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Visuoperceptual rehabilitation with repetitive transcranial magnetic stimulation in chronic cortical blindness: a case report

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ABSTRACT

This study aims to reveal the effect of visuoperceptual rehabilitation combined with neuromodulation on visual impairment recovery in chronic cortical blindness. A 71-year-old patient with cortical blindness was assessed using perimetry, pattern electroretinogram (pERG), Canadian Occupational Performance Measurement (COPM), and Montreal Cognitive Assessment (MoCA) at baseline and after treatment. After 12 rTMS sessions and 50 visual perceptual rehabilitation sessions, perimetry, pERG, COPM, and MoCA significantly improved the visual field and daily functioning. Both COPM-MoCA scores exceeded clinical significance. The results indicate that combining vision therapy with rTMS may improve vision field, daily function, and satisfaction in a chronic blindness case.

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KEYWORDS
Cortical blindness; transcranial magnetic stimulation; rehabilitation; visual perception; case report

Introduction

Cortical blindness (CB) results from damage to the primary visual cortex (V1) or its immediate afferents, producing a loss of vision in the contralateral visual hemifield (Cowey & Stoerig, 1991). The major reason of CB is stroke due to damage to the posterior or middle cerebral arteries (Fujino & Kigizawa, 1986). Some spontaneous improvements in vision may occur within the first few months after stroke, but significant residual visual defects usually remain (Zhang et al., 2006). Although CB affects daily activities such as driving, reading, and navigating complex visual environments (Das & Huxlin, 2010), rehabilitation and recovery options are limited in this population. However, several perceptual training methods have achieved success in reducing the size of perimetrically blind fields (Das & Huxlin, 2010; Shibuki et al., 2020), and it is also stated that noninvasive brain stimulation such as transcranial direct current stimulation may affect the visual domain (Gall et al., 2015), but no data regarding the effects of repetitive transcranial magnetic stimulation (rTMS) application on CB was found in the literature.

The aim of this study is to display the effects of visuoperceptual rehabilitation combined with transcranial magnetic stimulation (TMS) on the recovery of visual impairment in a case with chronic CB

Case description

This case report was designed in line with the case report guidelines of SCRIBE (Tate et al., 2016). Written consent was obtained from the patient before the study, which was conducted in the Cognitive Rehabilitation Unit of Medipol University Hospital between November 2021 and February 2022.

A 71-year-old man with high blood pressure and diabetes was hospitalized for COVID-19 in March 2021. After 14 days in the intensive care unit, he realized not able to see. He could only see silhouettes of people. An MRI scan in April showed subacute infarct areas with hemorrhagic transformation in the bilateral occipital lobes (Figure 1) He was placed on blood thinners and discharged with recommendations. A month later, a neurological exam found only the vision loss. He was then started on ginkgo biloba 120 2 × 1, alpha-lipoic acid 600 1 × 1, and was evaluated for visual therapy.

Assessments

An ophthalmologist carried out the assessments. Visual field was evaluated with Automated Static Perimetry (Humphrey 30–2 SITA-Standard), clinical electrophysiology of his visual system with pattern electroretinogram (pERG) (Robson et al., 2018), global cognitive skills with Montreal Cognitive Assessment (Nasreddine et al., 2005), and performance and satisfaction with performance in self-selected everyday life goals with Canadian Occupational Performance Measurement (COPM) (Law et al., 1990). Fixation controls were employed during the measurement of visual fields. All measurements were made at the baseline and after the treatment.

In the ophthalmological examination, the visual acuities were hand motion in both eyes. There was no abnormality in both eyes in the slit-lamp examination. Both eyes reacted sluggishly to direct light. Pupils were isochoric in both eyes. Intraocular pressure was 14 mmHg in both eyes. Fundus examination revealed normal findings in both eyes. There was mild asymmetric cupping.

Optical coherence tomography derived cross-sectional images of the fovea was normal in both eyes. Retinal nerve fiber layer (RNFL) thickness analysis and fundus

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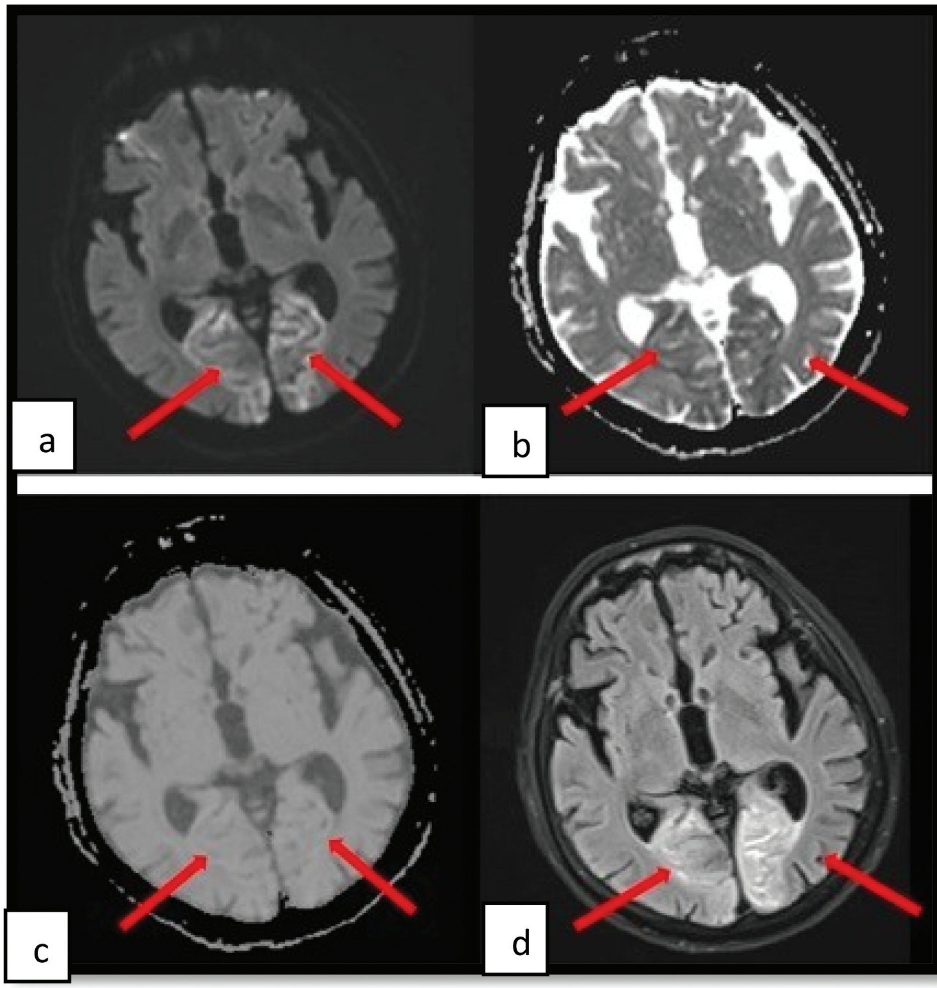

Figure 1. Magnetic resonance (MR) brain, bilateral occipital lobe infarcts indicated by arrows.

autofluorescence imaging yielded normal results in both eyes. The response of Pattern ERG was subnormal in both eyes. N95/P50 ratio was 2.3 in the right and 1.6 in the left eye. Ganzfeld ERG results were normal under scotopic and photopic conditions in both eyes. Humphrey automated static perimetry (30–2) revealed bilateral generalized absolute scotoma in both eyes, and only a peripheral midline upper relative scotoma area was observed in both eyes. The results are presented in Table 1.

In the clinical examination, he could not see the objects in his field of vision. However, when verbally directed, he could focus on red things and follow them in a short time. Although he could see the objects, he had trouble identifying them. He attempted to identify them by touching them. Identifying numbers and letters was easier. It was observed that when he tried to reach the objects, he perceived them 5 cm to the right of their actual location. MM was able to detect light but reported difficulty seeing it clearly.

Table 1. Pre- and post-treatment assessments.

	Pre-treatment		Post-treatment	
Assessments	Right Eye	Left Eye	Right Eye	Left Eye
Perimetry				
MD	−30.95	−30.82	−30.17	−29.86
PSD	4.06	4.51	5.12	6.33
Retinal sensitivity	42	63	83	131
pERG				
N95/P50	2.3	1.6	1.3	2.0
MoCA	16		18	
COPM				
Performance Score	3.3		6.3	
Satisfaction Score	1.6		7.6	

PD: Pattern Deviation; **PMD**: Perimetric Mean Deviation; **MD**: Mean Deviations.

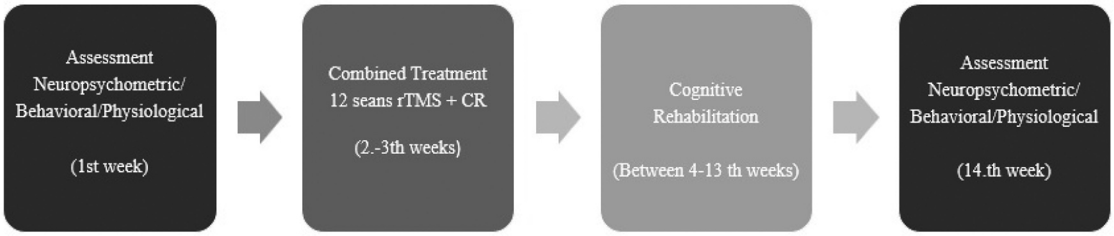

Figure 2. Study flow chart. CR: Cognitive Rehabilitation

Interventions

MM was followed up neurologically, ophthalmologically, and electrophysiologically for 14 weeks and received 12 sessions of rTMS and 50 sessions (3–4 sessions per week) of therapy for visuoperceptual disorders (Figure 2). TMS and visual rehabilitation protocols are described below.

rTMS protocol

Via magnetic stimulation using a figure-eight coil, rTMS was applied to the right and left posterior parietal lobes. The target location was identified on the first day when rTMS was administered, which was based on the International 10/20 System for EEG and applied on the right and left posterior parietal cortex (PPC). TMS intensity was set at a maximum of 110% of MM's resting motor threshold, which was determined daily following the recommendations of the International Federation of Clinical Neurophysiology (Schutter & van Honk, 2006). Trains of rhythmic high-frequency (20 hz) rTMS were delivered for short periods (3.75-s duration), separated by longer, no-stimulus periods (45 s), during each daily session. A total of 3000 pulses were applied each day (75 stimuli/train, 40 trains) for a total of 12 sessions. The patient was applied 12 sessions of rTMS (Figure 3).

Figure 3. rTMS application.

Visuoperceptual rehabilitation program

The intervention program was composed of remedial and compensatory approaches and was supported with psychoeducation (Pollock et al., 2011). The patient attended 45-min sessions 3–4 times a week and was followed up for 14 weeks. In addition to the sessions, it was ensured that the patient continued to exercise every day with home exercises planned to last 1.5 h.

Remedial approaches

Remedial approaches were used predominantly in the intervention program rather than compensatory approaches. Among these approaches, computer-based exercises and TMS applications, which are among noninvasive stimulation methods, are included. The exercises in the intervention program were performed frequently and repetitively.

(1) *Step 1*: The perimetric evaluation of the patient who applied to our clinic showed that he had very limited vision, so vision tests could not be performed. Therefore, the initial goal of the treatment was to increase the visual field. For this purpose, horizontal-vertical and diagonal tracking of a remarkable stimulus was initiated with various applications such as ocular fixation, convergence and divergence exercises, motion perception, and awareness of stationary and moving stimuli within the field of view. The patient started the exercises at a level that he could manage, and the time and direction parameters were changed to increase the difficulty of the exercises.
(2) *Step 2*: The exercises in step 1 were continued by increasing the difficulty. The ability of the patient, who was able to focus on the sound or remarkable stimulus, to recognize the stimulus and follow the moving object was assessed. Reading and writing exercises were done. Computer-based exercises were used intensively in this step and it was observed that he recognized numbers and texts more easily, but had difficulty in recognizing

objects. It was thought that he might have apperceptive agnosia, but it could not be confirmed due to his loss of vision. To increase the difficulty of the exercises, objects that were too small or too large were shown, the display time was reduced, familiar and unfamiliar objects were shown, respectively, and objects placed outside the field of view were shown. It was tried to make the patient watch videos, but this was abandoned because the patient had difficulty in perceiving.

(3) *Step 3*: In this step, the goal was to transfer the acquired skills to daily life activities to maintain the improvements obtained in the sessions. In contrast, the step 1 and step 2 exercises (by increasing the degree of difficulty) continued. For this purpose, different activities were carried out such as finding the door to the treatment room, finding the buttons in the elevator, detecting the entrance to the hospital and finding the treatment room, following the bus coming from afar until it approaches the bus stop, reading the numbers on the bus, finding and returning a remarkable object in a different room while being the treatment room, and taking an object from a specified place and transporting it to another. It was observed in this step that the patient had optic ataxia and perceived objects approximately 5 cm to the right from their original place (Figures 4 5).

Compensatory approaches

Although remedial approaches were predominantly used in the rehabilitation program, some environmental adaptations and strategy trainings were also included during the treatment.

(a) ***Environmental adaptations:*** In order to ensure the patient's safety, it was requested to keep the living environment uncluttered, and to remove the objects that could be an obstacle such as coffee tables, cables, and boxes within the walking area in his house. He was also asked to remove items such as rugs and mats that might cause slipping, especially in the areas that are frequently used, such as the bathroom.

(b) ***Strategy training:*** Two different types of strategies, i.e., cognitive and organizational, were used on the case. Cognitive strategies such as visual scanning among the selected target points when he could not find the objects he was looking for, trying to find the object and increasing the perception through logical reasoning when he could not make sense of the objects he saw, and transferring what he learned in the sessions to his home activities were used. In addition, organizational strategies such as placing frequently used objects in the same place, establishing a certain routine in activities, using contrasting colors in the areas he was frequently using (eating on a red tablecloth, placing clothes to be worn on a white bedspread) were also used to compensate for the weakness in visual perception.

Psychoeducation

The patient and his companion were informed about his condition. The difficulties he was experiencing while performing the activities of daily living were determined, and the strategies to cope with the vision problem were taught to the patient. His weaknesses and strengths were clearly demonstrated.

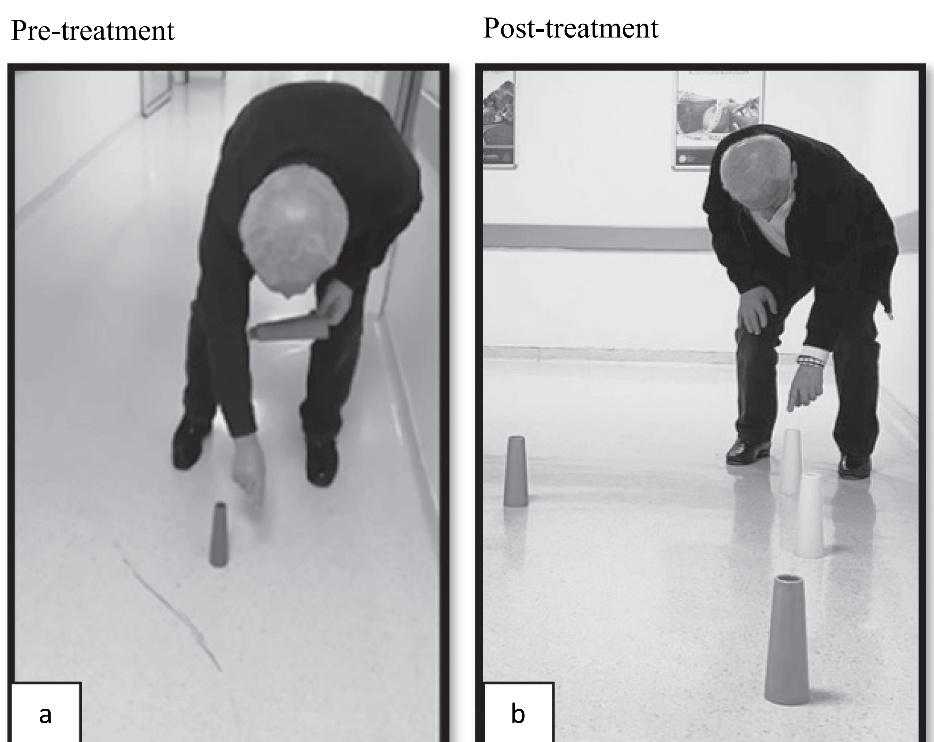

Figure 4. Exercise for optic ataxia.

Figure 5. Exercise examples during treatment.

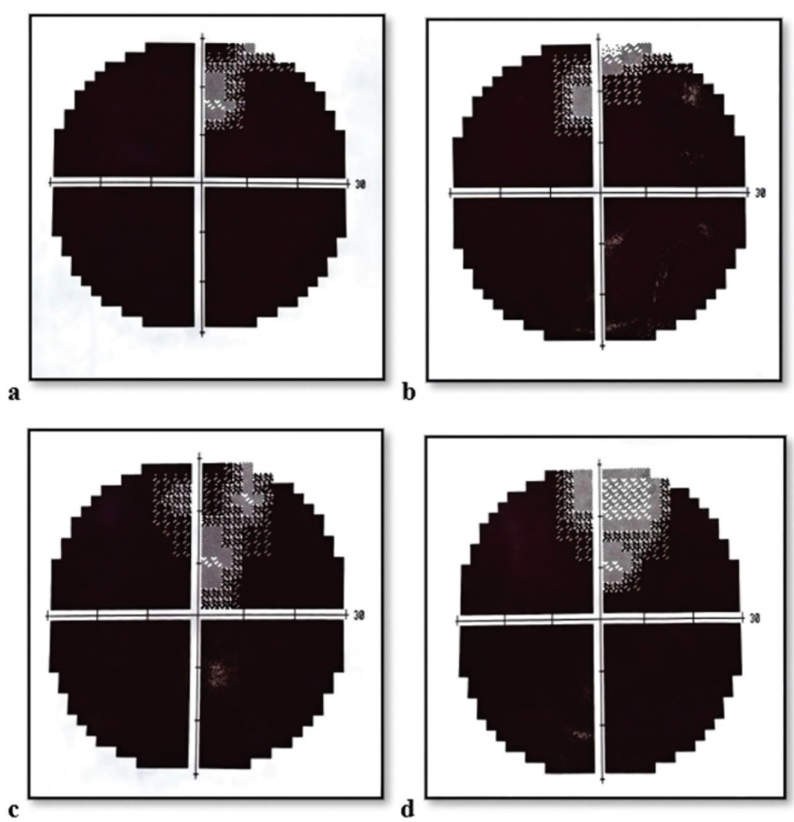

Figure 6. Perimetry results. a. Pre-treatment perimetry result of the right eye; b. Pre-treatment perimetry result of the left eye; c. Post-treatment perimetry result of the right eye; d. Post-treatment perimetry result of the left eye

Motivational speeches were given against negative thoughts that might have occured. The importance of continuing home exercises in a strict and regular manner was emphasized. It was underlined that it was necessary to transfer what was learned during the exercises to daily activities.

For the analysis of study data, the scales used before and after the treatment were evaluated for clinical significance. In addition, subjective comments of the patient were included. After the rehabilitation program, all results regarding the visual field, his cognitive situation, activity performance, and satisfaction were discussed in detail.

Results

In the initial ocular examination, the visual acuities were hand motion in both eyes; after the treatment, it was hand motion in the right eye and the patient can count finger from 50 cm distance in the left eye. The slit-lamp examination revealed no abnormality in both eyes. The response of Pattern ERG was subnormal in both eyes (Table 1). N95 response improved in both eyes. Gansfeld ERG results were normal under scotopic and photopic conditions in both eyes. Humphrey automated perimetry (30–2) results showed that the peripheral midline upper relative scotoma area improved in both eyes (Figure 6). All assessment results are presented in Table 1.

Subjective signs of improvement: In addition to the improvements obtained in the standardized evaluations of the patient, obvious changes in life activities such as changes in his gaze over time, increase in ocular following, going out of his own apartment by himself, being able to find breakfast items from the refrigerator and place them on the table, finding his own clothes in the wardrobe, being able to recognize the bus to take from afar (although not always), and being able to shave himself were reported by the relatives of the patients.

Discussion

This case report describes the treatment of a patient with CB that had occurred due to a stroke 1.5 years earlier. To our knowledge, there have been no published data on CB treated with rTMS and visuoperceptual rehabilitation.

CB can develop for a variety of reasons, including stroke, trauma, infection, and tumor (Melnick et al., 2016). It was reported that spontaneous recovery occurs within the first 6 months in CB due to stroke, and then the improvements are limited (Zhang et al., 2006). Therefore, the importance of rehabilitation to ensure maximum efficiency is emphasized. The literature states that visual impairment can be partially corrected through appropriate training (Melnick et al., 2016). Sabel et al. revealed that Vision Restoration Therapy (VRT), which is performed to treat visual impairments occurring due to injuries after chiasma (post-chiasmatic injury), has therapeutic potential. Huxlin and Cavanaugh stated that intensive visual discrimination training given to cases with CB due to chronic stroke 5 days a week for 6 months improved the field of vision in perimetry (Cavanaugh & Huxlin, 2017). Saionz et al. stated that even when the blind spot is intensively treated with remedial approaches, recovery could be achieved partially, so the main factor in the rehabilitation of visual impairments is the combined use of compensatory and remedial approaches. It is also underlined that intervention approaches should start early and be in line with strategies that optimize their use in daily life in order to make the treatment more effective and to achieve the development of plasticity (Saionz et al., 2021). In light of this data, we designed the rehabilitation program for our case, implementing remedial and compensatory approaches, and supported it with psychoeducation. Oculomotor tracking, detecting stimuli in the visual field, and the use of moving stimuli formed the basis of the exercise program, which was structured in three steps of remedial approaches. It is stated that training the oculomotor tract improves the attention required for visual perception to the blind spot (Hadid & Lepore, 2017). The short- and long-term beneficial effects of the presentation of the moving stimulus in the impaired area are mentioned in a case who developed CB after 5 years of occipital infarction (Shibuki et al., 2020).

The remedial approaches we implemented in the rehabilitation program we designed were applied intensively, and the home exercise program, which was applied for 1.5 h a day, also supported this level of intensity. The subsequent steps of the program aimed to transfer the acquired skills such as using the scanning strategy while taking breakfast food from the fridge, directing attention to the daily objects around himself and trying to find out what they are, trying to use the visual stimulus as a guide instead of getting help from the tactile stimulus during the identification process, using red color as a guide and taking an active role in simple kitchen tasks (making a cup of tea and cleaning countertop), and ensuring personal hygiene by maintaining a heightened focus on daily life. The rehabilitation program was strengthened with compensatory approaches and psychoeducation to ensure maximum independence of the patient (Saionz et al., 2021). Although it is generally observed that the rehabilitation programs of CB cases are structured on maximizing the remaining vision and teaching compensatory strategies (Shibuki et al., 2020), there is currently no consensus on a specific method (Law et al., 1990; Pollock et al., 2011; Sabel et al., 2005).

Recently, noninvasive brain stimulation methods have been used in the treatment of visual field loss in addition to visual perceptual exercises, and it is stated that the effects of noninvasive brain stimulation should be investigated (Melnick et al., 2016; Saionz et al., 2021, 2022). It is not clear which type of stimulation should be used in which brain region. In their study comprising healthy individuals and those with cortical blindness, Herpich et al. utilized two different stimulation techniques, namely tRNS and tDCS, and targeted two distinct brain regions, the occipital and parietal lobes. In contrast to our study, they demonstrated that a 10-day short-term tRNS stimulation applied to the occipital lobe, combined with visual training, could lead to plastic changes and potential restoration in cases primarily characterized by unilateral V1 area damage (Herpich et al., 2019).

It is commonly observed that tDCS application is preferred for stimulation and occipital region stimulation is used (Alber et al., 2017; Plow et al., 2012). In our study, we stimulated the bilateral PPC of MM through TMS. The main reason why we chose the PPC as the stimulus in the treatment program of our patient, who had a stroke 1.5 years earlier, can be explained as follows. In addition to the visual information flow reaching the occipital cortex from the superior colliculus (SC) or thalamus and providing conscious vision, the information reaching the PPC from the SC or thalamus provides unconscious vision and is called blind vision (Shibuki et al., 2020). When damage occurs to the occipital cortex, healing occurs either spontaneously or partially through neural plasticity of the remaining cortical areas (Ajina et al., 2015; Marshall et al., 2008). However, as a third healing mechanism, it was reported that blind vision could turn into conscious vision with the neural synchronization between the neural group in blind vision and the other neural group that includes conscious vision (Melloni et al., 2007; Silvanto , 2015). Therefore, if this view turns out to be correct, stimulating the PPC in chronic cases will be effective in the evolution of blind vision to conscious vision (Shibuki et al., 2020). In addition, the PPC was reported to play a causal role in both primary awareness and visuospatial attention (Babiloni et al., 2007), and studies on virtual lesion of the parietal lobe with TMS support this (Fierro et al., 2000; Yan et al., 2016).

In cases of CB, the location and intensity of the visual field defect affects the individual's quality of life and independence (Gall et al., 2009). For this reason, it is important to determine the loss of vision by perimetry, which is a quantitative test (Hepworth & Rowe, 2018; Townend et al., 2006). While the intact visual field in the right eye was only in the outer upper quadrant before the treatment, the intact visual field in the outer quadrant expanded to include the inner quadrant after the treatment in the perimetric examination we implemented on our case. The retinal sensitivity in this field increased by 97%. As for the left eye, the intact field in the superior enlarged even further after the treatment, and retinal sensitivity increased by 107%. Although the angular measurements of the improved field could not be made, the post-treatment improvements were evident. It is possible to come across studies in the literature that report improvements in the visual field thanks to visual training and its effects on perimetry (Cavanaugh & Huxlin, 2017; Saionz et al., 2022). It is also stated in the literature that tDCS application, which is one of the brain stimulation methods applied on the occipital cortex, may be beneficial even if TMS is not implemented (Alber et al., 2017; Plow et al., 2012; Shibuki et al., 2020). The improvement observed in our case is consistent with the literature.

Although exercises for cognitive skills other than visual field and perception exercises were not performed in the rehabilitation program, it was observed that the MoCA score of the patient increased by 2 points after the treatment, which is above the level of minimal clinical significance (Wong et al., 2017). The increase of 2 points occurred in the attention subtest of the MOCA. That the visuoperceptual exercises applied as part of the rehabilitation program incorporated attention skills and the TMS application applied to the PPC, which is effective on attention, are thought to have an effect on this increase in the attention area (Babiloni et al., 2007).

In addition to standardized tests, a semi-structured scale called COPM was used to evaluate the performance and satisfaction of the patient in our study. After the treatment, the patient's performance score increased by 3 (from 3.3 to 6.3) and satisfaction by 6 (from 1.6 to 7.6). It was noted that these scores, especially the satisfaction score, were considerably higher than the clinical significance level determined for COPM (Wressle et al., 2002). In parallel with our findings, the literature holds that visual rehabilitation improves quality of life, which is related to individual satisfaction (Trauzettel-Klosinski, 2009). MM also stated that he could see and recognize a larger area, his independence in home and hygiene practices increased, and he could follow moving objects (bus approaching the stop) better after the treatment.

The literature states that noninvasive brain stimulation can be used to modulate neural network activity in addition to the rehabilitation approaches used in CB cases (Alber et al., 2017; Shibuki et al., 2020). In addition, it is highlighted that visual training before neurostimulation is necessary (Hadid & Lepore, 2017). In our study, which is compatible with these principles, the remedial and compensatory approaches that we applied intensively for 3 months for visuoperceptual disorders were supported by high-frequency rTMS. It was observed after our program that the patient's field of view expanded, and the increase in global cognitive skills, activity performance, and satisfaction reached the level of clinical significance. However, it should be kept in mind while interpreting the results that the subjective measurements the patients reported could be biased.

Limitations

There are several limitations to this study. First, due to its single-case study design, the effectiveness of this rehabilitation program may not be generalized for all cases with CB. Second, since a pilot study was not conducted beforehand, stimulation was performed according to the patient's needs, not within the usual stimulation fields.

Conclusion

This study presents the improvements in a case of CB to whom visuoperceptual rehabilitation was applied intensively through rTMS 1.5 years after the case had had a stroke. Intensive visuoperceptual rehabilitation combined with noninvasive brain stimulation holds promise in improving the visual field.

Disclosure statement

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Data availability statement

Data sharing is not applicable to this article because no datasets were generated or analyzed during the current study.

Patient consent statement

Written consent was obtained from the patient.

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