Enhancing Consolidation of a New Temporal Motor Skill by Cerebellar Noninvasive Stimulation

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Abstract

Cerebellar transcranial direct current stimulation (tDCS) has the potential to modulate cerebellar outputs and visuomotor adaptation. The cerebellum plays a pivotal role in the acquisition and control of skilled hand movements, especially its temporal aspects. We applied cerebellar anodal tDCS concurrently with training of a synchronization-continuation motor task. We hypothesized that anodal cerebellar tDCS will enhance motor skill acquisition. Cerebellar tDCS was applied to the right cerebellum in 31 healthy subjects in a double-blind, sham-controlled, parallel design. During synchronization, the subjects tapped the sequence in line with auditory cues. Subsequently, in continuation, the learned sequence was reproduced without auditory cuing. Motor task performance was evaluated before, during, 90 min, and 24 h after training. Anodal cerebellar tDCS, compared with sham, improved the task performance in the follow-up tests ($F_{1,28} = 5.107$, $P = 0.032$) of the synchronization part. This effect on retention of the skill was most likely mediated by enhanced motor consolidation. We provided first evidence that cerebellar tDCS can enhance the retention of a fine motor skill. This finding supports the promising approach of using noninvasive brain stimulation techniques to restore impaired motor functions in neurological patients, such after a stroke.

Key words: cerebellum, motor learning, rehabilitation, tDCS

Introduction

Many activities of daily life such as using new communication devices, learning to play a music instrument, or doing sports rely on the acquisition and retention of fine motor skills. Learning of such motor skills is a dynamic process with spatial and temporal components. Motor skill learning occurs on different scales and leads by practice to the acquisition of complex goal-oriented movements. Furthermore, it involves structural modifications (e.g., synaptogenesis, dendritic remodeling, or motor map reorganization) (Hosp and Luft 2011) and shares similar mechanisms of synaptic efficacy like long-term potentiation (LTP) (Rioult-Pedotti et al. 2000). Moreover, on the systems level, network structures are modified with learning (Dayan and Cohen 2011; Wolpert et al. 2011).

In behavioral studies, motor learning has been investigated using a variety of tasks, including visuomotor adaptation, isometric force production, and associative learning, among others. For sequential motor skill learning, a dynamic interaction within cortico-striato-thalamo-cortical and cortico-cerebello-thalamo-cortical loops depending on the time course and nature of the learned motor skill has been described (Doyon et al. 2003; Schulz et al. 2015). Within this motor learning network, the cerebellum...
serves as one central node. Its dentate nucleus is connected via the thalamus to primary and secondary cortical motor areas (Middleton and Strick 2000; Schulz et al. 2015). Previous animal studies were able to associate different motor learning stages with cerebellar substructures. Lesioning the dentate nuclei in monkeys impaired storage and retrieval of long-term memory (Lu et al. 1998) and automatization of motor sequences (Nixon and Passingham 2000).

Noninvasive brain stimulation (NIBS) is a feasible method for testing prior neurobehavioral concepts in the in vivo human brain. NIBS has been shown to interact with the processes of neuronal synaptic plasticity and reorganization and proven to enhance different stages of the learning process in healthy subjects (Nitsche et al. 2003; Reis et al. 2009; Zimerman et al. 2012) and in stroke patients (Zimerman et al. 2012). Among NIBS techniques, transcranial direct current stimulation (tDCS) is a safe and well-tolerated method that induces prolonged excitability changes, resulting in LTP-like synaptic modifications (Fritsch et al. 2010).

Recently, the cerebellum has been emphasized as an additional stimulation target for NIBS (Koch 2010; Grimaldi, Argyropoulos et al. 2014; Priori et al. 2014). Proof-of-principle studies showed that anodal cerebellar tDCS was able to enhance visuomotor adaptation (Galea et al. 2011), locomotor stimulation (Jayaram et al. 2012), and the acquisition of conditioned eyelid responses (Zuchowski et al. 2014). Additionally, cerebellar tDCS enhanced the performance of a serial reaction time task (SKTT), a model of implicit motor learning (Ferrucci et al. 2013). Interestingly, a recent study provided evidence that cerebellar cathodal tDCS impaired the overnight retention of a force field reaching task (Herzfeld et al. 2014).

Learning of explicit motor sequences and their temporal aspects, reflect in great part hand motor skill in everyday life situations (e.g., learning to play instruments or to use modern electronic devices). To our knowledge, the effect of cerebellar tDCS on the process of learning a rhythmic motor skill has not yet been addressed. Following this idea, we developed a relatively complex task that enables us to evaluate the acquisition of temporal aspects of a motor sequence with one effector.

In the present study, we investigated the effects of simultaneous application of ipsilateral cerebellar anodal tDCS during learning of a motor skill. We hypothesized that coupling of tDCS and training might potentiate skill acquisition.

Materials and Methods

Subjects

Thirty-eight right-handed, young, neurological healthy subjects were recruited for the present study. Thirty-one subjects participated in the main experiment (mean age 25.0 ± 2.7 years, 18 females, Edinburgh handedness inventory [EHI] 92.2 ± 12.0, Penhune index of musical training and experience [PIEMT] (Penhune et al. 1999) mean score of 3.1 ± 2.1, indicating strong right handedness and comparable musical training and experience). One subject in the main experiment had to be excluded from the study due to vertigo under stimulation. Seven subjects participated in the control experiment (mean age 24.1 ± 2.9 years, 3 females, EHI 95.7 ± 7.9, PIEMT mean score of 2.0 ± 2.4). None of the participants was taking any CNS active medication and none of them had any contraindications for tDCS. Written informed consent was obtained from all subjects according to the Declaration of Helsinki (www.wma.net/en/30publications) and from the local Ethics Committee of the University of Hamburg (PV3770).

Experimental Design

We used a double-blind, sham-controlled, parallel design. The subjects first underwent a familiarization of the learning task, in which they performed a simplified sequence (composed of 3 elements with 4 repetitions in synchronization and 2 in continuation). Next, they performed a baseline block, subsequently the task was trained for 20 min (training). The training period was subdivided into 7 blocks each lasting approximately 140 s separated by a 36-s break. During the main experiment, anodal or sham tDCS was applied concurrently with training. We used a block-randomization for assigning the subjects to one of the 2 intervention groups. To test retention after cessation of direct tDCS-related effects (Nitsche and Paulus 2000) motor performance was assessed at a 90-min (post-90) and 24-h (post-24) follow-up. The follow-up assessments consisted of three blocks with the same length and breaks (for detailed information, see Fig. 1). To investigate the polarity specificity of the tDCS-related effects, we further performed a control experiment in which cathodal (inhibitory) tDCS was applied in a different group of subjects within in a similar experimental design.

Motor Skill Acquisition Task

The participants were seated in an armchair in front of a 21-inch screen monitor during the study. The distance between the chair and mouse was adjusted for subject comfort and was kept constant during the whole study. Skill learning was tested using an adapted version of the motor synchronization continuation paradigm (Rao et al. 1997; Lewis et al. 2011), a task that relies on lateral cerebellar function (Ivry et al. 1988). In brief, the task consisted of different blocks separated by a short break. Each block was divided in 2 modes, which were synchronization and continuation (Fig. 1). In the synchronization mode, the subjects had to tap their right index finger on a standard computer mouse in line with auditory cues. The cues consisted of 250 Hz sinus waves with a duration of 300 ms, presented through speakers. Within each block, 8 predetermined interstimulus intervals (ISIs) were consecutively repeated and composed the sequence. We adopted 2 different sequences from (Lewis et al. 2011) (sequence A was 640–160–560–960–320–400–240–720 ms and B 320–1040–800–160–240–400–480–560 ms). The present sequences were introduced in a randomized allocation for baseline or training to avoid sequence specific effects. During synchronization, 8 trial runs of the sequence made up one block. In the continuation mode, the subjects had to reproduce the preceding temporal sequence without any cues. In this part, 4 trials formed one block.

The stimulus presentation and the recording of the behavioral tapping data was performed with a standard personal computer using Presentation Software (Neurobehavioral Systems, Inc., USA) and was analyzed offline. Additionally, in every training block, participants characterized their level of attention toward the task, perception of fatigue and the level of discomfort/tiredness of the practice hand in a visual analog scale (VAS) questionnaire.

Transcranial Direct Current Stimulation

The protocol for cerebellar tDCS was adjusted from previous work (Galea et al. 2009). tDCS was applied in a double-blind, sham-controlled, parallel design. For cerebellar stimulation, the active (anodal) electrode was fixed 3 cm lateral to the inion (Ugawa et al. 1995; Galea et al. 2009) and the reference (cathodal) electrode over the buccinator muscle both ipsilateral to the training right hand. A current of 2 mA was applied through 25 cm2 (5 × 5 cm)
sponge electrodes soaked with sodium chloride solution leading to a current density of 0.08 mA/cm² (Eldith, DC-stimulator, Neuroconn, Germany). In the main experiment, we stimulated either with anodal or sham tDCS. In all conditions, the current was applied with a 8-s fade-in and fade-out interval to attenuate itching sensations and avoid phosphenes (Nitsche et al. 2008). For the anodal condition, we stimulated 20 min. During sham, we applied 30 s of anodal tDCS, a procedure demonstrated to warrant successful blinding (Gandiga et al. 2006; Galea et al. 2009). In the control experiment, the electrode montage was reversed (cathode electrode was fixed 3 cm lateral to the inion and anode was positioned over the buccinators muscle) with the same stimulation parameters as in the main experiment.

Data Analysis

For the behavioral analyses, we calculated the tapping error. In synchronization, this was the absolute time interval where the acoustic cue and the key press did not overlap (tapping error = abs[cueON – keyON] + abs[cueOFF – keyOFF], see Fig. 1) (Steele and Penhune 2010). With this analysis, we were able to measure the learning of the precise key on- and offset relative to the acoustic stimulus, instead of just focusing on the decrease in reaction times. To calculate a simple measure of the timing accuracy in continuation, we aligned the played tapping interval (IKI) with the referring ISI and calculated the absolute difference (tapping error = abs[ISI – IKI]) (Wright et al. 2012).

The subjects were instructed that, during continuation, all taps had to be completed for the next sequence to start. Furthermore, the actual position within the sequence was displayed on a computer screen. In the rare case of stops and abnormal long breaks, the subjects were instructed to continue and the trial was rejected.

Trial and block values for each subject were obtained by averaging the tapping error data (see Fig. 1).

Statistical Analysis

The 2 modes of the task, synchronization and continuation, were analyzed separately. The statistical analysis was based on the computed block values. To meet the assumptions of the central limit theorem and to reach normal distribution, we performed a natural logarithmic transformation of the data.

In the main experiment, we used repeated-measure analysis of variance (ANOVA-RM) to evaluate: 1) the training with the factors BLOCK and INTERVENTION; 2) the retention index (see below) using the factors SESSION and INTERVENTION; and 3) the level of attention, fatigue and discomfort/tiredness of the practicing hand with the factors BLOCK and INTERVENTION. Online gains were assessed by calculating the ratio of the last (T7) and the first (T1) training block. To evaluate consolidation of the motor task, defined as changes in performance after completion of the training phase (offline effects), we calculated a retention index (Robertson et al. 2004; Reis et al. 2009). This index was defined as the ratio of the mean of the blocks of a follow-up session (AVG_FU) and the last training block (T7) (retention index = AVG_FU/T7).

For analyzing the control experiment, we generated a control group by drawing baseline-matched pairs from the sham tDCS group of the main experiment. The remaining statistical analysis resembled the main experiment. For data arrangement and
Results

The participants were unable to distinguish between anodal tDCS and sham stimulation. The correct stimulation type was named at chance level by 19 of 37 subjects (51.4%). The type of stimulation did not influence attention \( (F_{2,34} = 0.049, P = 0.953) \), perception of fatigue \( (F_{2,34} = 0.409, P = 0.667) \), or discomfort/tiredness of the practicing hand \( (F_{2,34} = 0.331, P = 0.721) \) during the main and control experiment.

Synchronization: Learning Curves

The anodal and sham tDCS group showed comparable performance at baseline \( (t_{28} = -0.464, P = 0.646) \). The analysis of the learning curves revealed a significant effect of BLOCK \( (F_{6,168} = 62.493, P < 0.001) \). This documented that during synchronization the subject improved in this learning paradigm. No significant effects were found for INTERVENTION \( (F_{1,28} < 0.001, P = 0.985) \) or the BLOCK by INTERVENTION interaction \( (F_{6,168} = 0.166, P = 0.892) \) (see Fig. 2A). Further analysis of online gains showed no difference between interventional groups \( (t_{28} = -0.168, P = 0.868) \).

Synchronization: Consolidation

ANOVA-RM revealed a significant SESSION \( (F_{1,28} = 30.224, P < 0.001) \) and INTERVENTION \( (F_{1,28} = 5.107, P = 0.032) \) effect without any SESSION by INTERVENTION interaction \( (F_{1,28} = 0.172, P = 0.682) \). Exploration of the group means \( (\text{AVG} \pm \text{SEM}, \text{tDCS}_{90 \, \text{minFU/T7}} = 0.94 \pm 0.02, \text{Sham}_{90 \, \text{minFU/T7}} = 1.03 \pm 0.03, \text{tDCS}_{24 \, \text{hFU/T7}} = 0.82 \pm 0.03, \text{Sham}_{24 \, \text{hFU/T7}} = 0.92 \pm 0.04) \) indicated that the significant INTERVENTION effect was due to a superior retest performance of synchronization in the anodal tDCS group both at 90 min as well as 24-h follow-up (see Fig. 2B).

Continuation: Learning Curves

In continuation, both intervention groups showed comparable performance at baseline \( (t_{28} = 0.203, P = 0.841) \). Analysis of the training revealed a significant effect of BLOCK \( (F_{6,168} = 8.556, P < 0.001) \), INTERVENTION \( (F_{1,28} = 0.116, P = 0.736) \) and the BLOCK by INTERVENTION interaction \( (F_{6,168} = 0.334) \) had no significant influence on the dependent variable. Evaluation of online gains during training showed no significant difference between the intervention groups \( (t_{28} = 1.300, P = 0.204) \) (see Fig. 3A).

Continuation: Consolidation

The analysis of the consolidation in continuation revealed no significant SESSION \( (F_{1,28} = 2.678, P = 0.113) \) or INTERVENTION \( (F_{1,28} = 0.068, P = 0.796) \) effect, nor a SESSION by INTERVENTION \( (F_{1,28} = 0.068, P = 0.796) \) interaction (see Fig. 3B).

Control Experiment (Polarity-Specific tDCS Effects):

Synchronization

Baseline comparison did not show significant difference between intervention groups \( (t_{12} = 0.154, P = 0.880) \). Evaluation of training
revealed a significant effect of BLOCK (F_{6,72} = 13.730, P < 0.001), but not for INTERVENTION (F_{1,12} = 0.275, P = 0.609) or for the BLOCK by INTERVENTION interaction (F_{6,72} = 0.198, P = 0.848). Analysis of online gains showed no significant group differences (t_{12} = -0.076, P = 0.941). The retention index showed a significant SESSION effect (F_{1,12} = 19.691, P = 0.001), but was not modulated by INTERVENTION (F_{1,12} = 0.567, P = 0.466) or the SESSION by INTERVENTION (F_{1,12} = 2.683, P = 0.127) interaction.

Control Experiment (Polarity-Specific tDCS Effects): Continuation

Performance at baseline did not show a significant difference between interventional groups (t_{12} = -0.062, P = 0.952). The analysis of the learning revealed a significant effect of BLOCK (F_{6,72} = 3.458, P = 0.013). INTERVENTION (F_{1,12} = 0.440, P = 0.844) and the BLOCK by INTERVENTION interaction (F_{6,72} = 1.101, P = 0.368) had no significant effect during training. Analysis of online gains during training did not show a significant difference between intervention groups (t_{12} = -1.267, P = 0.229).

The consolidation of the task was not significantly influenced by SESSION (F_{1,12} = 3.783, P = 0.076). INTERVENTION (F_{1,12} = 2.262, P = 0.158), nor the SESSION by INTERVENTION (F_{1,12} = 0.061, P = 0.809) interaction.

Discussion

The main finding of this interventional study was that cerebellar anodal tDCS applied concurrently with training of a temporal motor skill enhanced the performance in the follow-up sessions of the synchronization mode. At first glance, these results were quite surprising based on recent work, for example, by Galea et al. (2011), in which the authors showed enhanced acquisition during adaptation in a visuomotor transformation task without influencing retention. In the present study, we did not see any effects of cerebellar tDCS on online improvements during the training period. However, significant offline improvements after the training session, most likely mediated by increased motor consolidation mechanisms, were apparent. Further support for the present findings come from recent studies using cerebellar stimulation during motor adaptation (Herzfeld et al. 2014) and learning of voluntary arm movements (Li Voti et al. 2014). These studies applied cathodal cerebellar tDCS (inhibitory) or cerebellar cTBS (inhibitory) and demonstrated an impairment of retention with these interventions. Thus, they point toward relevance of the cerebellum for retention and consolidation, supporting the findings of the present work. The tasks used in these studies addressed different aspects of motor learning compared with the motor synchronization continuation task. Furthermore, there are differences in the experimental design, such as the timings of evaluation of retention of the trained motor skill, here, for example, 24 h after training including night sleep was assessed. Thus, the differences in experimental design and learning tasks might explain the differential findings of cerebellar tDCS on the acquisition phase.

Motor consolidation in general refers to motor memory trace formation after training based on two main mechanisms: (1) offline-improvement leading to better performance of the task without further training and (2) memory stabilization, a process by which motor skills are transformed from an initial fragile state, in which they are prone to being disrupted or lost by, for example, training of another motor act, to a more solid state (Walker et al. 2003; Robertson et al. 2005). The present study design did not include means to address (2), as no additional other motor act was trained in a vulnerable period. Thus, it is conceivable that anodal cerebellar tDCS may have primed the consolidation process within the cerebellum through enhancing the offline effects after training of the motor task.

Cerebellum and Motor Consolidation

Behavioral studies demonstrated offline gains in timed motor sequence learning (Wright et al. 2012). The functional neuroanatomy mediating these processes has in part been revealed. During early learning of timed motor sequences, there is a strong interaction between the cerebellum and the primary motor cortex (M1) (Penhune and Doyon 2005). Early cerebellar activation is associated with poorer performance and might serve as an error correction mechanism (Shadmehr et al. 2010), whereas later increase in M1 activation is associated with better performance and could be interpreted as strengthened motor representations (Penhune and Doyon 2005). Within the cerebellum, a transfer of recruitment from cortex to dentate has been described during motor consolidation (Doyon et al. 2002). A recent study showed that activation in cerebellum and striatum serve as a memory function in learning of a temporal motor skill (Lewis et al. 2011).

The proposed cellular mechanisms of motor consolidation in the cerebellum are diverse. Synaptogenesis (Klein et al. 2002), change in discharge properties of Purkinje cells (Medina and Lisberger 2008; Wulff et al. 2009), error-driven induction of long-term depression (Ito 2000), among others have been reported. The neuroanatomical substrates of the motor synchronization continuation task on the cellular and molecular level remain largely unknown. Therefore, possible cellular mechanisms in the next section are discussed using the rather well-defined eyelblink classical condition paradigm (EBCC) as a model of associative motor learning. In EBCC, an unconditioned stimulus (US), for example, electric stimulus or air puff, is repeatedly paired with a conditioned stimulus (CS), for example, a tone, until the CS itself elicits a conditioned response, a reflexive eye blink. The US is relayed by the climbing fiber, the CS via the mossy fiber—parallel fiber pathway. Both systems convey to the Purkinje cells in the cerebellar cortex and the deep cerebellar nuclei. EBCC learning is mediated by synaptic and nonsynaptic plasticity at both sites (De Zeeuw and Yeo 2005). Recently, it could be shown that acquisition and timing of EBCC is modified by cerebellar tDCS in a polarity-dependent manner (Zuchowski et al. 2014). In addition, in a recent study, fast- and slow-learning memory components of EBCC could be dissociated with cerebellar theta-burst stimulation (cTBS) (Monaco et al. 2014). Extinction (fast learning), but not consolidation (slow learning) was impaired by inhibitory cTBS. This is pointing toward a diverse susceptibility of the underlying neuronal microcircuitry to NIBS.

It is highly speculative whether these mechanisms are in part a universal mechanism of motor learning and consolidation or are rather task-specific. Interestingly, adaptation of the horizontal optokinetic response showed similar features (Okamoto et al. 2011). In this context, anodal tDCS might to some extent have enhanced these inherent mechanisms of systemic and cellular neuroplasticity in the cerebellar cortex and nuclei.

Cerebellar tDCS

In the present study, we demonstrated that cerebellar tDCS can modify the retention of a cerebellum-dependent motor skill. The stimulation effect was polarity specific, since the enhanced consolidation in the synchronization mode was not apparent in
the control experiment with cathodal stimulation. Mechanisms mediating this effect are to date not fully understood and currently under investigation. Although speculative, it has been suggested that tDCS interacts with mechanisms of neuroplasticity like LTP (Fritsch et al. 2010) and GABAergic neurotransmission (Stagg et al. 2011). In vitro experiments with mammalian cerebellar slices revealed that white-matter DC stimulation modified the discharge properties of Purkinje cells (Llinas and Sugimori 1980). Furthermore, phase-specific optogenetic activation of the Purkinje cell or climbing fiber system was able to induce learning of the vestibulo-ocular reflex (VOR) (Nguyen-Vu et al. 2013).

In humans cerebellar output channels, measured neurophysiologically, for example, with cerebellobrain inhibition (Ugawa et al. 1995), could be modified by tDCS (Galea et al. 2009). Moreover, comparable tDCS montages as used in this study failed to alter neurophysiological measures of motor cortex, brainstem, and visual cortex excitability (Galea et al. 2009, 2011) indicating the location of action within the cerebellum. In addition, a recent modeling study demonstrated that cerebellar tDCS generates the highest current density amplitude near the active electrode at the cerebellar cortical level (Parazzini et al. 2014).

**Synchronization versus Continuation**

It is of interest that a statistically significant stimulation effect was only observed for the retention of synchronization, but not for the continuation mode. This is in line with recent work showing that inhibitory 1-Hz rTMS interfered with the performance of 2-Hz finger tapping in synchronization but not during continuation (Del Olmo et al. 2007). Following this finding, both modes of training (synchronization vs. continuation) might have a different susceptibility toward interference via noninvasive brain stimulation.

However, exploratory analysis revealed a similar trend at the first follow-up blocks (F1 and F4) in both modes. To account for this, we performed a statistical subanalysis, by calculating a retention index just considering the first follow-up blocks (F1/T7 and F4/T7). Although, the visual inspection suggested a trend, the ANOVA-RM revealed no significant difference (INTERVENTION F1,T38 = 2.522, P = 0.123) for enhanced retention by cerebellar anodal tDCS in the continuation mode.

Despite this, several features distinguish both modes. There is evidence they recruit slightly different neuroanatomical networks (Rao et al. 1997; Lewis et al. 2004). In our design, they differ in repetition rate. In continuation, the repetitions were reduced to four trials per block compared with synchronization. Continuation seems to rely more on working memory. Interestingly, recent evidence suggested that cerebellar tDCS can interfere with working memory tasks (Ferrucci et al. 2008). Furthermore, the continuation mode showed a larger intersubject variability.

**Implications for Translational Research**

We provide support that cerebellar anodal tDCS stimulation can influence cerebellar functions and motor learning in young healthy subjects. In particular, retention of a temporal motor skill was enhanced by anodal tDCS. The acquisitions of most everyday life skills are dependent on temporal components of the motor acts. In future studies, it will be interesting to investigate, whether this enhancement also applies to motor learning in general and if patients with learning deficits will benefit from the present approach (Pope and Miall 2014). Although speculative until now, animal studies demonstrated that chronic electric stimulation of the lateral cerebellar nucleus improved motor recovery after ischemic stroke in a rat model (Machado et al. 2009). A recent study provided evidence that age related declines in motor adaptation can be diminished by concurrent cerebellar tDCS stimulation in healthy aging (Hardwick and Celnik 2014).

First proof-of-principle studies in patients with cerebellar ataxia found a favorable effect of anodal cerebellar tDCS on the long-latency stretch reflex (Grimaldi and Manto 2013) and of cerebellocerebral tDCS on upper limb tremor and dysmetria (Grimaldi, Oulad Ben Taib et al. 2014).

Based on present work together with our previous findings, one interesting working hypothesis would be that patients with altered cortical or dentato-thalamo-cortical excitability, like cerebellar stroke (Liepert et al. 2004) or cerebral ataxias (Manto and Ben Taib 2008), in which therapeutic options are still limited, could potentially benefit from anodal cerebellar tDCS applied concurrently with specific physical training (Machado and Baker 2012). This concept may not only hold true for immediate behavioral improvement but also for enhancing consolidation effects of acquired motor skills.

**Limitations of the Study**

Overall, a limitation of this study is that tDCS lacks spatial precision. It is not possible to differentiate which cerebellar subarea was exactly stimulated and mediated the behavioral effect. We cannot completely rule out that stimulation of adjacent brain areas, such as the brainstem, temporal lobe, and the cortico-striatal system, although unlikely, also mediated parts of the effect. Furthermore, the mechanisms how tDCS enhances neuroplasticity are to date not fully understood. This makes the interpretation concerning possible underlying mechanisms speculative.

**Summary**

To conclude, we provided further evidence that cerebellar tDCS has the potential to modulate cerebellar function, especially aspects of learning of temporal aspects of motor acts. These findings support the interventional potential of cerebellar noninvasive stimulation in neurological patients, such as after stroke. To further put forward this concept and translate it into clinical life, upcoming studies have to investigate and help to better understand possible underlying mechanisms and optimizing its application for patients with cerebellar disorders.

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**References**


Zuchowski ML, Timmann D, Gerwig M. 2014. Acquisition of conditioned eyeblink responses is modulated by cerebellar tDCS. Brain Stimul. 7:525–531.