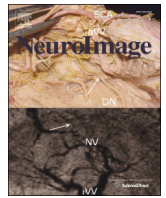




Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Review

Transcranial cerebellar direct current stimulation (tcDCS): Motor control, cognition, learning and emotions

Roberta Ferrucci¹, Alberto Priori^{*}

Centro Clinico per la Neurostimolazione, le Neurotecnologie ed i Disturbi del Movimento, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, via F. Sforza 35, 20122 Milano, Italy
 Università degli Studi di Milano, Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, via F. Sforza 35, 20122 Milano, Italy

ARTICLE INFO

Article history:

Accepted 28 April 2013
 Available online xxxxx

Keywords:

Cerebellum
 Cerebellar stimulation
 tDCS
 Neuroenhancement

ABSTRACT

The neurological manifestations of cerebellar diseases range from motor to cognitive or behavioral abnormalities. Experimental data in healthy subjects extend the cerebellar role to learning, emotional and mood control. The need for a non-invasive tool to influence cerebellar function in normal and pathological conditions led researchers to develop transcranial cerebellar direct current stimulation (tcDCS). tcDCS, like tDCS, depends on the principle that weak direct currents delivered at around 2 mA for minutes over the cerebellum through surface electrodes induce prolonged changes in cerebellar function. tcDCS modulates several cerebellar skills in humans including motor control, learning and emotional processing. tcDCS also influences the cerebello-brain interactions induced by transcranial magnetic stimulation (TMS), walking adaptation, working memory and emotional recognition. Hence tcDCS is a simple physiological tool that can improve our physiological understanding of the human cerebellum, and should prove useful also in patients with cerebellar dysfunction or psychiatric disorders and those undergoing neurorehabilitation to enhance neuroplasticity.

© 2013 Elsevier Inc. All rights reserved.

Contents

Introduction	0
Motor control and motor learning	0
Neuroplasticity	0
Cognition, learning and emotions	0
Working memory	0
Learning	0
Emotion recognition	0
tcDCS mechanism of action and safety	0
Conclusion and future perspectives	0
Conflict of interest	0
References	0

Introduction

Patients with cerebellar disorders have various neurological impairments including motor disturbances, and cognitive or behavioral abnormalities (D'Angelo and Casali, 2012; De Smet et al., 2013; Stoodley et al., 2012). The human cerebellum also contributes to cognitive and affective deficits (Schmahmann and Caplan, 2006; Stoodley, 2012). Experimental ablation or stimulation of the cerebellar cortex or cerebellar nuclei in human alters behavior and cerebellar ablation impairs integrative functions such as learning and perception (Cooper, 1978). Direct electrical cerebellar stimulation results in enhanced arousal and activation, changes that in turn may indirectly improve specific functions such as

Abbreviations: tDCS, transcranial direct current stimulation; tcDCS, cerebellar transcranial direct current stimulation; TMS, transcranial magnetic stimulation; CBI, cerebello-brain inhibition; CBIRC, CBI recruitment curve; LTP, long-term potentiation; PAS, paired associative stimulation; mSI, motor surround inhibition; SRRT, serial reaction time task; VAS, visual analog scale; DLPC, dorso-lateral prefrontal cortex.

^{*} Corresponding author at: Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, via F. Sforza 35, Milano 20122, Italy.

E-mail addresses: roberta.ferrucci@policlinico.mi.it (R. Ferrucci), alberto.priori@unimi.it (A. Priori).

¹ The authors equally contributed to this work and are in alphabetical order.

perception, learning or emotion in humans (Riklan et al., 1976a, 1976b). Data in healthy subjects extend cerebellar roles to emotional and mood control (Baumann and Mattingley, 2012; Schutter and van Honk, 2006). The neurophysiological technique customarily used over the past decades for non-invasively stimulating the cerebellum has been transcranial magnetic stimulation (TMS) (Minks et al., 2010). Several years ago, we proposed a simpler technique than TMS for non-invasive cerebellar neuromodulation namely, transcranial cerebellar direct current stimulation (tcDCS) (Ferrucci et al., 2008). tcDCS is based upon the same principle as transcranial direct current stimulation (tDCS): weak direct currents (DC) below 2–3 mA delivered for minutes over the scalp through a pair of surface electrodes induce prolonged changes in the underlying brain areas (Priori, 2003). As tDCS has done over the past ten years (Nitsche and Paulus, 2011), tcDCS promises to receive progressively increasing attention owing to its low-cost and safety (Priori et al., 2009). Last, but more important, tcDCS – like tDCS – delivers an “ecological” stimulation because it can stimulate the cerebellum “online” while the subject engages in various activities, ranging from motor to cognitive or behavioral tasks.

Ample evidence that we review here therefore supports the conclusion that tcDCS is a simple and novel approach for investigating human cerebellar function.

Motor control and motor learning

Seeking to explore how tcDCS affects the cerebello-brain interaction, Galea et al. (2009) studied 16 healthy individuals in three different experiments. TMS over the cerebellum elicits a short-latency inhibitory effect on the motor potential evoked by contralateral motor cortex TMS: this inhibitory interaction is known as cerebello-brain inhibition (CBI) (Ugawa et al., 1991). In the first experiment Galea and coworkers, assessed changes in excitability in primary motor cortex (M1), brainstem, and CBI in 8 subjects before and after anodal, cathodal, or sham tcDCS applied at 2 mA intensity for 25 min over the right cerebellar cortex. They found that tcDCS modulated CBI in a polarity specific manner: cathodal tcDCS decreased CBI, whereas anodal and sham tcDCS left it unchanged. In the second experiment they evaluated the CBI recruitment curve (CBIRC) after anodal tDCS. CBI was measured using five different conditioning stimulation intensities. The investigators showed that after anodal tcDCS all the stimulation intensities elicited CBI, even intensities that when tested before tcDCS elicited no CBI. Finally, to assess how long the cathodal tcDCS-induced changes in CBI lasted, they measured CBI immediately after, 30 min and 50 min after tcDCS ended. The last set of experiments showed that after 2 mA cathodal tcDCS CBI decreased, and the decrease persisted for at least 30 min. Galea et al. (2009) produced direct evidence that the technique influences excitability in the cerebello-brain circuit.

More recently, to investigate whether tcDCS enhances locomotor learning, Jayaram et al. (2012) used a cerebellum-dependent split-belt walking task. During this task one leg is set to move three times faster than the other. This test procedure initially disrupts coordination between the legs so that the fast and slow leg steps are asymmetric. Over time, subjects learn to predict and account for the perturbation (Reisman et al., 2005). They investigated the laterality of adaptive changes in 40 healthy subjects by separately delivering tcDCS (anodal, cathodal and sham) over the cerebellar hemisphere ipsilateral to fast and slow lower limb. tcDCS was delivered, only during locomotor adaptation, through two sponge electrodes (one electrode over the cerebellum 3 cm lateral to the inion, the other on the ipsilateral buccinator muscle), tcDCS intensity was set at 2 mA for 15 min. Anodal tcDCS applied during walking improved locomotor adaptation, whereas cathodal tcDCS worsened it, without affecting the rate of de-adaptation to the new locomotor pattern. The investigators speculated that anodal tcDCS acts in different ways: it could broaden the Purkinje cell populations that are available for learning or increase their dynamic range. In conclusion, Jayaram et al. (2012) provided important information

showing that tcDCS can influence locomotor learning, a function classically thought to come mainly under cerebellar control. The results suggest that tcDCS could be used as a tool to modulate locomotor training in patients with neurological gait disturbances.

Seeking to dissociate the roles of the cerebellum and M1 during adaptive learning, Galea et al. (2012) applied anodal tDCS during a visuomotor adaptation paradigm in 72 healthy subjects in three different experiments. The first experiment included 3 groups each with different tDCS electrode placements. For the tcDCS group, the anodal electrode was positioned on the right cerebellar cortex and the cathodal electrode on the right buccinator muscle; for the M1 group the anodal electrode was placed over the left motor “hotspot” identified by single TMS pulses, and the cathodal electrode on the contralateral supraorbital region; for the sham group electrodes were applied over the right cerebellar or left M1 positions chosen at random. Anodal stimulation was set at 2 mA. The subjects underwent a visuomotor adaptation paradigm consisting of 6 blocks of trials and anodal tDCS was applied during blocks 2 and 3. During these 2 blocks, the groups differed in tDCS electrode positioning (tcDCS and M1) and in the amount of stimulation received (SHAM). During adaptation, the tcDCS group reduced their errors faster than the SHAM and M1 groups, but the total reduction in errors was similar across groups. In experiment 2, a new group of subjects underwent de-adaptation trials without visual feedback. Given that subjects could not observe movement errors, the investigators could assess whether tDCS over the cerebellum or M1 specifically influenced the forgetting rate for the previously acquired visuomotor transformation (Fig. 1). When three groups underwent the same experimental procedures used in experiment one, during adaptation the tcDCS group reduced their errors faster than the other 2 groups (as happened in experiment 1). At de-adaptation onset, all groups made the same number of initial errors. During de-adaptation, the M1 group increased their ability to retain the newly acquired visuomotor transformation. In an experiment to assess whether the results found depended on cerebellar or occipital cortex (OC) modulation, two additional groups of subjects performed the same behavioral task as in experiments 1 and 2 but the task included only the initial 3 blocks. The last experiment showed that during adaptation the tcDCS reduced their errors faster than the OC and SHAM groups. Anodal tcDCS caused faster adaptation to the visuomotor transformation, as shown by a rapid reduction in movement errors. In contrast, tDCS over M1 left adaptation unchanged, but markedly increased the retention of the newly learnt visuomotor transformation.

One mechanism that the central nervous system uses to produce independent finger movements is motor surround inhibition (mSI). Seeking information on the mechanisms underlying mSI, Sadnicka et al. (2013) used tcDCS to examine the cerebellar role in mSI. Twelve healthy subjects completed a three session cross-over study in which mSI was measured before and after 20 min sham, anodal and cathodal tcDCS. The researchers found that neither anodal nor cathodal tcDCS modulated the magnitude of mSI suggesting that modulation of cerebellar excitability does not affect human mSI.

Neuroplasticity

The method commonly used to induce LTP-like plasticity is paired associative stimulation (PAS). The PAS technique entails delivering slow-rate repetitive low-frequency median nerve stimulation combined with transcranial magnetic stimulation (TMS) over the contralateral motor cortex. This protocol induces plastic changes in excitability in the human motor cortex (Classen et al., 2004). In their later study Hamada et al. (2012) found that concurrent anodal or cathodal tcDCS blocked PAS25-induced plasticity. tcDCS was applied simultaneously with PAS at an intensity of 2 mA for 15 min, one electrode was placed on the right cerebellar cortex the other on the right buccinator muscle. The measured variables were resting and active motor thresholds, MEP amplitude, recruitment curves and short afferent inhibition. Twelve

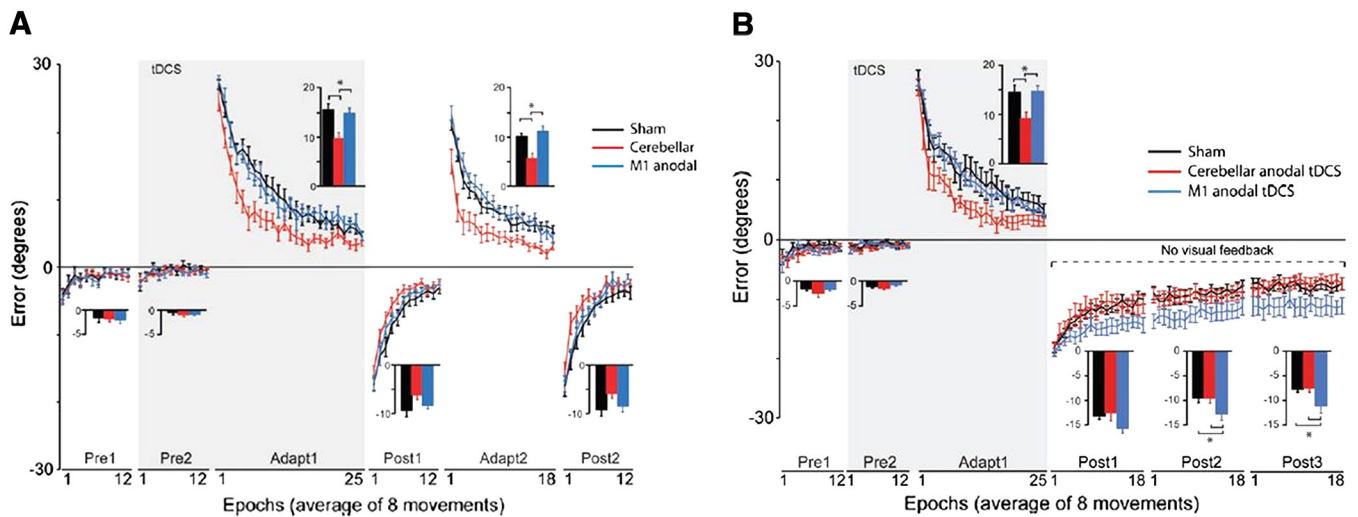


Fig. 1. The figure shows that cerebellar transcranial direct stimulation (tcDCS) caused faster adaptation to the visuomotor transformation, as shown by a rapid reduction in movement errors whereas tDCS over M1 left adaptation unchanged, but resulted in a marked increase in retention of the newly learnt visuomotor transformation. A: Group data for experiment 1. End point error (degrees) are shown during baseline (Pre1 and 2), adaptation (Adapt1 and 2), and deadaptation (Post1 and 2) blocks, for the SHAM (black), tcDCS (red), and M1 (blue) groups. B: Group data for experiment 2. End point error (degrees) are shown during baseline (Pre1 and 2), adaptation (Adapt) and deadaptation blocks with no visual feedback (Post1, 2, and 3) for the SHAM (black), tcDCS (red), and M1 (blue) groups. Positive values indicate counterclockwise deviation. The shaded area represents blocks in which tDCS was applied. Bar graph insets indicate mean end point error in degrees (\pm SEM). * $P > 0.05$. From Galea et al. (2012), with permission.

subjects participated in the first experiment, which consisted of three randomized ordered sessions, each separated by at least 1 week (anodal tcDCS-PAS25, cathodal tcDCS-PAS25 and sham-PAS25). The investigators found that sham tcDCS-PAS25 induced a lasting increase in MEP size but anodal tcDCS-PAS25 and cathodal tcDCS-PAS25 induced no consistent changes in motor cortical evoked responses. To investigate whether the tcDCS modulated PAS in a timing specific manner, Hamada and coworkers, also explored anodal tcDCS-induced effects on PAS21.5 ms. Eight subjects who were also enrolled in experiment 1 participated in the second experiment, entailing two randomized ordered sessions, separated by at least 1 week (anodal-PAS21.5 and sham-PAS21.5). Sham tcDCS-PAS21.5 induced a lasting increase in MEP sizes and the increase was larger after anodal-PAS21.5 than after sham-PAS21.5.

To test how tcDCS influenced cortical processing of sensory input, in the third experiment SEPs were recorded before and after anodal or sham tcDCS in a crossover design. Eight subjects of whom six were not enrolled in experiments 1 and 2 participated in the study. The investigators concluded that tcDCS had no effect on the early median-nerve SEP components. They showed that tcDCS blocks the PAS-induced LTP-like effects when the interval elapsing between peripheral and motor cortical stimuli is 25 ms, but not when it is 21.5 ms. They therefore speculated that separate mechanisms mediate PAS-induced changes in these two interstimulus intervals and that PAS25-induced changes depend specifically upon the cerebellum.

The blocking effect on PAS agrees with the tcDCS-induced blocking effect on learning that originally allowed Ferrucci et al. (2008) to describe tcDCS (see Section Cognition, learning and emotions). Hence, tcDCS can influence neuroplastic changes taking place elsewhere in the central nervous system thus making the cerebellum a potential “window” for modulating widely ranging neural functions.

Cognition, learning and emotions

Working memory

Even though the cognitive and behavioral cerebellar functions in humans are probably the least understood, tcDCS-induced changes in these functions were first assessed in a cognitive task involving

working memory. In this study (Ferrucci et al., 2008), in 13 healthy subjects we tested whether tcDCS – delivered through a surface electrode placed over the cerebellum for 15 min, at 2 mA – modified the practice-dependent increase in the proficiency of a working memory task. We found that anodal and cathodal tcDCS both impaired the practice-dependent improvement in the reaction times. In addition, to test whether tcDCS induced specific cerebellar changes in working memory, we compared tcDCS-induced changes after delivering tDCS over the dorsolateral prefrontal cortex (DLPC). In this series of experiments, unlike tcDCS, tDCS over the DLPC induced an immediate change in the working memory task but left its practice-dependent proficiency unchanged demonstrating that the tcDCS-induced

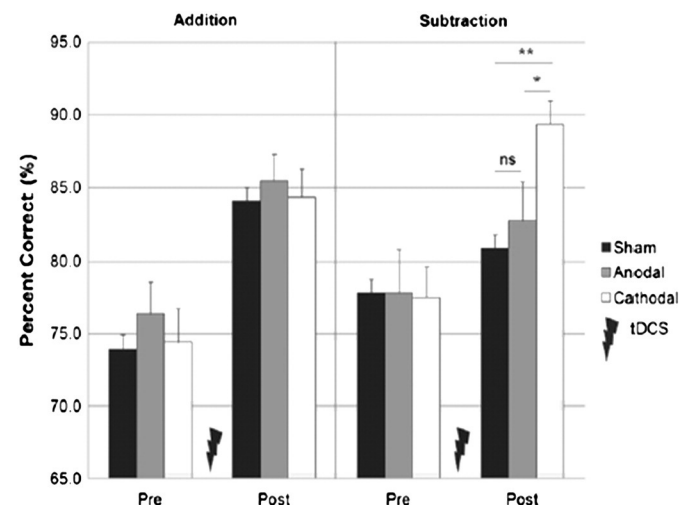


Fig. 2. The figure shows the results obtained before and after cerebellar transcranial direct current stimulation (tcDCS) in the addition Paced Auditory Serial Addition Task (PASAT) and subtraction Paced Auditory Serial Subtraction Task (PASST). Note that the accuracy in the subtraction task, but not in the addition task, was significantly greater after cathodal, than after anodal or sham stimulation. * $P > 0.05$. Error bars are standard error of the mean. From Pope and Miall (2012), with permission.

changes are structure specific. Finally, to assess whether tDCS influenced the visual cortex, we also assessed changes in visual evoked potentials. This last experiment failed to disclose tDCS-induced changes in visual evoked potentials therefore ruling out visual cortex involvement. We therefore concluded that tDCS specifically impairs the practice-dependent proficiency of a verbal working memory task. To explain our findings we speculated that tDCS influences neuronal excitability in the cerebellar cortex thus interfering with neuronal function, and ultimately impairing the practice-dependent cerebellar changes but not the working memory per se.

Four years later, Boehringer et al. (2012) substantially reproduced these results. In 40 healthy young participants they investigated how cathodal tDCS influences verbal working memory as measured by forward and backward digit spans before and after applying right cathodal tDCS (2 mA, stimulation duration 25 min). In addition, they tested tDCS-induced changes in word reading, finger-tapping and a visually-cued sensorimotor task. In line with our findings (Ferrucci et al., 2008), they showed that tDCS reduced forward digit spans and blocked the practice-dependent increase in backward digit spans. Hence current knowledge shows that tDCS can block the practice-dependent proficiency increase thus providing the rationale for using this technique for contrasting maladaptive plasticity after an acquired central nervous system lesion.

Extending research on tDCS in memory processes, Pope and Miall (2012) reported that cathodal tDCS over the right cerebellum improved cognitive performance in the Paced Auditory Serial Subtraction Task (PASST) evaluating the arithmetic aspects of working memory and attention. Three groups of 22 participants each performed the PASST and the Paced Auditory Serial Addition Task (PASAT) two cognitive tasks that require comparable motor skills, but different levels of working memory and attention, before and after anodal or cathodal tDCS for 20 min, at 2 mA, with one electrode positioned on the right cerebellar cortex and the other on the right deltoid muscle. Participants' performance in the difficult PASST task improved significantly after cathodal

tDCS but remained unchanged after sham or anodal tDCS. All three stimulation conditions elicited similar improvement in the easier PASAT. These findings suggest that right cathodal tDCS affects working memory and attention differentially depending on task difficulty (Fig. 2).

The variability in the cathodal tDCS-induced changes in working memory in the foregoing studies probably depends on differences in electrode location (right cerebellum, or bilateral cerebellum). Another explanation involves variance in the cognitive and neural processes associated with the cognitive tasks used.

In conclusion, available studies show that tDCS can influence working memory. Understanding how to manipulate the ability to form new memories and acquire new skills gives an exciting opportunity to extend tDCS use from a neuroscience research tool to a therapeutic option in patients.

Learning

The cerebellum participates also in procedural learning, a major learning type that takes place daily without our intent or conscious awareness, and plays a major role in structuring our skills, perceptions, and behavior (O'Halloran et al., 2012). We investigated whether tDCS influences procedural learning as measured by the serial reaction time task (SRTT), in which subjects make key press responses to visual cues (Ferrucci et al., 2013). Twenty one participants did the SRTT, a visual analog scale (VAS) and a visual attention task, before and 35 min after receiving anodal and sham tDCS for 20 min at 2 mA. The main finding in this study is that anodal tDCS influenced procedural learning as indexed by the SRTT in healthy subjects. Because mood and fatigue VAS and visual attention task remained unchanged, the tDCS-induced changes in SRTT performance did not reflect changes in arousal or alertness. Hence tDCS modulated and improved healthy subjects' performance during procedural learning suggesting that tDCS could be a useful new tool for studying cerebellar cognitive functions.

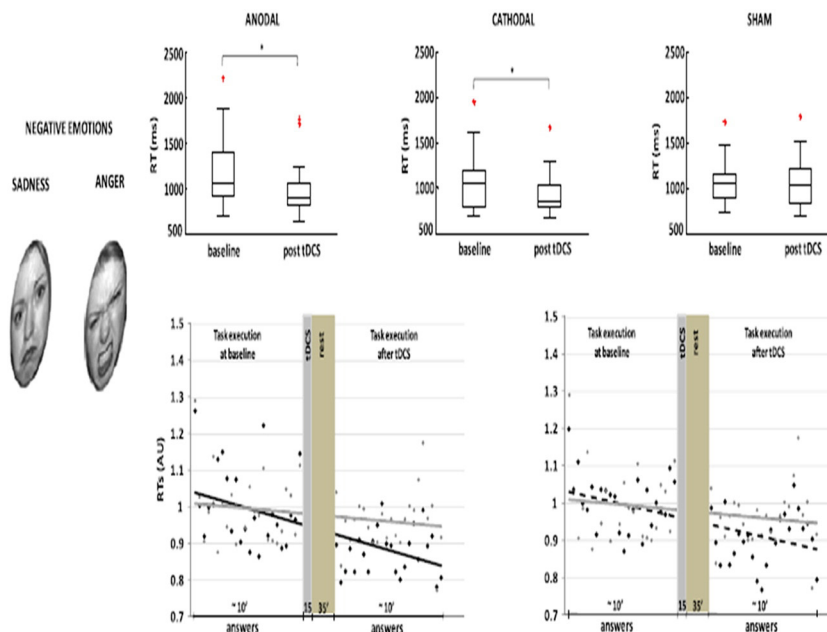


Fig. 3. The figure shows changes induced by cerebellar transcranial direct current stimulation (tDCS) in negative emotional recognition in healthy subjects. On each box the central mark is the median, the edges of the box are the 25th and 75th percentiles, the whiskers extend to the most extreme data points not considered outliers, and each outlier is plotted individually (cross). y-Axis: RTs (ms). Trial-to-trial grand average ($n = 21$) of reaction times (RTs) across task stimulus presentation before tDCS stimulation (24 answers) and after tDCS stimulation (24 answers). x-Axis: answers, note that the x-axis graphically represents the time elapsing between the end of the task execution before stimulation and the beginning of the task execution after tDCS; y-axis: RTs (arbitrary units, AU). Note that anodal and cathodal cerebellar tDCS both reduce baseline RTs for negative emotions. * $P > 0.05$. The trial-to-trial representation highlights the finding that anodal and cathodal curves differ from sham curves for negative emotions. From Ferrucci et al. (2012), with permission.

Emotion recognition

Continuing research into non-motor cerebellar functions, in another study we assessed whether tcDCS influences facial emotion recognition (Ferrucci et al., 2012). To do this we assessed 21 healthy subjects with a facial emotion recognition task before and after tcDCS (2 mA, 20 min). All the subjects were also assessed with a visual attention task and a VAS for mood. Anodal and cathodal tcDCS significantly enhanced the response to negative facial emotions leaving perception of positive and neutral facial expression unchanged (Fig. 3). To assess the specificity of our findings we tested our subjects also before and after right prefrontal cortex stimulation but observed no significant effect. These results suggest that brain processing of negative facial expressions involves at least two dissociable, but interlocking systems. One responds to facial stimuli (sad) involved in social conditions; the other implicates regions involved in behavioral extinction by responding to angry facial expressions. tcDCS alters the way healthy subjects recognize specific facial expressions thus showing that the cerebellum plays a direct role in recognizing negative emotions. This finding could have interesting applications in psychiatry.

In conclusion, whatever the mechanisms, overall our experiments imply that the cerebellum facilitates practice-dependent proficiency (i.e. learning) in the working memory task but exerts an inhibitory control over recognition of negative facial emotion.

tcDCS mechanism of action and safety

Overall the studies we reviewed show that tcDCS influences cognitive and motor functions. But they left open a major question, namely

how the electric field generated by tcDCS actually reaches the cerebellum? A recent study provides interesting clues (Ferrucci et al., 2013). To estimate electric fields (E) and current density (J) distributions we applied a computational electromagnetic method on a model for a healthy subject (a 26-year-old female) based on high-resolution magnetic resonance (MR) images, and segmented into a voxel-based format at a resolution of 1 mm. The model comprised up to 77 different tissues, whose dielectric properties were defined (Parazzini et al., 2011, 2012). The electrodes were rectangular pads ($\sigma = 5.9 \times 10^7$ S/m) with a sponge ($\sigma = 0.3$ S/m) placed directly under the electrode. The tcDCS intensity was 2 mA. This preliminary modeling study demonstrated that the extra-cephalic electrode montage (active electrode over the cerebellum with a reference electrode over the right arm) generated the maximum electric field amplitude in the cerebellum without substantial spread to the brainstem or other brain structures (Ferrucci et al., 2013) (Fig. 4).

Once the electric field actually reaches the cerebellum, another important issue is how tcDCS influences cerebellar activity. tcDCS could interfere with Purkinje cell LTD by altering the membrane potential fine-tuning and the relative pace-making properties. Induced cerebellar functional changes presumably act on the cortical structures primarily involved in motor, cognitive and emotional processing through the cerebellar efferent projections.

A further important point is tcDCS polarity-specificity. In their study investigating this feature, Galea et al. (2009) found a clearly polarity-specific effect on cerebello-brain inhibition. This finding seemingly contrasted with our two studies on cognitive and emotional processing (Ferrucci et al., 2008, 2012). The lack of polarity specificity,

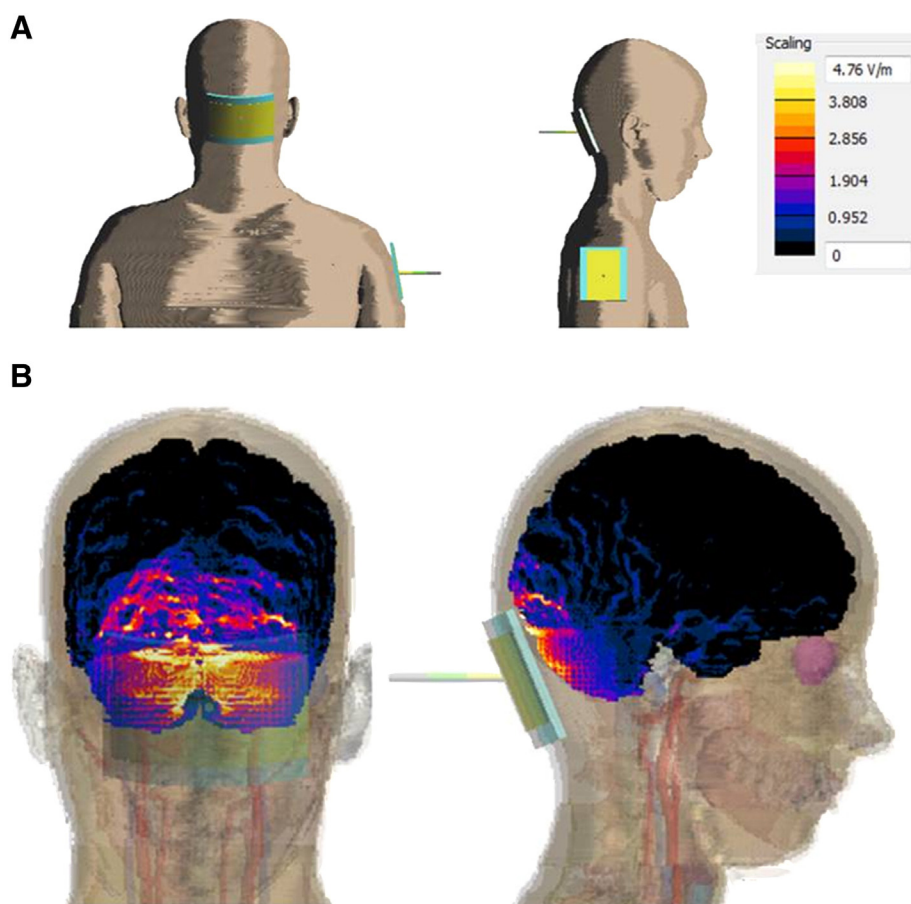


Fig. 4. The figure shows a preliminary modeling study demonstrating that an extra-cephalic electrode montage (active electrode over the cerebellum with an extra-cephalic reference) generates the maximum electric field amplitude in the cerebellum. A. Back and lateral views of the electrode positioning. B. Back and lateral views of the E field distributions on the cortex and cerebellum with the reference color scale for intensity. From Ferrucci et al. (2013), with permission.

besides possibly arising from methodological differences (i.e. the geometry of the electric field and the position of the stimulating electrodes), agrees, however, with earlier experiments testing the tDCS-induced changes in cognitive variables (Marshall et al., 2005) and could also depend upon the relative current strength in tDCS (Batsikadze et al., 2013). The lack of a polarity effect could arise also from polarity-dependent changes in neuronal function. This interpretation receives support from an early study reporting that anodal and cathodal polarization blocks axonal conduction (Lorente De No, 1947).

Conclusion and future perspectives

Available data provide evidence that tDCS modulates human cognitive and motor cerebellar functions, further studies need to find out how tDCS works and develop optimum stimulation settings. This information will be important in developing new therapeutic interventions using cerebellar modulation in conditions characterized by cerebellar dysfunction, such as, ataxia, Parkinson's disease, autism and schizophrenia (Massaquoi, 2012; Wu and Hallett, 2013; Yeganeh-Doost et al., 2011).

Cerebellar involvement in autism, schizophrenia, and other cognitive disorders is typically associated with prefrontal cortical dysfunction. In mice, stimulation applied to the dentate nucleus evokes dopamine release in the medial prefrontal cortex. Extending these findings to patients, Rogers et al. (2012) suggested that the neuropathological changes in the cerebellum commonly observed in autism, schizophrenia, and other cognitive disorders could result in aberrant dopaminergic activity in the medial prefrontal cortex. Dopamine and glutamatergic dysregulation may be associated with deficits in working memory, reward and motivation and tDCS might readjust dopaminergic system in patients.

Future studies designed to investigate whether tDCS can improve specific features related to motor or cognitive performance in cerebellar disorders must take into account evidence that the cerebellar cortex exerts a predominant inhibitory effect on the cerebellar nuclei given that these nuclei can be variably affected by the disease, the lesion's location in the cerebellar circuitry, and possible extracerebellar lesions along the afferent pathways.

Research findings already provide evidence that tDCS can influence motor adaptation, learning, memory and emotional processing in healthy humans. Despite the scanty literature, our review suggests that tDCS holds promise for restorative neurology and rehabilitation also thanks to its simplicity, low cost, and suitability for use online.

Conflict of interest

The authors are stakeholders in Newronika s.r.l., a spin-off company formed by the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico and Università degli Studi di Milano.

References

Batsikadze, G., Moliadze, V., Paulus, W., Kuo, M.F., Nitsche, M.A., 2013. Partially non-linear stimulation intensity-dependent effects of direct current stimulation on motor cortex excitability in humans. *J. Physiol.*

Baumann, O., Mattingley, J.B., 2012. Functional topography of primary emotion processing in the human cerebellum. *NeuroImage* 61 (4), 805–811.

Boehringer, A., Macher, K., Dukart, J., Villringer, A., Pleger, B., 2012. Cerebellar transcranial direct current stimulation modulates verbal working memory. *Brain Stimul.* <http://dx.doi.org/10.1016/j.brs.2012.10.001>.

Classen, J., Wolters, A., Stefan, K., Wycislo, M., Sandbrink, F., Schmidt, A., et al., 2004. Paired associative stimulation. *Suppl. Clin. Neurophysiol.* 57, 563–569.

Cooper, S., 1978. *Cerebellar Stimulation in Man*. Raven Press, New York.

D'Angelo, E., Casali, S., 2012. Seeking a unified framework for cerebellar function and dysfunction: from circuit operations to cognition. *Front. Neural Circ.* 6, 116.

De Smet, H.J., Paquier, P., Verhoeven, J., Marien, P., 2013. The cerebellum: its role in language and related cognitive and affective functions. *Brain Lang.* <http://dx.doi.org/10.1016/j.bandl.2012.11.001>.

Ferrucci, R., Marceglia, S., Vergari, M., Cogiamanian, F., Mrakic-Sposta, S., Mameli, F., et al., 2008. Cerebellar transcranial direct current stimulation impairs the practice-dependent proficiency increase in working memory. *J. Cogn. Neurosci.* 20 (9), 1687–1697.

Ferrucci, R., Giannicola, G., Rosa, M., Fumagalli, M., Boggio, P.S., Hallett, M., et al., 2012. Cerebellum and processing of negative facial emotions: cerebellar transcranial DC stimulation specifically enhances the emotional recognition of facial anger and sadness. *Cogn. Emot.* 26 (5), 786–799.

Ferrucci, R., Brunoni, A.R., Parazzini, M., Vergari, M., Rossi, E., Fumagalli, M., et al., 2013. Modulating human procedural learning by cerebellar transcranial direct current stimulation. *Cerebellum.* <http://dx.doi.org/10.1007/s12311-012-0436-9>.

Galea, J.M., Jayaram, G., Ajagbe, L., Celnik, P., 2009. Modulation of cerebellar excitability by polarity-specific noninvasive direct current stimulation. *J. Neurosci.* 29 (28), 9115–9122.

Galea, J.M., Vazquez, A., Pasricha, N., de Xivry, J.J., Celnik, P., 2012. Dissociating the roles of the cerebellum and motor cortex during adaptive learning: the motor cortex retains what the cerebellum learns. *Cereb. Cortex* 21 (8), 1761–1770.

Hamada, M., Strigaro, G., Murase, N., Sadnicka, A., Galea, J.M., Edwards, M.J., et al., 2012. Cerebellar modulation of human associative plasticity. *J. Physiol.* 590 (Pt 10), 2365–2374.

Jayaram, G., Tang, B., Pallegadda, R., Vasudevan, E.V., Celnik, P., Bastian, A., 2012. Modulating locomotor adaptation with cerebellar stimulation. *J. Neurophysiol.* 107 (11), 2950–2957.

Lorente De No, R., 1947. *A Study of Nerve Physiology*. Rockefeller Institute for Medical Research, New York.

Marshall, L., Molle, M., Siebner, H.R., Born, J., 2005. Bifrontal transcranial direct current stimulation slows reaction time in a working memory task. *BMC Neurosci.* 6, 23.

Massaquoi, S.G., 2012. Physiology of clinical dysfunction of the cerebellum. *Handb. Clin. Neurol.* 103, 37–62.

Minks, E., Kopiczkova, M., Marecek, R., Streitova, H., Bares, M., 2010. Transcranial magnetic stimulation of the cerebellum. *Biomed. Pap. Med. Fac. Univ. Palacky Olomouc Czech Repub.* 154 (2), 133–139.

Nitsche, M.A., Paulus, W., 2011. Transcranial direct current stimulation—update 2011. *Restor. Neurol. Neurosci.* 29 (6), 463–492.

O'Halloran, C.J., Kinsella, G.J., Storey, E., 2012. The cerebellum and neuropsychological functioning: a critical review. *J. Clin. Exp. Neuropsychol.* 34 (1), 35–56.

Parazzini, M., Fiocchi, S., Rossi, E., Paglialonga, A., Ravazzani, P., 2011. Transcranial direct current stimulation: estimation of the electric field and of the current density in an anatomical human head model. *IEEE Trans. Biomed. Eng.* 58 (6), 1773–1780.

Parazzini, M., Rossi, E., Rossi, L., Priori, A., Ravazzani, P., 2012. Numerical estimation of the current density in the heart during transcranial direct current stimulation. *Brain Stimul.* <http://dx.doi.org/10.1016/j.brs.2012.05.007>.

Pope, P.A., Miall, R.C., 2012. Task-specific facilitation of cognition by cathodal transcranial direct current stimulation of the cerebellum. *Brain Stimul.* 5 (2), 84–94.

Priori, A., 2003. Brain polarization in humans: a reappraisal of an old tool for prolonged non-invasive modulation of brain excitability. *Clin. Neurophysiol.* 114 (4), 589–595.

Priori, A., Hallett, M., Rothwell, J.C., 2009. Repetitive transcranial magnetic stimulation or transcranial direct current stimulation? *Brain Stimul.* 2 (4), 241–245.

Reisman, D.S., Block, H.J., Bastian, A.J., 2005. Interlimb coordination during locomotion: what can be adapted and stored? *J. Neurophysiol.* 94 (4), 2403–2415.

Riklan, M., Cullinan, T., Shulman, M., Cooper, I.S., 1976. A psychometric study of chronic cerebellar stimulation in man. *Biol. Psychiatry* 11 (5), 543–574.

Riklan, M., Kabat, C., Cooper, I.S., 1976. Psychological effects of short term cerebellar stimulation in epilepsy. *J. Nerv. Ment. Dis.* 162 (4), 282–290.

Rogers, T.D., Dickson, P.E., Heck, D.H., Goldowitz, D., Mittleman, G., Blaha, C.D., 2012. Connecting the dots of the cerebro-cerebellar role in cognitive function: neuronal pathways for cerebellar modulation of dopamine release in the prefrontal cortex. *Synapse* 65 (11), 1204–1212.

Sadnicka, D.A., Kassaveti, D.P., Saifee, D.T., Parees, D.I., Rothwell, P.J., Edwards, D.M., 2013. Cerebellar transcranial direct current stimulation does not alter motor surround inhibition. *Int. J. Neurosci.* <http://dx.doi.org/10.3109/00207454.2012.763165>.

Schmahmann, J.D., Caplan, D., 2006. Cognition, emotion and the cerebellum. *Brain* 129 (Pt 2), 290–292.

Schutter, D.J., van Honk, J., 2006. An electrophysiological link between the cerebellum, cognition and emotion: frontal theta EEG activity to single-pulse cerebellar TMS. *NeuroImage* 33 (4), 1227–1231.

Stoodley, C.J., 2012. The cerebellum and cognition: evidence from functional imaging studies. *Cerebellum* 11 (2), 352–365.

Stoodley, C.J., Valera, E.M., Schmahmann, J.D., 2012. Functional topography of the cerebellum for motor and cognitive tasks: an fMRI study. *NeuroImage* 59 (2), 1560–1570.

Ugawa, Y., Day, B.L., Rothwell, J.C., Thompson, P.D., Merton, P.A., Marsden, C.D., 1991. Modulation of motor cortical excitability by electrical stimulation over the cerebellum in man. *J. Physiol.* 441, 57–72.

Wu, T., Hallett, M., 2013. The cerebellum in Parkinson's disease. *Brain* 136 (Pt 3), 696–709.

Yeganeh-Doost, P., Gruber, O., Falkai, P., Schmitt, A., 2011. The role of the cerebellum in schizophrenia: from cognition to molecular pathways. *Clinics (Sao Paulo)* 66 (Suppl. 1), 71–77.