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Transcranial direct current stimulation in the treatment of cerebellar ataxia: A two-phase, double-blind, auto-matched, pilot study

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ABSTRACT

Objective: To assess the impact of tDCS on posture, gait and coordination of movements in subjects with cerebellar ataxia.
Patients and methods: This is a two-phase, double blind, auto matched, pilot study. Seven people were selected to participate in the study aged from 14 to 57. tDCS and sham-tDCS were applied at different times to all participants for 40 min over five consecutive days so that they were blind to which of the two techniques was applied at any one time. The area stimulated was the bilateral motor cortex. Subjects were evaluated before and after the interventions using the Scale for Assessment and Rating of Ataxia (SARA) and specific tests to measure posture and balance were carried out using the Wii Fit platform and CvMob software.
Results: The study indicates a statistically significant improvement in respect of gait parameters and the total score of the SARA scale and Wii Fit platform after tDCS when compared with data obtained from sham-tDCS trials (p: 0,03). The adverse events relating to tDCS were all self-limiting and from mild to moderate intensity.
Conclusion: Despite the small sample size, tDCS showed positive results in some motor parameters and could be considered a valuable new option for the treatment of cerebellar ataxias.

1. Introduction

Cerebellar ataxias represent a broad and heterogeneous group of diseases. Among these, two categories are highlighted: hereditary ataxias and acquired ataxias [1]. Hereditary ataxias are genetic diseases defined by the progressive degeneration of the cerebellum and are often accompanied by systemic and neurological symptoms [2,3]. Acquired ataxias, in turn, include diseases caused by a variety of events, such as intoxication, endocrine disorders, vitamin deficits, or infections [1]. Cerebellar dysfunction can result in significant functional difficulty of the upper and lower limbs, oculomotor control, balance, and gait [4]. These difficulties considerably reduce the quality of life of individuals, as well as reduce their integration and occupational activities, which, in turn, can impose greater financial burdens [5,6].

Acquired ataxias can mostly be treated by reverting causing disturbances. On the other hand, there are very limited therapeutic options available for the treatment of hereditary ataxias for the control of neurodegeneration, despite their being widely studied for their genetic aspects [1]. For this reason, other rehabilitation strategies in patients with cerebellar ataxia should be investigated.

Transcranial direct-current stimulation (tDCS) has emerged in the scientific community as a promising technique and has proved to be satisfactory in the rehabilitation of various neuropsychiatry disorders in addition to being non-invasive, safe and promoting long-term neuroplasticity [7–14]. Studies have shown that, in acute and degenerative cerebellar disease, the excitability of cortical motor areas is severely depressed functionally [15,16]. Ben Taib et al. hypothesized that tDCS has the potential to modulate the excitability of the hypoexcitable motor cortex after acute cerebellar dysfunction, and possibly reverse this condition to an appropriate level of excitability [17].

In this context, the aim is to measure the effects of tDCS on gait, posture, and coordination of movements in subjects with cerebellar

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ataxia, evaluating this technique as a rehabilitation tool.

2. Materials and methods

2.1. Subjects and study design

This is a two-phase, double blinded, auto-matched, pilot study. The study sample consists of seven individuals, of both sexes, diagnosed with cerebellar ataxia, accompanied by the Neurology Division of the Professor Edgar Santos University Hospital (HUPES) from the Federal University of Bahia (UFBA). Recruitment took place between June and November, 2014.

This trial, which has been registered on the Clinical Brazilian Trials website (http://www.ensaiosclinicos.gov.br/rg/RBR-358sm6/), was comprised of individuals with non-progressive or slowly progressive cerebellar ataxia, who were literate, possessing independent gait, and had MRIs that showed diffuse cerebellar atrophy.

The trial excluded subjects with treatable cerebellar ataxia or other diseases, with debilitating intellective deficit, poor brain formation, or severe visual or hearing impairment. Since it was a clinical trial evaluating the impact of transcranial direct current stimulation, the participants did not undergo any other therapeutic intervention before or during the study period.

Seven people were selected to participate in the study. Table 1 presents clinical and demographic characteristics of the population selected. There was a predominance of females (4:3), and the patients' age ranged from 14 to 57. Four patients (57.1%) had slowly progressive cerebellar ataxia, while the other three (42.9%) had non-progressive ataxia. All participants had MRIs of diffuse cerebellar atrophy.

Participants were assigned to the sham-group, first phase, and the active group, second phase. For participants in the intervention group, transcranial direct current stimulation (tDCS) was applied, while sham-tDCS was applied to the control group. The procedures were performed for five consecutive days, while clinical evaluations and analysis of posture and balance before and after the intervention were performed. A one-month washout period was used, as per other tDCS studies [18,19]. After the washout period all members from the control group were allocated to the intervention group. By the end of the study, all participants received tDCS and sham-tDCS at some point. The subjects were blind to the procedures performed.

2.2. Clinical evaluation using scale for assessment and rating of Ataxia (SARA)

Before the start and after the last day of the stimulation periods, all participants were filmed while performing the commands of the Scale for Assessment and Rating of Ataxia (SARA) [20–22]. To avoid the bias of the evaluator, the pre- and post- intervention videos were randomly classified into video A and video B and assessed by blinded neurologists. The SARA scale has been widely used in studies involving subjects with ataxias [23,24]. Whilst it is a subjective instrument it has high inter-rater agreement. The SARA score depends on the severity of the cerebellar condition and the predominance of symptoms (axial or appendicular) [20]. The scale has been validated in previous studies, including those involving children, and is considered a safe and reproducible instrument when following-up subjects with cerebellar ataxia [25,26]. The SARA scale has eight parameters as following: (1) Gait - walks parallel to a wall in tandem without support: scale 0 (Normal, no difficulties) to 8 (Unable to walk, even supported); (2) Stance - stands in with feet together in parallel and in tandem: scale 0 (Normal, able to stand in tandem for > 10 s) to 6 (Unable to stand for > 10 s even with constant support of one arm); (3) Sitting - sits on a bed without support of feet, arms outstretched: scale 0 (Normal, no difficulties > 10 s) to 4 (Unable to sit for > 10 s without continuous support); (4) Speech disturbance - Speech is assessed during normal conversation: scale 0 (Normal) to 5 (Only single words understandable); (5) Finger chase - examiner performs 5 consecutive pointing movements in a frontal plane. Proband follows with index finger: scale 0 (No dysmetria) to 4 (Unable to perform 5 pointing movements; (6) Nose-finger test - points with index finger from nose to examiner's finger: scale 0 (No tremor) to 4 (Unable to perform 5 pointing movements); (7) Fast alternating hand movements - performs 10 cycles of repetitive alternation of pro- and supinations of the hand on thigh: scale 0 (Normal), no irregularities to 4 (Unable to complete 10 cycles); (8) Heel-shin slide - lies on bed and lifts one leg. Point with the heel to the opposite knee, slide down along the shin to the ankle, and lay the leg back on the bed: scale 0 (Normal) to 4 (Unable to perform the task).

2.3. Analysis of posture and balance through the Wii Fit platform and CvMob software

All participants were assessed before and after each week of intervention through the Wii Fit platform and CvMob software [27].

Wii Fit, developed by Nintendo® for the video game console Nintendo Wii®, is a platform that grades weight distribution on its surface, consisting of four quadrants, and maps the location and trajectory of the individual's center of pressure. With this feature, and through specific software developed by researchers at the Center for Technological Innovation in Rehabilitation (NITRE), it was possible to project the data from the Wii Fit platform to a computer to evaluate the standard deviation of the oscillation of the individual's center of pressure in the anteroposterior and latero-lateral axis, as well as the median and the standard deviation of each leg's load [28].

CvMob software was used to describe the physical characteristics (speed, time, acceleration, trajectory) from points previously marked in the video. Using this software, it was possible to measure some parameters in order to estimate the oscillation of the lower limbs and head in the anteroposterior and latero-lateral axis. The parameters were the total trajectory of the displacement during one minute at specific points on the glabella, knees, pterion and fibular head. The maximum speed with which the participants stood up from a chair without using their hands was also evaluated [29].

Table 1
Clinical and demographic data of the participants.

Patient	Sex	Age (years)	Associated manifestations	Clinical evolution
1	F[(a)]	18	Mild cognitive impairment; dyspraxia	Non-progressive
2	F	27	Pyramidal release in the lower limbs	Slowly progressive
3	F	43	No	Slowly progressive
4	M[(b)]	42	No	Slowly progressive
5	M	55	No	Non-progressive
6	M	57	No	Non-progressive
7	F	14	Mild cognitive impairment	Slowly progressive

[(a)] F, female.
[(b)] M, male.

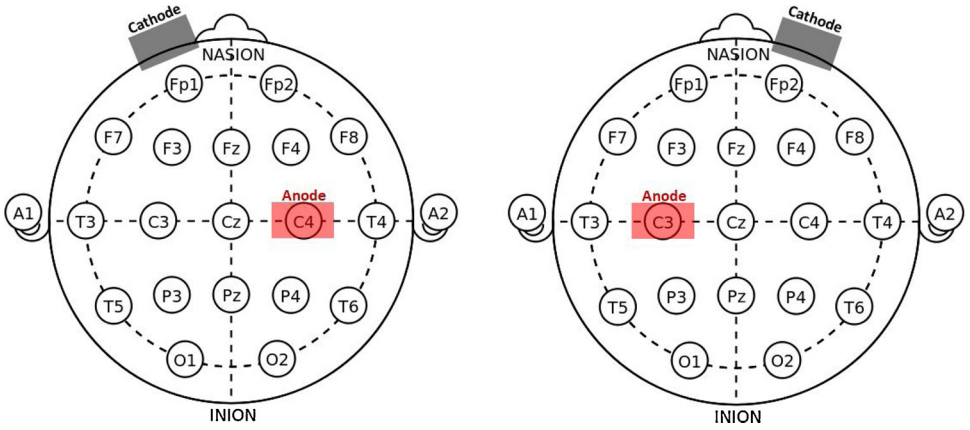


Fig. 1. Placement of electrodes for anodic transcranial direct current stimulation. The anode (in red) was placed on the motor área (C3 or C4) as determined by the 10–20 International electroencephalography system. The cathode (in black) was placed on the opposite supraorbital region (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

2.4. Performing transcranial direct current stimulation

The procedure (tDCS) involved the application of direct current from two electrodes (5 cm × 7 cm) in saline-soaked sponges for 20 min on each motor cortex (total 40 min for session). The electrodes were held in place by elastic bandages and five sessions were conducted over five consecutive days. The intensity of the current was 2 mA, except for the first and last minutes of each session when it was reduced to 1 mA [30]. To maintain participants in the sham-tDCS phase blinded, the device was turned on for one minute at around 1 mA to provide a sensation of current flow similar to that occurring during tDCS and was then turned off. Thus, subjects were unable to distinguish if sham-tDCS or tDCS was received at the time of stimulation [31]. The positioning of the electrodes was similar in the intervention group. The anode was positioned in the motor area (C3 or C4) in accordance with the 10–20 system. The cathode was placed in the opposite supraorbital region (Fig. 1). The device used was the Striat (Ibramed, Amparo-SP, Brazil), approved.

2.5. Application of scale of adverse effects

At the end of each tDCS day, patients were asked if adverse effects occurred during the procedure or after the intervention period, as proposed by Brunoni et al. [32]. The adverse effects studied were headache, neck pain, pain or discomfort in the scalp, tingling, itching, burning sensations, localized redness, drowsiness, difficulty concentrating, acute mood swings, and irritability, all being classified as mild, moderate, or severe.

2.6. Application of the patients' global impression of improvement scale (PGI-I)

After the end of each intervention period, the Patients' Global Impression of Improvement (PGI-I) scale was applied. The PGI-I is a subjective scale of global patient assessment. It translates the impression of change after a certain event as a number, ordered sequentially. Their values are 1 (much better); 2 (moderately better); 3 (slightly better); 4 (no change); 5 (slightly worse); 6 (moderately worse); and 7 (much worse). PGI-I is limited in assessing the efficacy of tDCS but provides additional information about the subjective perception of results and tolerability of the technique and its adverse effects.

2.7. Data analysis

The data provided by the Scale for Assessment and Rating of Ataxia (SARA) and the other instruments were inserted into statistical analysis software (Origin version 9.0). To analyze the data, the Wilcoxon Signed-Rank Test was used for paired data, where associations presenting $p \leq 0.05$ were considered significant.

2.8. Ethical aspects

Participants were recruited using invitation letters from clinics. The head of the departments of several neurological outpatient clinics were contacted in Salvador, Brazil. After acceptance by the physician to collaborate with the study, the patients who were willing to be enrolled in the trial were informed about the objectives, steps, and safety of the study and only those who signed the free and informed consent form (ICF) as well as the assent form for minors (for those between 14 and 18) and who were cognitively able, were included. This study was approved by the Research Ethics Committee of the Medical School of Bahia, Federal University of Bahia (UFBA), based in Largo do Terreiro de Jesus, in accordance with consent nº661.955 of May 15th, 2014.

3. Results

Table 2 shows the results of evaluations using the Scale for Assessment and Rating of Ataxia (SARA). This table shows the improvement of each participant after tDCS and after sham-tDCS calculated by subtracting scores obtained via SARA before and after, so that positive values represent a reduction and, therefore, an improvement. Table 3 shows the statistical analysis of data obtained through SARA (Table 2) using the Wilcoxon Signed-Rank Test for paired data, comparing the results of tDCS with those obtained by sham-tDCS.

As shown in Table 3, the results indicate that separate testing of the tDCS and sham-tDCS groups showed no significant differences, except for the parameters relating to the movement ($p = 0.03$). Moreover, significant difference was observed in the total score ($p = 0.03$), which was the sum of the individual parameters.

Table 4 and Graph 1 represent the analysis of the results obtained with the Wii Fit platform. We used the Wilcoxon Signed-Rank Test for paired data and compared the gain after tDCS and after sham-tDCS. Statistically significant associations were not identified when comparing tDCS and sham-tDCS using the individual parameters generated by the platform. However, the analysis of the overall gain (being the sum of the individual parameters) resulted in $p = 0.03$ with a median of 4.64 in the tDCS group and -1.36 in the sham-tDCS group. This result points to a significant improvement after tDCS when all of the parameters are taken into consideration.

Table 5 and Graph 2 show the results obtained from CvMob. The total trajectory was obtained by calculating the sum of all the movement across all measurements.

Analysis of the gain after tDCS and sham-tDCS using CvMob does not point to any significant gain ($p > 0.05$). However, the median of the total gain in the tDCS group was superior to the sham-tDCS group.

Table 6 shows the grade given by patients through the Patient Global Impression of Improvement scale (PGI- I). All participants reported improvement by the PGI-I after tDCS, with the highest score (1, much better) being reported by three of the participants; a score of 2 by

Table 2
Results obtained through the application of SARA[a].

Patient		Stage	Gait	Posture	Feeling	Speech	Finger-to-finger	Finger-to-nose	RAM[b]	Heel-to- Knee	Total
1	tDCS[c]	Baseline	2	0	0	1	1	1	3	1.5	9.5
		After	2	0	0	1	1	1	1	1	7
		Gain	0	0	0	0	0	0	2	0.5	2.5
	Sham-tDCS	Baseline	1	0	0	1	1	0	2	1	6
		After	1	0	0	1	1	1	1	1	6
		Gain	0	0	0	0	0	−1	1	0	0
2	tDCS	Baseline	3	1	2	2	1	1	2.5	1	13.5
		After	1	0	1	1	1.5	1	1.5	1	8
		Gain	2	1	1	1	−0.5	0	1	0	5.5
	Sham-tDCS	Baseline	2	1	2	1	1	1.5	1.5	1	11
		After	1	0	1	1	1	1	1.5	1.5	8
		Gain	1	1	1	0	0	0.5	0	−0.5	3
3	tDCS	Baseline	2	1	0	1	1.5	1	1.5	1	9
		After	1	0	0	1	1	0.5	1.5	1	6
		Gain	1	1	0	0	0.5	0.5	0	0	3
	Sham-tDCS	Baseline	2	0	0	0	0.5	1	1.5	1	6
		After	3	1	0	1	1	0.5	1	1	8.5
		Gain	−1	−1	0	−1	−0.5	0.5	0.5	0	−2.5
4	tDCS	Baseline	3	5	1	1	1	1	1	1	14
		After	1	0	0	0	0.5	0	1	1	3.5
		Gain	2	5	1	1	0.5	1	0	0	10.5
	Sham-tDCS	Baseline	3	2	0	0	0	0	0.5	1	6.5
		After	4	4	1	0	0.5	0.5	0.5	1	11.5
		Gain	−1	−2	−1	0	−0.5	−0.5	0	0	−5
5	tDCS	Baseline	4	4	0	0	1	1	0.5	1	11.5
		After	1	2	0	1	0.5	0	0	0.5	5
		Gain	3	2	0	−1	1	2	1	0	6.5
	Sham-tDCS	Baseline	2	1	0	0	0.5	0	0	0	3.5
		After	2	2	0	0	0	0	0	0.5	4.5
		Gain	0	−1	0	0	1	0	0	−1	−1
6	tDCS	Baseline	2	1	0	1	1.5	1	1.5	1	9
		After	1	0	0	1	1	0.5	1.5	1	6
		Gain	1	1	0	0	0.5	0.5	0	0	3
	Sham-tDCS	Baseline	2	0	0	0	0.5	1	1.5	1	6
		After	3	1	0	1	1	0.5	1	1	8.5
		Gain	−1	−1	0	−1	−0.5	0.5	0.5	0	−2.5
7	tDCS	Baseline	4	1	0	0	0.5	0.5	1	0	7
		After	3	1	0	0	0.5	1	1	1	7.5
		Gain	1	0	0	0	0	−0.5	0	−1	−0.5
	Sham-tDCS	Baseline	2	1	0	0	0.5	0.5	0.5	0	4.5
		After	2	1	0	0	0	0.5	0.5	0	4
		Gain	0	0	0	0	0.5	0	0	0	0.5

[a] SARA, Scale for Assessment and Rating of Ataxia.
[b] RAM, rapid and alternate movement.
[c] tDCS, transcranial direct current stimulation.

Table 3
Analysis of SARA[a] results.

Parameter	Median tDCS[b]	Median sham-tDCS	p
Gait	1	0	0.03
Posture	1	−1	0.09
Sitting	0	0	1
Speech	0	0	0.42
Finger-to-finger	0	0	0.40
Finger-to-nose	0	0	0.20
RAM[c]	0.5	0	0.12
Heel-to-knee	0	0	0.34
Total	2.5	−1	0.03

[a] SARA, Scale for Assessment and Rating of Ataxia.
[b] tDCS, transcranial direct current stimulation.
[c] RAM, rapid and alternate movement.

another three, and a 3 by one patient. All participants, except for patient 1, reported a lower grade after sham-tDCS, five reported no change and one reported slight improvement.

Adverse events reported in the study were itching, burning sensation, local erythema, tingling, headache, pain in the scalp, and drowsiness. None were reported as severe (Table 7).

Table 4
Analysis of the Wii Fit platform results.

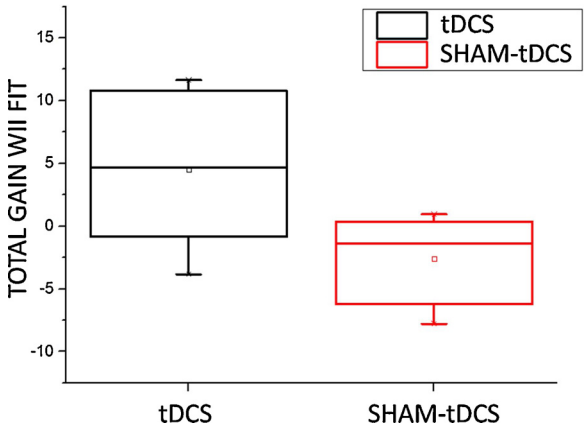
Parameter	Median tDCS[a]	Median sham-tDCS	p
S.D.[b] of AP[c] center of pressure (m)	0.510	0.305	0.67
S.D. of LL[d] center of pressure (m)	0.236	−1.179	0.14
Average right load (Kg)	−0.482	−0.352	1
Average left load (Kg)	3.710	−0.141	0.05
S.D. of right load (Kg)	0.020	−0.178	0.40
S.D. of left load (Kg)	−0.183	−0.245	1
Total	4.648	−1.368	0.03

[a] tDCS, transcranial direct current stimulation.
[b] S.D., standard deviation.
[c] AP, anteroposterior.
[d] LL, latero-lateral.

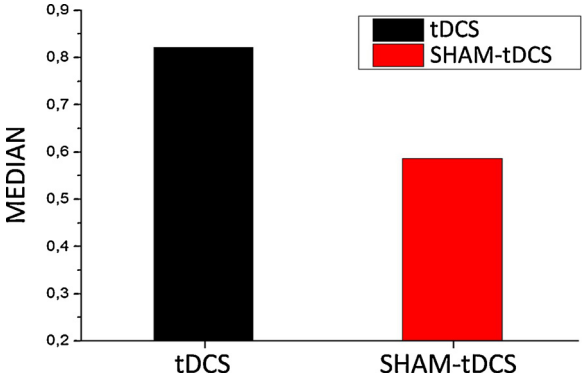
4. Discussion

The data presented reinforces the safety and reliability of tDCS. The adverse events were self-limited and were experienced for a limited duration, as reported by others [9,32,33].

Studies show that the anodic tDCS induces local changes, leading to



Graph 1. Total gain using Wii Fit platform after tDCS[a] and sham-tDCS.



Graph 2. Median of total gain (m) using CvMob after tDCS[a] and sham-tDCS.

the neuromodulation of the directly activated area [17]. The effects at the beginning and during stimulation are neuromodulatory because they generate change in neuronal firing. Late effects are neuroplastic and occur due to several factors, such as gene induction (c-Fos and c-Jun) and long-term potentiation in systems that use glutamate as a neurotransmitter. However, although these effects have been identified in animal and human studies by functional neuroimaging, the relevance of tDCS is apparent from clinically proven effects [34,35].

A question emerges as to the best place for the positioning of the active electrode. Hypoexcitability of the cerebral cortex has been identified in cerebellar lesions [16]. It follows that activation of the primary motor cortex would generate more stabilization in motor actions, and lead to the reduction of ataxia. Grimaldi et al. showed that the anodal stimulation of the cerebellar cortex enhances the inhibitory activity of this structure over the cerebellar nuclei and consequently accelerates the process of motor learning, working memory, and locomotor adaptation [8]. Thus, in some studies, motor cortex stimulation was performed, whilst, in others, stimulation was directed to the cerebellar cortex [36–42]. Considering the pathophysiological aspects involved in cerebellar lesions, the area chosen for stimulation in this study was both motor cortices (C3 and C4) in order to reduce local hypoexcitability provided by cerebellar injury.

Regarding the difference in the average leg load between the sides identified in Table 4, all subjects were right-handed and the dominant side was activated within maximum motor performance. This could explain the absence of any difference in motor power on the right side when compared to the left. We cannot rule out that in right-handed individuals there was a pre-existing motor functional optimization in the right hemisphere. Moreover, it is not possible to conclude that the differences in the average leg load between sides is clinically significant since there was not a predominantly affected side. More likely this

Table 6
Results after application of PGI-I[a].

Patient	tDCS[b]	Sham-tDCS
1	1	1
2	2	4
3	1	4
4	2	4
5	3	4
6	2	3
7	1	4

[a] PGI-I, Patient Global Impression of Improvement scale.
[b] tDCS, transcranial direct current stimulation.

Table 7
Incidence of adverse effects after tDCS[a].

Adverse effects	Incidence (%)	Light (%)	Moderate (%)	Severe (%)
Headache	7.5	7.5	0	0
Neck pain	0	0	0	0
Pain in the scalp	5	2.5	2.5	0
Tingling	17.5	15	2.5	0
Itching	37.5	27.5	10	0
Burning sensation	15	10	5	0
Local erythema	2.5	2.5	0	0
Drowsiness	2.5	2.5	0	0
Difficulty in concentration	0	0	0	0
Sharp mood swings	0	0	0	0
Irritability	0	0	0	0

[a] tDCS, transcranial direct current stimulation.

Table 5
Analysis of CVMOB results.

Parameter		Median tDCS[a]	Median sham-tDCS	P
Frontal plane	TT[b] of the head (m)	0.074	0.150	0.67
	TT of the LL[c] (m)	0.420	0.035	0.35
Sagittal plane	TT of the head (m)	−0.074	0.112	0.09
	TT of the RLL[d] (m)	0.016	0.055	1
	TT of the LLL[e] (m)	0.047	0.000	0.40
Standing up	TT (m)	−0.109	−0.102	0.67
	Time	0.737	0.161	0.40
	Total	0.821	0.587	0.83

[a] tDCS, transcranial direct current stimulation.
[b] TT, total trajectory.
[c] LL, lower limbs.
[d] RLL, right lower limb.
[e] LLL, left lower limb.

variation is due to the lack of homogeneity in a small sample.

Despite the small sample size, improvement in gait and overall SARA grade, as well as increased motor performance measured by the Wii Fit platform after tDCS were observed. Pozzi et al., in an open trial with three participants, showed similar results with improved gait, posture, and instrument-specific parameters (SARA) [41]. However, the resources of the objective evaluation of posture adopted by Pozzi were different from those used in this study (Wii Fit platform and CvMob), so it was not possible to compare the outcomes.

Benussi et al. conducted a clinical trial with 19 patients with cerebellar ataxia and rated the response after a single cerebellar anodic stimulation session and after Sham. In this study, there was a significant improvement in gait and SARA scores after stimulation when compared to Sham [42].

The study showed that in respect of SARA, the Wii Fit platform, and CvMob, there was little or no improvement when isolated parameters were evaluated. However, significant improvement was found when comparing the total scores provided by these instruments. This suggests that participants experienced improvement within various parameters, which is expected when the sample is heterogeneous [43,44]. Another possibility is that the small sample size does not allow for identification of differences in specific parameters. However, taking the sum of the parameters into consideration in a total score lends weight to the validity of the study. Due to the limited sample, it was not possible to perform sub-analyses between the improvement of the participants and demographic variables such as gender and age.

Subjectively, tDCS was accompanied by the perception of more significant improvement by patients than when sham-tDCS was applied. All subjects noticed improvement after tDCS, presenting higher scores than those observed after sham-tDCS. An area of discussion concerns the functional improvement that is not always associated with positive change in the objective parameters, and vice-versa. Thus, the perception of the subjects about the changes should be valued in sham-controlled studies.

It is still not possible to guage long-term effects and to determine whether repeated cycles of stimulation could affect a late prognosis of ataxia. These questions were not addressed in the current study although could be subsequently dealt with in randomized trials with a longer casuistic and longer follow-up time.

Further studies on the use of tDCS in individuals with cerebellar ataxia can be methodologically improved in several areas, for example to compare the improvement of cerebellar tDCS and motor cortex tDCS and to measure the results. Studies involving tDCS need objective parameters, not just clinical criteria, to assess both its benefits and adverse effects. In this study, the Wii Fit platform and CvMob software, both innovative tools in motion analysis, were used but in the literature, there is still no consensus about the best mechanisms available to obtain this data. Finally, there is a need for further investment in evaluating the motor cortex after stimulation.

5. Conclusion

tDCS seems to improve objective and subjective parameters of motor function in patients with cerebellar ataxia after five sessions, although it is important to consider that the small sample size and heterogeneity of the sample are limiting factors in this trial. Moreover, different disease entities had been examined which has to be mentioned when interpreting the results. In the case of cerebellar diseases in which the therapeutic resources are limited, identifying positive results in motor parameters makes tDCS a very promising therapeutic option, especially due to its low cost and technical ease of use. However, further randomized, double blinded, sham-controlled studies with larger sample sizes and greater observation times are essential to determine the therapeutic potential of long-term tDCS and the corresponding impact on the prognoses of these individuals.

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Conflict of interest

The authors declare that they have no conflict of interest.

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