Rehabilitative effect of the patterned stimulation with MP1 microperimeter in homonymous hemianopia

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Abstract

Background: MP-1 microperimeter (NIDEK Technologies) is equipped with a visual rehabilitation tool used until now to rehabilitate patients with low visual acuity. Because the patterned stimulation might activate surviving neurons in areas of residual vision, in our work we want to verify the possibility to rehabilitate patients with visual field defects and foveal sparing, to obtain vision restoration and visual field enlargement.

Methods: Ten consecutive patients (7 females, 3 males; median age of 42.3 ± 11.63 years) with homonymous visual field defect resulting from lesions of the central visual pathways and foveal sparing were enrolled for visual rehabilitation with MP-1 microperimeter (NIDEK Technologies). Subjects underwent an ophthalmic evaluation at baseline, after rehabilitative pathway performed by flickering pattern and at 3 months of follow-up. Outcomes measured included visual field exams and microperimetries.

Results: Compared with the baseline time point, all patients showed a statistically significant reduction of the scotoma points and visual field Mean Deviation and a statistically significant increasing of the mean retinal sensitivity. All results showed a major statistical significance after 3 months since the end of the visual stimulation.

Conclusions: The MP1 pattern stimulation is a valid method to perform a behavioral training and rehabilitate patients with visual field defects following lesions of the central visual pathways.

Keywords

Homonymous hemianopia; Visual rehabilitation; Microperimeter; Visual stimulation

Introduction

Homonymous visual field (VF) defects are a common complication of stroke, cranial trauma and brain tumors. Among them, the homonymous hemianopia (HH) is the one found most frequently. Because this impairment can affect a variety of cognitive visual functions, including visual search, safe navigation through changing environments and reading, and given the poor rate of spontaneous recovery, several rehabilitative programs have been proposed to help patients recover. Three main different approaches have been developed to treat patients with HH: (1) substitution, including special devices such as optical...
This last approach is based on the concept of brain plasticity. Just as plasticity after brain damage is well recognized in other functional systems (motor, somatosensory), plasticity of the visual system has been recognized as a useful mechanism whereby the brain compensates for its functional loss, either spontaneously or by repetitive visual stimulation (Safran, 1988; Sabel et al., 2005; Schofield and Leff, 2009; Matteo et al., 2016).

About visual stimulation aimed to restore the VF in HH patients, 2 major kinds of behavioural stimulation were applied: the blindsight training and the border-field training. The blindsight training accomplishes goals by training pathways left intact after the damage, which project directly or indirectly to higher cortical regions, the border-field training by strengthening the function of partially damaged regions at the VF border or in islands of residual vision inside the blind field (Sabel et al., 2011).

For the VF border training, different visual rehabilitative programs were used, including repetitive VF testing (Zihl and von Cramon, 1979; Zihl and von Cramon, 1985), reaction perimetry treatment (Zihl & Werth, 1984) and the vision restoration therapy (VRT) (Sabel et al., 2005; Kasten et al., 1998; Julkunen et al., 2003; Julkunen et al., 2006; Marshall et al., 2008; Mueller et al., 2008; Romano et al., 2008; Sabel and Kasten, 2000; Widdig et al., 2003; Werth, 2008); moreover Bergsma and van der Wildt found an enlargement of the VF in their patients which was independent of the type of stimulus-set used during training (Bergsma and van der Wildt, 2010).

Since September 2009, is possible to perform repetitive visual stimulation also by the MP-1 microperimeter (NIDEK Technologies, Padua, Italy), using a program of visual pattern with structured stimuli. The MP-1 is a diagnostic and rehabilitative device, currently used to train patients with central vision loss. It is equipped with a visual rehabilitation tool consisting of flickering pattern, which allows patients with unstable fixation to develop a new preferred retinal locus (PRL). The patterned stimulation has highly significant recognition shape that increase inner retina integration processes and optimize stimulus processing and recognition and brain transmission and it was suggested that it can involve residual surviving cells, as well as amplify and integrate retinal and brain cortical plasticity (Verboschi et al., 2013; Markowitz and Reyes, 2013). For these characteristics, this photostimulation program might activate surviving neurons in areas of residual vision in patients with VF defects as well as other behavioral stimulation. Moreover, thanks to its eye-tracking module, the MP1 allows the operator to observe eye movements throughout the training session. In our study we want to verify the possibility to rehabilitate patients with VF defects and central vision preserved, using the MP1 patterned stimulation.

based practices that have yielded positive results for their students, which we will share here. After describing the challenges that people who have restricted visual fields or visual acuity loss may have with horizontal lateral scanning for vehicles at uncontrolled crossings, we will explain the accommodative strategies that were found to help them address those difficulties, and a procedure that

**Methods**

**Subjects**

11 patients (4 males and 7 females) with homonymous VF defect resulting from lesions of the central visual pathways and foveal sparing, were enrolled, after having given consent to participate in the study. The study protocol adhered to the tenets of the Declaration of Helsinki, and was approved by the Ethical Committee of the Polyclinic A. Gemelli. All participants were recruited in our Low Vision (LV) Centre, inside the Polyclinic A. Gemelli in Rome, between the 2016 and the 2017. Causes of the homonymous defects included stroke (3 patients), cerebral tumors (5 patients) and trauma (3 patients); 7 patients had right homonymous visual defect, the remaining had left. In all cases, more than 1 year had passed from the onset of the VF defects, in order to exclude spontaneous recovery (Table 1). To make the sample more homogeneous, all the patients underwent a neuropsychological evaluation, aimed at excluding the impairment of other cognitive functions, besides the hemianopia. Neuropsychological test battery had the purpose of evaluating memory, praxis, attention, visuo-spatial perception and neglect, and consisted in:
1. Mini Mental State Examination (MMSE)
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3. Rey–Osterrieth complex figure test (ROCF)
4. Letter Cancellation test
5. Barrage test
6. Clock drawing
7. Visual Object and Space Perception Battery (VOSP) (Screening Test, Dot Counting, Incomplete Letters, Silhouettes, Object Decision and Cube Analysis)
8. MFTC Multiple Features Targets Cancellation task

After neuropsychological tests, 1 patient (male, with right hemianopia after brain trauma) was excluded because a memory deficit was found.

Functional Assessment

We examined 20 eyes out of 10 patients. Mean age of participants was 42.3 years (± 11.63 SD). Patients enrolled in the study underwent standard protocol of clinical and functional assessment, by measuring the following:

1. **Best Corrected Visual Acuity (BCVA):** evaluated by Early Treatment Diabetic Retinopathy Study charts. BCVA was expressed in logMAR values obtained data distance of 4 meters with the best refractive correction.

2. **Contrast sensitivity:** evaluated with Pelli-Robson boards at 1 meter distance with the addition of +1 sph to the distance refractive correction.

3. **Fixation stability:** evaluated with the MP-1 microperimeter (NIDEK Technologies). Patients were asked to focus on a central target for about 20 seconds. The standard target was represented by a white cross with an extension of 1°.

4. **Retinal threshold sensitivity:** evaluated with the MP-1 microperimeter (NIDEK Technologies) expressed in decibels, using an automated mode, 4-2 threshold strategy, Goldmann III stimulus.

5. **Peripheral VF:** evaluated with Humphrey Field Analyzer (ZEISS), automated static perimeter, based on three threshold stimuli program that measures 30 degrees temporally and nasally and tests 76 points.

Each patient was evaluated in the same way at baseline, at the end of the rehabilitative pathway (consisted in 30 training sessions) and at the follow up (after 3 months). All patients had BCVA 0.0 LogMAR and central and stable fixation.

**Treatment**

Our rehabilitative program consisted in 30 visual training sessions, lasting 15 minutes for each eye, performed twice a week. In each session we used the MP1 pattern, a flickering at 20 Hz chessboard with retinal overlay of 8 degrees and squares stimuli of 0.5 degree. The pattern was centered on the fixation point, so the stimuli were located in the intact field, at the border zone and in the blind field.

**Statistical analysis**

Analyses were performed on data from the 10 participants (20 eyes), who completed the intervention. The data obtained were inserted on an Excel worksheet. Analyses were performed using Stata/IC for Mac software version 14.2 (Rev. 01.29.2018, StataCorp, Lakeway, College Station, TX 77845, USA). The Type-I error rate for this experimental intervention was set at α = 0.05 for all the tests. Descriptive data were summarized using continuous variables and were analysed using means and standard deviations (Mean ± Standard Deviation), after assessing the normal distribution of the variables through Shapiro-Wilk test. Potential differences in baseline characteristics were evaluated by unpaired t tests (or Wilcoxon rank sum test, according to the normality of distribution of the analyzed variables). The effect of the 30 visual training sessions intervention on each study outcome was analyzed with a separate two-way repeated-measures ANOVA and confirmed with General Linear Model. Dependent variables were the change in each result from baseline to each follow-up visit. Model effects included intervention, follow-up visit (post-intervention, 3-months retention) and their interaction. Models were adjusted for age and sex and Tukey’s post-hoc testing was used to compare factor means of significant models (Moscato et al., 2014).
Results

Visual field examination

Compared with the baseline time point, all patients showed a statistically significant reduction of the VF Mean Deviation (VFMD) and scotoma points (VFSP), consequently an improvement in the VF (Figure 1,2). Before stimulation the mean of the VFMD was -15.02 dB ± 3.42 SD (p < 0.000) and became -14.16 dB ± 3.97 SD after 30 visual training sessions; at the follow-up it was −13.97 ± 3.94 SD (p < 0.000). The mean of the VFSP was 30.85 ± 6.56 SD at baseline and decreased by 29.05 ± 7.96 SD (p < 0.000) after the training and by 27.8 ± 7.47 SD (p < 0.000) at the 3-months follow-up.

Microperimetry examination

Compared with the baseline time point, all patients showed a statistically significant reduction of the scotoma points (MPSP) and a statistically significant increasing of the mean retinal sensitivity (MPRS) (Figure 3,4). The eye-tracker monitored the fixation during all examinations, and it remained stable for all patients before and after training, and at the 3-months follow-up. At baseline, the mean of the MPSP was 23.6 ± 8.88 SD; at the end of the rehabilitative pathway it was 21.35 ± 9.64 SD (p < 0.000) and at follow-up 21.25 ± 9.10 SD (p < 0.000). The mean of MPRS was 10.95 dB ± 2.31 SD and increased by 12.24 dB ± 2.48 SD (p < 0.000) after training and by 12.14 ± 2.45 SD (p < 0.000) at the follow-up.

All results showed a major statistical significance after 3 months since the end of the visual stimulation, recording a further reduction of the campimetric damage. In percentage terms, if we compare the baseline and the follow-up values, the improvement recorded through the VF examination is 6.95% for the mean deviation and 9.88% for the scotoma points, while that recorded through the Microperimetry examination is 10.85% for the retinal sensitivity and 9.95% for the scotoma points.

None of the patients reported any complications or adverse events associated with rehabilitation treatment.

Discussion

Brain injuries (stroke, cerebral hemorrhage, cerebral trauma or brain surgery outcomes) are the most common causes of the damage of the retrochiasmal visual pathways, resulting in homonymous VF defects, as quadrant defects or complete hemianopia or more. The HH presents a spontaneous improvement in the first month in 50% of cases, many cases continue this process up to the 3rd
month, only rarely up to the 6th. The spontaneous recovery is complete in 38% of cases (Zhang et al., 2006). During the last decade, the traditional view that visual system damage is permanent has given way to a more optimistic view, because visual loss does not remain unchanged, but it can recover spontaneously to some extent. Even when the period of spontaneous recovery has ended, there is still additional potential of plasticity and regeneration. The neuroplasticity approach has shown that residual structures can be reactivated by repetitive stimulation. This can be achieved by different means: visual experience, visual training or electrical brain stimulation (Sabel et al., 2011). Concerning the visual training, several kinds of visual stimulation have already been used in ophthalmology for the treatment of hemianopic patients with the aim to restore the VF (Kasten and Sabel, 1995; Polat et al., 2004; Sahraie et al., 2006; Henriksson et al., 2007; Raninen et al., 2007; Jobke et al., 2009; Hayes et al., 2012). The border-field training is the most frequently used method and is based on exercises specifically targeting the transition zone between intact and damaged VF (Kasten et al., 1998; Schmielau and Wong, 2007). According with Residual Vision Activation Theory (Sabel et al., 2011), clinically relevant plasticity occurs not primarily in regions of “absolute blindness” but in “areas of residual vision”, known also as “relative defects”, typically located at the VF borders. It is hypothesized that repeated stimulation (training) of the transition zone induces a synaptic plasticity of the partially damaged structures and downstream areas, stabilizing their synchronous firing, even after the treatment period. This improved or stabilized synchronization is one of the proposed neurophysiological mechanism of vision restoration. Previous studies have demonstrated the efficacy of LV rehabilitation by means of microperimeter MP1 biofeedback in patients with central LV, reporting improvements in visual acuity, fixation behavior, retinal sensitivity and reading speed (Melillo et al., 2020; Vingolo et al., 2009). The MP1 is an automated retina scotometry and sensitivity measuring system, which monitors the fundus image at the same time, and thanks to the biofeedback tool, it can be used as a rehabilitating device. Training with a visual target or a pattern, connected to an acoustic signal that measured the best fixation position, leads to improve unconscious functions (fixation and visual acuity). This kind of procedure was ideated for the LV patients who have lost fovea fixation capabilities, to increase their fixation stability or to train to relocate their PRL into a different region, called trained retinal locus. On the other hand, for the intrinsic characteristics of the flickering stimulation pattern, we thought to use the MP1, for the first time, to rehabilitate patients with VF defect and we obtained hopeful results. Thanks to the eye-tracker system, we can guarantee that the fixation was stable in all patients during all examinations and that the VF en-
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largement was not due to saccadic movements (Sabel & Trauzettel-Klosinski, 2005). In conclusion, our results indicate that MP1 pattern stimulation induces a little improvement of the VF in hemianopic patients, restoring areas of residual visual function. So the MP1 can be dedicated to rehabilitate also patients with peripheral defects, even in longstanding cases of cerebral accident. Since to the best of our knowledge there are no studies exploring the effect of MP1 patterned stimulation for the rehabilitation of the peripheral LV, considering the easy availability of the MP1 device in the LV Centers, we wanted to make our preliminary findings known, although the absolute change is low, to encourage the study of the applications of the MP1 also for the rehabilitation of the VF defects and to contribute to the best possible rehabilitative care for LV patients.

Large-scale studies are necessary to confirm our preliminary findings and to investigate the effects on visual exploration performance. Other limits of the current study are the lack of the long-term follow-up after treatment period and the lack of a control group (which was excluded from the training or was treated with a placebo training), although spontaneous recovery can be excluded. Compared with the baseline time point, all patients showed a statistically significant reduction of the VF Mean Deviation (VFMD) and scotoma points (VFSP), consequently an improvement in the VF (Figure 1,2). Before stimulation the mean of the VFMD

Conflicts of Interest

The authors report no conflicts of interest and have no commercial interest in any of the materials mentioned in this article.

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