative fixation stability parameter. It represents the area of an ellipse that encompasses the cloud of fixation points for a given proportion based on standard deviations of the horizontal and vertical eye positions during the fixation procedure. BCEA 95% describes the area in which the retinal locus is 95%, and BCEA 63% represents the area in which the retinal locus is 63%.

With improvements in fixation stability, P1 and P2 values were expected to increase while BCEA 95% and 63% decreased.[19,20]

Patients having eyes with eccentric and unstable fixation based on the software were recruited for the study. If both eyes fulfilled the criteria, the eye with lower visual acuity was preferred. The decision to proceed with TRL was based on the location of the initial and final PRL which was determined automatically by the microperimeter software and the localization of the scotoma.

The initial PRL was determined after the initial 10 seconds of the examination, the point when patients make their strongest effort to hold a steady fixation (labeled with a pink dot in the data). It defines the center of the MAIA (CenterVue®, Padova, Italy) stimuli grid. The final PRL, labeled with a blue dot in the printout, is found at the end of the MAIA (CenterVue®, Padova, Italy) examination and serves as the reference point for calculating fixation stability. Patients with stable fixation will present both PRLs in the same anatomical location, while longer distance PRLs show more unstable fixation and less visual acuity. To estimate the TRL, the initial and final PRLs, the BCEA including all fixation points, the size and extent of the scotoma, and localization of the fovea are evaluated. Among the fixation points, the one closest to the estimated fovea but the farthest possible distance from the scar in the superior quadrant and is preferred. Additionally, to facilitate reading tasks, a fixation locus with horizontal neighbor points, and high sensitivity in the superior quadrant is chosen as the TRL.[21]

For eligible patients with a suitable TRL and who were willing to participate regularly in the training program, the average threshold of retinal sensitivity and the values for P1, P2, and BCEA in the full threshold 4-2 test were recorded (Figure 1a, Figure 1b).

To better determine the rehabilitation program's effects, contrast sensitivity using the CSV 1000E Contrast Sensitivity Test (VectorVision® Dayton, OH) at eight feet, and reading speed using the Turkish version of the MNREAD reading chart, were conducted with reading glasses under adequate lighting conditions. Reading acuity, critical print size, and maximum reading speed were calculated according to the instructions for the reading cards.[22] Reading speed and contrast sensitivity tests performed before and after treatment were performed in the same room, in the same ambient lighting and at the same time of day.

Additionally, the impact of treatment on the quality of life was evaluated with the Turkish version of the 25-item National Eye Institute Visual Function Questionnaire (NEI-VFQ-25).[23] This questionnaire was composed of 12 groups of questions: general health (one item), general vision (one item), ocular pain (two items), near vision (three items), distance vision (three items), social function (two items), mental health (four items), role limitations (two items), dependency (three items), driving (two items), color vision (one item), and peripheral vision (one item). The points received from these sections and the overall average score was calculated and analyzed. The questions were read and scores are recorded by a nurse (SO). The total point calculation and data analysis was performed by main researcher (ABO).

Our study was preliminary in evaluating the change in fixation parameters during each session of training. The values for P1, P2, BCEA 63%, BCEA 95% were recorded at the end of each session and documented for statistical analysis.

The outcome parameters included best-corrected visual acuity (VA); fixation stability parameters P1, P2, BCEA 63% and 95%; contrast sensitivity; reading speed; and quality of life. The parameters were continuously recorded for one week after the training program and compared with the parameters before the training.

Exercise Techniques

Patients were invited to the TRL treatment, preferably on the same day and time each week during the eight-week testing period. There is no consensus in the literature about

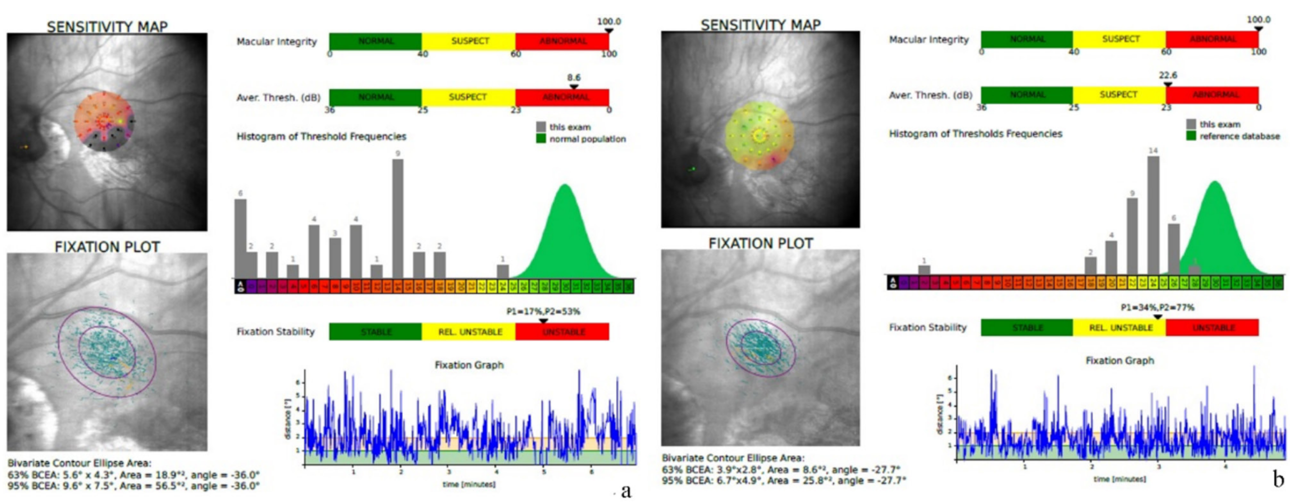

Figure 1: The change in the fixation area used by the patient after training sessions. According to the MAIA (CenterVue®, Padova, Italy) normative studies, the decibel scale is color-coded where green represents the normal value, yellow suspect, red the abnormal, and black absolute scotomas. (a) The sensitivity map before training, where the difficulty in the fixation can be observed. (b) The blue fixation points converge after treatment, meaning that fixation behavior is more stable. The new sensitivity map (after rehabilitation) shows the same assessment area as the first map.

the optimum duration of the training program. Based on the experience in similar studies, and to guarantee the compatibility of patients with the program, we scheduled eight sessions once per week for 10 minutes.[18] Patients were allowed to rest for 15 minutes before training. During the 10-minute exercise, patients tried to fix their eyes on the previously-determined TRL point. As the patient got closer to the locus intended for the fixation, a sound with increasing volume was heard in addition to positive comments from the clinician, who was reading from the screen. Patients were also asked to remember the gaze movement performed during the training sessions and try to reproduce the same movement in their daily lives when attempting to focus on a target.

Statistical Analysis

All obtained data were uploaded to the software after proper encoding. The Statistical Package for the Social Sciences version 18.0 (SPSS, Inc., Chicago, IL, USA) Windows software package was used for the statistical analysis. The data were analyzed for normal distribution; the best-corrected VA was analyzed with Mann-Whitney U-test. Other parameters were analyzed using the parametric paired t-test. Data related to the follow-up controls were evaluated using the repeatability measurement test. If any significant change was detected, the data were analyzed in paired groups using the paired t-test. For all analyses, $p<0.05$ was considered statistically significant.

Results

A total of 29 subjects, recruited with a mean age of 68.72±8.34 years, agreed to participate in the study and met the required criteria. Eighteen of the patients (62.1%) were males, and 11 (37.9%) were females. There was no significant difference between male and female patients considering their age ($p>0.05$). In 27 of the patients, AMD was the etiological cause of the central scotoma; trauma was the cause in the remaining two patients. Of the AMD patients,13 had geographic atrophy, and 14 had disciform scars. Patients who completed all training sessions are analyzed.

The median value for best-corrected VA was initially 0.8 (0.2 – 1.6) logMAR and increased to 0.8 (0.1 – 1.6) logMAR after eight weeks of PRL treatment. This change was statistically significant (p=0.003). The median value of the best-corrected VA of fellow eye was 0.5 (0.0 – 1.0) logMAR. The mean value of the average threshold before training was 12.96±1.16 dB. It showed a slight increase to 13.24±1.33 dB. However, it was not significant in the statistical analysis (p = 0.900).

Preceding the training fixation stability parameters P1 and P2 were 21.28±3.08% and 52.79±4.53% respectively. After training, the values increased to 32.69±3.69% for P1 (p = 0.001) and 68.31±3.89% for P2. This incline was found statistically significant (p = 0.001). BCEA 63% was 16.11±2.27 deg^2 before training and decreased to 13.34±2.26 deg^2 after training. Similarly, BCEA 95% decreased from 45.87±6.72 deg^2 before training and to 40.01±6.78 deg^2 after training. This change was not statistically significant (p = 0.127, p = 0.247 respectively) (Figure 2). Further subgroup analysis of initial and final VA and fixation parameters P1, P2, BCEA 63%, BCEA 95%, according to scar etiology as geographical atrophy, disciform scar and trauma revealed no statistically significant difference before and after the treatment (p= 0.77, p=0.67, p=0.33, p=0.98, p=0.46, p= 0.96, p= 0.98, p=0.87, p=0.91, p=0.85 respectively).

The intersession variation of fixation parameters P1 and P2 values showed a consistent rise in each session. Statistical analysis of intersessional change showed statistically significant increases at the fifth session ($p<0.001$) compared to the pretraining value ($p<0.001$). BCEA 63% and BCEA 95% demonstrated fluctuations in each session with no statistically significant difference ($p>0.05$) (Figure 3).

The contrast sensitivity was evaluated in four categories, as shown in Table 3: a) 3 cycles/degree, b) 6 cycles/degree, c) 12 cycles/degree, and d) 18 cycles/degree. The pre-and post-training values of each category presented a statistically significant increase (p values were $p<0.001$, $p<0.001$, p = 0.01, p = 0.001 respectively). For reading speed, the mean values for reading acuity, critical print size, and maximum reading speed (wpm)

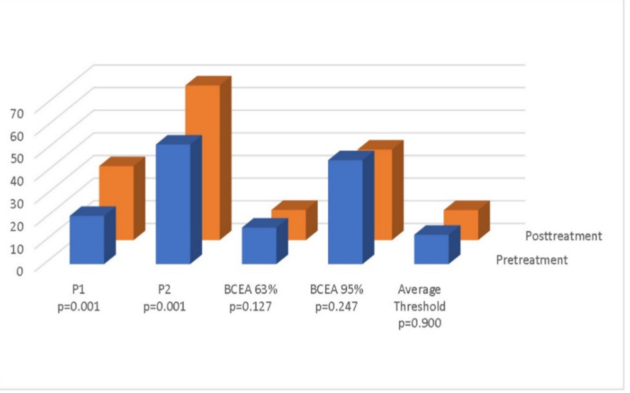

Figure 2: P1 and P2 values increase significantly in full threshold 4-2 tests conducted before and after PRL training. Despite the numerically positive change in BCEA 63%, BCEA 95%, and the average threshold, this change is statistically insignificant.

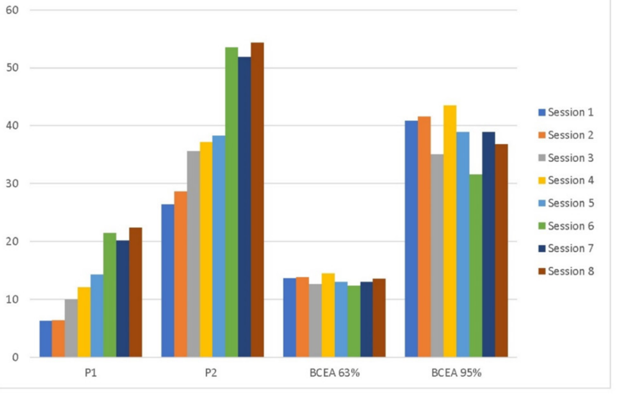

Figure 3: P1 and P2 values noted over eight sessions increased significantly after the 5th session, with no significant changes in BCEA 63% and BCEA 95% values.

changed significantly at the final visit compared to pretraining (for all parameters: p<0.001) (Table 1).

The quality of life questionnaire results demonstrated a statistically significant improvement in overall composite scores and all sections except general health and ocular pain. The scores are shown in Table 2.

Discussion

According to data from the World Health Organization (WHO), there are 285 million people with low vision problems worldwide.[24] Over the years, several rehabilitation methods have been developed for this group of patients. Equipment such as magnifiers, text shifting, or prisms is focused on the improvement of reading skills.[6,25,26] To improve perceptual skills, rehabilitation methods such as training based on eccentric imaging, oculomotor control, and perceptual learning were introduced.[26,27] They enable effective emotional improvement through technical training and can be easily implemented during clinical practice because they do not require expensive equipment.[28] Research on integrating perceptual and oculomotor training to induce a new fovea was further developed with the addition of auditory feedback.[8] In some studies, additional oculomotor exercises at home following training are shown to increase reading speed and decrease readable font size.[29,30]

The rehabilitation method uses eccentric imaging to look directly at the relatively healthy retina locus to improve visual function. The retinal locus, called TRL, is in an area advantageous to reading.[31] Nilsson et al.[8] reported the initial outcomes for TRL training and found improved reading rates of the scotomatous eye following training for 5.4 hours with SLO. Watson et al.[32] trained the better-seeing eye and proposed the development of a TRL that is easily and fast. In contrast, Baker

Table 1: Contrast sensitivity and reading speed before and after treatment

	Pretreatment (Mean±SD)	Posttreatment (Mean±SD)	p value
Contrast Sensitivity			
3 cycles/degree (A)	1.07±0.056	1.19±0.061	**p<0.001**
6 cycles/degree (B)	1.23±0.051	1.36±0.061	**p<0.001**
12 cycles/degree (C)	0.91±0.05	1±0.056	**p=0.01**
18 cycles/degree (D)	0.37±0.04	0.48±0.05	**p=0.001**
MNREAD reading chart			
Reading acuity	1.05±0.05	0.96±0.06	**p<0.001**
The critical print size	1.12±0.04	1.07±0.05	**p<0.001**
Maximum reading speed (wpm)	38.28±6.25	45.34±7.35	**p<0.001**

SD, standard deviation; wpm, words per minute

Table 2: Quality of life questionnaire scores before and after treatment

	Pretreatment (Mean±SD)	Posttreatment (Mean±SD)	p value
General health	46.552±25.63	48.276±24.93	p=0.480
General vision	30.172±29.41	43.965±28.07	**p<0.001**
Ocular pain	72.413±19.30	75±20.04	p=0.083
Near activities	30.169±21.29	42.239±21.47	**p<0.001**
Distance activities	24.699±20.35	31.319±20.97	**p<0.001**
Social functioning	34.052±24.52	44.396±23.76	**p<0.001**
Mental health	27.802±18.26	34.482±19.23	**p<0.001**
Role difficulties	18.534±19.93	23.706±20.41	**p=0.001**
Dependency	30.170±28.90	34.480±27.52	**p=0.001**
Driving*	58.33±8.33	66.663±8.33	p=0.102
Color vision	34.483±27.88	43.965±26.43	p=0.001
Peripheral vision	28.448±27.32	35.345±24.56	p=0.005
Overall composite score	32.945±17.81	40.795±16.97	p<0.001

SD, standard deviation
*This question was asked only to them because there are 3 people driving

et al.[4] observed that eyes with more severe foveal scarring are more prone to reorganization. In our study, we also preferred the weakest eye for training, and the patient's improvement after training supported this hypothesis.

Initial trials were performed with basic systems like AccommotracVision Trainer, Visual Training System (VTS), or the improved Biofeedback Integrated System (IBIS) device.[10,33] Significant advancements in rehabilitation methods have been made by developing a software package uploaded to the microperimeter. There are limited studies in the literature reporting on the therapeutic outcome of visual rehabilitation programs containing an auditory feedback mechanism in several disorders. They include nystagmus, AMD, glaucoma, anisometropia, amblyopia, retinitis pigmentosa, oculocutaneous albinism, myopic maculopathy, vitelliform dystrophy, posttraumatic macula scarring, and cone dystrophy.[14] These studies differ in several aspects. Some evaluate training the PRL to increase fixation stability, while some identified a TRL and trained to force fixation from that point. In addition, the intensity, frequency, and duration of training are different. The optimum training program required to transport the central fixation locus to the nearby healthy retinal locus permanently is already a challenge.[34,35]

Two devices currently use this available software training: the MP-1 (Nidek Instruments, Italy) and MAIA (CenterVue®, Padova, Italy). Although the aim is similar, there are small differences that hinder a head-to-head comparison. MP-1 doesn't present objective fixation stability parameters like P1, P2, or BCEA. Typically, reading speed and visual acuity are assumed to be primary outcomes in studies. Vingolo et al.[10] reported improved results in 15 AMD patients who underwent bilateral BFT with the MP-1 device once per week for ten 10-minute sessions. They claimed that five follow-up training sessions every three months would maintain visual performance. In 2009 Tarita-Nistor et al.[2] applied BFT using the MP-1 device for five sessions lasting one hour to the relocate PRL; they reported improved fixation stability and better reading performance.

In another study, Raman et al.[36] applied BFT to both eyes with myopic maculopathy using the MP-1 device and demonstrated that visual acuity did not change after exercise; only retinal sensitivity and fixation stability improved. The most extensive study with the most extended follow-up using MP-1 was conducted by Pacella et al.[33], who reported results for 171 eyes on 99 patients. They applied 16 TRL training sessions and showed improved visual acuity in 76.02% of the patients. Of those, 19.23% lost the benefits of training after 12 months.

Our study, conducted with the MAIA (CenterVue®, Padova, Italy) microperimeter, achieved significant improvement in best-corrected VA, average retinal sensitivity, and fixation stability parameters P1 and P2 after eight sessions of BFT. The initial values were 16.11 ± 2.27 deg^2 for BCEA 63% and 45.87 ± 6.72 deg^2 for BCEA 95%. In the MAIA (CenterVue®, Padova, Italy) microperimeter, the normal value range was 2.40 ± 2.04 deg^2 for BCEA 95% and 0.80 ± 0.68 deg^2 for BCEA 63%. The BCEA 63% and BCEA 95% has been reported to serve as the single and accurate parameter to evaluate fixation stability.[19] Although not statistically significant, a decline in BCEA 63% and BCEA 95% values were observed at the end of the study. This insignificance could be explained by the low number of subjects included and fewer training sessions than recent studies that typically scheduled 10 sessions.[11,12,36-38]

We preferred to train the optimum locus with higher sensitivity, which, in our opinion, would enhance plasticity more efficiently. Recent studies support our hypothesis. Morales et al.[7] compared training for the PRL and TRL and suggested that a selected TRL would improve fixation stability more after training. They postulated that spontaneously-developed plasticity reflects a compensatory motor pattern rather than a true recovery and that selected locus training may enhance plasticity more efficiently. Raman et al.[36] also showed improved fixation stability and retinal sensitivity after TRL training and maintained at one-year follow-up program. A study reporting on the outcome of PRL therapy in AMD patients published by Vingolo et al.[10] could not find statistical significance in best-corrected VA, except for a statistically significant difference in the effect of font size on reading rates. Vingolo et al.[37] reported that the P100 latency value changed significantly in the VEP examination conducted in the pre-and post-treatment periods. However, the effect of this finding on daily life is unknown.

Another study evaluated BFT with the MAIA (CenterVue®, Padova, Italy) microperimetry on nine patients' eyes. They underwent macular hole surgery and applied three sessions lasting 10 minutes each. Within three months, the patients showed a statistically significant increase in best-corrected VA. The fixation stability, BCEA 63%, and reading speed also improved; however, the results were not statistically significant like the BCEA 63% values in our study. The investigators attributed the results to the small number of subjects in their study.[39] In our opinion, the low number of sessions might have influenced the study outcome. Pacella et al.[33] conducted a study with a larger sample size and demonstrated a statistically significant improvement in the best-corrected VA, reading rate, and fixation behaviors. Etiology of macular scar might be another confounding factor for different outcomes in various studies. We have enrolled patients with disciform scar, geographic atrophy and traumatic macular scar in the study. However subgroup analysis demonstrated no statistically significant difference in the short term evaluation. As macular degeneration is progressive in contrast to macular hole or traumatic scar, different outcomes in duration of training effect might be expected in the long term.

As training process is static, assessing its functionality during dynamic situations is essential because they occur in everyday life while moving objects or performing tasks involving eye movement such as reading. According to our data, the new TRL appeared to improve reading speed, contrast sensitivity, and quality of life. Our study findings were preliminary in that they were the first to address contrast sensitivity and quality of life among those studies evaluating the same training method. The data demonstrated statistically significant improvements in all frequencies, a finding consistent with substantial improvement in other parameters (visual acuity, reading speed, and fixation stability). Our findings indicated that TRL treatment made positive contributions to visual quality. This promising effect is also observed in two patients with a VA higher than 0.4 logMAR. They were enrolled regarding unstable fixation parameters and complains about reading. As their number was limited, a subgroup analysis according to VA level could not be performed. Their visual acuity increased 1 line after training and a slight improvement could be achieved in fixation parameters which in turn improved their reading speed and quality of life according to questionnaire scores.

The Turkish version of the National Eye Institute Visual Functioning Questionnaire (NEI-VFQ) was used to compare the quality of life in pre-and post-treatment periods. Except for general health and ocular pain, the overall scores changed significantly with the treatment. Only a limited number of studies focused on the evaluation of this questionnaire after PRL treatment. A re-evaluation of the NEI-VFQ-25 questionnaire after exercises revealed statistically significant changes consistent with our study findings.[40] Scuderi et al.[14] implemented BFT treatment for TRL in a patient with Stargardt disease who experienced reduced visual acuity during the previous three years. Based on the NEI-VFQ-25 quality of life questionnaire, they observed an increase in visual acuity, reading speed, and overall satisfaction. The meta-analysis conducted by Hamade et al.[41] reported that eccentric viewing training showed the most improvement in reading speed among the low-vision rehabilitation strategies. However, there was no significant effect on the scores for depression.

The total number of BFT sessions required for permanent, stable fixation is challenging. In the majority of studies, the BFT program was set at 10 sessions of 10 minutes each. In the literature, the number of sessions typically varied between three and 16.[7,33,39,42] In our study, we preferred a program consisting of eight sessions of 10 minutes each. This schedule was in response to the difficulty in adhering to hospital visiting rules for AMD patients due to age and poor vision. Based on our follow-up sessions, the changes in the P1, P2, and BCEA showed that fixation stability increased in each session. The changes in the P1 and P2 percentages became significant after the fifth session ($p = 0.001$). This finding should be considered when planning the training schedule.

In their study, Estudillo et al.[43] showed improvement after one week in visual acuity, fixation parameters P1 and BCEA 95%, and reading speed. They claimed that the short duration of treatment enabled them to attribute the changes directly to the treatment. In our study, we also repeated the control test one week after the last session to determine the real effects of BFT.

Despite promising results, the effect of training duration is unknown. Ratra et al.[38] reported continued effects up to six months with a slight reduction in fixation stability. Raman et al.[36] observed that these changes continued during the one-year follow-up period and suggested that treatment provided permanent results through the mechanism called the phenomenon of remapping between retinal neurons and the brain. Morales et al.[7] also showed a slight reduction in fixation parameters after three months and scheduled two sets of 12 weeks with three-month intervals between sets. They suggested that training for more extended periods was warranted to achieve permanent results.

We do not plan any long-term follow-up visits because the underlying disease is progressively fibrotic. Any deterioration might be attributed to fibrosis instead of the dwindling effects of training. However, repeated training might be useful in possible patients. Another bias about this visual rehabilitation method among the studies is laterality. Some studies performed bilateral training. We preferred the worst eye to avoid adverse effects like diplopia. Estudillo et al.[43] preferred the same approach.

Another confounding factor in our study was the selection criteria for training eye. However, as our subjects were old and had central scotoma, the dominant eye was difficult to determine. We preferred the worse eye with more severe foveal scar to treat as it was shown to present better reorganization capacity.[44] The TRL was one of the existing fixation points and the effect of eye dominance was already reflected in the reference microperimetry which we used to schedule the training. Additionally the treatment outcome is also assessed monocularly. The only exceptions are the measurement of reading speed and the NEI-VFQ-25 questionnaire. The outcome of both outcome parameters should be evaluated regarding this confounding factor.

With prolonged life expectancy in the modern world, the number of AMD patients is increasing significantly. This increase, in turn, added to the number of AMD patients with macular scars. Because the disease gives rise to central scotoma, serious problems may arise in patients' daily activities, particularly their reading activity, as reflected in our quality of life questionnaire. A locus with higher sensitivity in the peripheral retina outside of the fovea may provide higher visual quality as a means of adaptation. The goal of BFT was to enable the patient to use that selected area for visual tasks.

Our results demonstrated that patients with macular scar might improve during an eight-session BFT program on the selected TRL; this adaptation positively affects reading speed, contrast sensitivity, and quality of life in patients with impaired fixation stability. A patient with good comprehension skills is warranted for effective training. To our knowledge, age-related hearing loss is frequent among AMD patients.[45] This fact should be kept in mind when selecting eligible patients. Our short-term follow-up revealed significant improvement in fixation parameters after the 5th BFT session. The optimum duration and session interval for maintenance of training effects is already a matter of debate that should be addressed with further studies. Etiology of macular scar seem to be insignificant in the short term however effects in the long term should be evaluated with duration of fixation stability improvement. The need for repeat sessions and frequency of control visits are major issues that should be addressed in the future. However the effect of TRL training on reading and daily life is promising as a low vision rehabilitation tool.

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