



Case Study

Transcranial direct current stimulation (tDCS) combined with blindsight rehabilitation for the treatment of homonymous hemianopia: a report of two-cases

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Abstract. [Purpose] Homonymous hemianopia is one of the most common symptoms following neurologic damage leading to impairments of functional abilities and activities of daily living. There are two main types of restorative rehabilitation in hemianopia: “border training” which involves exercising vision at the edge of the damaged visual field, and “blindsight training,” which is based on exercising the unconscious perceptual functions deep inside the blind hemifield. Only border effects have been shown to be facilitated by transcranial direct current stimulation (tDCS). This pilot study represents the first attempt to associate the modulatory effects of tDCS over the parieto-occipital cortex to blindsight treatment in the rehabilitation of the homonymous hemianopia. [Subjects and Methods] Patients TA and MR both had chronic hemianopia. TA underwent blindsight treatment which was combined with tDCS followed by blindsight training alone. MR underwent the two training rounds in reverse order. [Results] The patients showed better scores in clinical-instrumental, functional, and ecological assessments after tDCS combined with blindsight rehabilitation rather than rehabilitation alone. [Conclusion] In this two-case report parietal-occipital tDCS modulate the effects induced by blindsight treatment on hemianopia.

Key words: Stroke, Visual field, Hemianopsia

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INTRODUCTION

Homonymous hemianopia (HH) is the result of retro-chiasmal pathway damage and is a common symptom of neurologic damage affecting 20–70% of stroke survivors^{1, 2)}.

HH is characterized by a visual field impairment on the same side in both eyes due to a lesion contralateral to the defect. Vision impairments may vary from blindness of an entire hemifield to loss of only a part of the affected field. HH has many negative effects on functional abilities and the activities of daily living^{3, 4)}: the most common problem is diminished visuospatial exploration, which can impact on reading, mobility, and driving⁵⁾.

In general, spontaneous recovery occurs within three months of the event; after six months, significant improvement is unlikely^{6, 7)}. Techniques used for rehabilitation of HH are designed to help the brain activate residual vision⁸⁾ by training the patient to detect stimuli falling in their blind hemifield⁹⁾. There are two main kinds of restorative rehabilitation of hemianopia: “border training,” which involves exercising vision at the edge of the damaged visual field, and “blindsight training,”

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Table 1. Characteristics of patients

Case	Gender	Age	Side of lesion	Type of lesion	Age of the lesion
TA	Male	39	Left	Ischemic	12 months
MR	Female	27	Right	Ischemic	14 months

which is based on exercising the unconscious perceptual functions deep inside the blind hemifield^{10–14}). Both techniques have proven to be useful for recovery of different visual functions^{15–23}), and functional imaging studies have shown neuroplasticity and cortical reorganization following restorative rehabilitation^{24–30}).

For HH, Plow et al.³¹), Plow et al.³²) and Arber et al.³³) reported that border rehabilitation training results obtained with a combination of training and anodal transcranial direct current stimulation (tDCS) were superior to the results obtained with training alone. tDCS treatment, in fact, influenced recovery speed and entities. Studies on offline tDCS with hemianopic patients showed an improvement of motion perception in the healthy hemifield and, in one case, the increase speed of blindsight^{34, 35}). Although these studies documented the efficacy of tDCS in association with border rehabilitation, its effects on blindsight rehabilitation have not yet been studied. In the present study, we hypothesized a modulatory effect of tDCS when combined with blindsight rehabilitation. Therefore, we present a pilot study of blindsight rehabilitation after tDCS over the parieto-occipital cortex in two patients affected by chronic HH.

SUBJECTS AND METHODS

The study complies with the Declaration of Helsinki and was performed following approval by the ethics committee of University of Milan-Bicocca (date: 21/09/2016). Written informed consent was obtained from both patients. The study design was a crossover AB BA.

TA was a 39-year-old right-handed salesman (Table 1). He presented with right HH due to a first-ever unilateral embolic infarction in the left hemisphere. His ischemic lesion was located on the left paramedial occipital cortex. Patient TA had a corrected-to-normal visual acuity and was able to maintain fixation. He was alert and cooperative. The rehabilitation program started 12 months after the event causing the visual field defect.

MR was a 27-year-old right-handed unemployed woman who presented with left HH (Table 1). Magnetic resonance imaging showed a right parieto-occipital first-ever ischemic stroke. She had normal visual acuity and was vigilant and compliant and able to maintain fixation. Her rehabilitation program started 14 months after the event causing the visual field defect.

Patients underwent blindsight therapy in two rounds of training.

TA underwent tDCS during the first round of rehabilitation, MR was treated with tDCS during the second round of rehabilitation. Each round is composed by twenty one-hour sessions of training occurring three times a week with a two-week interval between two rounds (Fig.1).

During each one-hour session, the patients were seated in front of a 19-inch monitor with a white screen in background at a distance of 50 cm, subtending a visual angle of $45^\circ \times 27^\circ$, in a darkened room. Patients were asked to maintain central fixation and were exposed to visual stimuli in their blind hemifield. The patients' task was to detect and/or discriminate between stimuli. They were presented according to a random sequence with respect to exposure time (from 1 to 10 s), color, shape (geometrical figures or letters), and frequency (from 0 to 5 Hz). The size of each stimulus was subtended approximately by $5^\circ\text{--}2^\circ$ of visual angle (dimension of the stimuli varied from 5 to 2 cm). The patients were subjected to around 700 different stimuli variously associated in space and/or time. During all the exercise times, fixation stability was required of the patient, and this was monitored by a Tobii X2 eyetracker.

tDCS treatment was carried out simultaneously to the training in one round. The stimulation started at the beginning of the rehabilitation session, and continued for the first 30-min training period, then tDCS stopped and training continue in order to complete the one-hour session.

Anodal tDCS was applied, using a battery-driven constant current stimulator (BrainStim, E.M.S. s.r.l., Bologna, Italy, <http://brainstim.it>), and a pair of surface saline-soaked sponge electrodes (5×5 cm). Current intensity was 2 mA (Fade-in/-out=10 s), for a total duration of 30 min. The anode was placed over the parieto-occipital cortex of the affected hemisphere (PO4 for TA. PO3 for MR; according to the international reference EEG 10-20 system). The cathode was placed in the contralateral supraorbital position.

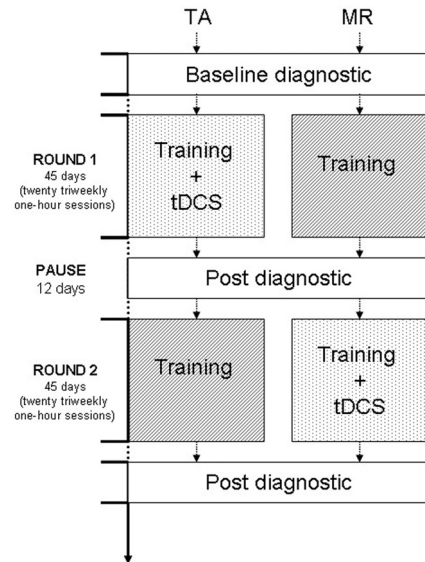
**Fig. 1.** Study design

Table 2. Clinical-instrumental and functional assessment for TA and MR

Case	Assessment	Baseline	After round 1		After round 2	
		Abs. value	Abs. value	% of change	Abs. value	% of change
TA	VF sensitivity (dB)	34.5	70	103%	73	4%
	VF extension (deg)	95	130	37%	143	10%
	Detected stimuli (no)	4	10	150%	11	10%
	Reaction Time (ms)	2,835	2,623	7%	2,525	4%
MR	VF sensitivity (dB)	168.5	238	41%	439.5	85%
	VF extension (deg)	134	130	3%	175	35%
	Detected stimuli (no)	20	20	0%	29	45%
	Reaction Time (ms)	2,031	2,024	0%	1,608	21%

Outcome variables in absolute values and in percentage of change are reported.

VF sensitivity: value in decibel in Humphrey SITA-standard 30-2 program; VF extension: total extension in degrees of vision in Vienna Schuhfried PP-R test; Detected stimuli: number of perceived stimuli in affected hemifield in TAP, v. 2.3, visual field 92 stimuli subtest; Reaction time: average of reaction time in the affected hemifield in TAP, v. 2.3, visual field 92 stimuli subtest

To assess the improvement after rehabilitation, we used clinical, functional, and ecological endpoints.

Clinical-instrumental assessment: A threshold visual field Humphrey SITA-standard 30-2 program was used to measure the central 30 degrees of visual perception. To treat perimetric data, the Sahraie et al. method²¹⁾ was used.

For peripheral visual field testing, the Schuhfried Vienna PP-R test was used to measure visual perception up to 180 degrees. During the test, a second simultaneous task in central vision (following a moving target) was performed in order to verify test reliability.

Functional visual field assessment: The test for attention performance (TAP, v. 2.3) visual field 92 stimuli subtest³⁶⁾ was performed.

Ecological assessment: During the initial and final interviews, data for an International Classification of Functioning (ICF) profile of the subject was collected. The profile included mainly the activity and participation categories of ICF as recommended by de Haan et al³⁷⁾. A clinical assessment was also carried out to verify the absence of confounding factors such as comorbidities, including neurological, psychiatric, or ophthalmological pathology and to exclude the presence of visuo-spatial neglect. In order to verify satisfaction of the inclusion criteria for non-invasive brain stimulation³⁸⁾, clinical and instrumental investigations were performed before treatment.

RESULTS

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

TA Quality of fixation, registered by means of the TobiiX2 eyetracker, was registered as stable. During rehabilitation, his fixation remained stable and the standard deviation of the fixations was 1.35 degrees.

As shown in Table 2, the TA sensitivity in the blind hemifield in the threshold test increased by 35.5 dB (+103%) after training combined with tDCS, and it improved by only 3 dB (+4%) after training without tDCS.

The TA Schuhfried Vienna PP-R test showed an increase in the peripheral stimuli perception by 35 degrees (from 95° to 130° –that represents an improvement of 37%) with an enhanced accuracy in tracking task (deviation from 14 to 4.2 mm). At the end of second training round—without tDCS—we observed a further enlargement of peripheral perception of 13° (+10%) and the accuracy was almost stable (from 4.2 to 5.3 mm).

The TA TAP Battery subtest of the visual fields recorded 4 points (of 46 points tested in the affected hemifield) at the patient's baseline. After training with tDCS, the detected stimuli increase to 10, and after training without, they were 11. Therefore, we observed a gain of 6 points (+150%) of vision after the first round, and one additional point after the second round (+10%).

Regarding the response speed, for TA there was a decrease of reaction time after both rehabilitative rounds, averaging 212 ms after the rehabilitation combined with tDCS and 98 ms after blindsight rehabilitation alone.

As regards the ecological improvement, the rehabilitation had a positive effect in all ICF codes considered (Table 3).

In particular, as observed from the subjective qualitative questionnaire, TA reported an improvement in the perception of people and objects in his blind hemifield. Although he was not able to define them clearly, he felt their presence. The patient also often noticed a distorted view at the edge of the scotoma, with elongated shapes and washed out colors.

MR quality of fixation, registered by means of the TobiiX2 eyetracker, was registered as stable. During rehabilitation, her fixation remained stable, as indicated by the standard deviation of all fixations in every session of 0.9 degrees. As shown in Table 2, after the first training round—without tDCS— MR sensitivity in the affected hemifield documented an increase of 69.5 dB (+41%). After the second round, the testing showed a further improvement of 201.5 dB (+85%) associated with tDCS. Both the stimulus detection and tracking tasks were stable in the Schuhfried Vienna PP-R test after the first round

Table 3. Patient TA ICF activity and participation report

Code	Pre	0	1	2	3	4	Post	0	1	2	3	4
d110	S						S					
	T						T					
d155	S						S					
	T						T					
d210	S						S					
	T						T					
d230	S						S					
	T						T					
d360	S						S					
	T						T					
d460	S						S					
	T						T					
d475	S						S					
	T						T					
d620	S						S					
	T						T					
d630	S						S					
	T						T					
d640	S						S					
	T						T					
d660	S						S					
	T						T					
d850	S						S					
	T						T					
d920	S						S					
	T						T					

List of capacity before and after training. S: Self report; T: Test Report; Functions: d110 Watching, d155 Acquiring skills, d210 Undertaking a single task, d230 Carrying out daily routine, d360 Using communication devices and techniques, d460 Moving around in different locations, d475 Driving, d620 Acquisition of goods and services, d630 Preparing meals, d640 Doing housework, d660 Assisting others, d850 Self-employment, d920 Recreation and leisure

Table 4. Patient MR ICF activity and participation report

Code	Pre	0	1	2	3	4	Post	0	1	2	3	4
d110	S						S					
	T						T					
d155	S						S					
	T						T					
d210	S						S					
	T						T					
d230	S						S					
	T						T					
d360	S						S					
	T						T					
d460	S						S					
	T						T					
d475	S						S					
	T						T					
d620	S						S					
	T						T					
d630	S						S					
	T						T					
d640	S						S					
	T						T					
d660	S						S					
	T						T					
d850	S						S					
	T						T					
d920	S						S					
	T						T					

List of capacity before and after training. S: Self report; T: Test Report; Functions: d110 Watching, d155 Acquiring skills, d210 Undertaking a single task, d230 Carrying out daily routine, d360 Using communication devices and techniques, d460 Moving around in different locations, d475 Driving, d620 Acquisition of goods and services, d630 Preparing meals, d640 Doing housework, d660 Assisting others, d850 Self-employment, d920 Recreation and leisure

of rehabilitation. After the second round of rehabilitation with tDCS, peripheral stimulus detection increased by 45 degrees (35%) and the tracking task improved by 0.4 mm.

At baseline, patient MR recorded 20 out of 46 stimuli in her blind hemifield in the TAP test. After the first rehabilitation round, the detected points remained unchanged, and after the tDCS rehabilitation round, they increase to 29 (+45%). Patient MR show an average reduction of response time of 7 ms after blindsight rehabilitation and a further reduction of 416 ms more after rehabilitation combined with tDCS.

The rehabilitation had a positive effect in all ICF codes considered (Table 4). In particular, MR regained an independent life. She was able to return to living independently (she went to live in her parent’s house after the event) and was able to take care of her son and resume gainful employment.

DISCUSSION

Both patients showed major positive training effects when blindsight exercises were combined with tDCS.

From the clinical-instrumental point of view in the threshold test, we observed an improvement of visual field sensitivity with a higher improvement when tDCS is utilized for rehabilitation. This led us to think that tDCS could enhance the effects of rehabilitation. From the functional point of view, a two-fold positive effect was induced by the TAP battery. Improvements occurred in visual perception and response speed in stimulus detection. Interestingly, reaction times became faster after tDCS-rehabilitation³⁹).

Furthermore, to the best our knowledge, this is the first study of HH rehabilitation with a computerized evaluation of up to 180 degrees to test the effectiveness of the treatment on the extremes of peripheral vision (using the Schuhfried Vienna PP-R). The degree of peripheral visual field extension in the PP-R test increased after rehabilitation treatment. This is probably the reason for the improvement in the patients’ quality of life. Given that space exploration and mobility are the most impaired functions in hemianopic patients⁵), improved lateral visual field usage allowed the resumption of key activities of daily living such as driving, cooking, and leisure time pursuits.

When we analyzed the ICF profile (Tables 3 and 4), it was noted that the capacity increased after rehabilitation. This

supports the idea that there had been improvement in the patient's ADLs and social life activity⁴⁰). The monitoring and the checking of stability fixation by means of eyetracker during rehabilitation sessions led us to exclude the possibility that the observed improvements can be induced by compensative eye movements⁴¹).

Therefore, the two cases presented here show for the first time that ipsilesional parieto-occipital anodal tDCS influences the effects induced by blindsight treatment. It can be argued that stimulation of visual associative areas is useful to promote and enhance the blindsight phenomenon.

Our previous paper⁴²) strongly suggest that blindsight rehabilitation improves the processing of visual stimuli, so it is possible that stimulation of associative areas could facilitate this processing mechanism.

We have reason to believe that even in these patients, this may have occurred by way of the cortical rearrangement via long-term potentiation mechanisms⁴³). The neuroplasticity hypothesis is consistent with the literature⁸) concerning border rehabilitation associated with tDCS^{31–33, 44}). In light of this primary results, we recommend further studies to investigate the tDCS effects on blindsight treatment in HH.

Although there is presently no evidence in the literature regarding the best stimulation protocols and electrode montage to obtain the greatest rehabilitation effect on HH⁴⁵), the hypothesis of anodal stimulation over PO3 and PO4 merits further investigation.

In conclusion, the results of the two case studies indicate that positive effects could occur after rehabilitation treatment of HH, by enhancing blindsight. This is consistent with prior reports in the literature^{22, 23}). The results obtained in these two case reports seem to be promising. However, it is not possible to generalize from these individual cases: the results show an improvement but they do not provide conclusive or statistical evidence. Thus, our two case study may be able to guide further studies in order to validate the results with a larger population, using a sham-controlled study design, with correlated functional images and monitoring of the long-term stability using an appropriate series of follow-up evaluations.

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