Anodal Transcranial Direct Current Stimulation (tDCS) Decreases the Amplitudes of Long-Latency Stretch Reflexes in Cerebellar Ataxia

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Abstract—Recent studies suggest that the neuromodulation of the cerebellum using transcranial direct current stimulation (tDCS) could represent a new therapeutic strategy for the management of cerebellar disorders. Anodal tDCS of the cerebellum increases the excitability of the cerebellar cortex. We tested the effects of anodal tDCS applied over the cerebellum in ataxic patients. We studied (a) stretch reflexes (SR) in upper limb (SLSR: short-latency stretch reflexes; LLSR: long-latency stretch reflexes), (b) a coordination functional task in upper limbs based on mechanical counters (MCT: mechanical counter test), and (c) computerized posturography. tDCS did not change the amplitude of SLSR, but reduced significantly the amplitudes of LLSR. tDCS did not improve the MCT scores and did not modify posture. We suggest that anodal tDCS of the cerebellum reduces the amplitudes of LLSR by increasing the inhibitory effect exerted by the cerebellar cortex upon cerebellar nuclei. The absence of effect upon upper limb coordination and posture suggests that the cerebello-cerebral networks subserving these functions are less responsive to anodal tDCS of the cerebellum. Anodal tDCS of the cerebellum represents a novel experimental tool to investigate the effects of the cerebellar cortex on the modulation of the amplitudes of LLSR.

Keywords—Direct current stimulation, Anodal, Cerebellum, Long-latency stretch reflexes, Excitability, Plasticity.

ABBREVIATIONS

AS20	Ataxia scale on 20 points
dX	Medial–lateral displacement
dY	Anterior–posterior displacement
ECR	Extensor carpi radialis
EMG	Electromyography
FCR	Flexor carpi radialis
LLSR	Long-latency stretch-responses
MCT	Mechanical counter test
PEYO	Eyes open and feet apart
PEYF	Eyes closed and feet apart
PJYO	Eyes open and feet together
PJYF	Eyes closed and feet together
SLSR	Short-latency stretch responses
t-DCS	Transcranial direct current stimulation
TTW	Total travelled way

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INTRODUCTION

Cerebellar disorders represent a heterogeneous group of diseases.[10] These disabling disorders, also called human cerebellar ataxias, manifest primarily with an impaired control of voluntary movement.[7] Voluntary movement is ataxic, affecting not only single-joint and multi-joint movements in limbs, but also posture. We currently lack efficient drug therapies for most of the cerebellar disorders encountered during daily practice. There is an urgent need to identify novel strategies to antagonize cerebellar motor deficits or to enhance the effects of rehabilitation on this group of disabling disorders.

There is a growing interest in non invasive electrical or magnetic stimulation methods as research techniques to promote neuroplasticity or as therapeutic tools. In particular, transcranial direct current stimulation (tDCS) applied over the cerebellum is a tool currently under investigation to speed up learning of reaching or adaptation during locomotion.[6,9] In tDCS, a steady current of small intensity (usually 0.5, 1 or 2 mAmp) passes between two large electrodes affixed on the scalp. Continuous or intermittent anodal tDCS induces a polarity-dependent site-specific modulation of brain activity.[13,14] Anodal tDCS induces a

depolarization of the neural tissue immediately below the electrode, inducing a subthreshold membrane potential shift and increasing neural firing rate, therefore enhancing the overall neural activity of the stimulated area.[1] Anodal tDCS of the cerebellum increases the excitability of the cerebellar cortex.[5]

We recently found in rats that anodal epidural DCS of the cerebellum tunes the excitability of the motor cortex and re-shapes corticomotor maps of couples of agonist/antagonist limb muscles.[15] We also observed that anodal epidural DCS of the cerebellum enhances the spinocerebellar evoked potentials associated with peripheral electrical stimulation and—very attractively—increases cerebellar blood flow both at the level of cerebellar cortex and cerebellar nuclei. These observations strengthen the idea that tDCS should be tested in human cerebellar ataxias, trying to assess patients at a very early stage of the disease if possible.

We assessed the effects of anodal tDCS of the cerebellum in a group of cerebellar patients. We studied the effects on (a) short-latency stretch responses (SLSR) and long-latency stretch reflexes (LLSR), the amplitude of these latter is known to be increased in cerebellar ataxias,[2,12] (b) a quantitative coordination task in upper limbs designed specifically for cerebellar ataxias,[3,8] and (c) posture (which is a major source of disability in cerebellar disorders) using a computerized technique. We tested the hypothesis that anodal tDCS of the cerebellum would improve the three measurements. We assumed that anodal tDCS of the cerebellum would restore, at least partially, the activity of the cerebellar cortex, especially the activity of the Purkinje neurons which exert physiologically an inhibitory effect upon cerebellar nuclei. We speculated that this would improve cerebellar function.

SUBJECTS AND METHODS

We enrolled nine patients (two female) who gave their informed consent following approval by the Ethical Committee of ULB. The mean age ($\pm$SD) was 51.3 ± 14.0 years. All the patients were right-handed and shared a core cerebellar syndrome characterized by oculomotor ataxia, dysarthria, limbs dysmetria and ataxic posture in association with cerebellar atrophy demonstrated by brain MRI. The group included the following cerebellar disorders (Table 1): immune ataxia ($n = 1$), paraneoplastic ataxia ($n = 1$), adult-onset ataxia of unknown origin ($n = 3$), autosomal recessive ataxia ($n = 1$), dominant ataxia ($n = 3$). Severity of ataxia and global disability of our patients was evaluated with the ataxia scale on 20 points (AS20), which is highly correlated with the speed and accuracy of the three-dimensional movements of upper

limb and takes also into account the impact of the disease on patients' quality of life.[10]

We investigated during distinct experimental sessions held on separate days (at least 6 days; every effort was made to limit each session time to a maximum of 3 h) the effect of tDCS on three experimental paradigms: (a) stretch reflexes (SR) in upper limbs, (b) upper limb dexterity and coordination using a mechanical counter test (MCT), and (c) computerized posturography. For each session, data were collected at baseline, after a sham stimulation, and after anodal tDCS applied over the cerebellum. For sham and anodal stimulation, the anode—a sponge electrode; size: 50×40 mm—positioned at the level of the posterior fossa was applied (a) on the right side with the center of the sponge at about 3 cm to the right of the inion[5,6] for SR test and MCT test (in order to target the right cerebellar hemisphere, given the lateralized cerebellar functions for upper limbs),[10] and (b) in front of the vermis at the inion level for postural tests (in order to target the vermis, given the critical role played by medial cerebellar structures on postural control.[10] The second sponge electrode—the cathode; same size of anode—was applied over the contralateral supra-orbital area. Electrodes were soaked (with a solution of NaCl 0.9%). The period of stimulation lasted 20 min both for sham and active stimulation. Current delivered was 1 mAmp (portable stimulator with a 9 V battery; CES, Canada). Current was increased gradually from 0 to 1 mAmp over 30 s, as confirmed by the analysis of the current using a Fluke PM3384A Combiscope. For sham stimulation, once the current reached the plateau, it was gradually decreased to zero over a period of about 1 min, so that patients were blinded as to whether they were receiving sham stimulation or anodal tDCS.[6] In order to assess a possible dose response effect, we also compared at different days the effects of an intensity of stimulation of 2 mAmp with the effects of an intensity of stimulation of 1 mAmp in three patients for the three experimental paradigms. We found no difference for the results of SR, MCT and postural tests between the two intensities of stimulation (variations were below 5%). In order to exclude a possible cathodal inhibitory effect over the frontal lobe, the cathode was put on right shoulder in 3 patients. Results were unchanged as compared to the supra-orbital location.

Stretch Reflex Responses (n = 6 Patients)

We investigated the dominant side. We recorded surface electromyographic (EMG) activities (Bagnoli system, Delsys electrodes, USA) of the right flexor carpi radialis muscle (FCR) during passive rapid wrist extension movements, and we analyzed SLSR and

TABLE 1. Demographics of patients.

| Patient | Age (years) | Sex | Duration of disease (years) | Diagnosis | CNS-acting drugs | Global disability scale | Procedure applied | | |
							SR response (n = 6)	MCT (n = 8)	Computerized posturography (n = 6)
1	56	M	4	Sporadic adult-onset ataxia	Tandospirone Memantine	B		X	X
2	33	F	9	Autosomal recessive ataxia	Escitalopram Baclofen Memantine	B	X	X	X
3	75	F	3	Sporadic adult-onset ataxia		C	X	X	X
4	52	M	34	Sporadic adult-onset ataxia	Memantine	D	X	X	
5	40	M	9	Immune ataxia		C		X	
6	68	M	11	Paraneoplastic ataxia	Gabapentine	D	X	X	
7	54	M	10	Dominant ataxia		B	X	X	X
8	36	M	21	Dominant ataxia		A	X	X	X
9	48	M	8	Dominant ataxia		A			X

A: fully independent, B: requiring some help, C: external aid often required, D: dependent.

LLSR in three experimental conditions: baseline, post-sham, post-tDCS. The method of SR analysis is based on a robotic technique (myohaptic) reported earlier.[12] Subjects were comfortably seated, with the shoulder relaxed and the upper arm perpendicular to the forearm. The hand and forearm were affixed with straps. The wrist joint was carefully aligned with the motor axis. Movements were performed in the horizontal plane. Extensions, imposed *via* a rapid extension of the wrist joint (at a peak velocity of 4.7 rad/s; time to peak: 30 ms—triangular velocity profile), were applied randomly every 5–10 s. The wrist joint was in a neutral position at the onset of the stretch and patients are asked to slightly activate their FCR muscle throughout the procedure, using a visual feedback of the EMG activity. Sampling rate was of 2048 Hz. EMG traces were full-wave rectified and averaged for 50 trials (Bandpass filter: 20–500 Hz). The averaging process allows a better estimation of the electrical activity generated by the muscle and has a smoothing effect on the EMG pattern. Calibration of surface EMG activities is critical to compare EMG activities within subjects and across subjects.[11] To this aim, we assessed the maximal contraction in an isotonic task (MIC, maximal isotonic contraction; the motor is opposing a controlled force): subjects were asked to perform a maximal wrist flexion (10 trials) against a torque of 20 Nm controlled by the computer. Corresponding EMG activities were rectified and averaged. The calibration area was defined as the integrated area below the averaged EMG trace (traces are first rectified before averaging) corresponding to a torque value from 0 to 6 Nm.[12] We evaluated the following parameters of muscle stretch responses: maximal amplitude (peak) of SLSR, Integral of the interval 25–40 ms, peak of LLSR, Integral of the interval 55–85 ms. The intervals 25–40 and 55–85 ms were selected on the basis of previous experiments on muscle stretch responses because they are robust markers of amplitudes of SLSR and LLSR.[12] We also computed the ratios of the peak of LLSR divided by the peak of SLSR, and the ratios of the Integral 55–85 ms divided by the Integral 25–40 ms.

Mechanical Counter Test (n = 8 Patients)

The MCT is a validated test to quantify upper limb function in ataxic patients.[3,8] The test is highly reproducible in cerebellar disorders. The patients were comfortably seated during the task. Two procedures were applied in each upper limb: a task of clicking repeatedly with the thumb on a single mechanical counter (MCT-U: unilateral; upper limb maintained at rest with forearm on the ipsilateral thigh during the task), and a task of clicking alternatively with the index finger on two mechanical counters separated by a
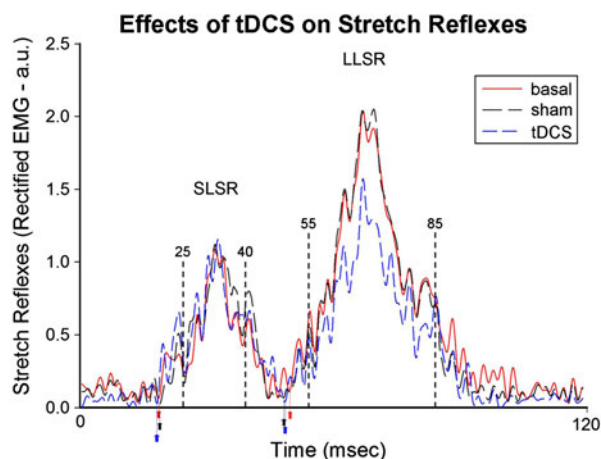
FIGURE 1. Effect of tDCS on SR in upper limb. Representative EMG activities for the FCR during rapid stretches of the wrist (extensions) in a cerebellar patient at baseline (red trace), after sham stimulation (black dashed trace) and after anodal tDCS of the cerebellum (blue dashed trace). Stretch responses are superimposed. The amplitudes of the SLSR are similar in the three conditions. The amplitudes of the LLSR are similar between baseline and sham stimulation. However, the intensity of LLSR is reduced by anodal tDCS. Each trace corresponds to an average of 50 trials. EMG responses are full-wave rectified before averaging. Stretch responses are calibrated in arbitrary units (a.u.) (see "Subjects and Methods"). Arrows at the bottom of the traces indicate the onset latencies of SLSR and LLSR. Vertical dotted lines: intervals 25–40 and 55–85 ms.

distance of 39.5 cm in the horizontal plane (MCT-A: alternate). For each side and each task, three practice trials of 10 s were performed, followed by three assessments at 10, 20 and 30 s, respectively (total of 9 measurements for each upper limb in each of the two procedures). Each procedure (in each side, starting by the dominant side) was repeated in the three experimental conditions: basal, post-sham, post-tDCS. A rest of 15 s was applied between each measurement to avoid muscle fatigue.

Computerized Posturography (n = 6 Patients)

Posture recordings were made with a calibrated FootScan pressure platform (Footscan, RSScan International, Olen, Belgium). Patients were assessed in 4 successive conditions: eyes open and feet apart (PEYO), eyes closed and feet apart (PEYF), eyes open and feet maintained together (PJYO), eyes closed and feet maintained together (PJYF). For conditions PEYO and PEYF, we used tape affixed on the platform to identify the position of the feet associated with a subjective feeling of stability allowing the patients to keep the upright position without any external support. Patients were asked to keep the standing position with the arms hanging loosely by the sides. A rest period of at least 3 min was applied between each of

the 4 conditions. A series of nine trials of 15 s duration was performed in each condition. Between each trial, a rest period of 15 s was applied if the patient perceived any degree of fatigue. These 4 sets of measurements were repeated in the 3 experimental conditions: basal, post-sham, post-tDCS. Anterior–posterior (dY), medial–lateral (dX) displacements and total travelled way (TTW)[17] were calculated using the system's software. Moreover, we computed the ratios PEYF/PEYO in order to isolate the vision effect, and check whether tDCS influenced this parameter.

STATISTICAL ANALYSIS

Statistical analysis was performed with Sigma Plot (Jandel Scientific, Germany). The normality of data was assessed with the Kolmogorov–Smirnov test. To evaluate the effects of sham stimulation and active tDCS on peaks of SLSR, peaks of LLSR, integrals 25–40 ms, integrals 55–85 ms, we applied the repeated measure analysis of variance, followed by the Holm–Sidak test for pairwise multiple comparison procedure. The same analysis was performed for the ratios peak of LLSR/peak of SLSR and integral 55–85 ms/integral 25–40 ms. The Spearman correlation coefficient and a linear regression analysis were applied to study the relationship between the AS20 score and the peak of LLSR, as well as for the relationship between peak of SLSR and peak of LLSR. To assess the relationship between the integral 25–40 ms and the integral 55–85 ms, we applied the Pearson product moment coefficient and a linear regression analysis. For MCTU and MCTA scores, we looked for an inter-group effect between baseline, post-sham stimulation and post-tDCS in both sides (dominant and non dominant) by using the repeated measure analysis of variance or the Friedman repeated measures analysis of variance on ranks according to the results of the normality assessment. The same procedure was applied for the parameters of the computerized posturography.

RESULTS

Stretch Reflexes

Figure 1 illustrates a typical example of SR responses in the three experimental conditions in one patient. At baseline, a first stretch response (SLSR) occurs at a short latency, followed by a second response (LLSR). The latencies of the responses remained similar following sham stimulation or anodal tDCS. Sham stimulation did not change the amplitude of SLSR. Moreover, sham procedure did not modify the amplitude of LLSR response. Anodal tDCS did
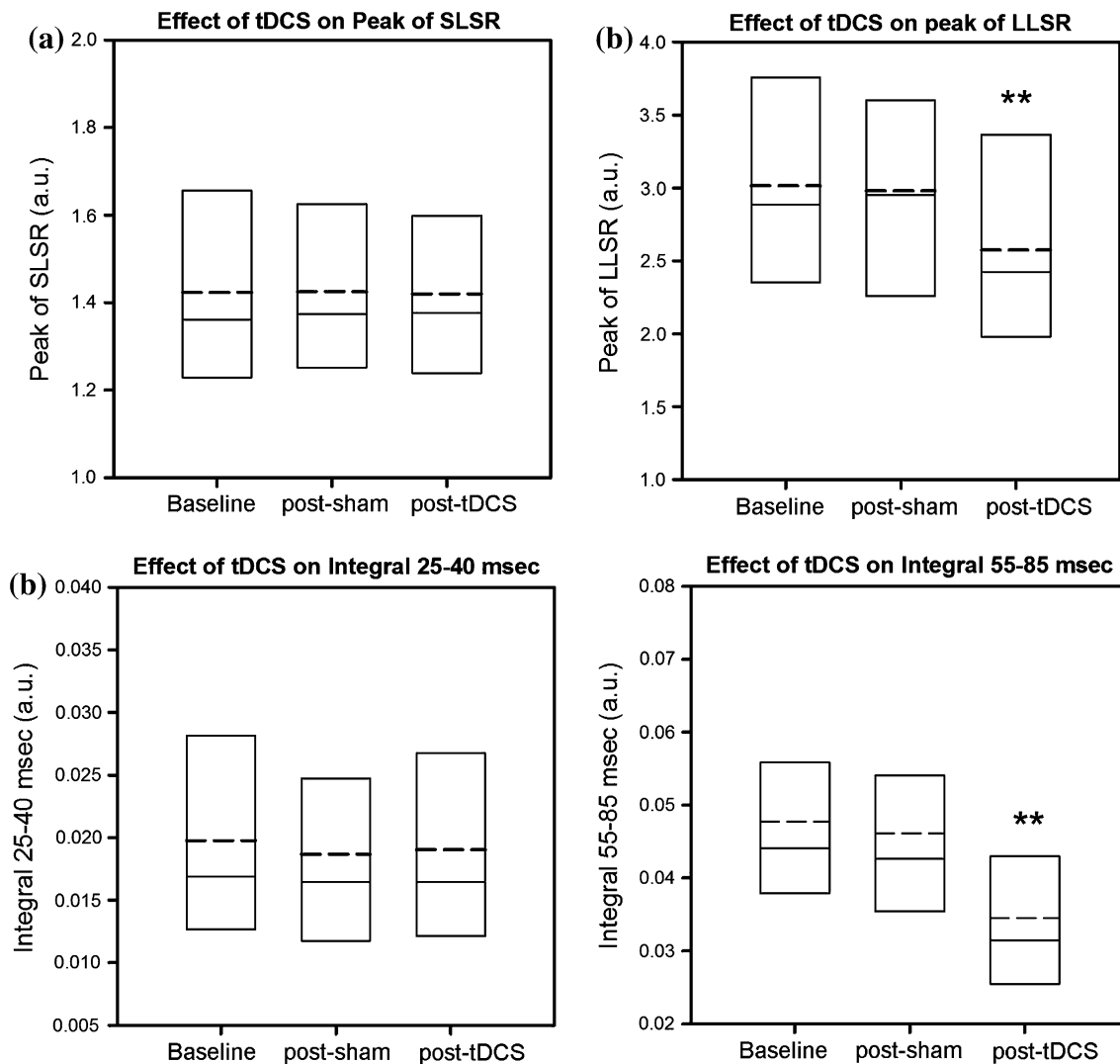
FIGURE 2. Effect of tDCS on SLSR and LLSR. (a) Box plots corresponding to the data obtained in the three experimental conditions (baseline, post-sham, post-tDCS) for peak of SLSR (left panel) and peak of LLSR (right panel). (b) Box plots of the integrals 25–40 ms (left panel) and 55–85 ms (right panel). Mean (dashed lines), median (continuous lines) values, as well as the 5–95th percentiles are shown. Data are expressed in a.u. (see also "Subjects and Methods"). **$p < 0.001$.

not affect the amplitude of SLSR but reduced clearly the amplitude of LLSR response. This observation was confirmed by the statistical analysis of peaks of stretch responses in the group of patients. We found no inter-group difference between baseline, post-sham and post-tDCS for peaks of SLSR (F: 0.0861; $p = 0.918$) and for integrals 25–40 ms (F: 1.249; $p = 0.328$) (Fig. 2). By contrast, active tDCS reduced markedly the amplitudes of LLSR responses as compared to baseline and sham stimulation, with a highly significant inter-group difference both for peaks of LLSR (F: 21.375; $p < 0.001$) and for integrals 55–85 ms (F: 54.280; $p < 0.001$). Ratios of peaks of LLSR/peaks of SLSR were significantly reduced by anodal tDCS as compared to baseline and sham stimulation (Fig. 3;

inter-group effect; F: 19.482; $p < 0.001$). A similar observation was made for ratios of integrals 55–85 ms/integrals 25–40 ms (F: 31.386; $p < 0.001$).

Patients with the largest peaks of LLSR responses were the more severely affected clinically, as confirmed by the correlation between the AS20 score and peak of LLSR at baseline (Fig. 4; Spearman correlation coefficient = 0.771; linear regression analysis: $p = 0.04$). At baseline, the peak of SLSR was linearly correlated with the peak of LLSR (Fig. 5, left; Spearman correlation coefficient = 0.829; linear regression analysis: $p = 0.033$). The integral 25–40 ms was linearly correlated with the integral 55–85 ms (Fig. 5, right; Pearson product moment correlation = 0.949; linear regression analysis: $p = 0.0037$).
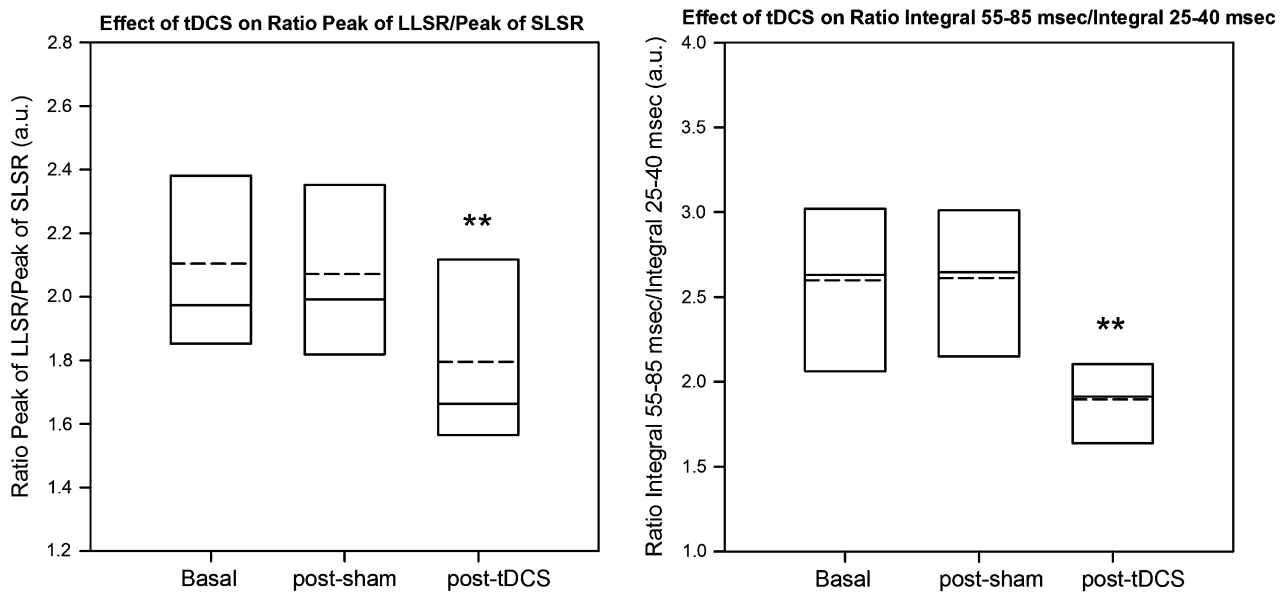
FIGURE 3. Effect of tDCS on ratios peak of LLSR/peak of SLSR (left panel) and on ratio integral 55–85/25–40 ms (right panel) in the three experimental conditions (baseline, post-sham, post-tDCS). Box plots showing mean values (dashed lines), median values (continuous lines), as well as the 5–95th percentiles. Data are expressed in a.u. (see "Subjects and Methods"). **$p < 0.001$.
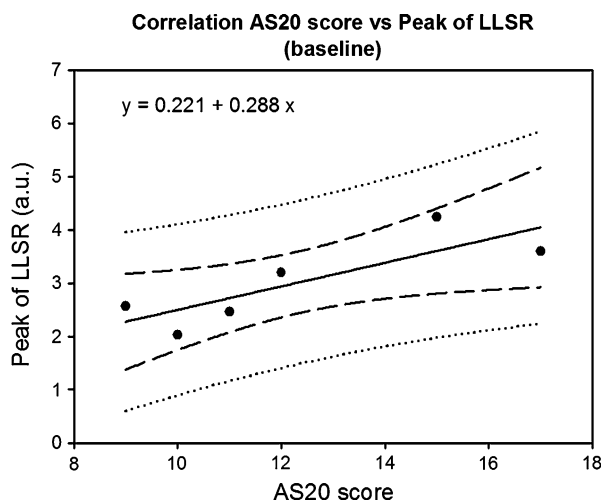

FIGURE 4. Linear correlation between severity of symptoms and peak of LLSR. Severity of symptoms evaluated with AS20 score (on x axis). Peaks of LLSR are expressed in a.u. 95% confidence interval (long dash) and 95% prediction interval (dotted) are shown.

Mechanical Counter Test

Both on the dominant and non dominant side, sham stimulation and anodal tDCS did not improve the scores of MCTU-10 (Fig. 6; inter-group difference for dominant side: F: 1.022, $p = 0.385$; non dominant side: F: 0.243, $p = 0.788$), MCTU-20 (F: 0.171, $p = 0.844$; F: 1.064, $p = 0.371$, respectively) and MCTU-30 ($p = 0.654$; F: 0.025, $p = 0.975$, respectively). Sham stimulation and anodal tDCS did not increase the

scores of MCTA-10 (Fig. 7; inter-group difference for dominant side: $p = 0.794$; non dominant side: F: 0.409, $p = 0.672$), MCTU-20 (F: 0.417, $p = 0.667$; F: 0.511, $p = 0.611$, respectively) and MCTU-30 ($p = 0.531$; F: 0.931, $p = 0.417$, respectively).

Computerized Posturography

Figure 8 illustrates an example of the path of the center of pressure in one patient in condition 1 (eyes open, feet apart) at baseline, after sham stimulation and after tDCS. No reduction of the path in the latero-lateral or anterior-posterior direction occurred. Considering the group of patients in each of the 4 conditions, the parameters of posture (dX, dY, TTW) remained unchanged following sham stimulation or tDCS stimulation (Fig. 9). For dX, the inter-group difference had a p value of 0.786 (F: 0.247), 0.947 (F: 0.0545), 0.463 (F: 0.877) and 0.163 (F: 2.95) for the conditions PEYO, PEYF, PJYO and PJYF, respectively. For dY, p value for the inter-group difference was 0.430, 0.956, 0.092 (F: 3.636) and 0.571 (F: 0.646) for the 4 conditions, respectively. For TTW, p value for the inter-group difference was 0.05 (trend towards larger values for sham and tDCS as compared to baseline; F: 4.096), 0.648, 0.936 (F: 0.067) and 0.279 (F: 1.789) for the 4 conditions, respectively. tDCS had no effect on the vision ratio (Fig. 10), as confirmed by the absence of significant inter-group difference for dX (F: 0.589, $p = 0.573$), dY (F: 0.93, $p = 0.426$) and TTW ($p = 0.184$).

Correlation Peak of SLSR vs Peak of LLSR (baseline)

$y = -0.646 + 2.571\ x$

Correlation Integral 25-40 msec vs Integral 55-85 msec (baseline)
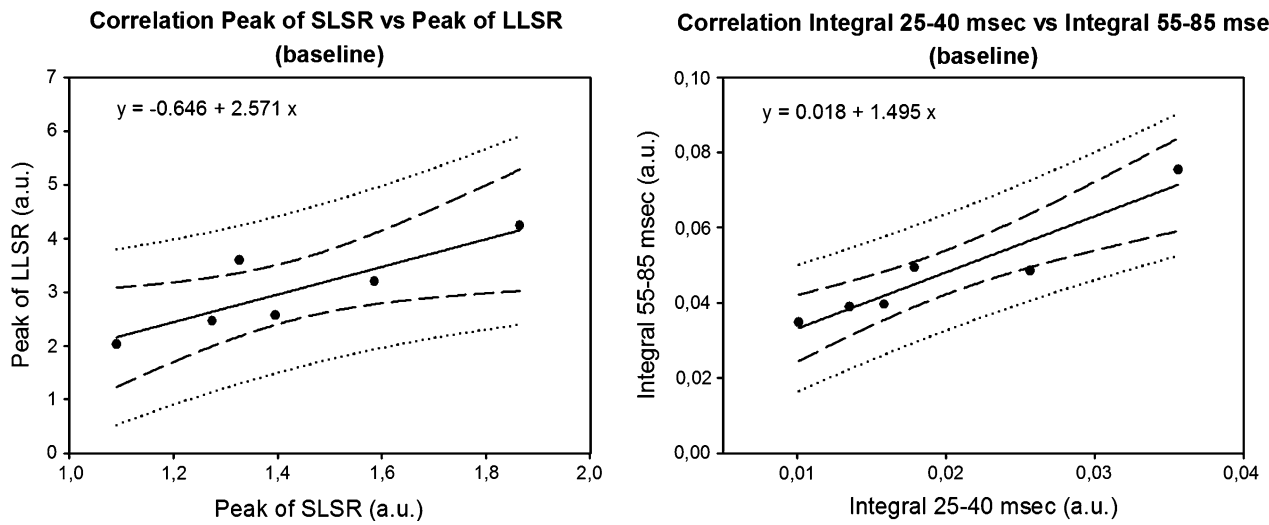
$y = 0.018 + 1.495\ x$

FIGURE 5. Correlation between SLSR responses and LLSR responses in basal condition. Left panel: peaks of SLSR and peaks of LLSR are linearly correlated. Right panel: integrals in the interval 25–40 ms (corresponding to SLSR) and integrals in the interval 55–85 ms (corresponding to LLSR) are correlated in a linear fashion. Peak of SLSR, peak of LLSR, integral 25–40 ms and integral 55–85 ms are expressed in a.u. 95% confidence interval (long dash) and 95% prediction interval (dotted) are shown.
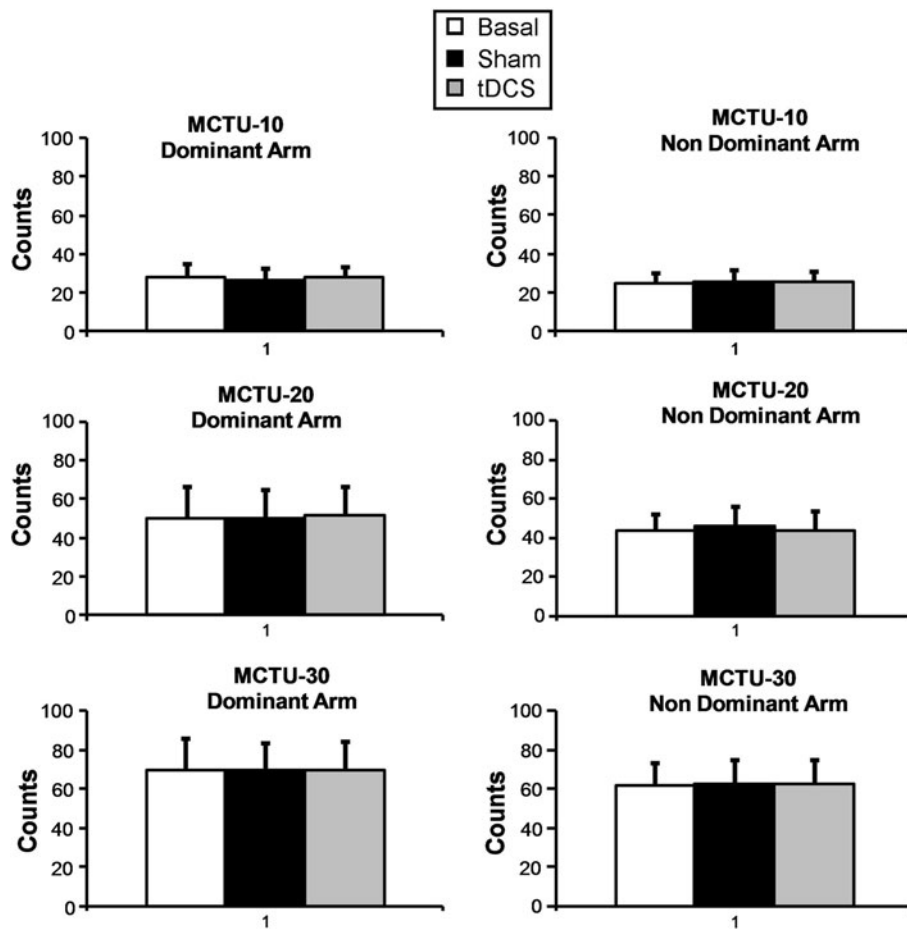

FIGURE 6. Effects of tDCS on MCT (unilateral; MCT-U task). Number of clicks performed with the thumb in the three experimental conditions (baseline: white bars; post-sham: black bars; post-tDCS: gray bars) for recordings of 10 s (MCTU-10), 20 s (MCTU-20) and 30 s (MCTU-30). Left panels: dominant side; right panels: non dominant side. Vertical bars correspond to mean values (±SD).
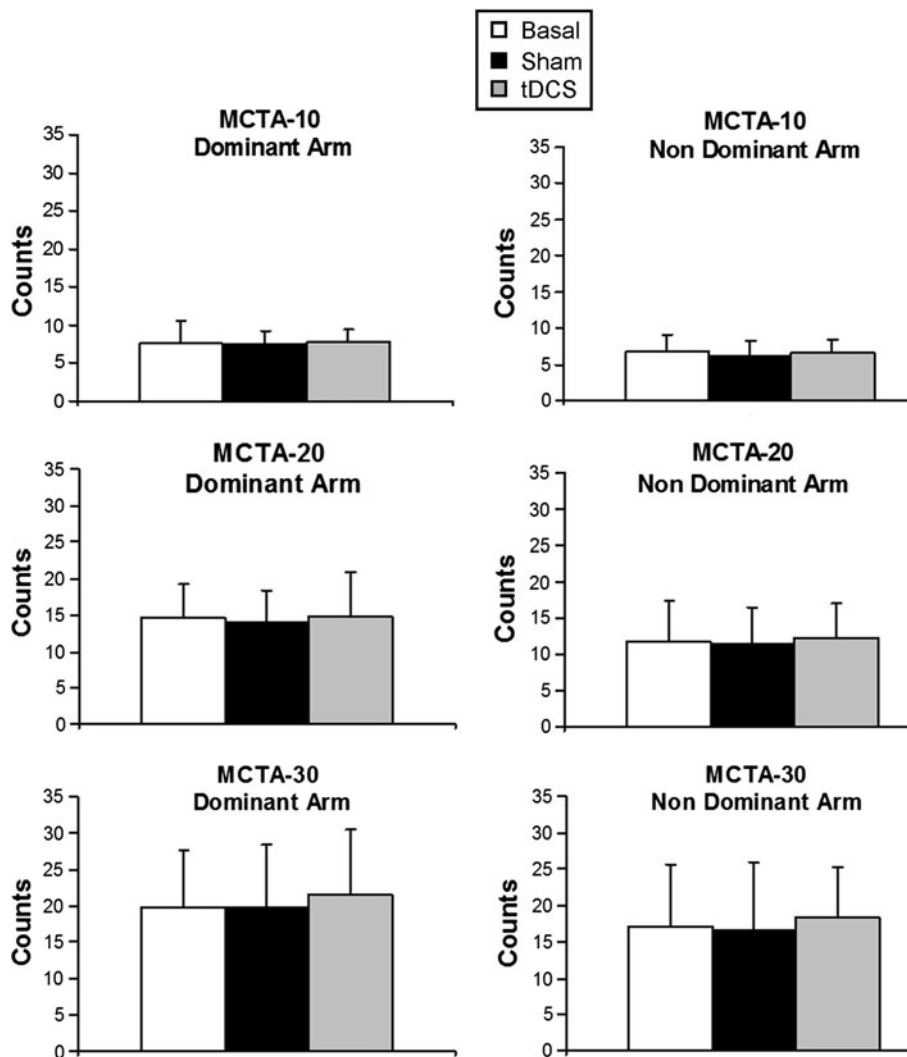
FIGURE 7. Effects of tDCS on MCT-A task. Number of clicks performed during the alternate task in the three experimental conditions (baseline: white bars; post-sham: black bars; post-tDCS: gray bars) for recordings of 10 s (MCTA-10), 20 s (MCTA-20) and 30 s (MCTA-30). Left panels: dominant side; right panels: non dominant side. Vertical bars correspond to mean values (±SD).

DISCUSSION

Our study shows that anodal tDCS of the cerebellum (1) exerts a favorable effect on amplitudes of LLSR without changing the amplitudes of SLSR, (2) does not improve a coordination functional task in upper limbs, and (3) does not improve postural parameters as assessed by computerized posturography in ataxic patients. We did not find differences amongst the different groups of patients. The amplitudes of LLSR is known to be increased in cerebellar patients with atrophy of the cerebellar cortex.[2] Indeed, cerebellar cortex exerts a physiological inhibition upon cerebellar nuclei. Therefore, nuclei are disinhibited when the cerebellar cortex is damaged. This disinhibition contributes to the enhanced long-latency central responses following peripheral stretches applied over limb segments.[2] Our results show that anodal tDCS applied over the cerebellum reinforces the inhibitory activity exerted by the cerebellar cortex over cerebellar nuclei. Anodal tDCS of the cerebellum appears as a novel method to study the modulation of LLSR by the cerebellar cortex. The effects of cerebellar anodal tDCS on SR is unlikely the consequence of an extra-cerebellar effect, such as a direct stimulation of brainstem nuclei. Indeed, the studies by Jayaram et al.[9] and Galea et al.[5,6] have shown no effect of cerebellar tDCS on the excitability of brainstem nuclei such as vestibular or trigeminal nuclei. However, it could be argued that the position of the return electrodes may influence results due to an effect of current flow direction. Earlier studies used the buccinator muscle to position the return electrode.[5,9] Others have used the shoulder, although a possible interference with
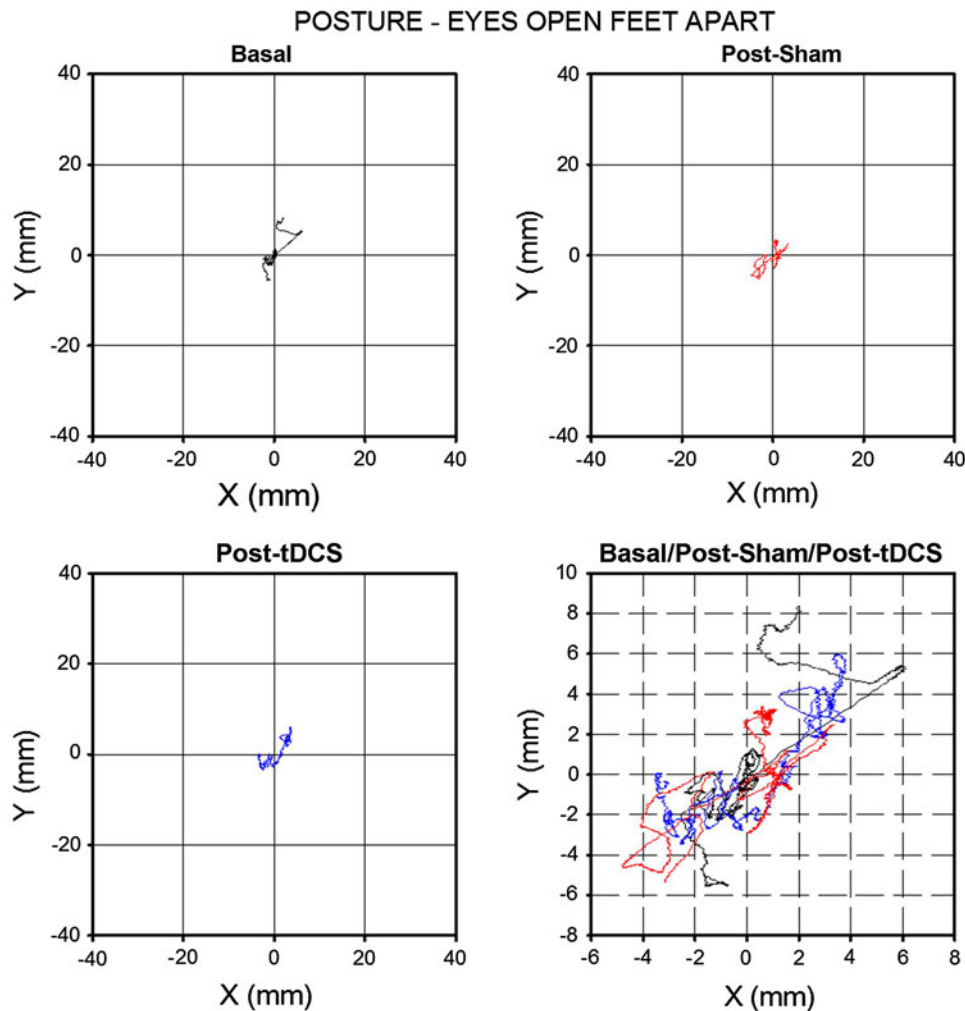
FIGURE 8. Example of effects of tDCS on posture. Traces obtained by computerized posturography in one patient. Projection of the center of pressure on the platform in the medio-lateral (X) axis and anterior–posterior axis (Y). Upper left: basal trace; upper right: post-sham; lower left: post-tDCS. Data obtained during the task eyes open and feet apart (PEYO). Lower right panel: superimposition of the traces obtained in the 3 experimental conditions. Values are expressed in mm.

peripheral nerves has been suggested if the electrode is located nearby the brachial plexus. Nevertheless, we did not find differences between different positions for the return electrode. For instance, having the return electrode on the supra-orbital area or the shoulder did not change the effects observed. The impairments of the cerebellar circuits in our patients may render the cerebellum much less susceptible to changes induced by tDCS, or even lead to a more erratic distribution of currents as a result of the heterogeneous loss of neurons known to occur in cerebellar ataxias.

Neither the MCT scores, nor the postural parameters were improved by anodal tDCS of the cerebellum. One explanation to explain these discrepancies with the effects on LLSR is that both functional tasks depend on the integrity of diffuse cerebello-cerebral networks whose activity could not restored by a spatially-selective anodal tDCS. This opens the possibility that a

hierarchy exists in terms of responsiveness of cerebellar deficits to tDCS: some elemental deficits such as LLSR might be responsive, whereas others might be refractory and require another approach which could be for instance more extensive in terms of spatial application. In this sense, large electrodes surrounding the whole posterior fossa could be envisioned, given the excellent safety features of tDCS. Another possibility is that tDCS should be delivered at a very early stage of the cerebellar disorder in order to be effective, especially for functional tasks. Indeed, in the majority of cerebellar ataxias associated with cerebellar atrophy, a substantial loss of cerebellar cortical neurons has already developed when the patient comes to medical attention. Otherwise, the clinical usefulness of cerebellar tDCS might be generally limited. The possibility of an insufficient intensity of stimulation is unlikely since we did not observe any change by increasing the
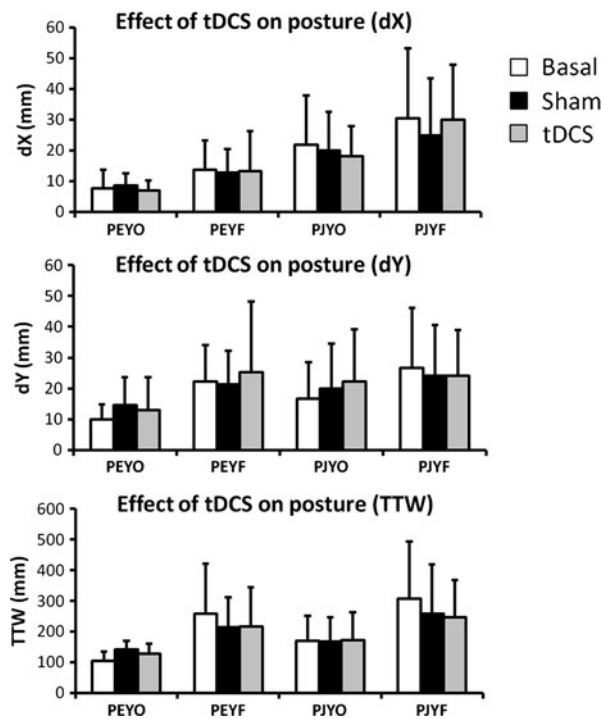
FIGURE 9. Effect of tDCS on postural parameters obtained by computerized posturography. The figure shows the results in the four tasks (PEYO: eyes open and feet apart; PEYF: eyes closed and feet apart; PJYO: eyes open and feet together; PJYF: eyes closed and feet together) during the three experimental conditions (baseline: white bars; post-sham: black bars; post-tDCS: gray bars). Top panel: medial–lateral displacements (dX, expressed in mm). Middle panel: anterior-posterior displacements (dY, expressed in mm). Bottom panel: TTW (expressed in mm). Vertical bars correspond to mean values (±SD).
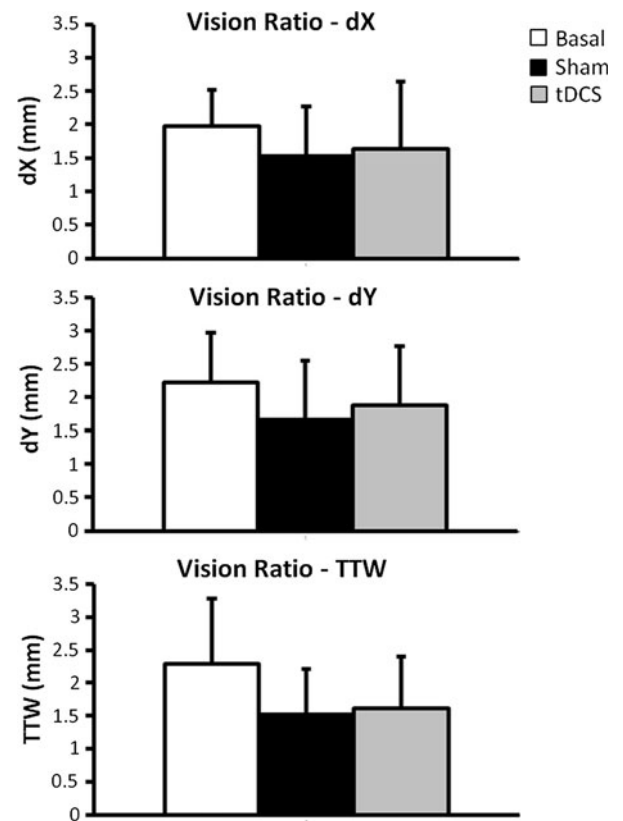

FIGURE 10. Effects of tDCS on vision ratio for the medial–lateral displacements (dX, top panel), the anterior-posterior displacements (dY, middle panel) and the TTW (bottom panel). Vision ratio corresponds to the ratio of the values obtained during the task eyes closed feet apart (PEYF) divided by the values obtained during the task eyes open feet apart (PEYO). Vertical bars correspond to mean values (±SD). Values are expressed in a.u.

intensity of tDCS. With the advent of novel biomarkers of cerebellar degeneration, one can expect that the disorders will be detected at an early stage, at a time when the neuronal populations are not heavily affected and could respond to tDCS.

A conceptual framework for the applications of tDCS over the cerebellum is slowly evolving in various domains. Indeed, developments of tDCS research occur at a time when our understanding of cerebellar functions and their underlying anatomical substrates in terms of networks is growing in a tremendous way. tDCS of the cerebellum is being investigated to promote neuroplasticity and as a therapeutical tool for cerebellar deficits. Recent works have addressed the effects of tDCS on the connectivity between the cerebellum and the motor cortex during learning.[9] The inhibition exerted by Purkinje neurons over cerebellar nuclei decreases during the early phase of learning in healthy subjects and there is a correlation between this reduction and the degree of learning.[18] Anodal tDCS of the cerebellum accelerates the process of learning a reaching task and locomotor adaptation tasks.[6,9] In terms of cognitive operations, cerebellar stimulation

with cathodal tDCS improves the performances during a word generation task. The beneficial effects on working memory could be due to a disinhibition of prefrontal areas.[16] Indeed, cathodal tDCS applied over the cerebellum depresses the activity of the cerebellar cortex. Therefore, the excitatory disynaptic pathway between cerebellar nuclei and the contralateral motor cortex is more active and its effects upon the contralateral cerebral cortex are more widespread. A recent study indicates that tDCS of the cerebellum impacts on recognition of expression of emotions such as sadness and anger.[4] tDCS is thus being applied to study the roles of the cerebellum not only in the motor domain, but also in the cognitive and affective domains.

Future studies are required to better define how tDCS affects cerebellar symptoms. One possible future direction in the emerging field of cerebellar neuromodulation is to combine tDCS of the cerebellum with tDCS of the motor/premotor cortex. Indeed, experimental studies show that anodal tDCS of the motor cortex antagonize efficiently the hypoexcitability of the

motor cortex associated with an extensive damage of the contralateral cerebellar hemisphere.[14] The decreased excitability of the motor cortex with enhanced inhibition associated with cerebellar lesions is considered as one of the mechanisms participating in the deficits of skilled movements.[19,20] This is particularly relevant since cerebellar tDCS in healthy subjects modulates the cerebello-cerebral inhibition in a polarity specific manner, without changing M1 and brainstem excitability.[5] So, a next study could be to combine simultaneously anodal tDCS of the cerebellum and anodal tDCS of the contralateral motor cortex.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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