The Cerebellum (2024) 23:2487–2496
https://doi.org/10.1007/s12311-024-01748-0

RESEARCH

Potentiation of Motor Adaptation Via Cerebellar tACS: Characterization of the Stimulation Frequency

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Accepted: 23 September 2024 / Published online: 22 October 2024

Abstract

Motor adaptation is critical to update motor tasks in new or modified environmental conditions. While the cerebellum supports error-based adaptations, its neural implementation is partially known. By controlling the frequency of cerebellar transcranial alternating current stimulation (c-tACS), we can test the influence of neural oscillation from the cerebellum for motor adaptation. Two independent experiments were conducted. In Experiment 1, 16 participants received four c-tACS protocols (45 Hz, 50 Hz, 55 Hz, and sham) on four different days while they practiced a visuomotor adaptation task (30 degrees CCW) with variable intensity (within-subject design). In Experiment 2, 45 participants separated into three groups received the effect of 45 Hz, 55 Hz c-tACS, and sham, respectively (between-subject design), performing the same visuomotor task with a fixed intensity (0.9 mA). In Experiment 1, 45 Hz and 50 Hz of c-tACS accelerated motor adaptation when participants performed the task only for the first time, independent of the time interval between sessions or the stimulation intensity. The effect of active c-tACS was ratified in Experiment 2, where 45 Hz c-tACS benefits motor adaptation during the complete practice period. Reaction time, velocity, or duration of reaching are not affected by c-tACS. Cerebellar alternating current stimulation is an effective strategy to potentiate visuomotor adaptations. Frequency-dependent effects on the gamma band, especially for 45 Hz c-tACS, ratify the oscillatory profile of cerebellar processes behind the motor adaptation. This can be exploited in future interventions to enhance motor learning.

Keywords Cerebellum · Transcranial alternating current stimulation · Motor adaptation · Motor learning · Frequency-dependent effect

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Introduction

Motor learning is an essential human capacity for achieving daily actions under different conditions. The capacity to update the motor performance in new dynamic or kinematics conditions is called motor adaptation. For instance, when we comb our hair in front of a new mirror, we must adjust the motor commands to achieve the desired movement of our hand. Motor adaptation involves mapping motor acts and their sensory consequence, requiring updating such a relationship represented by internal models [1]. In particular, adapting motor command requires the assessment of sensory error and predicting future consequences, making the cerebellum a key structure of both processes [2–4]. Previous research has described the effects of transcranial direct current stimulation (tDCS) on the cerebellum in motor adaptation paradigms. For example, Galea et al. [5] and Hardwick and Celnik [6] have reported that cerebellar tDCS reduces the error of movement direction when people are exposed to external perturbations, facilitating the error-based recalibration process. This effect is specific to stimulation of the cerebellum, not the motor cortex [5].

Adaptation of motor commands requires the integration of neural computations distributed in both cortical and subcortical regions [7], with synchronization of neural oscillations being a proposed mechanism for transferring information between distant areas of the nervous system and implementing operations such as motor adaptation [8–11]. However, the possibilities for testing this proposed mechanism are limited.

Transcranial alternating current stimulation (tACS) has been tested to entrain or potentiate neural activity in a particular oscillatory rhythm [12]. In particular, tACS on the cerebellum (c-tACS) in the gamma band modifies the excitability of the motor cortex, promoting the adjustment of a finger tapping task [13], as well as modifying performance in functional tasks of the Wolf test [14]. In parallel, theta but not gamma c-tACS improves motor motor in finger and reaching tasks [15]. Likewise, the effect of c-tACS, in parallel to motor cortex stimulation, decreases error in a visuomotor finger task only for participants with poor performance in the basal condition [16]. Otherwise, c-tACS do not influence the acquisition of grip strength tasks [17] and show opposite effects in motor sequences learning [18]. Thus, while the evidence suggests a positive impact of c-tACS on motor performance, our knowledge about their effect on motor learning is emerging. The optimal brain stimulation parameters (e.g., stimulation frequency) should be adjusted for the individual-specific activity. Thus, the possibility of influencing ongoing oscillatory activity is more significant if the stimulation frequency is close to the endogenous frequency of each individual [12]. Although in the field of motor control, this idea has been barely tested, in visual attention paradigms, it has been reported that performance and neural activity are significantly enhanced if the frequency of tACS is matched to the predominant frequency of electroencephalographic activity, as compared to stimulation at a single frequency for all participants [19, 20]. This evidence suggests examining a range of frequencies, rather than a single frequency, to characterize the effects of tACS on motor learning.

Most c-tACS studies have tested 50 Hz as the effective stimulation frequency to modulate cerebellar functions [21]. This is related to the basal activity of the cerebellar cortex [22], attempting to modulate the cerebellum region closest to the stimulation electrodes. However, in light of the evidence presented above, examining a wide range of frequencies around 50 Hz seems necessary to investigate their effects on motor learning. In this investigation, we aim to evaluate the effect of c-tACS for a range of 45 to 55 Hz during a visuomotor adaptation task. We hypothesized that c-tACS is an effective method to accelerate motor adaptation for frequencies around 50 Hz.

Materials and Methods

Experimental Design

The study was experimental, longitudinal, randomized, and double-blinded.

Ethics Statement and Consent to Participate

This study followed all the guidelines of the Helsinki Declaration and was approved by the ethical review committee of the University of Santiago de Chile. All participants signed the informed consent N° 313/2022 arranged to execute the DIUMCE 20-2022-FGI project.

Participants

61 young people (27 females and 34 males with a mean age of 21.8 years) with a right-handed manual preference (confirmed by the Edinburgh laterality questionnaire) were included in the study. Inclusion criteria were: (a) adults between 18 and 40 years; (b) less than 5 h per week of video game experience during the last six months; and (c) reporting a night's rest of at least 7 h the night before testing. In addition, we excluded participants if they had: (a) medical contraindications for the application of tACS such as pacemakers, defibrillators, invasive brain stimulators, metallic implants in the craniocervical area, and skin alterations at the electrode placement sites; (b) medical diagnosis of

epilepsy and (c) consumption of drugs with effects on the central nervous system.

Procedures

Two independent and consecutive experiments were conducted. In Experiment 1 (16 participants), each participant attended four experimental sessions on different days, with an interval of at least two days between sessions. Participants sat 1 meter away from a 23” monitor (1920 × 1080 pixels resolution), holding a joystick (Hotas Wartog, Truthmaster, France) with their right hand, intending to position the elbow at a 90° angle. The joystick controlled a cursor on the screen. The visuomotor task consisted of moving the cursor from the center of the screen to a target that changed its location at each trial. The instruction for the task was: “Move the cursor with the joystick as fast and straight as possible to the target”. Each trial consisted of the following consecutive events: (1) a central point was displayed on the screen, indicating the onset of the trial (500 ms of duration); (2) the cursor was displayed in green in the center of the screen, together with a circular target that appeared in one of four excentric positions distributed equally in the upper half of the screen (position 22º, 67º, 112º, and 157º regarding a 360º plane, 400 pixels radially distant). At this time, the cursor was allowed to move to the target (for 1000 ms maximum) (3). The target and the cursor were displayed statically, independently of the joystick state (at 1000 ms) (4). A black screen was displayed (500 ms).

Each session (280 trials) was divided into three stages involving 80, 120, and 80 trials, respectively. In stage 2, a 30° counterclockwise (CCW) distortion of the cursor trajectory feedback was imposed (Fig. 1-a and b). The c-tACS (45 Hz, 50 Hz, 55 Hz, or Sham) was applied 5 min before stage 2 and lapsed until the end of the stage.

In Experiment 2, we set up three groups (15 participants each) to receive 45 Hz, 55 Hz, or sham c-tACS in a single session. The session involved 400 trials, divided into three stages of 120, 160, and 120 trials, respectively. As in Experiment 1, c-tACS was applied before the onset of stage 2 (5 min) and lapsed until the end of this stage. The same visuomotor task and distortion on feedback trajectory during stage 2 were employed (Fig. 1-c).

Transcranial alternating current stimulation was delivered by the DC-STIMULATOR PLUS device (neuroConn, Ilmenau, Germany) in each session and according to the stimulation protocol. A 15-second ramp up and down was also considered.

For Experiment 1, the stimulation lasted ~ 16 min (120 trials). In each session, one of the following frequencies was applied: 45 Hz, 50 Hz, 55 Hz, or sham. The order of the tACS protocol was pseudo-randomly scheduled to ensure that 4 participants were stimulated with 1 of the four options in the first session. The following sessions involved the remaining options randomly. For sham stimulation (30 s

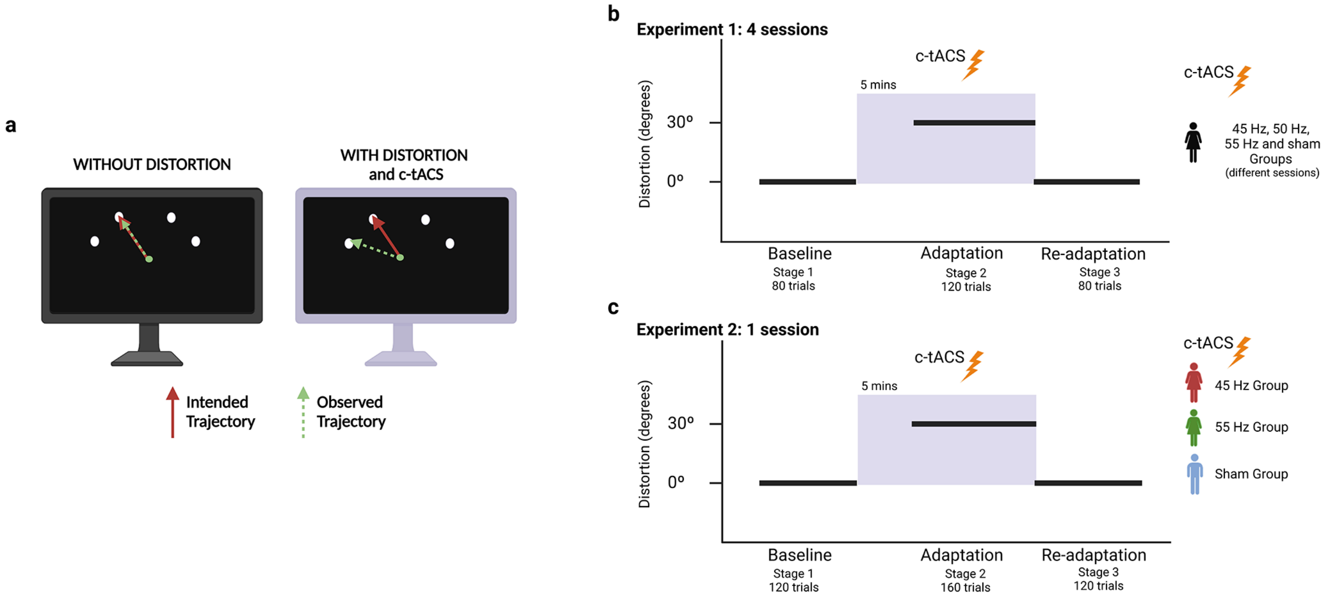

Fig. 1 Visuomotor task and learning protocol. **a** - On the left, we illustrate cursor movement without distortion. The movement observed on the screen is the same as on the joystick (red and green arrows). On the right, we illustrate cursor movement with distortion. The movement observed on the screen (in green) resulted from a 30º CCW distortion of visual feedback of joystick trajectory (in red). **b**- Protocol for Experiment (1) The X-axis denotes the three stages of a session. The Y axis indicates distortion. Cerebellar tACS (c-tACS) was applied 5 min before stage 2 (light-grey box). Each participant took part in four tACS sessions. **c**- Protocol for Experiment (2) In this case, each stage increased in 40 trials. Participants took part in one session only

plus 15 s of ramp up and down), the frequency used was pseudo-randomly assigned, assuring that the three frequency options were employed equally in the sample. Active and sham stimulation was applied with a subthreshold intensity calculated by subtracting 0.1 mA from the intensity value at which the participant reported feeling any cutaneous sensation (tingling, burning, or itching) or phosphenes.

For Experiment 2, the stimulation lasted ~ 20 min (160 trials) for 45-Hz, 55-Hz or sham c-tACS. The intensity was set at 0.9 mA (average subthreshold intensity recorder from Experiment 1). All other parameters and procedures were similar to Experiment 1.

In both experiments, we used sponge electrodes measuring 5 × 5 cm wetted with saline and attached with rubber straps to 2 sites: 3 cm to the right of the inion and over the right jaw angle. This configuration was chosen to obtain a focalized current density over the right cerebellar hemisphere [21]. The impedance for each c-tACS delivery was kept below 15 KΩ. At the end of each stimulation session, a side-effect survey was conducted. Also, each participant was asked whether they received real or sham stimulation.

Data Processing

Motor behavior was assessed using a custom code developed in Matlab software (version R2022a, Mathworks, Massachusetts, USA). For this purpose, we used the raw data from the instantaneous position of the cursor on the screen in pixel coordinates. First, we obtained a time series of instantaneous velocity that was filtered (low pass FIR filter, 15 Hz). After that, we determined the movement period as the continuous velocity period greater than 5% of the peak velocity. To determine the direction of movement, we calculated the angle subtended between the onset and cursor positions for the peak acceleration during the movement period.

The error in the reaching direction measured motor adaptation. This metric was calculated as the difference between the movement direction and the ideal direction to reach the target (the angle regarding the x-axis subtended by the rect between the target and the center of the screen). Motor performance was also characterized by reaction time, velocity, and movement duration. Complementarily, the stimulation intensity was also analyzed for each frequency.

The task was dissected in blocks of 10 trials, counting 28 blocks in the case of Experiment 1 and 40 blocks for Experiment 2. We set specific block comparisons to analyze the effect of feedback distortion, and c-tACS applied in stage 2. These were the first block of stage 2 versus the last block of stage 1 (period of initial feedback distortion), the block progression on stage 2 (adaptation), the first block of stage 3 versus the last block of stage 2 (initial re-adaptation), and the block progression on stage 3 (re-adaptation). To account for differences between subjects in their initial performance, the variables analyzed were referenced concerning each variable's average in the last four blocks of stage 1, using arithmetic subtraction of this value.

Statistical Analysis

Descriptive and inferential statistical analyses were performed in R and Rstudio (R Core Team. (2023). R: A language and environment for statistical computing (R studio Version 2023.06.2 + 561) https://www.R-project.org/). Mean and standard deviation, analysis of variance (ANOVA) for one (c-tACS protocol) or two factors (c-tACS protocol and blocks), and linear regression were used. The p-value was 0.05 for all effects. All data sets subjected to any test complied with their statistical assumptions. Also, post-hoc through multiple Student or Wilcoxon tests and correction by the Holm method was applied when needed. For survey analysis, we used the Chi-squared test. Effect sizes were calculated by Partial eta squared (η^2) in the case of ANOVA and D' Cohen (d) for pair comparisons.

In Experiment 1, the statistical analysis was performed for two datasets. The first included all sessions for 15 participants (one participant was discarded because it did not decrease the error in line with expected learning) in the within-subject design. The second dataset considered only the first session of each participant. Therefore, in a between-subject design, the sample size was reduced to 4 participants for each group, except for the sham group with 3 participants. In Experiment 2, a between-subject design was used.

Results

Experiment 1

Motor Performance

Angular error To determine the effect of c-tACS frequency on motor adaptation, first, we compared the complete dataset (Figs. 2 and 3 sessions for 15 participants). Our results indicate no significant differences in the angular error between c-tACS protocols for the four periods analyzed: (1) initial block of stage 2 (F(3,42) = 1.72, $p = 0.175$), (2) all blocks of stage 2 (F(3,42) = 1.54, $p = 0.217$), (3) initial block of stage 3 (F(3,42) = 1.48, $p = 0.231$), and (4) all blocks of stage 3 (F(3,42) = 0.87, $p = 0.46$). Concerning progress in angular error over time, both stage 2 (F(1, 14) = 61.25, $p < 0.0001$) and 3 (F(1, 14) = 78.92, $p < 0.0001$) showed a significant decrease, indicating adaptation and re-adaptation to distor-

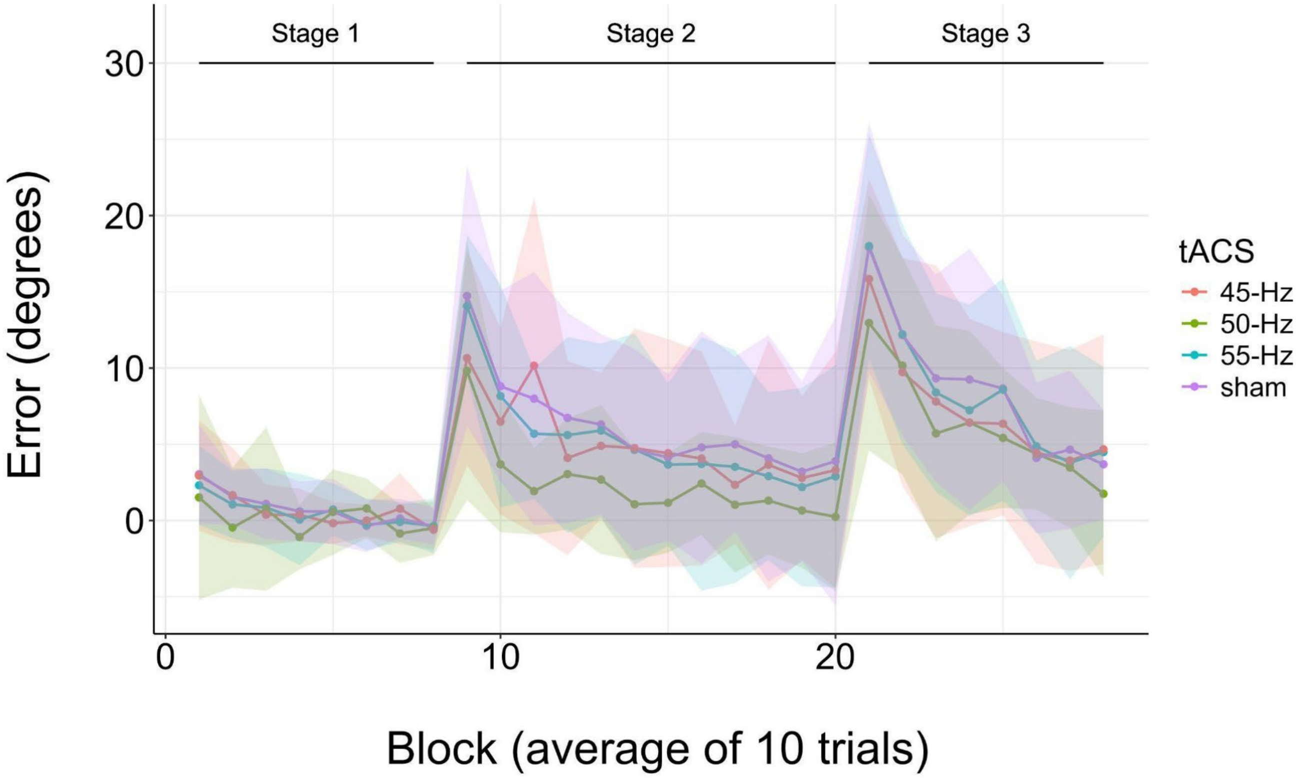

Fig. 2 Angular error for blocks of practice. Error during each tACS session is represented by a dotted line and shadow (mean ± standard deviation). During stage 2, c-tACS and distortion were applied. Error time series were corrected by the subtraction of the mean error for blocks 5 to 8 (stage 1)

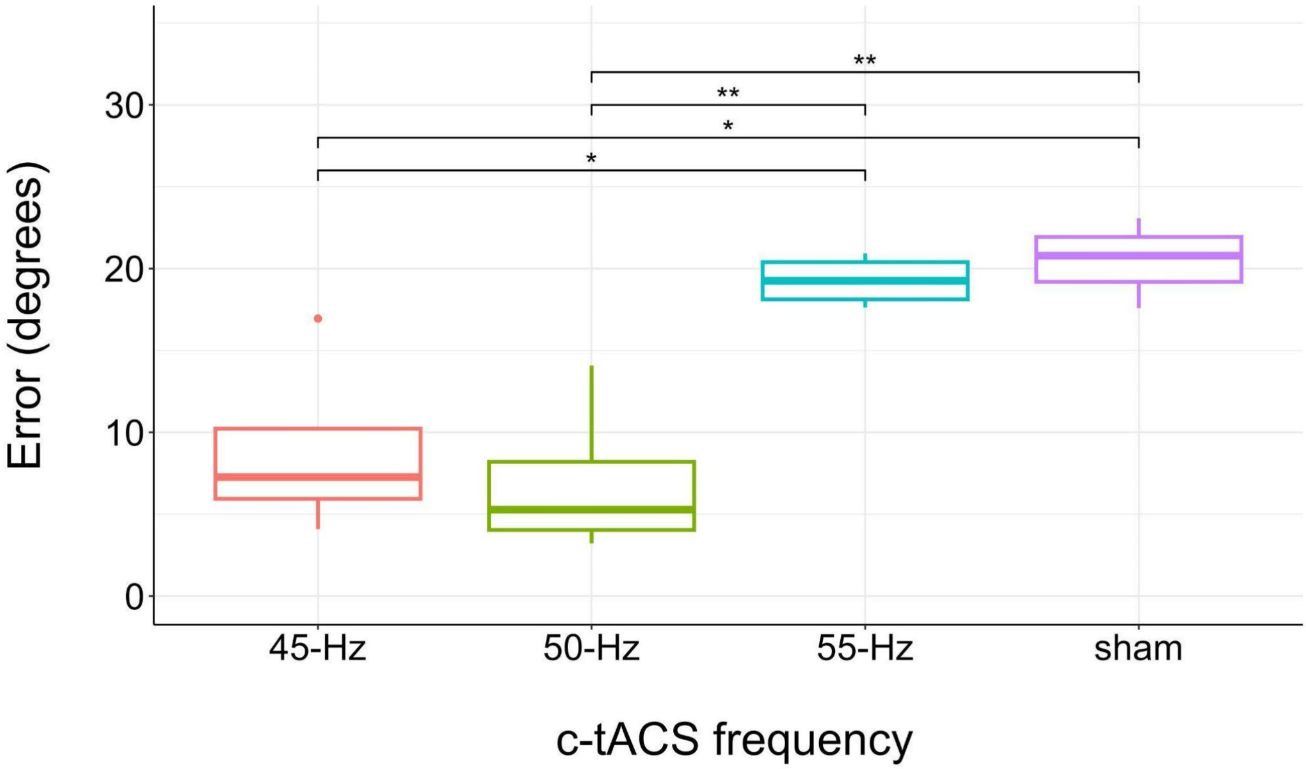

Fig. 3 Exploratory comparisons for error during the initial block of stage 2. Boxplots of errors for a subset of sessions (first c-tACS session), where participants were stimulated with 45 Hz ($n=4$), 50 Hz ($n=4$), 55 Hz ($n=4$), and sham ($n=3$) c-tACS. * means $p<0.05$, ** means $p<0.001$

tion, respectively. No interaction between c-tACS protocols and block factors was detected during stages 2 or 3.

Motivated by inspecting the effect of tACS in a single session, we performed an exploratory analysis for the first session of each participant. Thus, we included 4 participants for sessions with 45 Hz, 50 Hz, or 55 Hz c-tACS and 3 participants who received sham stimulation. Confronting c-tACS frequencies for the same task periods, we only obtained significant differences in error during the initial block of stage 2 (Fig. 4, F(3, 11) = 9.59, $p = 0.002$). Thus, the error was lower for 45 Hz vs. 55 Hz ($p = 0.015$) and sham ($p = 0.013$), as well as for 50 Hz vs. 55 Hz ($p = 0.0079$) and sham ($p = 0.0063$).

Reaction Time, Velocity, and Duration of Reaching Movement All variables were analyzed during the initial block of stage 2 and the complete stage 2. For reaction time, no significant differences were observed between c-tACS frequencies in both periods (F(3,42) = 0.09, $p = 0.961$ for block 9; F (3,42) = 0.941, $p = 0.43$ for stage 2). Similarly, movement velocity was not affected by s-tACS frequency of stimulation (F(3.42) = 0.416, $p = 0.742$) or the complete stage 2 (F(3.42) = 0.977, $p = 0.413$). Finally, movement duration showed also no effect of c-tACS frequency (F(3,42) = 0.239, $p = 0.868$ for block 9; F(3,42) = 1.03, $p = 0.389$ for stage 2).

Effect of Task Repetition

Given that in experiment 1 we used a within-subject design, reiteration of the task in successive sessions may improve performance. To evaluate this situation, we analyzed the effect of the execution order and the time interval between sessions, independent of the frequency of c-tACS. By linear regression of stage 2 initial error, no significant effects were detected for session 2 (β=-3.59, $p = 0.19$), session 3 (β=-2.79, $p = 0.32$), or session 4 (β = 0.98, $p = 0.72$), considering session 1 as reference. In the same line, the time interval (5.9 ± 6.2 days) between session 1 and sessions 2, 3, and 4 does not regress significantly the difference in initial error on stage 2 (β=-0.02, $p = 0.796$).

Stimulation Intensity

Because we set the intensity parameter of c-tACS as subthreshold, measured just before each session, the intensity differed for each session and participant. The average intensity was 0.91 +- 0.3 mA for 45-Hz tACS sessions, 0.94 +- 0.3 for 50-Hz tACS sessions, 0.91 +- 0.32 mA for 55-Hz tACS sessions, and 0.81 +- 0.33 mA for sham sessions. Such intensity differences between sessions were not significant (F(3,60) = 0.516, $p = 0.673$). To explore if the intensity could explain the initial error in stage 2, we first grouped the sessions in two groups according to intensity delivered below or above 0.9 mA. We compared the effect on error without significant differences for high (F(2, 22) = 0.625, $p = 0.545$) or low intensities (F(2, 17) = 2.145, $p = 0.148$).

Experiment 2

Motor Performance

45-Hz and 50-Hz c-tACS seem to favor the motor adaptation for a subset of the data in Experiment 1. To verify this preliminary result, we formed three independent groups (with 45 Hz, 55 Hz, and sham c-tACS, 0.9 mA), so we discarded any effect of task repetition or stimulation intensity. We did not include the 50 Hz c-tACS group to simplify the design since this frequency exhibited the same result as 45 Hz in Experiment 1. For the complete stage 2, the results show an overall favorable effect of c-tACS on motor error (F(2,42) = 3.46, $p = 0.041$, η2 = 0.14), as well as for blocks (F(15,630) = 138.9, $p < 0.0001$, η2 = 0.76) and the interaction of factors (F(30,630) = 2.3, $p = 0.0001$, η2 = 0.09, Fig. 3a). When looking at the initial block of stage 2 (initial distortion, block 13), there is a significant effect of c-tACS (F(2,42) = 5.39, $p = 0.008$, η2 = 0.2), where both 45 Hz ($p = 0.021$, d = 1.04) and 55 Hz ($p = 0.014$, d = 1.15) show lower error compared to sham, without differences between active c-tACS conditions ($p = 0.76$). To explore the effect of c-tACS at the initial adaptation period, we analyzed the period of fastest error decay (blocks 13 to 16, Fig. 3b). In this subset, both 45 Hz ($p = 0.032$, d = 0.35) and 55 Hz c-tACS ($p = 0.047$, d = 0.31) showed a positive effect on sham, again without differences between them ($p = 0.75$). On the other hand, when we analyzed the late adaptation period (Fig. 3c), corresponding to the average error between blocks 21 to 28, only 45 Hz c-tACS led to a lower error concerning sham ($p = 0.030$, d = 0.51), as well as regarding 55 Hz c-tACS ($p = 0.037$, d = 0.60). There were no differences between sham and 55 Hz ($p = 0.77$).

In stage 3, there was only a significant decrease in error (F(11,462) = 113.2, $p < 0.0001$, η2 = 0.73), without differences between c-tACS protocols (F(2,42) = 1.88, $p = 0.164$) neither interaction (F(22,462) = 0.69, $p = 0.844$).

Success of the Blinding (mask) Procedure

Participants were not informed about the c-tACS protocols applied in each session. When we examine the results from a survey that asked if the participants thought they received active or sham stimulation, we conclude that blinding was effective in experiments 1 and 2 ($X^2 = 0.17$, $p = 0.67$).

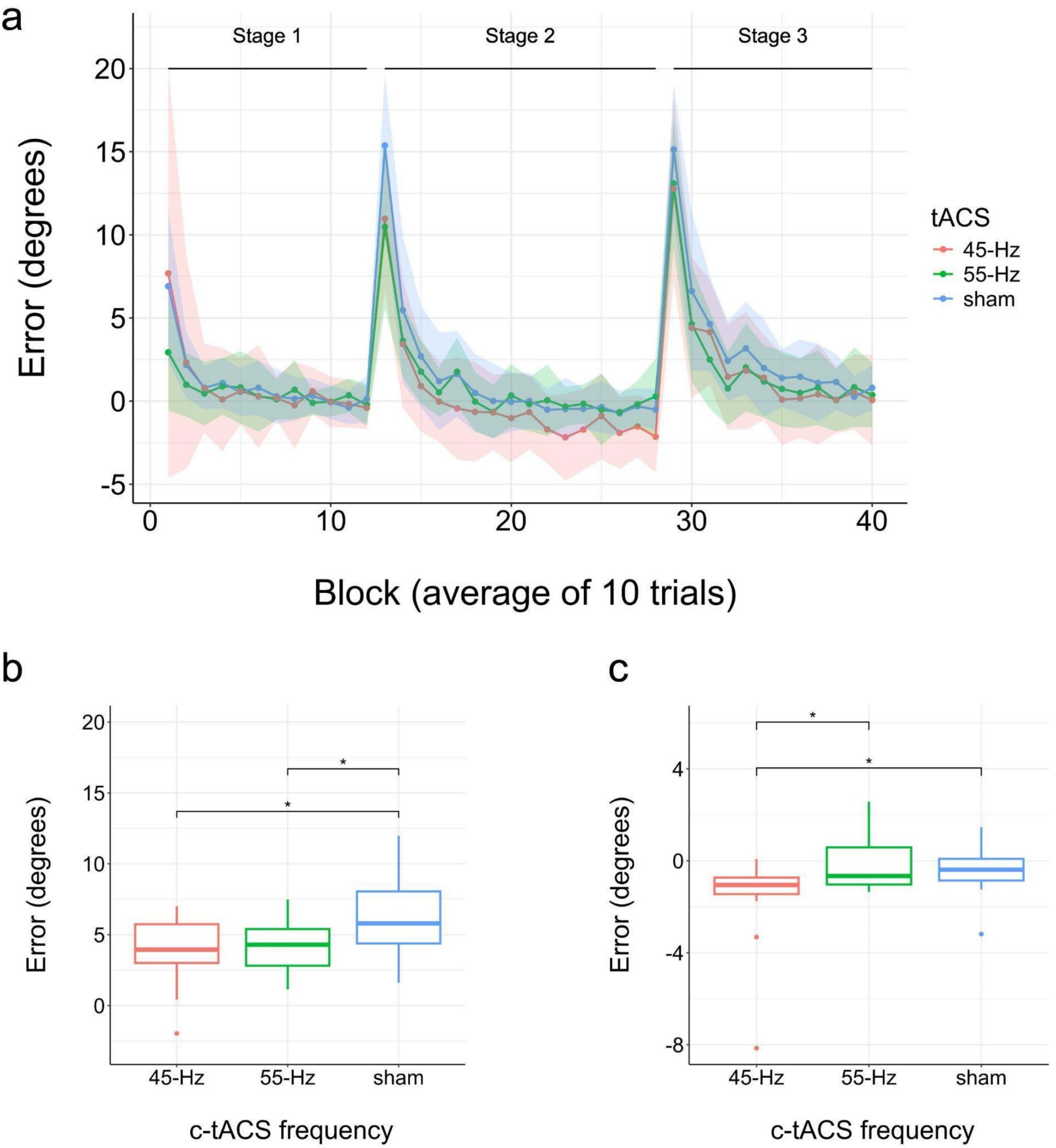

Fig. 4 Angular error for practice blocks in experiment 2. **a** - Error during each tACS session is indicated by a dotted line and shadow (mean ± standard deviation). During stage 2, c-tACS and distortion were applied. The mean error for blocks 5 to 8 (stage 1) was subtracted from the error time series to improve error comparisons. Significant differences were observed during stage 2. **b** - Boxplot of errors for the first blocks of stage 2 (13 to 16). * means $p < 0.05$. **c** - Boxplot of errors for the last blocks of stage 2 (21 to 28). * means $p < 0.05$

Discussion

The present work aimed to determine the effects of c-tACS at the gamma range on motor adaptation phenomenon. The results indicated a significant impact of cerebellar tACS stimulation at 45 Hz and 55 Hz on motor adaptation, extending over the entire stimulation period only in the case of 45 Hz. No effects in motor control parameters of reaching movement were detected, confirming the specific role of the cerebellum in motor learning and the possibility of being optimized by tACS.

As seen through the angular error, motor adaptation is supported by the cerebellum as a critical node responsible for acquiring, maintaining, and updating internal models [7, 24]. Thus, when the cerebellum updates these models during an adaptive motor task, fewer errors occur in the execution of motor commands [3]. Our results ratify this critical learning process, as cerebellar alternating stimulation significantly decays motor errors. At the same time, it does not significantly affect the other parameters, such as reaction times, duration, and movement velocity. This evidence suggests that c-tACS potentiates cerebellar processes related to neural operations like internal models. In this sense, c-tACS is potentially an effective strategy to enhance human performance based on motor adaptations.

There is consistent evidence showing positive effects of gamma c-tACS on connectivity between the cerebellum and the primary motor cortex during sensorimotor hand synchronization tasks [16], performance in motor sequence learning tasks [27], and corticospinal excitability [25]. However, studies also show null effects of c-tACS specifically for 50 Hz in motor learning tasks [17] and repetitive movements with the upper limb [15]. These mixed findings seek an explanation at the neurophysiological level in Purkinje cells (PCs), which have been proposed as the target of c-tACS [35]. The natural oscillatory activity of PCs is in the gamma band. Some studies have shown that the oscillatory frequency during upper extremity tasks tends to be in higher gamma frequencies [28]. However, in animal models, it has been observed that stimulation at 50 Hz shows promising results in regulating the discharge frequencies of the PCs [29], which is coherent with the behavioral effect reported for previous studies in humans [13, 14, 18]. In our case, we obtained positive effects for frequencies around 50 Hz, being more prolonged for 45 Hz c-tACS, which confirms that oscillatory processes in the gamma band are implicated in different modalities of motor learning, probably mediated by PC activity. Thus, our results expand the range of effective cerebellar stimulation described until now, which could motivate new studies to characterize the c-tACS effects for frequencies and stimulation periods.

The differential effects showed in experiment 2 for 45 Hz, and 55 Hz suggest that optimal frequency stimulation could be below 50 Hz (the most tested gamma-range c-tACS frequency). In this regard, examining endogenous oscillatory activity on the cerebellum could guide an individualized c-tACS approach, where both frequency and intensity are determinant parameters of the effectiveness of non-invasive techniques under the “Arnold Tongue” [33, 34] phenomenon. Future research that combines electro or magnetoencephalography with tACS can unveil the feasibility and effectiveness of a personalized tACS approach for motor learning.

A particular finding of our study was the differential effect of c-tACS depending, in part, on the protocol design. Previous studies with a between-subject design have shown the benefits of c-tACS in motor performance [13, 14] and tasks involving reaction times [18]. On the other hand, in a within-subject design, null effects on motor learning have been reported [16, 17, 25]. This raises the possibility that the c-tACS effect during experiment 1 (within-design) could be masked by the repetition of motor protocol, a possibility controlled in experiment 2 (between-design). Motor adaptation paradigms suffer from the saving effect [26], where repeated exposure to visual distortions generates a carry-over effect that enhances performance upon re-exposure. Although the order of stimulation was randomized in experiment 1, this saving effect could obscure the benefits of one frequency over another. In this way, determining possible carry-over phenomena can expand our knowledge of the cumulative effects of tACS.

Beyond motor adaptation, the null effect of different c-tACS frequencies on reaction time, movement speed, and movement duration was expected, as the control of these parameters does not lie primarily in the cerebellum but in areas related to movement execution like the primary motor cortex, as well as neuromechanical factors [30, 31].

Intensity has been proposed as a critical parameter of stimulation protocols. In this sense, the amount used with our participants was similar to what is generally employed in c-tACS, with values ranging around 1 mA [16, 25] and 2 mA [13, 14, 17, 18]. Such parameter did not yield statistically significant differences when analyzing the results of motor error for low intensity (<0.9 mA) versus high intensity (>0.9 mA and <1.8 mA), which is in line with the results of Miyaguchi and Cols, that showed a similar effectiveness of c-tACS stimulation at gamma frequency, independent of stimulation intensity [32]. So, a subthreshold intensity for sensory effect seems enough to potentiate cerebellar processing during motor adaptation. Although a personalized stimulation design that considers individual intensity thresholds confers the advantage of adjusting the stimulation dose to each participant, its effectiveness must be explored through studies with larger sample sizes than those usually used, which imposes a challenge to the field of neurostimulation.

We must acknowledge some limitations in our study. The first experiment was conceived with a within-subject design to control variability from an individual origin. However, this design imposes the challenge that all participants must perform every session in a specific time interval, which was impossible to achieve because of issues beyond our control. Even the time interval between sessions did not explain the participants' performance, this issue might explain some of the variance. Additionally, the reduced sample size when we compare only the first session between c-tACS frequencies limited the conclusions that could be drawn from these results. These limitations were addressed in the second experiment, where we adopted a between-subjects design, increased the sample size, and focused on specific stimulation frequencies (45 Hz, 55 Hz, and a sham condition as control). Such changes allowed us to compare different stimulation conditions more robustly and delve deeper into our initial findings.

Conclusions

This study provides significant evidence of the effects of cerebellar transcranial alternating current stimulation on motor adaptation. The results from two complementary experiments demonstrate that c-tACS has an enhancing impact on motor adaptation tasks, and this effect depends on the stimulation frequency used. The findings suggest that 45 Hz and 55 Hz frequencies are particularly effective, with 45 Hz showing greater consistency and broader effects on the adaptation period. These results open new avenues for future research and underscore the importance of careful parameter selection in applying c-tACS. The study encourages future investigations and clinical applications of c-tACS in the context of motor adaptation, with potential implications for the improvement of motor performance.

Author Contributions P.F., J.A., P.U., T.B., L.E., P.I. and J.M. conceived and designed the study, and wrote the main manuscript text. P.F., J.A., P.U, L.E., and J.M. participated in the recording and analysis of data. All authors reviewed the manuscript.

Funding The study was partially funded by the DIUMCE grant (code 20-2022-FGI) managed by the Universidad Metropolitana de Ciencias de la Educación.

Data Availability No datasets were generated or analysed during the current study.

Declarations

Ethical Approval This study was revised and approved by the scientific ethics committee of the Universidad de Santiago de Chile N° 313/2022 and followed the principles of the Helsinki Declaration. All participants signed the document of consent to participate before taking part in the procedures of the study.

Competing Interests The authors declare no competing interests.

References

1. Wolpert DM, Ghahramani Z. Computational principles of movement neuroscience. Nat Neurosci. 2000;3:1212–7.
2. Wolpert DM, Miall RC, Kawato M. Internal models in the cerebellum. Trends Cogn Sci. 1998;2(9):338–47.
3. Ito M. Control of mental activities by internal models in the cerebellum. Nat Rev Neurosci. 2008;9(4):304–13.
4. Tzvi E, Loens S, Donchin O. Mini-review: the role of the Cerebellum in Visuomotor Adaptation. Cerebellum. 2022;21(2):306–13.
5. Galea JM, Vazquez A, Pasricha N, Orban De Xivry JJ, Celnik P. Dissociating the roles of the Cerebellum and Motor Cortex during adaptive learning: the Motor Cortex retains what the Cerebellum learns. Cereb Cortex. 2011;21(8):1761–70.
6. Hardwick RM, Celnik PA. Cerebellar direct current stimulation enhances motor learning in older adults. Neurobiol Aging. 2014;35(10):2217–21.
7. Wolpert DM, Diedrichsen J, Flanagan JR. Principles of sensorimotor learning. Nat Rev Neurosci. 2011;12(12):739–51.
8. Varela F, Lachaux JP, Rodriguez E, Martinerie J. The brainweb: phase synchronization and large-scale integration. Nat Rev Neurosci. 2001;2(4):229–39.
9. Schwey A, Battaglia D, Bahuguna J, Malfait N. Different faces of Medial Beta-Band Activity reflect distinct visuomotor feedback signals. J Neurosci. 2023;43(49):8472–86.
10. Mariman JJ, Bruna-Melo T, Gutierrez-Rodriguez R, Maldonado PE, Burgos PI. Event-related (de)synchronization and potential in whole vs. part sensorimotor learning. Front Syst Neurosci. 2023;17:1045940.
11. Burgos PI, Mariman JJ, Makeig S, Rivera-Lillo G, Maldonado PE. Visuomotor coordination and cortical connectivity of modular motor learning. Hum Brain Mapp. 2018;(March):1–18.
12. Wischnewski M, Alekseichuk I, Opitz A. Neurocognitive, physiological, and biophysical effects of transcranial alternating current stimulation. Trends Cogn Sci. 2023;27(2):189–205.
13. Naro A, Leo A, Russo M, Cannavò A, Milardi D, Bramanti P, et al. Does Transcranial Alternating Current Stimulation

Induce Cerebellum plasticity? Feasibility, Safety and Efficacy of a novel electrophysiological Approach. Brain Stimulat. 2016;9(3):388–95.

14. Naro A, Bramanti A, Leo A, Manuli A, Sciarrone F, Russo M, et al. Effects of cerebellar transcranial alternating current stimulation on motor cortex excitability and motor function. Brain Struct Funct. 2017;222(6):2891–906.
15. Guerra A, Paparella G, Passaretti M, Costa D, Birreci D, De Biase A, et al. Theta-tACS modulates cerebellar-related motor functions and cerebellar-cortical connectivity. Clin Neurophysiol. 2024;158:159–69.
16. Miyaguchi S, Otsuru N, Kojima S, Saito K, Inukai Y, Masaki M, et al. Transcranial Alternating Current Stimulation with Gamma Oscillations over the Primary Motor Cortex and Cerebellar Hemisphere Improved Visuomotor performance. Front Behav Neurosci. 2018;12:132.
17. Wessel MJ, Draaisma LR, De Boer AFW, Park C, hyun, Maceira-Elvira P, Durand-Ruel M, et al. Cerebellar transcranial alternating current stimulation in the gamma range applied during the acquisition of a novel motor skill. Sci Rep. 2020;10(1):11217.
18. Giustiniani A, Tarantino V, Bracco M, Bonaventura RE, Oliveri M. Functional role of cerebellar Gamma frequency in motor sequences learning: a tACS study. Cerebellum. 2021;20(6):913–21.
19. Mioni G, Shelp A, Stanfield-Wiswell CT, Gladhill KA, Bader F, Wiener M. Modulation of individual alpha frequency with tACS shifts Time Perception. Cereb Cortex Commun. 2020;1(1):tgaa064.
20. Kemmerer SK, Sack AT, De Graaf TA, Ten Oever S, De Weerd P, Schuhmann T. Frequency-specific transcranial neuromodulation of alpha power alters visuospatial attention performance. Brain Res. 2022;1782:147834.
21. Wessel MJ, Draaisma LR, Hummel FC. Mini-review: Transcranial Alternating Current Stimulation and the Cerebellum. Cerebellum. 2022;22(1):120–8.
22. Llinás R, Sugimori M. Electrophysiological properties of in vitro Purkinje cell somata in mammalian cerebellar slices. J Physiol. 1980;305(1):171–95.
23. Rampersad SM, Janssen AM, Lucka F, Aydin U, Lanfer B, Lew S, et al. Simulating Transcranial Direct Current Stimulation with a detailed Anisotropic Human Head Model. IEEE Trans Neural Syst Rehabil Eng. 2014;22(3):441–52.
24. Ishikawa T, Tomatsu S, Izawa J, Kakei S. The cerebro-cerebellum: could it be loci of forward models? Neurosci Res. 2016;104:72–9.
25. Herzog R, Berger TM, Pauly MG, Xue H, Rueckert E, Münchau A, et al. Cerebellar transcranial current stimulation – an intra-individual comparison of different techniques. Front Neurosci. 2022;16:987472.
26. Wolpert DM, Flanagan JR. Computations underlying sensorimotor learning. Curr Opin Neurobiol. 2016;37:7–11.
27. Herzog R, Bolte C, Radecke JO, Von Möller K, Lencer R, Tzvi E, et al. Neuronavigated cerebellar 50 hz tACS: attenuation of Stimulation effects by Motor sequence learning. Biomedicines. 2023;11(8):2218.
28. Thach WT. Discharge of Purkinje and cerebellar nuclear neurons during rapidly alternating arm movements in the monkey. J Neurophysiol. 1968;31(5):785–97.
29. Nguyen-Vu TDB, Kimpo RR, Rinaldi JM, Kohli A, Zeng H, Deisseroth K, et al. Cerebellar Purkinje cell activity drives motor learning. Nat Neurosci. 2013;16(12):1734–6.
30. Paraskevopoulou SE, Coon WG, Brunner P, Miller KJ, Schalk G. Within-subject reaction time variability: role of cortical networks and underlying neurophysiological mechanisms. NeuroImage. 2021;237:118127.
31. Sartori M, Yavuz UŞ, Farina D. In vivo neuromechanics: Decoding Causal Motor Neuron Behavior with resulting Musculoskeletal function. Sci Rep. 2017;7(1):13465.
32. Miyaguchi S, Otsuru N, Kojima S, Yokota H, Saito K, Inukai Y, et al. Gamma tACS over M1 and cerebellar hemisphere improves motor performance in a phase-specific manner. Neurosci Lett. 2019;694:64–8.
33. Vogeti S, Boetzel C, Herrmann CS. Entrainment and spike-timing dependent plasticity – a review of proposed mechanisms of Transcranial Alternating Current Stimulation. Front Syst Neurosci. 2022;16:827353.
34. Huang WA, Stitt IM, Negahbani E, Passey DJ, Ahn S, Davey M, et al. Transcranial alternating current stimulation entrains alpha oscillations by preferential phase synchronization of fast-spiking cortical neurons to stimulation waveform. Nat Commun. 2021;12(1):3151.
35. Asan AS, Lang EJ, Sahin M. Entrainment of cerebellar purkinje cells with directional AC electric fields in anesthetized rats. Brain Stimulation noviembre de. 2020;13(6):1548–58.