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Original Article

Short-Term Clinical Results of Preferred Retinal Locus Training

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Abstract

Objectives: This study evaluated acoustic biofeedback training 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 acoustic biofeedback training 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); MAIA microperimeter full threshold 4-2 test parameters of average threshold value, fixation parameters P1 and P2, and bivariate contour ellipse area (BCEA) for 63% and 95% of fixation points; contrast sensitivity (CSV 1000E Contrast Sensitivity Test); reading speed using the Minnesota Low-Vision Reading Test (MNREAD reading chart); and quality of life (NEI-VFQ-25). In addition, 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. Median BCVA was initially 0.8 (0.2-1.6) logMAR and was 0.8 (0.1-1.6) logMAR after 8 weeks of preferred retinal locus training (p=0.003). The fixation stability parameter P1 improved from a mean of 21.28±3.08% to 32.69±3.69% (p=0.001) while mean P2 improved from 52.79±4.53% to 68.31±3.89% (p=0.001). Mean BCEA 63% decreased from 16.11±2.27$^{\circ 2}$ to 13.34±2.26$^{\circ 2}$ (p=0.127) and mean BCEA 95% decreased from 45.87±6.72$^{\circ 2}$ to 40.01±6.78$^{\circ 2}$ (p=0.247) after training. Binocular reading speed 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 fifth session, biofeedback training 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

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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 has become an important concern, and investigations aiming to improve or maintain visual performance are increasing.[1]

The human brain contains maps of the retina on the surface of the occipital lobes, called *retinotopic maps*. In patients with macular degeneration, the loss of foveal input leads to deprivation in the cortical regions responsive to foveal 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 magnetic resonance imaging studies in early childhood foveal vision loss.[4] However, Baseler et al.[5] demonstrated that large-scale remapping does occur in the adult brain. This raises concerns about peripheral reorganization in the retina, especially the macula.

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

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 specific ocular movements 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 from among patients' fixation points using special criteria. The latter is called a 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 causes 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 remapping phenomenon is based on this explanation.[10,12,13,14]

In the literature, a few studies and case reports have described promising outcomes with BFT. Even oculomotor exercises performed in BFT have been shown to improve fixation stability using either PRL or TRL. However, there is no consensus on the optimal duration, number of training sessions, or effect on patient quality of life.[2,10,15,16,17,18]

Our study aimed to assess the short-term efficacy of BFT on fixation stability. To better understand this effect, we analyzed intersessional changes in fixation parameters. Furthermore, we evaluated the effect of BFT on contrast sensitivity and quality of life in addition to reading speed.

Materials and Methods

This study is based on a non-comparative case series of patients with bilateral macular scarring treated in the retina unit of Selçuk University Faculty of Medicine, Department of Ophthalmology. The study protocol was designed according to the ethical principles of the Declaration of Helsinki and was approved by the Ethics Committee for Non-invasive Clinical Research of the Selçuk University Faculty of Medicine. Among the patients with macular disease, those whose disease was inactive for at least 1 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 audio signals from the device. 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 VA measurement with Snellen chart, biomicroscopic examination of the anterior segment and dilated fundus examination. VA values obtained by Snellen chart (in decimal) were converted to logMAR for statistical analysis using the following established formula: logMAR = $\log^{10}$ (1/VA).

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. Calculating the bivariate contour ellipse area (BCEA), which is believed to be the most representative fixation stability parameter. It represents the area of an ellipse that encompasses a given proportion of fixation points based on standard deviations of the horizontal and vertical eye positions during the fixation procedure. BCEA 95% describes the area that includes 95% of retinal loci and BCEA 63% represents the area containing 63% of retinal loci used for fixation.

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

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

The initial PRL was determined after the first 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). This point determines 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 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 distances between PRLs show more unstable fixation and lower VA. To estimate the TRL, the initial and final PRLs, the BCEA including all fixation points, the size and extent of the scotoma, and location 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 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 who had a suitable TRL and 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, b).

To better determine the effects of the rehabilitation program, contrast sensitivity was tested using the CSV 1000E Contrast Sensitivity Test (VectorVision® Dayton, OH) at 8 feet and reading speed was assessed using the Turkish version of the MNREAD reading chart, 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 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 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 is composed of 12 groups of questions regarding general health (1 item), general vision (1 item), ocular pain (2 items), near vision (3 items), distance vision (3 items), social functioning (2 items), mental health (4 items), role limitations (2 items), dependency (3 items), driving (2 items), color vision

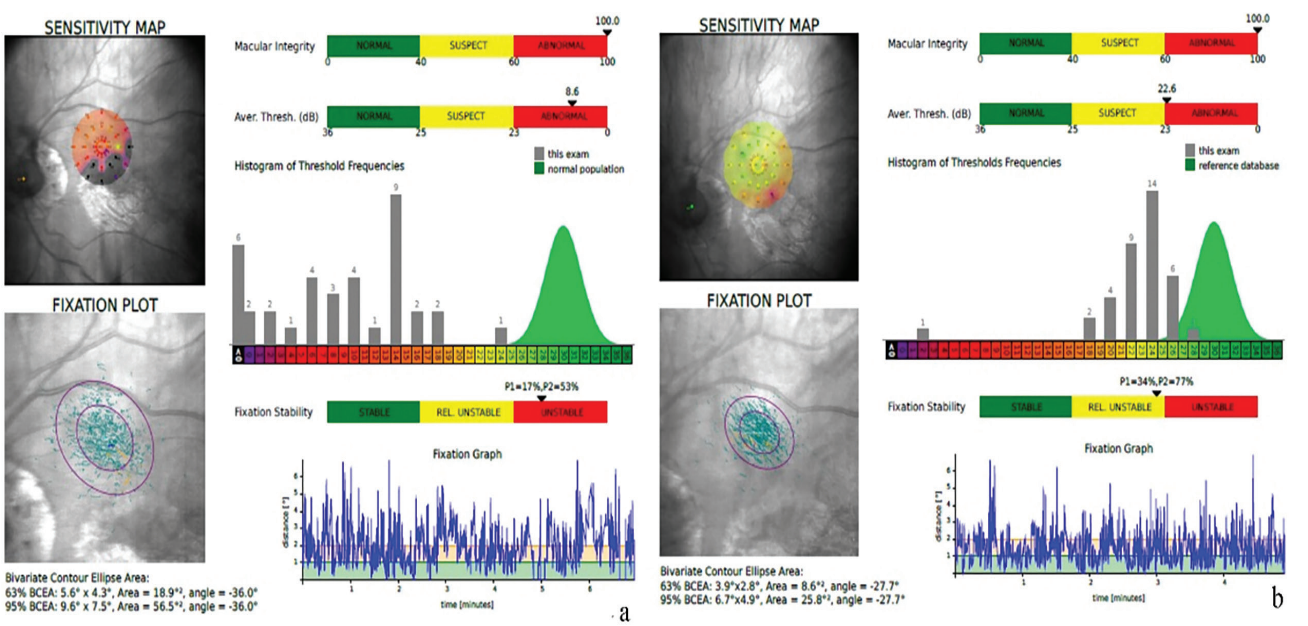

Figure 1. The change in the fixation area used by the patient after training sessions. According to the MAIA (CenterVue®, Padova, Italy) normative studies, the decibel scale is color-coded where green represents normal values, yellow suspect, red abnormal, and black absolute scotomas. (a) The sensitivity map before training demonstrates difficulty in fixation. (b) In the new sensitivity map (after treatment), assessment of the same area demonstrates convergence of the blue fixation points, indicating more stable fixation behavior

(1 item), and peripheral vision (1 item). The points received from these sections and the overall average score was calculated and analyzed. The questions were read to the patients and their scores were recorded by a nurse (S.O.). The total point calculation and data analysis were performed by the first researcher (A.B.O.).

Outcome parameters included best corrected VA; fixation stability parameters P1, P2, and BCEA 63% and 95%; contrast sensitivity; reading speed; and quality of life. P1, P2, BCEA 63%, and BCEA 95% values were recorded at the end of each session for analysis of changes in fixation parameters during training. To analyze changes after training, the parameters were reassessed 1 week after the training program and compared with pretreatment values.

Exercise Techniques

Patients were invited to TRL treatment preferably on the same day and time each week during the 8-week testing period. There is no consensus in the literature about the optimum duration of the training program. Based on experiences in similar studies and to increase the likelihood of adherence to the program, we scheduled 8 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 targeted fixation locus, they heard a sound increasing in volume as well as positive comments from the clinician, who was reading from the screen. The 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. Best corrected VA was analyzed with Mann-Whitney U-test; other parameters were analyzed using the parametric paired t-test. Data obtained during follow-up were evaluated using a repeated measures 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 patients with a mean age of 68.72±8.34 years at enrollment met the selection criteria and agreed to participate in the study. Eighteen (62.1%) of the patients were men and 11 (37.9%) were women. There was no significant difference between male and female patients in terms of age (p>0.05). In 27 of the patients, AMD was the etiology of the central scotoma, and trauma was the cause in the remaining 2 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 8 weeks of PRL treatment. This change was statistically significant (p=0.003). Median best-corrected VA in the fellow eye was 0.5 (0.0-1.0) logMAR. The mean average threshold value was 12.96±1.16 dB before training and showed a slight increase to 13.24±1.33 dB, but it was not significant in the statistical analysis (p=0.900).

Before 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 (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 to 40.01±6.78 deg^2 after training. However, these changes were not statistically significant (p=0.127 and p=0.247, respectively) (Figure 2). Further subgroup analysis of initial and final VA and fixation parameters P1, P2, BCEA 63%, and BCEA 95%, according to scar etiology (geographical atrophy, disciform scar, or trauma) revealed no statistically significant difference before and after 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, and p=0.85, respectively).

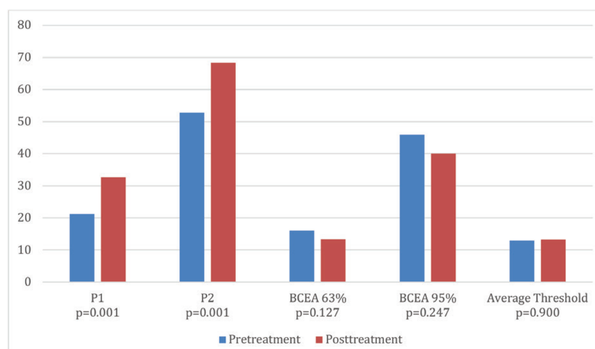

Figure 2. P1 and P2 values were significantly increased in full-threshold 4-2 tests conducted after preferred retinal locus training compared to before training. Despite favorable changes in BCEA 63%, BCEA 95%, and average threshold, they were not statistically significant

BCEA: Bivariate contour ellipse area

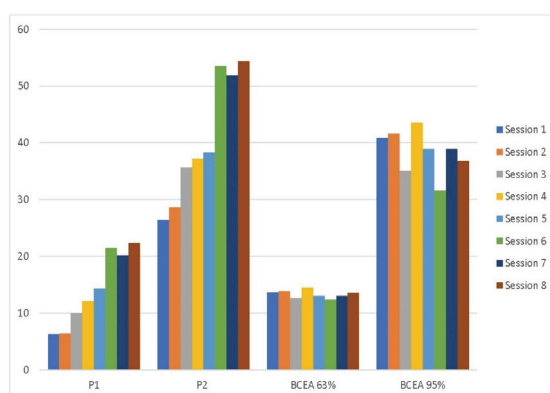

Figure 3. P1 and P2 values recorded over 8 sessions show a significant increase after session 5, while no significant changes were observed in BCEA 63% and BCEA 95% values

BCEA: Bivariate contour ellipse area

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 after the fifth session compared to the pre-training value (p<0.001). BCEA 63% and BCEA 95% demonstrated fluctuations in each session with no statistically significant difference (p>0.05) (Figure 3).

Contrast sensitivity was evaluated at four different spatial frequencies: 3, 6, 12, and 18 cycles/degree. The pre- and post-training values at each frequency demonstrated a statistically significant increase (p<0.001, p<0.001, p=0.01, and p=0.001, respectively). For reading speed, the mean values for reading acuity, critical print size, and maximum reading speed (words per minute) changed significantly at the final visit compared to before training (p<0.001 for all parameters) (Table 1).

The quality of life questionnaire results showed 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 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 improving 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 sensitivity 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

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

	Pre-treatment (mean ± SD)	Post-treatment (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

	Pre-treatment (mean ± SD)	Post-treatment (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 (n=3)*	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, *Only 3 of the patients were driving feedback.[8] In some studies, additional oculomotor exercises at home following training were shown to increase reading speed and decrease smallest readable font size.[29,30]

This rehabilitation method uses eccentric imaging to look directly at the relatively healthy retina locus to improve visual function. The retinal locus, called a TRL, is in an area advantageous to reading.[31] Nilsson et al.[8] reported initial outcomes for TRL training and found improved reading rates in scotomatous eyes following 5.4 hours of training with scanning laser ophthalmoscope. Watson et al.[32] trained the better-seeing eye and reported that the development of a TRL was easy and fast. In contrast, Baker et al.[4] observed that eyes with more severe foveal scarring were more prone to reorganization. In our study, we also preferred the weaker eye for training, and the patients' improvement after training supported this hypothesis.

Initial trials were performed with basic systems like the AccommotracVision Trainer, Visual Training System (VTS), or the Improved Biofeedback Integrated System (IBIS).[10,33] Significant advancements in rehabilitation methods have been made by developing a software package uploaded to the microperimeter. There are a few studies in the literature reporting the therapeutic outcomes of visual rehabilitation programs containing an auditory feedback mechanism in several disorders, including 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 evaluated training the PRL to increase fixation stability, while some identified a TRL and trained to force fixation on that point. In addition, the intensity, frequency, and duration of training were different. Establishing 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 purpose is similar, there are small differences that hinder a head-to-head comparison. The MP-1 does not present objective fixation stability parameters like P1, P2, or BCEA. Typically, reading speed and VA 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 in 10 weekly 10-minute sessions. They claimed that 5 follow-up training sessions every 3 months would maintain visual performance. In 2009, Tarita-Nistor et al.[2] applied BFT using the MP-1 device for 5 sessions lasting 1 hour to relocate the PRL and 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 VA did not change after exercise; only retinal sensitivity and fixation stability improved. The most extensive study with the longest follow-up using MP-1 was conducted by Pacella et al.[33], who reported results for 171 eyes of 99 patients. They applied 16 TRL training sessions and showed improved VA in 76% of the patients. Of those, 19.2% lost the benefits of training after 12 months.

Our study conducted with the MAIA microperimeter resulted in significant improvement in best-corrected VA, average retinal sensitivity, and fixation stability parameters P1 and P2 after 8 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%. Normal values for BCEA 95% and 63% in the MAIA microperimeter are 2.40±2.04 deg^2 and 0.80±0.68 deg^2, respectively. BCEA 63% and BCEA 95% have been reported to serve as an accurate, independent parameter with which to evaluate fixation stability.[19] Although not statistically significant, a decline in BCEA 63% and BCEA 95% values were observed at the end of this study. The lack of significance could be explained by the low number of subjects included and fewer training sessions than recent studies, which typically scheduled 10 sessions.[11,12,36-38]

We preferred to train the optimum locus with higher sensitivity, which we believe 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 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 that was maintained at 1-year follow-up. In a study reporting the outcomes of PRL therapy in AMD patients, Vingolo et al.[10] found no statistically significant change in best corrected VA but reported significant improvements in font size and reading rates. Vingolo et al.[37] reported that the P100 latency of visual-evoked potentials (VEP) changed significantly between pre- and post-treatment examinations. However, the effect of this finding on daily life is unknown.

In another study evaluating BFT with the MAIA microperimeter, 9 patients underwent macular hole surgery and 3 BFT sessions lasting 10 minutes each. Within 3 months, the patients showed a statistically significant increase in best corrected VA. Their fixation stability, BCEA 63%, and reading speed also improved but nonsignificantly, 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 may also have influenced the study outcome. Pacella et al.[33] conducted a study with a larger sample size and demonstrated a statistically significant improvement in best corrected VA, reading rate, and fixation behaviors. The etiology of macular scar might be another confounding factor contributing to the different results obtained in various studies. We enrolled patients with disciform scar, geographic atrophy, and traumatic macular scar in this study. However, subgroup analysis demonstrated no statistically significant difference in the short-term evaluation. As macular degeneration is progressive, unlike macular hole or traumatic scar, different long-term outcomes might be expected with different durations of training.

As the training process is static, assessing function during dynamic situations is essential because they occur in everyday life with moving objects or when 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 should be considered preliminary, as this is the first study on this training method to address contrast sensitivity and quality of life. The data demonstrated statistically significant improvements in contrast sensitivity at all spatial frequencies, a finding consistent with substantial improvement in other parameters (VA, reading speed, and fixation stability). Our results indicated that TRL treatment made positive contributions to visual quality. This promising effect was also observed in two patients with a VA higher than 0.4 logMAR who were enrolled due to unstable fixation parameters and complaints about reading. As their number was limited, a subgroup analysis according to VA level could not be performed. However, these patients showed a 1-line increase in VA and slight improvement in fixation parameters after training, which in turn improved their reading speed and quality of life according to questionnaire scores.

The Turkish version of the NEI-VFQ was used to compare quality of life before and after treatment. Except for general health and ocular pain, the overall scores changed significantly with treatment. Few studies have utilized 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 for TRL in a patient with Stargardt disease who experienced reduced VA over the previous 3 years. Based on the NEI-VFQ-25 quality of life questionnaire, they observed an increase in VA, reading speed, and overall satisfaction. A meta-analysis conducted by Hamade et al.[41] showed that eccentric viewing training caused 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 unclear. In most studies, the BFT program was designed as 10 sessions of 10 minutes each, although session numbers ranging from 3 to 16 have been reported in the literature.[7,33,39,42] For our study, we preferred a program consisting of 8 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. Changes in the P1 and P2 percentages became significant after the fifth session ($p=0.001$). This finding should be considered when planning a training schedule.

In their study, Estudillo et al.[43] showed improvement in VA, fixation parameters P1 and BCEA 95%, and reading speed after 1 week. 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 assessments 1 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 6 months with a slight reduction in fixation stability. Raman et al.[36] observed that these changes continued during the 1-year follow-up period and suggested that treatment provided permanent results through the mechanism of remapping between retinal neurons and the brain. Morales et al.[7] also showed a slight reduction in fixation parameters after 3 months and scheduled two sets of 12 weeks with 3-month intervals between sets. They suggested that training for more extended periods was needed 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 associated with fibrosis instead of the dwindling effects of training. However, repeated training might be useful.

Laterality is another source of bias related to this visual rehabilitation method among studies. Bilateral training was done in some studies. We preferred the worse 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 the 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 scarring for treatment because 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, treatment outcomes were also assessed monocularly except for 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, has 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 the 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 is to enable the patient to use that selected area for visual tasks.

Conclusion

Our results demonstrated that patients with macular scar might improve during an 8-session BFT program on the selected TRL and that this adaptation positively affects reading speed, contrast sensitivity, and quality of life in patients with impaired fixation stability. Patients should have good comprehension skills 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 fifth BFT session. The optimum duration and session interval for maintenance of training effects is already a matter of debate that should be addressed in further studies. Etiology of macular scar seems to be insignificant in the short term, but its effects in the long term should be evaluated with regard to the duration of improvement in fixation stability. 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 for low vision rehabilitation.

Ethics

Ethics Committee Approval: Approval was obtained from Selcuk University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee. (14.02.2017 date, 2017/06 number).

Informed Consent: Obtained.

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Authorship Contributions

Surgical and Medical Practices: A.B.O., B.T.Ö., Concept: A.B.O., B.T.Ö., B.B., Ş.Gö., Ş.Ge., S.O., Design: A.B.O., B.T.Ö., B.B., Ş.Gö., Ş.Ge., S.O., Data Collection or Processing: A.B.O., B.T.Ö., B.B., Ş.Gö., Ş.Ge., S.O., Analysis or Interpretation: A.B.O., B.T.Ö., Literature Search: A.B.O., B.T.Ö., Writing: A.B.O., B.T.Ö.

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