# Combining Visual Rehabilitative Training and Noninvasive Brain Stimulation to Enhance Visual Function in Patients With Hemianopia: A Comparative Case Study

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**Objective:** To standardize a protocol for promoting visual rehabilitative outcomes in post-stroke hemianopia by combining occipital cortical transcranial direct current stimulation (tDCS) with Vision Restoration Therapy (VRT).
**Design:** A comparative case study assessing feasibility and safety.
**Setting:** A controlled laboratory setting.
**Patients:** Two patients, both with right hemianopia after occipital stroke damage.
**Methods and Outcome Measurements:** Both patients underwent an identical VRT protocol that lasted 3 months (30 minutes, twice a day, 3 days per week). In patient 1, anodal tDCS was delivered to the occipital cortex during VRT training, whereas in patient 2 sham tDCS with VRT was performed. The primary outcome, visual field border, was defined objectively by using high-resolution perimetry. Secondary outcomes included subjective characterization of visual deficit and functional surveys that assessed performance on activities of daily living. For patient 1, the neural correlates of visual recovery were also investigated, by using functional magnetic resonance imaging.
**Results:** Delivery of combined tDCS with VRT was feasible and safe. High-resolution perimetry revealed a greater shift in visual field border for patient 1 versus patient 2. Patient 1 also showed greater recovery of function in activities of daily living. Contrary to the expectation, patient 2 perceived greater subjective improvement in visual field despite objective high-resolution perimetry results that indicated otherwise. In patient 1, visual function recovery was associated with functional magnetic resonance imaging activity in surviving peri-lesional and bilateral higher-order visual areas.
**Conclusions:** Results of preliminary case comparisons suggest that occipital cortical tDCS may enhance recovery of visual function associated with concurrent VRT through visual cortical reorganization. Future studies may benefit from incorporating protocol refinements such as those described here, which include global capture of function, control for potential confounds, and investigation of underlying neural substrates of recovery.
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## INTRODUCTION

Visual impairment that stems from cerebral damage such as stroke greatly impacts upon an individual's sense of independence and well-being [1]. Damage to the occipital cortex and/or the optic radiations results in a deficit within the contralateral half of the visual field of both eyes. This partial blindness, termed hemianopia [2-4], profoundly affects many important activities of daily living (ADL), including reading [5,6] and navigating safely within one's environment [7-9]. In the majority of cases, patients demonstrate less than 5° of central visual sparing [10], and complete spontaneous recovery occurs only rarely [9,11,12]. Given that relatively few therapeutic options exist for this condition, developing novel rehabilitation strategies to promote the recovery of visual function after cerebral damage is of great importance [13].

Author affiliations and disclosures are provided at the end of the article.

Disclosure Key can be found on the Table of Contents and at www.pmrjournal.org

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Multiple lines of evidence from animal and human clinical studies have highlighted the potential of the brain to reorganize itself within the context of functional recovery after injury [14-16]. Efforts also have been aimed at identifying interventions that can leverage and modulate these mechanisms [17-23]. One example emerges from work in motor recovery after stroke, which demonstrates that repeated systematic training combined with direct invasive electrical stimulation (delivered to areas of the motor cortex that correspond to the paretic hand) significantly improves functional rehabilitative outcomes [20,24-26]. Similar findings also have been reported when using adjunctive noninvasive forms of brain stimulation [21,27-31].

Translating these concepts to the case of hemianopia requires a visual analog of systematic rehabilitative training. One possibility is to incorporate computer-based visual training strategies such as Vision Restoration Therapy (VRT) (Novavision Inc, Boca Raton, FL). VRT trains patients to detect repeated presentations of visual stimuli concentrated within the area between blind and intact visual fields. This area of residual vision has been referred to as the "transition zone," and has been functionally characterized as an area of suboptimal visual perception that may physiologically correspond to partially surviving neurons associated with damaged visual areas [13,32,33]. By following a daily training regimen (typically lasting 6 months), a demonstrable expansion in visual field border has been reported [32-38]. Visual recovery may implicate the reactivation of surviving perilesional areas as well the recruitment of neighboring higher-order visual areas [32,39-42]. Thus, similar to motor recovery, cortical stimulation that targets areas implicated in repeated systematic training of the affected visual field may potentiate synaptic and network level neuroplastic changes and may lead to improved functional outcomes.

Based on these concepts, we developed a comparative case study protocol designed to test the feasibility and preliminary efficacy of combining VRT with noninvasive brain stimulation (transcranial direct current stimulation [tDCS]). TDCS has been gaining considerable interest not only for its ability to modulate cortical excitability but also for its relative simplicity of implementation and good safety profile [18,43]. Results of previous studies have shown that tDCS delivered to the occipital cortex can modulate visual perceptual functions, such as contrast sensitivity detection and motion perception [44-46]. We hypothesized that combining VRT with anodal tDCS (so as to upregulate the excitability of both the intact and lesioned hemispheres) would potentiate visual rehabilitative efficacy compared with VRT alone (ie, paired with sham tDCS).

We also incorporated a series of design refinements specifically aimed to address criticisms raised from previous studies regarding VRT [47-49]. First, by using online eye tracking, we investigated whether compensatory eye movements led to the erroneous appearance of visual field expansion [48-50]. Second, we included an ancillary assessment of visual field (by using a MP-1 microperimeter; NIDEK Technologies, Padova, Italy) to further compare and validate observed visual field changes after training. Third, we incorporated validated tests to capture associated functional benefits on ADLs. Fourth, we quantified the patients' own subjective changes in visual field deficit to address reported discontinuities between quantitative and qualitative outcomes [47,49]. Finally, we incorporated a functional magnetic resonance imaging (fMRI) study to characterize neural substrates associated with recovery after training [49].

## METHODS

### Subjects

Patients 1 and 2 (both women, aged 61 and 62 years, respectively) were both diagnosed with right-sided hemianopic visual field loss resulting from ischemic stroke and were in the chronic phase of visual recovery [9,11]. Neither patient presented with any additional confounding visual deficit (eg, ocular complications), nor was either patient concurrently involved in another form of rehabilitative training. Neither presented with any exclusion criteria drawn from safety guidelines associated with the use of noninvasive brain stimulation [51-53]. Briefly, this included the following: (1) history or familial history of seizure disorder; (2) metallic, mechanical, or magnetic implant in the head or body; and (3) chronic use of neurostimulants, anticonvulsants, or antidepressants.

Patient 1 was randomly assigned to receive VRT combined with active tDCS, whereas patient 2 received VRT combined with sham tDCS (Figure 1). Experimental blinding was implemented at the level of patients and the individuals who were assessing visual field outcomes. Both patients provided written informed consent, and the study was approved by the institutional review board of the Beth Israel Deaconess Medical Center, Boston, Massachusetts.

### Interventions

***VRT.*** The study was conducted in a controlled laboratory environment, which allowed for the standardization of the training environment and the opportunity to continually monitor and provide feedback on progress. A contracted VRT training regimen that lasted 3 months was used (ie, 2 half-hour sessions per day, 3 days per week for a total of 36 hours), which corresponded to approximately one-fourth of the typical schedule used in previous VRT studies (ie, 6 months, for a total of 144 hours) [32,33,35]. After comprehensive neurologic and ophthalmologic examinations, the patients' visual field function was assessed to characterize progress and also to guide the spatial parameters of customized VRT (see below for details).

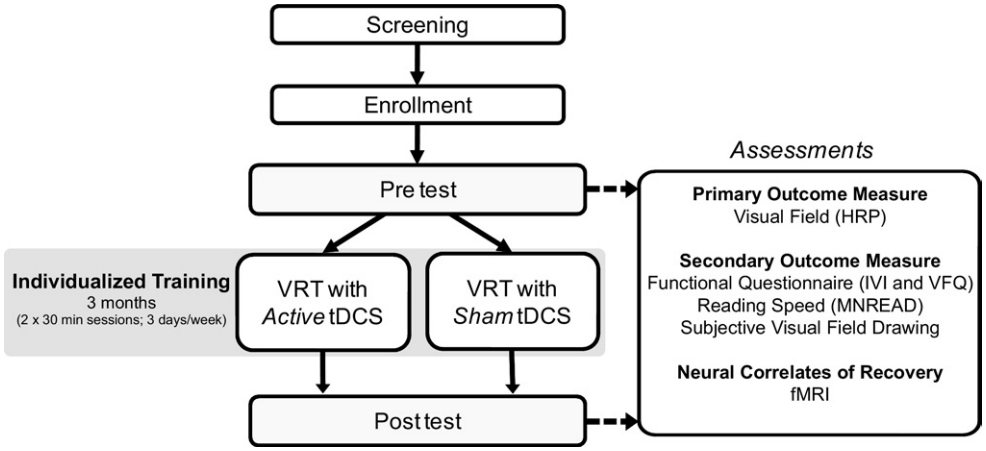


**Figure 1.** Overview of study design. Potential study participants are evaluated for eligibility based on predetermined inclusion and exclusion criteria. Baseline (pretest) measures of performance are obtained, including objective, subjective, and functional outcomes as well as a baseline fMRI. Participants are randomized to either VRT and active tDCS or VRT and sham stimulation, after which they undergo a 3-month visual rehabilitation program. Outcome measures of performance are again reassessed at monthly intervals and at the end (post-test). fMRI, functional magnetic resonance imaging; HRP, high-resolution perimetry; IVI, Impact of Vision Impairment; tDCS, transcranial direct current stimulation; VFQ, Visual Functional Questionnaire; VRT, Vision Restoration Therapy; MNREAD, Minnesota Low-Vision Reading Test.

During training, the patient was seated in front of a 15-in liquid crystal display monitor and at a constant viewing distance of 30 cm with the head supported comfortably in a chin rest (Figure 2). The patient was instructed to fixate with both eyes on a central target presented on the monitor (appropriate spectacle correction was used when necessary). During one 30-minute training session, 500 light stimuli were presented, primarily concentrated within the transition zone v (see primary outcome measure: visual field assessment for details). Each stimulus appeared for 2000 milliseconds, from low to high luminance (<1-50 cd/m$^2$) in a stepwise manner. The patient was instructed to respond as quickly as possible with a key press upon detecting the peripheral stimulus. As a built-in fixation monitoring strategy, the patient also was required to detect a color change of the fixation target within 750 milliseconds, presented at random intervals (for more details regarding the specifics of the VRT protocol, see Poggel et al [54]).

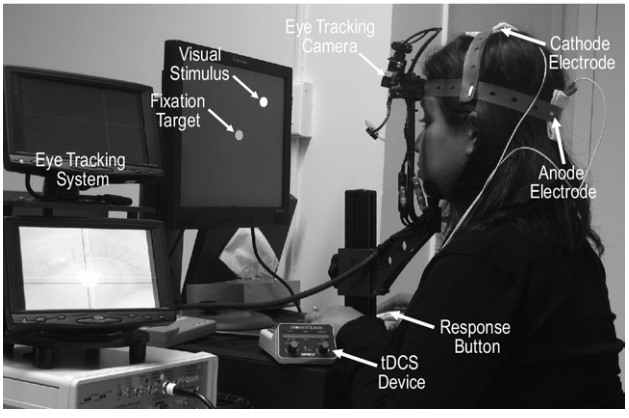


**Figure 2.** Experimental setup. The patient is seated in front of a computer monitor and instructed to fixate on a central target while responding (by using a response button) to the detection of visual stimuli presented. An eye-tracking camera monitors eye position throughout the experimental session. The stimulation montage consists of 2 electrodes connected to the transcranial direct current stimulation (tDCS) device. The anodal electrode is placed over the occipital pole (Oz), and the cathodal electrode is placed over the vertex (Cz).

***tDCS.*** tDCS was delivered by using 2 electrode sponges (5 × 7 cm, soaked in 0.9% saline solution) connected to a battery-operated unit that delivered continuous current (IOMED Inc, Salt Lake City, UT). Based on the 10-20 International EEG Coordinate System, the anode was placed overlying the Oz position, with the intention of stimulating the occipital cortex bilaterally, and the reference (cathode) was placed over Cz (vertex). The electrodes were secured in place by using nonlatex rubber straps (Figure 2). When a tDCS unit is turned on, current is slowly ramped up until the target current level is reached. During this initial period (approximately 30 seconds), subjects will typically report a tingling or itching sensation beneath the surface of the anode. The sensation subsides shortly thereafter (by habituation) and remains below the threshold of detection. This fact is exploited for the purposes of experimental blinding [18,52,55]. Specifically, in patient 1, once the current was ramped up to the target 2 mA/min, it was sustained throughout the duration of VRT training. For patient 2, the current was ramped down (to zero) after initial habituation. Thus, both patients remained unaware as to whether they were receiving active or

sham tDCS. Effective blinding was further verified at the exit interview.

## Outcome Measures

Outcomes were assessed at baseline (pretest) and at monthly intervals until completion of the 3-month training period (post-test), unless noted otherwise.

***Primary Outcome Measure: Visual Field Assessment.*** Visual fields were assessed by using high-resolution perimetry (HRP) (described in detail previously [33,56]), which is believed to correlate with more typical clinical visual field assessments [56]. As with standard automated perimetry, the patients were instructed to maintain fixation on a central target. Visual stimuli were randomly presented at suprathreshold intensity (luminance 95 cd/m$^2$) within the entire testing area (spanning 43°× 32° within an imaginary grid of 19 × 15 cells, each cell subtending 2°). The patients reported target detection by using a key press. Fixation monitoring strategy was similar to that used in VRT.

The final visual field map was generated by overlaying the results of 3 separate, consecutive tests. Intertest reliability was verified by consistent performance in stimulus detection, fixation performance, and false-positive rates. The composite visual field map comprised intact regions (areas where stimuli were detected on all 3 tests), blind (regions never detected), and transition zone (stimuli were detected on only one or 2 tests) (Figure 3). By convention, the visual field border was defined as the average horizontal distance between the central vertical meridian and the medial edge of 2 consecutive blind cells along each row in the imaginary grid [36].

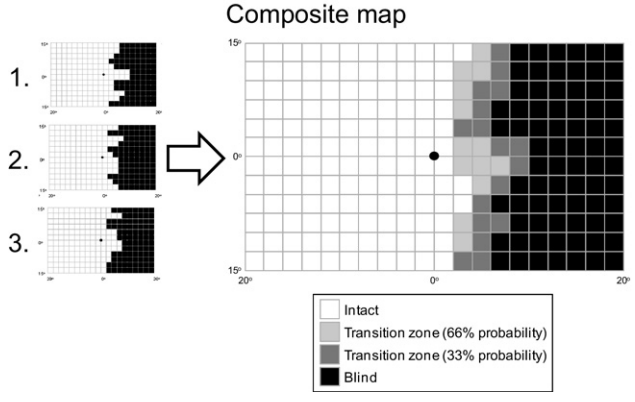


**Figure 3.** Assessment of the visual field by using high-resolution perimetry. The results of 3 separate suprathreshold perimetry tests are overlaid to generate a composite map that identifies the intact field, the blind field, and the transition zone of the visual field. The transition zone is further subdivided into regions where stimuli are detected once (33% probability) or twice (66% probability).

***Secondary Outcome Measures.***

- Functional Outcome Measures (Reading and ADLs): Functional outcomes of performance included the Impact of Vision Impairment (IVI) [57,58] and Veterans Affairs Low Vision-Visual Functional Questionnaire (LV-VFQ) [59,60]. Responses were rated by using a Likert-type scale (with 0 indicating "not affected" to 5 indicating "cannot do it at all" for the IVI; and 1 indicating "not difficult at all" to 4 indicating "impossible" for the LV-VFQ). Reading performance was assessed at pretest and post-test by using the Minnesota Low-Vision Reading Test (MNREAD) standardized test for reading speed (medium print size, 2M print size equivalent to 0.7 logarithm of the Minimum Angle of Resolution [logMAR]) [61] and was expressed in words per minute (wpm).
- Subjective drawings of the affected hemifield: To characterize a subjective visual field, the patients were instructed to fixate on a central target on a 9 × 12-in sheet of graph paper (similar in design to an Amsler grid) at a viewing distance of 40 cm. The patients then indicated the location of the intact visual border, and the drawings were then digitized and converted into dichotomous black and white figures with preserved aspect ratio [62]. The area of affected vision (represented by regions in black on digital images) was then calculated by using customized software (version 4.0.2; Scion, Frederick, MD).

***Ancillary Visual Field Assessment.*** As an ancillary outcome measure, visual field performance was assessed at pretest and at post-test by using a NIDEK microperimeter (MP-1). This device is gaining acceptance within the clinical community and allows luminance-based thresholded microperimetry with fixation tracking [63] using retinal fundus landmarks and false-positive rate measures [64,65]. The NIDEK MP-1 testing grid covered a circular area within central 20°, and a luminance-thresholded approach using a 4-2 strategy was used. Within the affected visual field, stimulus locations were categorized as "blind" (0-6 dB), "transition" (7-12 dB), and "intact" (13-20 dB) based on predefined thresholds of luminance of detection [64].

***Eye Movement Tracking.*** In addition to fixation monitoring built into the HRP system, we incorporated an independent measure of fixation performance by using a 2-dimensional infrared eye tracking device (Applied Science Laboratories, Bedford, MA). Tracking ocular pupillary and corneal reflections at a sampling frequency of 60 Hz (expressed in Cartesian coordinates) [66] allowed for online quantification of fixation performance during training and visual field testing. The "fixation moment" was defined as the instance in which the central gaze remained within 0.5° of a prior location for more than 12 milliseconds. The percentage time for which fixation moment was within the central 1° and 2° radius was then calculated.

***Functional Neuroimaging.*** fMRI has been used extensively in cognitive neuroscience and clinical neurology for its ability to localize brain activity [67-69]. Previous VRT studies have used fMRI to characterize patterns of neural activation with regard to the initial phases of VRT training [34] and with visual tasks designed for visual cortex mapping [34,70]. Here, we incorporated fMRI to identify patterns of activation associated with recovery of function.

The fMRI data were collected at baseline and at post-test for patient 1 (data could not be obtained for patient 2). Imaging parameters included blood oxygen level–dependent signal fMRI collected by using a whole-body Philips Achieva Intera 3T scanner equipped with an 8-channel SENSE head coil (Philips Medical Systems, Bothell, WA) and coregistered to the same-session high-resolution anatomical images. Analysis of functional data was performed to generate statistical fMRI activation maps by using the Brain Voyager QX 1.9 analysis software package (Brain Innovation, Maastricht, the Netherlands). Standard techniques for data preprocessing and analyses were used and have been previously described elsewhere [71].

By using a standard block design with alternating conditions of visual task and rest, stimuli were presented in the intact, blind, or the transition zone regions. The patient was required to detect and discriminate (1) the orientation of Gabor grating patches, and (2) the motion direction of random dot kinetograms. The patient responded with a key press to indicate whether the orientation of the gratings or the direction of moving dots was the same or different from that in the previous display. The position of stimuli was based on the HRP visual field map obtained at pretest and remained constant between baseline and post-test fMRI scanning sessions. These 2 stimuli were selected for their ability to activate lower-order (eg, primary visual cortex, V1) and higher-order (eg, hMT+/V5) visual areas, respectively [72].

## RESULTS

With regard to safety, neither patient experienced any complication or adverse event associated with the combined tDCS and VRT intervention. Furthermore, experimental blinding regarding active or sham delivery of tDCS was maintained and confirmed during the patient exit interview. Exit interviewing revealed that patient 1 believed that she received sham treatment, whereas patient 2 reported that she received real stimulation (note that these are the opposite conditions from those to which the patients were relegated).

Preliminary comparative findings were in agreement with our initial hypothesis. Specifically, HRP revealed a greater expansion in visual field border in patient 1 as well as recovery of the visual field that occurred within the periphery and extended toward the center (Figure 4). Ancillary visual field testing with the NIDEK MP-1 was in agreement with the HRP results. In patient 1, blind stimulus locations converted to transition zone (primarily in the inferior peripheral quadrant), whereas in patient 2, less visual field expansion was observed, with correspondingly fewer transition zone locations becoming intact (primarily in the macular region). Both

**Figure 4.** Changes in high-resolution perimetry (HRP) (top row) and subjective (bottom row) visual fields in 2 study participants. When comparing HRP assessments at pretest and post-test, patient 1 (Vision Restoration Therapy (VRT) and active transcranial direct current stimulation (tDCS)) shows a 3.55° expansion in her central visual field as well as a 4° shift inward from the periphery (lower right quadrant). Patient 2 (VRT and sham tDCS) shows a 0.9° expansion centrally. Contrary to HRP findings, a larger expansion in subjective visual field was reported by patient 2 (a change in the affected field of 53.75 $cm^2$) compared with patient 1 (a change of 24.14 $cm^2$) after training.

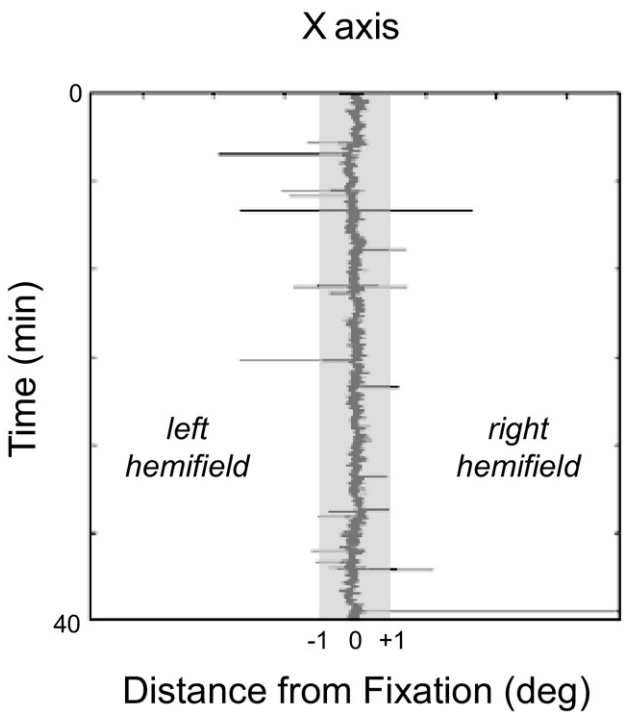


**Figure 5.** Online eye tracking trace from patient 1 (right hemianopia). Horizontal deviation of eye position (in visual field angle in degrees) from central fixation (marked at 0 on the x-axis) is shown during a continuous 40-minute trace captured during high-resolution perimetry (HRP) testing (sampled at 60 Hz). On average, the patient spends more than 95% of the time within ±1° of central fixation (shaded area).

patients maintained eye fixation within 2° of the central target 95% of the time (Figure 5). Quantitative secondary outcome measures, including IVI, LV-VFQ, and MNREAD reaffirmed that patient 1 received greater functional benefit after combined VRT and tDCS training. Patient 1 demonstrated considerable improvement on the IVI (from 48 to 4) and LV-VFQ (from 26 to 24) compared with patient 2 (from 22 to 14 and from 26 to 28, respectively). Similarly, improvement on MNREAD, which evaluates the reading ability for a medium print size (2M), was greater in patient 1 (150 to 200 wpm) versus patient 2 (200 to 150 wpm). Contrary to objective visual field results, patient 2 reported a greater subjective improvement in visual field recovery (Figure 4).

Finally, fMRI data obtained with patient 1 revealed differential patterns of activation after training (Figure 6). Task-related activation associated with motion discrimination in the intact and blind fields remained largely contralesional and implicated the motion-processing area hMT+/V5. However, motion discrimination in the transition zone was associated with a larger network of activation, including perilesional primary visual areas as well as V2/V3 and hMT+/V5 (Figure 6) following training. A similar pattern of activation associated with the Gabor orientation task (albeit less robust) also was observed (data not shown).

## DISCUSSION

In the present comparative case study, we have contrasted the effects of combining systematic visual rehabilitative training and noninvasive brain stimulation with training alone in improving visual functional outcomes in hemianopia. To our knowledge, this study represents the first attempt within the visual rehabilitation arena to replicate previous concepts drawn from stroke motor recovery.

Visual rehabilitative training (provided by VRT) combined with tDCS targeting the occipital cortex bilaterally enhanced visual field function to a greater degree than VRT alone. Besides assessing feasibility, the present case study protocol allowed us to incorporate study design refinements to help establish the foundation for more rigorous investigations in the future. Carried out in a controlled laboratory environment, we monitored the influence of potential confounds, such as ambient conditions and compensatory eye movements [48-50]. Regarding the latter point, we found that both patients were able to maintain accurate fixation throughout training and testing. Kasten et al [73] similarly concluded that improvements that resulted from VRT were not artifacts of compensatory eye movements (when using recordings for 3.5 minutes). Implementing online fixation monitoring for longer duration (as in the present report) has helped address previous concerns regarding the role of eye movements in visual field recovery (for further discussion, see Trauzettel-Klosinski and Reinhard [74]).

To compare and further characterize visual field recovery outcomes, we incorporated secondary perimetry assessment by using the NIDEK MP-1. Qualitatively, regional changes in the visual field were similar between NIDEK MP-1 and HRP. Although previous reports similarly suggest concordance between clinical perimetry and HRP [54,56], establishing quantitative agreement and clear correlations still requires further investigation [13,36].

Rehabilitative success has been operationalized by using objective measures that characterize visual field changes. To help capture functional changes, we also assessed reading performance (MNREAD) as well as standardized self-report questionnaires (IVI and VFQ). We found that increased visual field expansion was associated with improved performance of ADLs. Incorporating advanced methods of analyzing questionnaire-based functional assessments such as the Rasch analysis [75] may help to further characterize changes in visual function more accurately.

Interestingly, by studying both objective perimetry and subjective perception of visual field, we observed an apparent discontinuity between the two. This objective–subjective disconnect has been previously reported [47,49]. It is interesting to note that both patients reported that their tDCS status (ie, real or

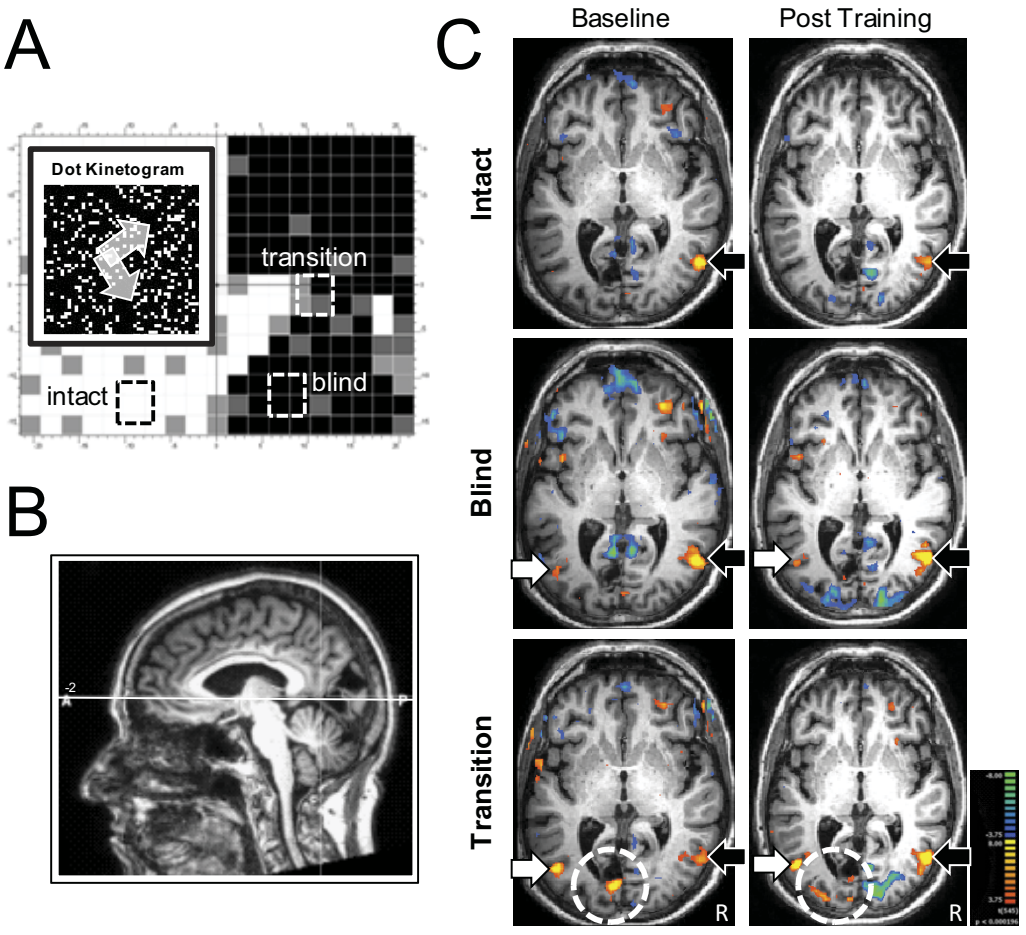


**Figure 6.** Functional neuroimaging results. (A) Visual stimuli used in the study include random dot kinetograms and Gabor patches (not shown). Behavioral performance on a direction-discrimination task is assessed with stimuli presented in either the intact field, the blind field, or the transition zone (as shown). (B) Structural magnetic resonance image (sagittal view) of patient 1 (Vision Restoration Therapy and active transcranial direct current stimulation), showing location of occipital lesion in the left hemisphere. The horizontal line illustrates the location of the axial slice shown in (C). (C) Visual motion perception–related activation as a function of stimulus location before and after training. When the visual stimulus is located in the intact visual field, activation within the contralateral area of V5/hMT+ is observed and is comparable at baseline and after training (black arrow). In the blind field, note the bilateral activation of V5/hMT+ in both the contralateral (white arrow) and ipsilateral visual (black arrow) at both baseline and after training. Finally, task performance with the visual stimulus presented in the transition zone at baseline is associated with bilateral V5/hMT+ activation as well as peri-lesional activation (dotted circle). Post-training activation related to visual motion perception in the transition zone, showing again bilateral activation of V5/hMT+ but now a greater spread of activation within the occipital pole. The threshold for significance was set at $P < .05$. A similar pattern of activation was observed with the Gabor patch visual stimulus, albeit with less robust activation.

sham) was opposite to what they actually received. Therefore, this disconnect may be related to their own expectations of outcome, or may reflect subjective differences in the functional relevance afforded to different regions of the visual field (eg, central visual versus peripheral sparing) [62]. Certainly, this issue confirms the need for accurate and reliable methods to assess visual function and the value of incorporating experimental blinding to help validate findings.

In an effort to elucidate recovery-associated mechanisms implicated in visual function recovery, we incorporated a neuroimaging component for patient 1 (VRT with active tDCS). After training, task-dependent and visual field location–specific reorganization implicated peri-lesional as well as bilateral higher-order visual areas. Although we cannot disentangle the contributory effects of VRT from tDCS, this widespread activation is in line with the view that visual recovery potentially reactivates surviving visual areas [32,39-42], a finding that is analogous to comparative work in post-stroke motor recovery [76-78]. The preliminary nature of these results warrants caution in interpretation. Incorporating additional specialized techniques and methods of analysis, such as tractography and functional connectivity, could further help to establish a relationship between cortical activity, neural pathways, and functional outcomes.

The potential neurophysiological mechanisms that underlie the combined benefit provided by VRT and tDCS remain unclear. Mechanisms may include increased neuronal excitability [29], induction of long-term potentiation [79-81], and functional reorganization of cortical maps [24], as well as increases in neuronal density [25,82].

At this juncture, it is difficult to surmise the impact of the electrode configuration of tDCS chosen for the present study in facilitating visual rehabilitative outcomes. Certainly, a variety of stimulation montages could have been used. However, because there was no *a priori* evidence that selective stimulation of either the lesioned or intact hemisphere would lead to a greater effect, we opted for a montage similar to previous studies that demonstrated that anodal stimulation delivered bilaterally to the occipital pole modulates a variety of neurophysiological outcomes, including phosphene thresholds and visual evoked potentials [46,83-85]. Interestingly, results of compartment-based current density modeling suggest that lesioned areas of the brain create an electrical shunt (due to the presence of cerebral spinal fluid), which affects the overall distribution of current between lesioned and nonlesioned areas [86,87]. Thus, it is possible that with the montage used here, peri-lesioned areas received preferentially greater current density by virtue of injury-related morphologic changes.

The greatest limitation of the study stems from the fact that we present results from only a single paired case study. Thus, our ability to generalize further from these observations is certainly limited. For example, although the combination of VRT and tDCS appeared to promote greater visual field recovery, differences in baseline visual deficits also could potentially lead to these same observations. It is possible that greater areas of residual vision present in patient 1 (ie, the size of the transition zone and the presence of peripheral islands of vision) could have been associated factors leading to greater visual field improvement from training. Indeed, the size of the transition zone has been reported to be an important predictor of overall visual field recovery [38,41,54]. Certainly, a larger randomized clinical trial is required not only to confirm these preliminary findings but also to help disentangle these multifactorial issues related to recovery and further validate the study design approach described here.

Finally, these preliminary findings hold promise not only from a functional outcomes perspective but also in terms of time and potential cost. Several groups have been pursuing computer-based training strategies [33,88-91] as well as novel cross-modal sensory approaches [92], and preliminary results have been encouraging. As with VRT, these strategies require thousands of repeated trials delivered over many months of training before beneficial effects are achieved. It is worthy of note that, in this study, a contracted training regimen was used (ie, one-fourth in the duration of the standard clinical paradigm). Yet, comparable changes in the visual field were possible (compared with the outcomes from previous studies of VRT), which suggests that combined stimulation may provide increased functional benefit and/or an acceleration of desired outcome achievement, either of which would be highly desirable from a rehabilitative standpoint.

## CONCLUSIONS

We present a comparative case study as well as feasibility and safety findings that describe the effects of combined visual rehabilitation (provided by VRT) with a form of noninvasive brain stimulation (tDCS) in patients with heminanopic visual field loss. Preliminary results are consistent with the hypothesis that the combination of visual rehabilitative training and noninvasive brain stimulation leads to an increase in functional visual recovery compared with visual rehabilitation alone. A larger randomized clinical trial is required to confirm these preliminary findings as well as to help uncover the potential neural correlates of functional recovery.

## ACKNOWLEDGMENTS

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**Footnotes Continued From Page 825.**

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