No consistent effect of cerebellar transcranial direct current stimulation (tDCS) on visuomotor adaptation

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RJ, CM & JG conceived experiment, RJ performed data collection, RJ & JG performed data analysis and RJ, CM and JG wrote the paper.

Abstract

Cerebellar transcranial direct current stimulation (ctDCS) is known to enhance adaptation to a novel visual rotation (visuomotor adaptation) and it is suggested to hold promise as a therapeutic intervention. However, it is unknown whether this effect is robust across varying task parameters. This question is crucial if ctDCS is to be used clinically, as it must have a consistent and robust effect across a relatively wide range of behaviours. The aim of this study was to examine the effect of ctDCS on visuomotor adaptation across a wide range of task parameters which were systematically varied. Therefore, 192 young healthy individuals participated in one of seven visuomotor adaptation experiments either in an anodal or sham ctDCS group. Each experiment examined whether ctDCS had a positive effect on adaptation when a unique feature of the task was altered: position of the monitor, offline tDCS, use of a tool, and perturbation schedule. Although we initially replicated the previously reported positive effect of ctDCS on visuomotor adaptation, this was not maintained during a second replication study, or across a large range of varying task parameters. At the very least, this may call into question the validity of using ctDCS within a clinical context where a robust and consistent effect across behaviour would be required.

New and Noteworthy: Cerebellar transcranial direct current stimulation (ctDCS) is known to enhance motor adaptation and thus holds promise as a therapeutic intervention. However, understanding the reliability of ctDCS across varying task parameters is crucial. To examine this, we investigated whether ctDCS enhanced visuomotor adaptation across a range of varying task parameters. We found ctDCS to have no consistent effect on visuomotor adaptation, questioning the validity of using ctDCS within a clinical context.

Keywords: Adaptation, Brain stimulation, Cerebellum, Motor learning, tDCS

Introduction

Motor adaptation is a specific form of motor learning, which refers to the error reduction that occurs in response to a novel perturbation (Krakauer, 2009, Shadmehr and Mussaivaldi, 1994). Specifically, when we make a movement with a defined goal, i.e. reaching to a visual target, the brain compares the actual and predicted sensory outcome of the executed movement. A sensory prediction error can be induced by a systematic perturbation such as a visual rotation or force-field. This perturbation induces prediction errors that inform the brain of an environmental change (Miall and Wolpert, 1996, Wolpert et al., 1998). To return to accurate performance, the brain gradually updates its prediction, and resulting motor commands, so that it accounts for the new dynamics of the environment (Yamamoto et al., 2006, Tseng et al., 2007).

Patients with cerebellar lesions show a pronounced impairment in their ability to adapt to novel perturbations (Yamamoto et al., 2006, Criscimagna-Hemminger et al., 2010, Diedrichsen et al., 2005, Martin et al., 1996, Maschke et al., 2004, Rabe et al., 2009, Smith and Shadmehr, 2005, Weiner et al., 1983, Donchin et al., 2012). Specifically, they are often unable to reduce the movement error induced by the visual rotation or force-field. This suggests that the cerebellum is crucial during the feedforward process required for successful motor adaptation. Although patient studies can provide us with a good insight regarding cerebellar function, there is a scarcity of patients with isolated cerebellar lesions. In addition, testing patients leaves the possibility that some changes, or the lack of them, are due to long-term compensation by other brain areas.

An alternative approach to investigate cerebellar function is to use non-invasive brain stimulation such as transcranial direct current stimulation (tDCS) in healthy participants. For instance, Galea et al., (2011) applied tDCS over the cerebellum (ctDCS) during adaptation to a visual rotation (visuomotor adaptation). It was found that anodal ctDCS led to faster adaptation, relative to either primary motor cortex (M1) anodal tDCS or sham tDCS (Galea et al., 2011). Such positive effects of ctDCS on cerebellar function have been replicated in visuomotor adaptation (Galea et al., 2011, Cantarero et al., 2015, Hardwick and Celnik, 2014, Block and Celnik, 2013), force-field adaptation (Herzfeld et al., 2014), locomotor adaptation (Jayaram et al., 2012), saccade adaptation (Panouilleres et al., 2015, Avila et al., 2015), motor skill learning (Cantarero et al., 2015), and language prediction tasks (Miall et al., 2016). As a result, it has been suggested that cerebellar tDCS is not only a useful tool to understand cerebellar function but also as a possible clinical technique to restore cerebellar function in patients suffering cerebellar-based disorders (Grimaldi et al., 2014). However, there are also inconsistencies regarding the impact of ctDCS with several studies reporting ctDCS having no effect on motor learning (A. Mamlins, 2016, Steiner et al., 2016).

In order for ctDCS to be applied in a clinical context, we must first understand how consistent the effects of ctDCS are within a particular learning context. Therefore, we examined the influence of anodal ctDCS on visuomotor adaptation across a range of different task parameters. Specifically, we examined whether ctDCS produced a reliable behavioural effect when manipulating task parameters such as screen orientation, tDCS timing, tool-use and perturbation schedule.

Materials and Methods

Participants

192 healthy young individuals participated in this study (120 female, 25 ± 7yrs). Each participated in one of seven experiments and received either anodal or sham ctDCS. All were blinded to the stimulation, naive to the task, self-assessed as right handed, had normal/corrected vision, and reported to have no history of any neurological condition. The study was approved by the Ethical Review Committee of the University of Birmingham and was in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants. Participants were recruited through online advertising and received monetary compensation upon completion of the study. At the end of the session, participants were asked to report their attention, fatigue, and quality of sleep

using a questionnaire with a scale from 1-7, and also reported their perceived tDCS as active (1) or placebo (0), and their hours of sleep in the previous night (table 1). These self-reports were collected from 164 participants, excluding one from experiments 1 and 2, thirteen (either anodal or sham) from experiment 5 and all 13 sham participants from experiment 7.

Experimental Procedure

Participants were seated, with their chin supported by a rest, in front of a computer monitor (30 -inch; 1280×1024 pixel resolution; 105 cm from chin rest). A Polhemus motion tracking system (Colchester, VT, USA) was attached to their pronated right index finger and their arm was placed underneath a horizontally suspended wooden board, which prevented direct vision of the arm (Fig. 1 A, C). This was unlike the original Galea et al., (2011) study where participants used a digitised pen and wore goggles to prevent vision of their hand. The visual display consisted of a 1cm-diameter starting box, a green cursor (0.25 cm diameter) representing the position of their index finger, and a circular white target (0.33 cm diameter). For all experiments, targets appeared in 1 of 8 positions (45˚ apart) arrayed radially at 8 cm from the central start position. Targets were displayed pseudo-randomly so that every set of 8 consecutive trials (an "epoch") included 1 movement towards each target position. Participants controlled the green cursor on the screen by moving their right index finger across the table (Fig. 1A). At the beginning of each trial, participants were asked to move their index finger to the start position and a target then appeared. Participants were instructed to make a fast 'shooting' movement through the target such that online corrections were effectively prevented. At the moment the cursor passed through the invisible boundary circle (an invisible circle centred on the starting position with an 8 cm radius), the cursor was hidden and the intersection point was marked with a yellow square to denote the terminal (endpoint) error. In addition, a small square icon at the top of the screen changed colour based on movement speed. If the movement was completed within 100-300 msec, then it remained white. If the movement was slower than 300 msec, then the box turned red (too slow). Importantly, the participants were reminded that spatial accuracy was the main goal of the task. After each trial subjects moved back to the start, with the cursor only reappearing once they were within 2cm of the central start position.

Cerebellar transcranial direct current stimulation (ctDCS)

Anodal tDCS was delivered (NeuroConn, Germany) through two 5 x 5 cm^2 electrodes soaked in a saline solution (Wagner et al.). The anodal electrode was placed over the right cerebellar cortex, 3 cm lateral to the inion. The cathodal electrode (reference) was placed over the right buccinator muscle (Galea et al., 2011). At the onset of stimulation, current was increased in a ramp-like fashion over a period of 10 seconds. In the anodal groups, a 2 mA current (current density 0.08 A/cm^2) was applied for up to 25 minutes. As adaptation involved additional trials, cerebellar tDCS was applied for ~8 minutes longer than in the original study (Galea et al., 2011). In the sham groups, tDCS was ramped up over a period of 10 seconds, remained on for a further 10 seconds before being ramped down over 10 seconds. Participants were blinded to whether they received anodal or sham tDCS (table 1).

Experiment 1: vertical screen

The aim of experiment 1 was to replicate the findings of Galea et al., (2011). However, unlike the original Galea et al., (2011) study, participants did not use a digitising pen and did not wear goggles to prevent vision of their hand. 28 participants (8 male, 21 ± 4 yrs) were split into two groups (anodal/sham; 14 in each group) and exposed to 8 blocks of 96 trials (1 block = 12 repetitions of the 8 targets) during a reaching task in which the computer screen was placed in a vertical position (Fig. 1A). The first 2 blocks acted as baseline and consisted of veridical feedback with (pre 1) and without (pre 2) online visual feedback. During the no visual feedback trials, the target was visible, but once the subjects had moved out of the starting position the cursor indicating their hand position was hidden. In addition, subjects did not receive terminal feedback. Participants were instructed to continue to strike through the target. Following this, participants were exposed to 3 blocks (adapt 1-

3) of trials in which an abrupt 30° counter clockwise (CCW) visual rotation (VR) was applied. Finally, to assess retention, three blocks (post 1-3) were performed without visual feedback. TDCS was applied from the start of pre 2 until the end of adapt 3 and lasted for approximately 25 minutes (Fig. 1E).

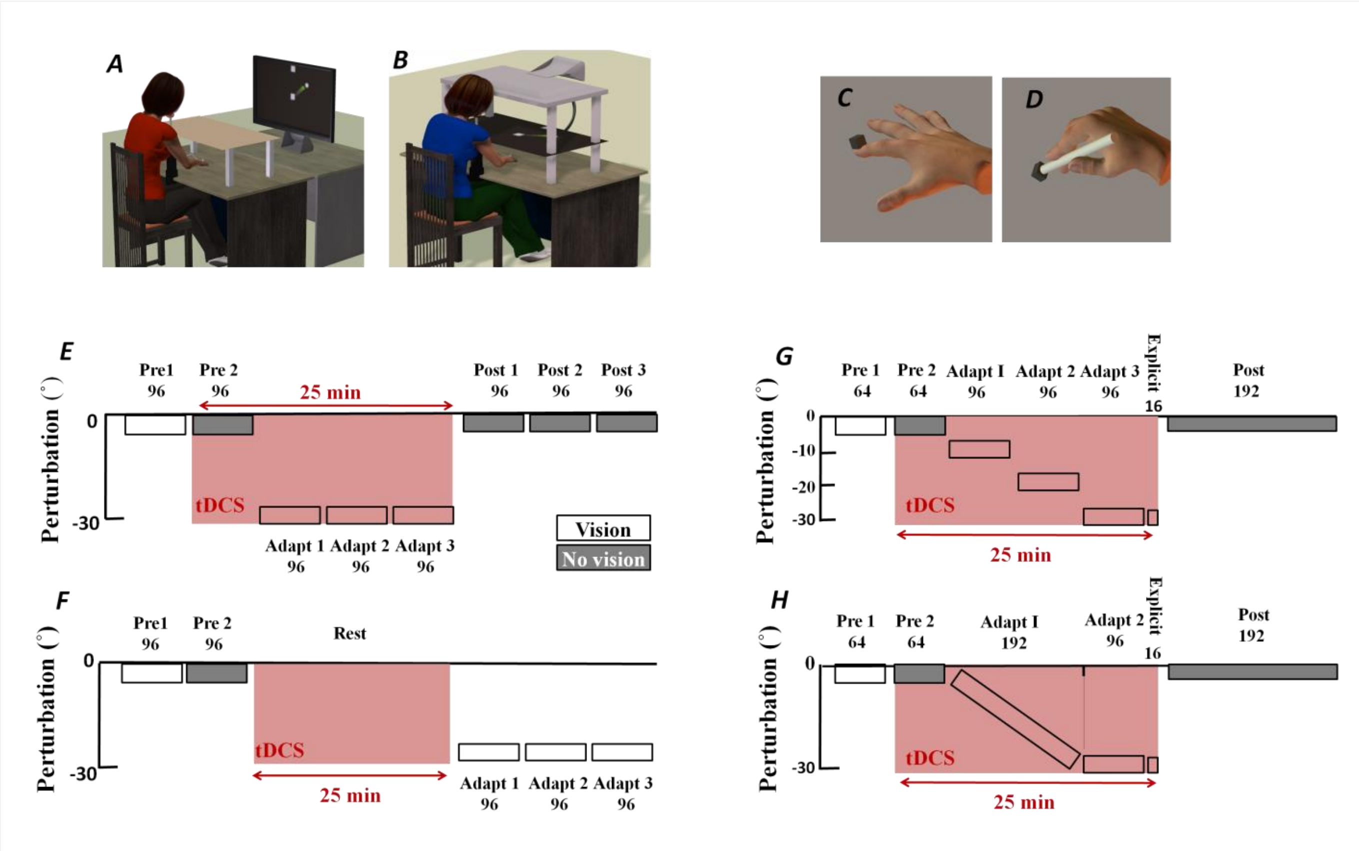

Fig. 1(A) Vertical screen set up; participants sat behind a table facing a vertically-orientated screen placed 105 cm in front of them **(B)** Horizontal screen set up; participants sat in front of a horizontally suspended mirror. The mirror prevented direct vision of the hand and arm, but showed a reflection of a computer monitor mounted above that appeared to be in the same plane as the hand. **(C)** Finger; Initial experiment started with the Polhemus sensor attached to the right index finger. **(D)** Pen tool**;** Sensor was attached to a pen-shape tool. Participants were asked to hold the top part of the pen. **(E)** Abrupt 30˚ visual rotation (VR) protocol: Following 2 baseline blocks (96 trials: pre 1-2), an abrupt 30˚ counter-clockwise VR was applied to the screen cursor and was maintained across 3 blocks (adapt 1-3). CtDCS (anodal/sham) was applied from pre 2 until adapt 3 (pink area). Following this, retention was examined by removing visual feedback (grey) for the final 3 blocks (post 1-3). **(F)** Offline ctDCS protocol: ctDCS (anodal/sham) was applied for 25 minutes during rest between pre 2 and adapt 1. Due to the length of the experiment, retention (no visual feedback blocks) was not examined. **(G)** Step adaptation protocol: Following 2 baseline blocks (64 trials: pre 1-2), a 30˚ VR was applied to the cursor in steps of 10˚ per block (96 trials: adapt 1-3). A short block (16 trials; explicit) followed this in which participants verbally reported their planned aiming direction. This is thought to measure the participant’s level of cognitive strategy (Taylor et al., 2014). Finally, retention was examined through one long block (192 trials) with no visual feedback. **(H)** Gradual adaptation protocol: A 30˚ VR was applied to the cursor gradually (0.156˚ per trial) across 192 trials. It was then maintained at 30˚ for 96 trials (Adapt). A short block (16 trials; explicit) followed this in which participants verbally reported their planned aiming direction. Finally, retention was examined through one long block (192 trials) with no visual feedback.

Experiment 2: horizontal screen

A large proportion of motor learning studies have been performed whilst the visual feedback is provided in the same plane as the movement e.g. (Shabbott and Sainburg, 2010). Therefore, experiment 2 investigated whether the positive influence of ctDCS on visuomotor adaptation was observed when the screen orientation was flipped to a horizontal position (Fig. 1B). 20 participants (5 male, 22 ± 4yrs) were split into two groups (anodal/sham; 10 in each group) and experienced an identical experimental protocol as in experiment 1 (Fig. 1E), except now the participants pointed with their semi-pronated right index finger underneath a horizontally suspended mirror. The mirror prevented direct vision of the hand and arm, but showed a reflection of a computer monitor mounted above that appeared to be in the same plane as the finger (Fig. 1B). Once again, participants controlled a cursor on the screen by moving their finger across the table.

Experiment 3: tool use

Several visuomotor studies have required participants to hold a digitising pen instead of a sensor attached to their finger (Galea et al., 2011, Schlerf et al., 2012). Therefore, in experiment 3 we changed the motion tracking arrangement so that the Polhemus sensor was attached to the bottom of a pen shaped tool (Fig. 1D). As a result, this was a closer replication of the task design used in Galea et al., (2011) than experiment 1. However, unlike Galea et al., (2011) participants did not wear googles that restricted vision of the hand. 27 subjects (2 male, 21 ± 4 yrs) were split into two groups (14 anodal/13 sham) and experienced an identical experimental protocol as experiment 1 (Fig. 1E; vertical screen) except that now participants controlled the cursor on the screen by holding the ‘pen’ and moving it across the surface of the table (Fig. 1D).

Experiment 4: offline cerebellar tDCS

Previous work has applied anodal ctDCS during rest and found both physiological and behavioural changes after the cessation of stimulation (Galea et al., 2009, Pope and Miall, 2012). This indicates that anodal ctDCS applied during rest (offline ctDCS) could have a beneficial effect on visuomotor adaptation tested after the cessation of stimulation. To examine this, 24 participants (7 male, 20 ± 4 yrs) were split into 2 groups (anodal/sham: 12 in each group) and experienced a 25 minute rest period between pre 2 and adapt 1. During this time, offline anodal ctDCS was applied (Fig. 1F) whilst participants sat quietly and kept their eyes open. In order to maintain a similar overall task length, retention (no visual feedback) was not assessed. All other task parameters (vertical screen, tDCS montage) were identical to experiment 1.

Experiment 5 and 6: step and gradual perturbation schedules

Visuomotor adaptation involves multiple learning mechanisms whose contribution to performance is determined by the task parameters (McDougle et al., 2015). For instance, McDougle suggest that large abrupt visual rotations reduce cerebellar-dependent learning from sensory-prediction errors and enhance strategic learning (development of a cognitive plan). In contrast, smaller gradual visual rotations are thought to bias responses towards sensory-prediction error learning. If true, then ctDCS should have a particularly beneficial effect on adaptation when the 30˚ visual rotation is introduced either through multiple small steps (visual rotation introduced in 3 steps of 10˚; Experiment 5) or a gradual paradigm (visual rotation is introduced gradually by 0.156˚ per trial; Experiment 6).

For experiment 5, 36 participants (1 male, 20 ± 1 yrs) were split into 2 groups (anodal/sham; 18 in each group). Following 2 baseline blocks (64 trials) with (pre 1) and without (pre 2) visual feedback, 3 adaptation blocks (96 trials; adapt 1-3) exposed participants to a 10°, 20°, and 30° CCW visual rotation (Fig. 1G). To examine the degree of cognitive strategy used by each participant, we included a task developed by Taylor et al., (2014). Specifically, following adapt 3, participants were asked to verbally report the direction they were aiming towards (Fig. 1G, explicit). For these trials (16 in total), the target was presented at the centre of a semi-circular arc of numbers displayed at 5° intervals. Those CW of the central target were labelled with negative numbers from 1-19, and those CCW of the central target were positive numbers from 1-19. Participants were asked to report which number they were planning to move their finger towards (McDougle et al., 2015, Bond and Taylor, 2015, Taylor et al., 2014). Once they had provided this verbal response, the numbers disappeared and the participants performed the reaching movement without visual feedback. If a participant was fully aware of the visual rotation, they would report reaching towards number -6 (30° CW). Whereas if they were unaware, participants would report aiming to 0 despite moving their finger 30° CW. Finally, a single block (192 trials) without visual feedback examined retention (post).

For experiment 6, 32 participants (4 male, 19 ± 1 yrs) were split into 2 groups (anodal/sham; 16 in each group). Following 2 baseline blocks (64 trials) with (pre 1) and without (pre 2) visual feedback, 1 long adaptation block (288 trials; adapt 1) involved the 30° CCW visual rotation being applied at rate of 0.156˚ per trial over 192 trials (Fig. 1H). The rotation was then maintained at 30° for a further 96 trials. Participant's level of cognitive strategy was again assessed (16 trials; explicit) after adaptation. Following this, one block of 192 trials without visual feedback examined retention (post).

Experiment 7: experiment 1 validation

Finally, we aimed to validate the results of experiment 1 by using the same task parameters in a new set of participants. Therefore, 26 participants (7 male, 21 ± 4yrs) were split into two groups (anodal/sham; 13 in each group) and exposed to the same protocol as utilised in experiment 1.

Data analysis

The 2-D index finger (X & Y) position data was collected at 120 Hz. For each trial, angular hand direction (°) was calculated as the difference between the angular hand position and angular target position at the point when the cursor intersected an 8-cm invisible circle centred on the starting position. During veridical feedback, the goal was for hand direction to be 0°. However, with a visuomotor rotation, hand direction had to compensate; that is, for a −30° (CCW) visuomotor rotation, a hand direction of +30° (CW) relative to the target was required. Positive values indicate a CW direction, whereas negative values indicate a CCW direction. In addition, reaction time (RT: difference between target appearing and the participant moving out of the start position) and movement time (MT: difference between reaction time and movement end) were calculated for each trial. We removed any trial in which hand direction, RT or MT exceeded 2.5 standard deviations above the group mean. This accounted for 8.78 ± 3.04% of trials. One participant in experiment 4 was removed from the study as a result of failing to follow the task instructions.

Epoch averages were created by binning 8 consecutive movements, 1 towards each target. For each participant, average hand direction was calculated for each target position for pre1 (vision baseline) and pre2 (no vision baseline). These values were then subtracted to trial-by-trial performance to that particular target in each visual feedback condition (Δ hand direction). Specifically, pre1 was subtracted away from adaptation performance and pre2 was subtracted away from retention performance. For baseline, we averaged hand direction across all epochs of pre1 and pre2 and compared the anodal and sham groups' using 2-tailed independent sampled t-tests. For adaptation, we initially compared Δ hand direction in the first trial of adapt 1 to ensure all participants experienced a similar initial error in response to the visuomotor rotation. We then calculated an average across all the epochs of adaptation excluding epoch 1. We believe this best represented the total amount of adaptation expressed by each participant. For retention, we averaged Δ hand direction across all the epochs of retention. For each experiment, the anodal and sham groups were compared using 2-tailed independent sampled t-tests. The threshold for all statistical comparisons was $P < 0.05$. Effect sizes are reported as Cohen's *d*. All data presented represent mean ± standard error of the mean, unless otherwise specified. Data and statistical analysis was performed using MATLAB (The MathWorks, USA) and SPSS (IBM, USA).

Results

Experiment 1: vertical screen

Despite a slightly different set up from Galea et al., (2011), we showed that anodal ctDCS led to a greater amount of adaptation relative to sham ctDCS (Fig. 2 & 3). First, both groups behaved similarly during baseline with there being no significant differences between groups during pre1 or pre 2 (Table 2). In addition, when initially exposed to the 30° VR, both groups showed a similar level of performance during the first trial of adapt 1 (Table 2). However, following this, the anodal group displayed a greater amount of adaptation to the VR compared to the sham group ($t_{(26)}$= 2.9, p=0.007, *d*=1.17). Retention in the anodal group appeared to be greater than in the sham group; however this did not reach statistical significance ($t_{(26)}$=1.2, p=0.24, *d*=0.4). There were no significant differences between groups for either RT or MT during adaptation or retention (Table 3).

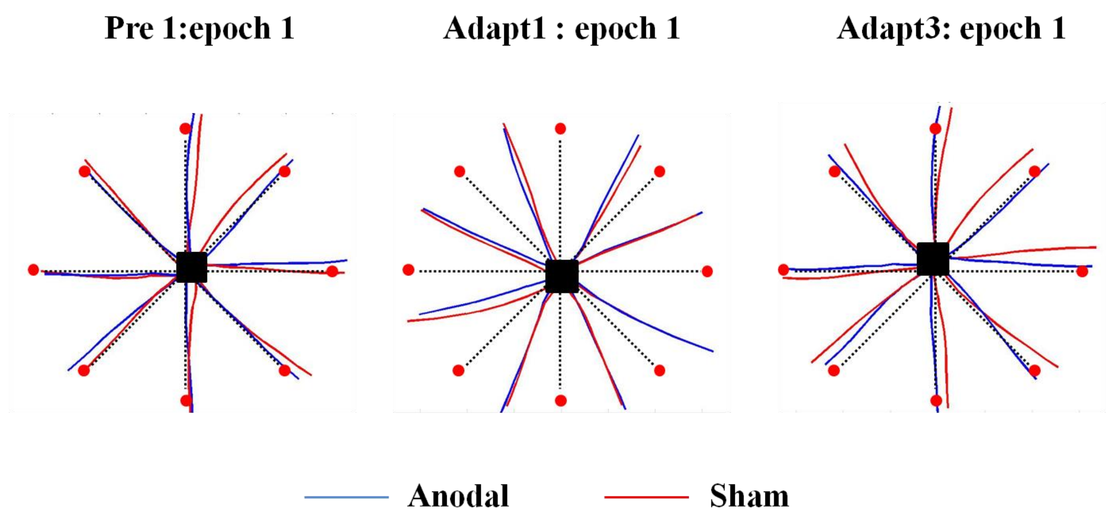

Fig 2. Kinematic data for two sample participants in experiment 1 (blue = anodal; red = sham). Both participants performed similarly during pre 1 (left). In addition, they showed similar initial error when exposed to the 30 degree CCW visual rotation (middle). However, by the end of adaptation the participant in the anodal group displayed a reduced amount of error in their movement trajectories (right).

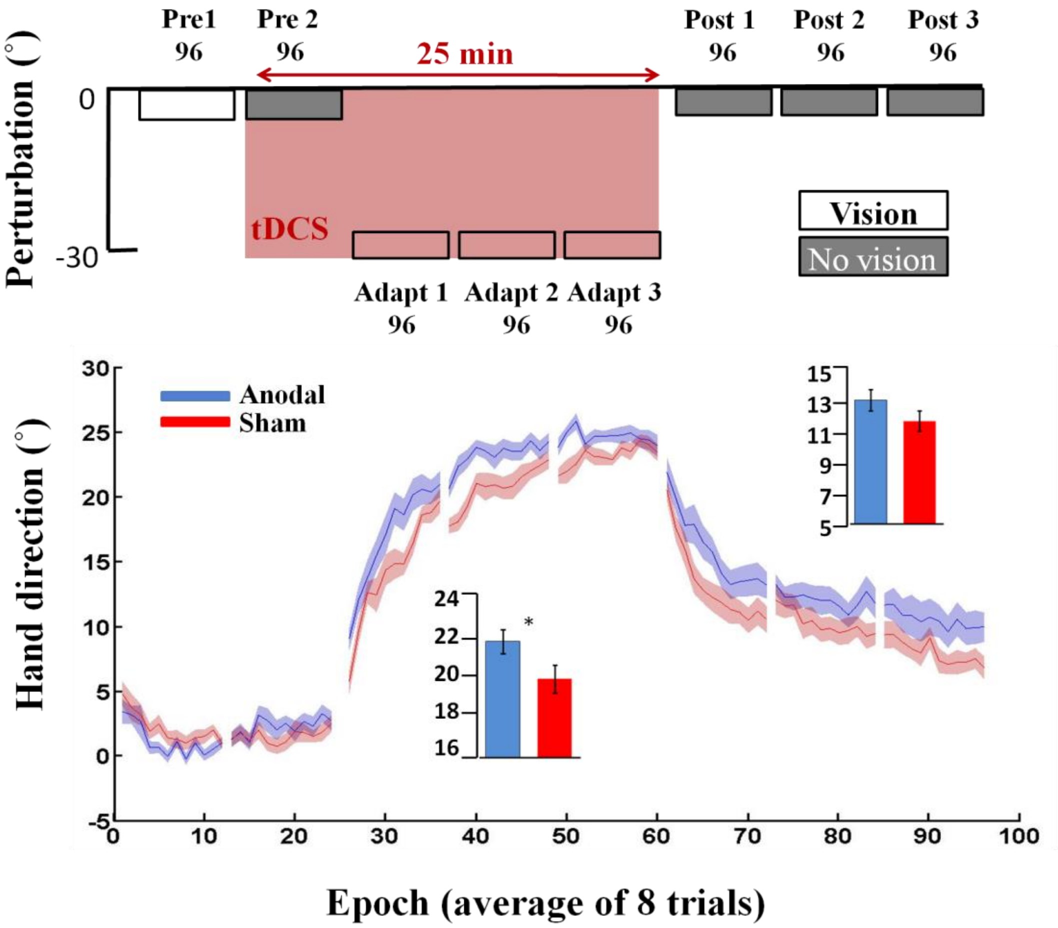

Fig. 3 Experiment 1: Vertical screen. Epoch (average across 8 trials) uncorrected angular hand direction (˚) data for the anodal (blue) and sham (red) ctDCS groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3) and retention (post 1-3). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Solid lines, mean; shaded areas/error bars, S.E.M. There was significant difference between the anodal and sham ctDCS groups (14 in each group) during adaptation ($t_{(26)}$= 2.9, p=0.007, *d*=1.17).

Experiment 2: horizontal screen

In experiment 2, an identical stimulation and testing protocol as experiment 1 was used; however now the visual feedback was in the same plane as the movement (horizontal screen). Surprisingly, anodal ctDCS was no longer associated with greater adaptation (Fig. 4). First, we found no significant differences between groups for pre 1, pre 2 or the first trial of adapt 1 (Table 2). In addition, there were no significant differences between the anodal or sham groups during adaptation

($t_{(18)}$=-0.005, p=0.9, d=0.00; Fig. 4) or retention ($t_{(18)}$=0.39, p=0.69, d=0.14). Finally, there were no significant differences between groups for either RT or MT during adaptation or retention (Table 3).

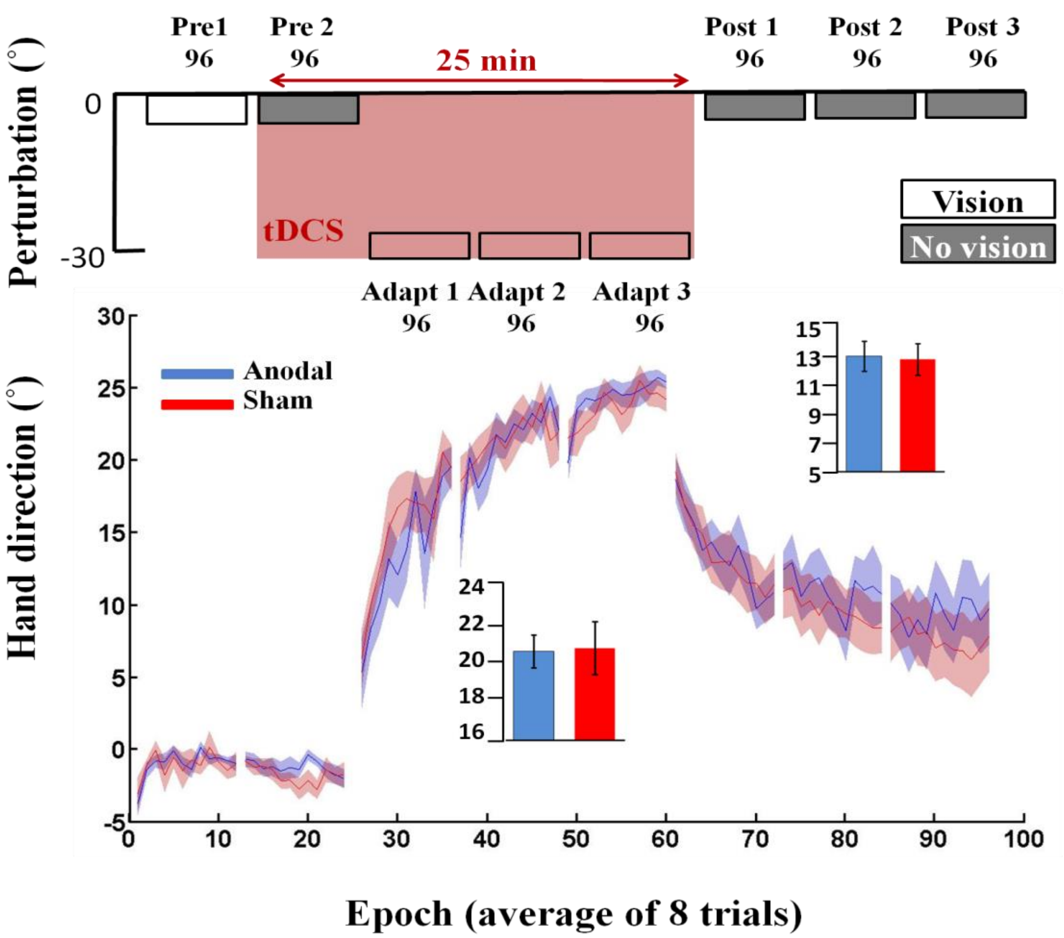

Fig. 4 Experiment 2: Horizontal screen. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3) and retention (post 1-3). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Performance of both groups was identical. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (10 in each group) during adaptation ($t_{(18)}$=-0.005, p=0.9, d=0.00).

Experiment 3: tool

In experiment 3 participants once again experienced an identical protocol as experiment 1; however, instead of performing the task with the sensor attached to their index finger, they held a digitising pen. This experimental manipulation led to the anodal and sham ctDCS groups behaving similarly across all experimental blocks (Fig. 5). Specifically, there were no significant differences between groups during pre 1, pre 2 or the first trial of adapt 1 (Table 2). In addition, no significant differences were observed during adaptation ($t_{(25)}$=- 0.28, p=0.78, d=0.09; Fig. 5) or retention ($t_{(25)}$= -1.15, p=0.13, d=0.6). Finally, there were also no significant differences between groups for either RT or MT during adaptation or retention (Table 3).

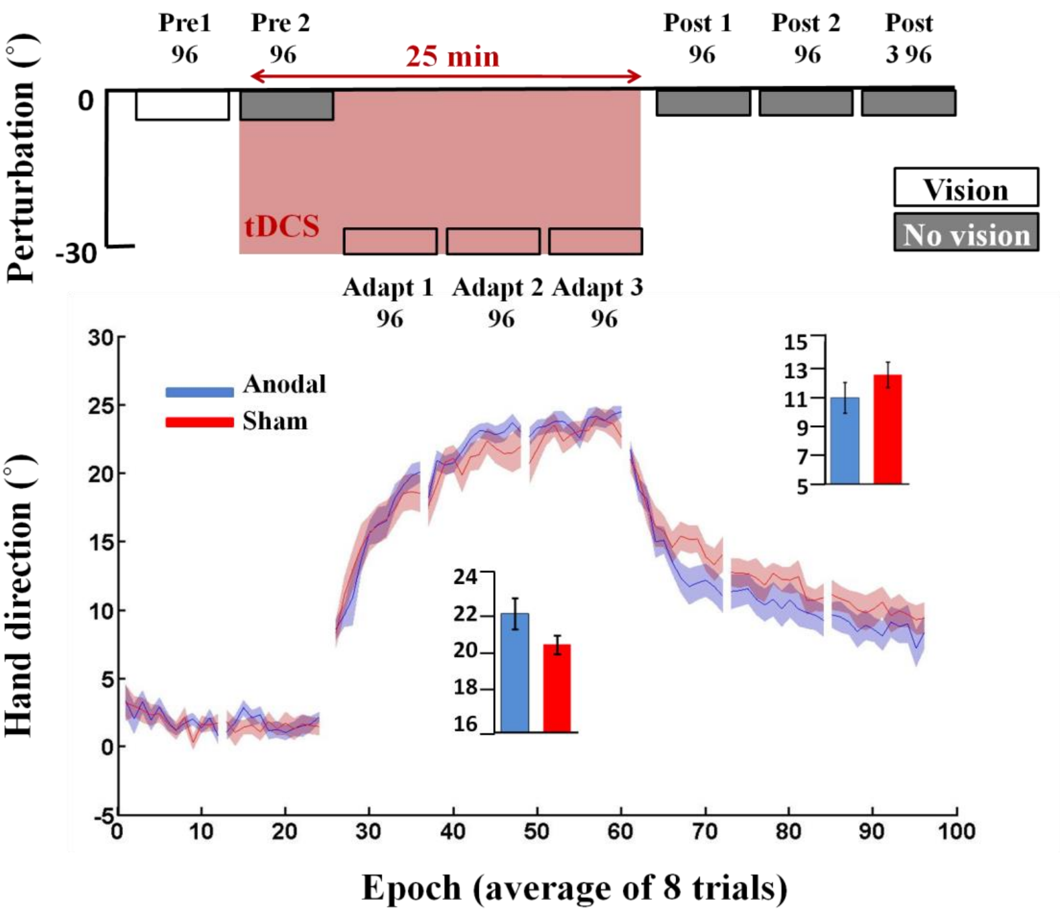

Fig. 5 Experiment 3: tool. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3) and retention (post 1-3). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (14 anodal/13 sham) during adaptation ($t_{(25)}$=- 0.28, p=0.78, d=0.09).

Experiment 4: offline cerebellar tDCS

Next, experiment 4 examined whether ctDCS applied offline (during 25 mins of rest) had a beneficial effect on subsequent visuomotor adaptation. Contrary to our predictions, offline anodal ctDCS did not cause greater adaptation relative to offline sham ctDCS (Fig. 6). Unfortunately, there was a significant difference between groups during pre 1, suggesting a small variation (approx. 1˚) in baseline performance between groups. However, after correcting the baseline, there was no significant difference between the anodal and sham ctDCS groups during adaptation ($t_{(21)}$=0.37, p=0.71, d=0.15). Lastly, there were no significant differences between groups for either RT or MT during adaptation or retention (Table 3). Because of the extended rest period prior to the adaptation phase (Fig. 6), this experiment did not include a retention block.

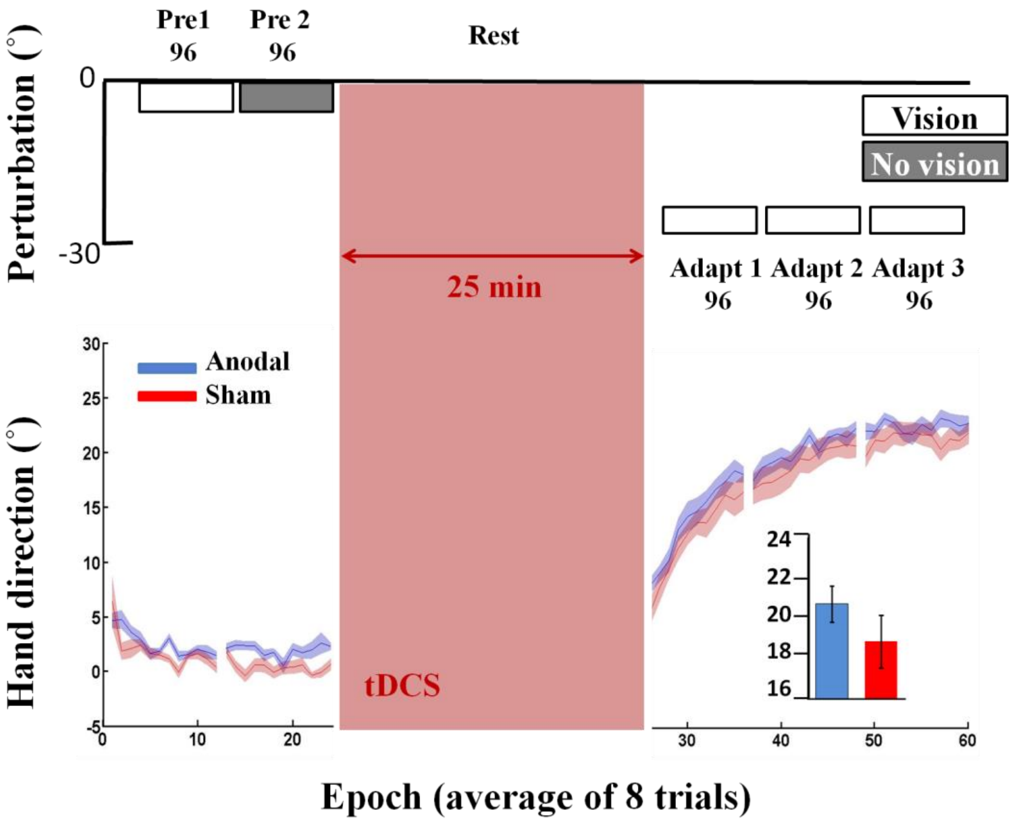

Fig. 6 Experiment 4: offline cerebellar tDCS. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3). This was determined for each participant by averaging consecutive epochs. Independent t-tests compared these values between groups. There was a clear difference between groups during pre 1. However, there were no significant differences between groups during adaptation when using either hand direction. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (12 anodal/ 11 sham) during adaptation ($t_{(21)}$=0.37, p=0.71, d=0.15).

Experiment 5 & 6: step and gradual perturbation schedules

Finally, experiments 5 and 6 tested whether anodal ctDCS was more effective when the 30˚ visual rotation was introduced either with a stepped (visual rotation was introduced in three steps of 10˚; Experiment 5) or gradual paradigm (visual rotation was introduced gradually by 0.156˚ per trial; Experiment 6). However, once again, we found no significant effect of anodal ctDCS on adaptation (Fig. 7 and 8).

In experiment 5, there were no significant differences between the anodal and sham groups during pre 1, pre 2 or when initially exposed to the 10˚ VR (Table 2). In addition, no significant differences were observed across adaptation ($t_{(34)}$=-0.35, p=0.72, d=0.1; Fig. 7) or retention ($t_{(34)}$=-0.9, p=0.37, d=0.3). To examine the degree of cognitive strategy used by each participant, after adapt 3 we asked participants to verbally report the direction they were aiming towards (Fig. 1G, explicit). Despite displaying a hand direction of approximately 20-25˚ (Fig. 7), both groups reported a similar aiming direction towards the target (Anodal explicit report: 1.7±2.1°, Sham: 1.4±4.1°, independent t-test $t_{(34)}$=0.47, p=0.64, d=0.09). This indicates that all participants had developed only a minimal cognitive aiming strategy. During this explicit block, although there was no significant difference between groups for Δ hand direction ($t_{(34)}$=-1.8, p=0.07, d=0.61), there did appear to be a trend for the anodal group to display reduced hand direction relative to the sham group (Fig 7). In addition, there were no significant differences between groups for either RT or MT during adaptation or retention (Table 3).

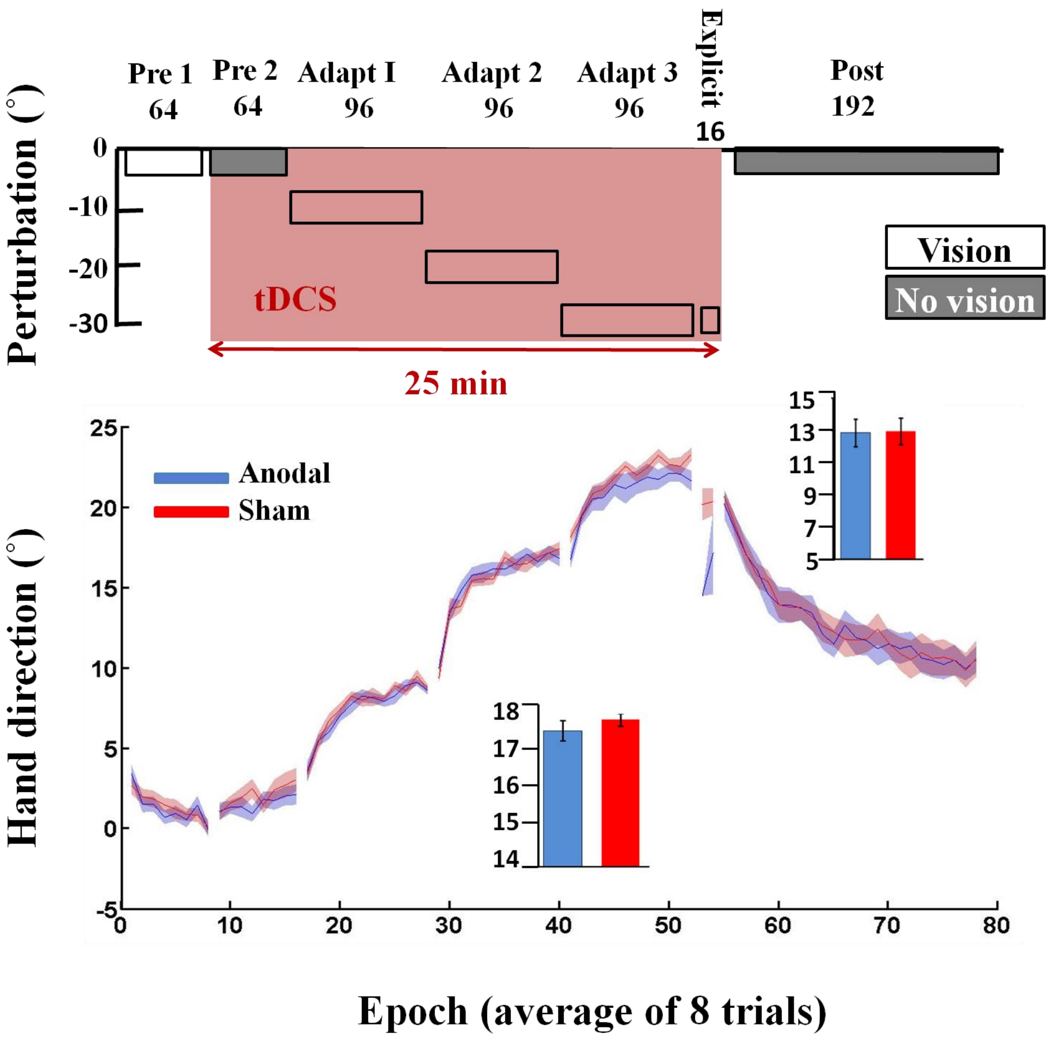

Fig. 7 Experiment 5: step perturbation schedule. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3) and retention. This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Performance of the anodal and sham groups was identical throughout the experiment. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (18 in each group) during adaptation ($t_{(34)}$=-0.35, p=0.72, d=0.1).

In experiment 6, there was a significant difference between groups during pre 1 (Table 2), suggesting a small variation (1°) in baseline performance between groups. Again, to account for these differences, we subtracted each participant's average hand direction during pre 1 from their subsequent performance, there was no significant difference between the anodal and sham ctDCS groups during adaptation ($t_{(30)}$=0.01, p=0.9, *d*=0.00; Fig 8) or retention ($t_{(30)}$= -1.00, p=0.3, *d*=0.35).

Similarly to experiment 5, despite displaying a hand direction of approximately 20-25° (Fig. 8), both groups reported a similar aiming direction towards the target (Anodal: 0.64±1.5°, Sham: 0.37±0.7°, independent t-test ($t_{(30)}$=0.67, p=0.51, d=0.23). This indicates that all participants had developed only a minimal cognitive aiming strategy. During this block, there was also no significant difference between groups for actual Δ hand direction ($t_{(30)}$= -0.9, p=0.4, *d*=0.3). There were no significant differences between groups for either RT or MT during adaptation or retention (Table 3).

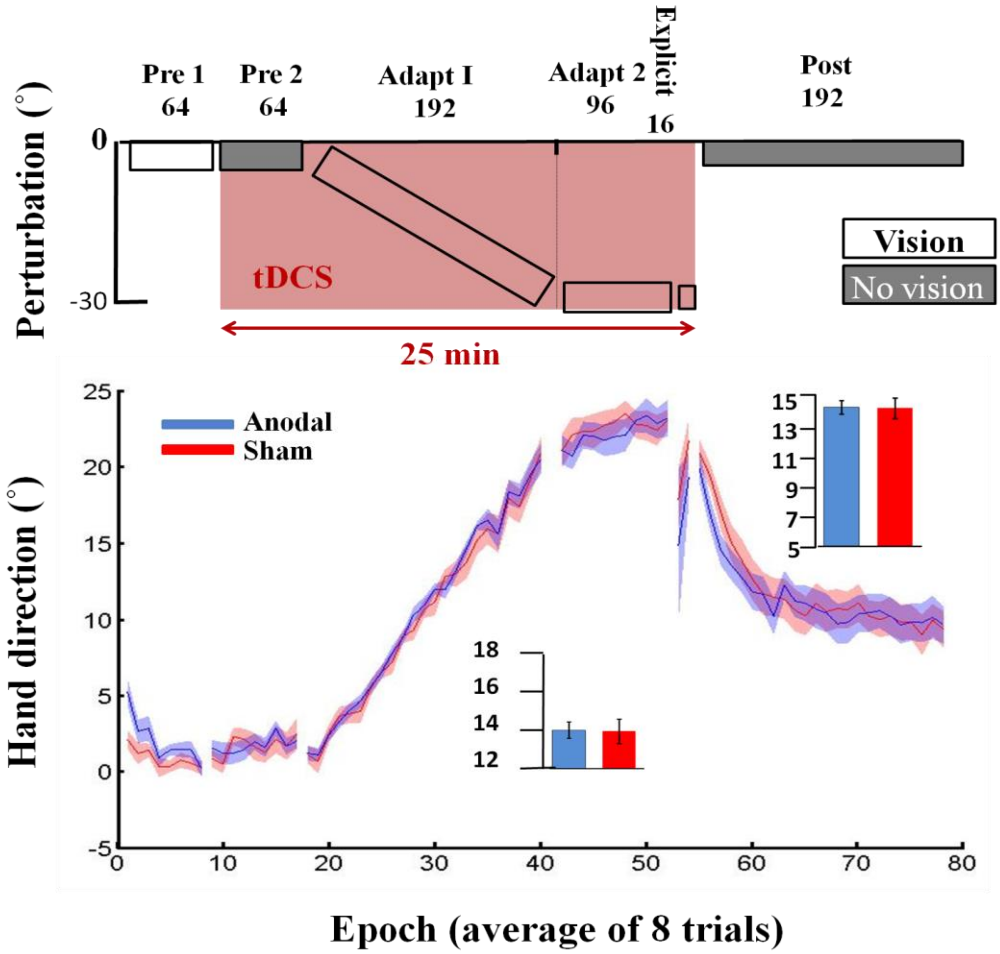

Fig. 8 Experiment 6: gradual perturbation schedule. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation blocks and retention (post). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Performance of the anodal and sham groups was identical throughout the experiment. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (16 in each group) during adaptation ($t_{(30)}$=0.1, p=0.9, *d*=0.00).

Experiment 7: experiment 1 validation

To validate our only positive result, we repeated experiment 1 with 2 new groups (anodal/sham) of naive participants. Unfortunately, we found no significant difference between the anodal and sham ctDCS groups. There were no significant differences between groups during pre 1, pre 2 or when initially exposed to the 30˚ VR (Table 2). In addition, there were no differences between groups across adaptation ($t_{(24)}$=-2.5, p=0.8, d=0.1; Fig. 9) or retention ($t_{(24)}$=0.23, p=0.8, d=0.1). Finally, there were no significant differences between groups for either RT or MT during adaptation or retention (Table 3).

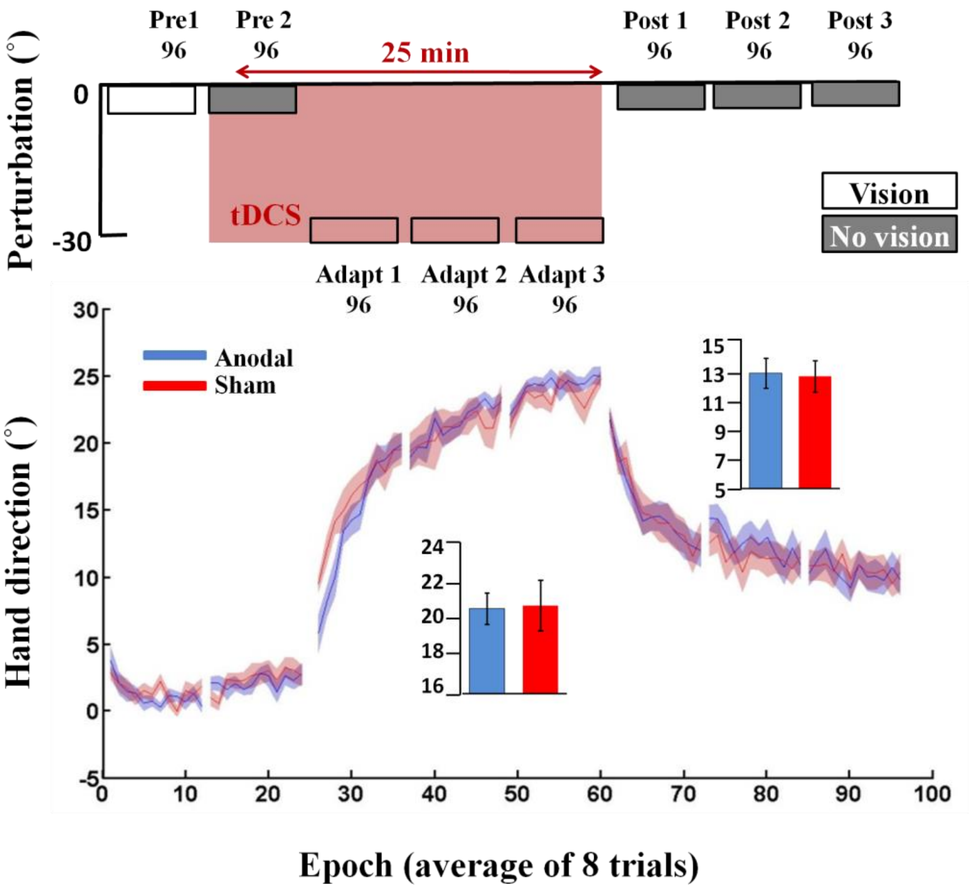

Fig. 9 Experiment 7: experiment 1 validation. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation blocks and retention (post). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Performance of the anodal and sham groups was identical throughout the experiment. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (13 in each group) during adaptation ($t_{(24)}$=-2.5, p=0.8, d=0.1).

Despite the differences between the current experimental set up and Galea et al., (2011), such as number of trials, duration of tDCS and use of tool, we pooled data across experiments 1 and 2 from Galea et al., (2011) and experiments 1,3 and 7 from the current study. For each participant, we calculated an average Δ hand direction across all adaptation epochs, excluding epoch 1 and performed an independent t-test between the pooled anodal (n=61) and sham (n=60) groups. This pooled data showed a significant difference between anodal (20.1± 2.9) and sham ctDCS (17.5± 4.1; $t_{(119)} = 3.9$, $p = 0.0005$, $d = 0.7$). Interestingly though, the effect size was substantially smaller than the positive results found in experiment 1.

Self-reported ratings of attention, fatigue, and sleep

There were no significant differences between groups across all experiments for the self-reported ratings of attention, fatigue and quality of sleep (table 1).

Discussion

Across all seven experiments, participants showed a clear ability to adapt to the novel visuomotor rotation. In experiment 1, we were able to show that anodal cerebellar tDCS caused a greater amount of adaptation relative to sham tDCS; however, this did not hold when we repeated the same experiment with a new set of participant (experiment 7). Although similar, these experiments differed to the original Galea et al., (2011) study in which participants used a digitised pen and wore goggles to prevent vision of the hand. When manipulating experimental parameters such as screen orientation (experiment 2), use of a tool (experiment 3), tDCS timing (experiment 4) and the perturbation schedule (experiments 5 and 6), we found anodal cerebellar tDCS to have no effect on visuomotor adaptation.

tDCS did not enhance visuomotor adaptation when using a horizontal screen

Although the facilitatory effect of cerebellar tDCS on motor learning has been shown across visuomotor adaptation (Galea et al., 2011), force-field adaptation (Herzfeld et al., 2014), locomotor adaptation (Jayaram et al., 2012), saccade adaptation (Panouilleres et al., 2015, Avila et al., 2015), motor skill learning (Cantarero et al., 2015) and language prediction tasks (Miall et al., 2016), the sensitivity of this effect to specific task parameters had not been previously documented. As a large proportion of motor learning studies are performed whilst the visual feedback is provided in the same plane as the movement (Shabbott and Sainburg, 2010, Herzfeld et al., 2014), we were first motivated to examine whether the positive influence of tDCS on visuomotor adaptation can be observed when the screen orientation was flipped to a horizontal position. Thus experiment 1 and 2 addressed this issue by first replicating the screen display used in Galea et al. (2011), and then showing that tDCS was not associated with greater adaptation in the more typical in-plane feedback condition. The posterior part of the cerebellum is important for visuomotor adaptation (Rabe et al., 2009) and heavily connected with the posterior parietal cortex (O'Reilly et al., 2010), which is crucial for visuomotor control (Culham et al., 2006). As modelling studies suggest cerebellar tDCS mainly activates the posterior part of the cerebellum (Ferrucci et al., 2012, Parazzini et al., 2014, Rampersad et al., 2014), the increased visuomotor complexity and presumed greater reliance on the posterior cerebellum with a vertical screen orientation may optimise the effects of cerebellar tDCS on visuomotor adaptation.

tDCS did not improve visuomotor adaptation even when participants used a tool

Next, we were unable to replicate the original Galea et al., (2011) study where participants held a tool/digitizing pen (Galea et al., 2011; Block et al., 2012). Although experiment 3 was a closer replication of Galea et al., (2011) than experiment 1 and 7, participants still did not wear googles to restrict vision of the hand. While not significant, Figure 5 does suggest there was a trend towards the anodal tDCS group adapting by a greater amount.

tDCS after-effect did not affect visuomotor adaptation

It has also been reported that anodal cerebellar tDCS applied during rest can lead to both physiological and behavioural changes over a period of 10-30 minutes after the cessation of stimulation (Galea et al., 2009, Pope and Miall, 2012). This indicates that the after-effect of cerebellar tDCS could have a beneficial effect on visuomotor adaptation. However, following 25 minutes of offline anodal cerebellar tDCS, we found no observable differences between the anodal and sham groups. One significant issue is that despite having neurophysiological evidence regarding the changes associated with offline cerebellar tDCS (Galea et al., 2009), no such data exists for its online effects. Therefore, we currently do not know whether the online and offline effects of cerebellar tDCS are consistent or whether one is more potent than the other.

tDCS did not enhance adaptation when the perturbation was applied gradually

The contribution of the cerebellum to abrupt and gradual perturbation paradigms is an area of continued interest within the motor adaptation literature. For example, Criscimagna-Hemminger et al., (2013) showed cerebellar-lesion patients were unable to adapt to abrupt perturbations but preserved the capacity to adapt to gradual perturbations. Similarly, Schlerf et al., (2012) reported modulation of cerebellar excitability for abrupt, but not gradual, visuomotor adaptation (Schlerf et al., 2012). However, Gibo et al., 2013 showed that cerebellar-lesion patients may use non-cerebellar strategic learning to successfully adapt (Gibo et al., 2013). In line with this argument, other recent work suggests that large abrupt visual rotations reduce cerebellar-dependent sensory-prediction error learning and enhance strategic learning, whilst smaller visual rotations bias learning towards sensory-prediction error learning (McDougle et al., 2015, Bond and Taylor, 2015, Taylor et al., 2014). This suggests that cerebellar tDCS may have been more effective with small or gradual perturbation schedules. However, we found that tDCS did not show any significant effect on adaptation when the perturbation was applied in small steps (experiment 5) or gradually (experiment 6).

The positive effect of cerebellar tDCS in experiment 1 was not replicated

Finally, we wanted to see whether the positive effect of cerebellar tDCS on visuomotor adaptation observed in experiment 1 could be replicated in a new set of naïve participants. Unfortunately, this positive effect was not observed, with experiment 7 showing no significant difference between the anodal and sham tDCS groups during adaptation. This suggests that the positive effects of cerebellar tDCS in experiment 1 were either observed by chance or that the effect size of cerebellar tDCS is significantly smaller than one might imagine. Although our sample sizes (10-15 per group) were in the range of previously published tDCS papers (Galea et al., 2011, Cantarero et al., 2015, Hardwick and Celnik, 2014, Block and Celnik, 2013), a recent study indicates this could be significantly under powered (Minarik et al., 2016). Minarik et al., in 2016 showed that with a suggested tDCS effect size of 0.45, the likelihood of observing a significant result with 14 participants (per group) was approximately 20%. To examine this further, we pooled data across experiments 1 and 2 from Galea et al., (2011) and experiments 1, 3 and 7 from the current study. This pooled data showed a significant difference between anodal and sham ctDCS however, the effect size was substantially smaller (0.6) than what was initially observed in experiment 1. At present it is difficult to determine a true effect size for not only cerebellar tDCS, but tDCS in general due to the clear publication bias in the literature towards positive effects. Through informal discussion with many colleagues, it is clear that researchers are observing null effects with cerebellar tDCS, but have so far been slow to publish these results. Although this is beginning to change (Steiner et al., 2016, A. Mamlins, 2016, Westwood SJ, 2016), we believe a more accurate representation of the effect size, and so the required participant numbers, of cerebellar tDCS will only be achieved if null results are published more often.

Another possible limitation with the current design is the use of a between-subject paradigm. Previous work has shown large inter-individual variation in motor learning rates (Stark-Inbar et al., 2017), implementation of motor learning processes (Christou et al., 2016) and responsivity to stimulation (Wiethoff et al., 2014). These factors may all negatively affect our ability to observe consistent between-subject tDCS differences in motor learning. Although a within-subject design would overcome many of these issues, it would also introduce the substantial problem of carry-over effects being observed with visuomotor adaptation weeks after initial exposure (Krakauer, 2009).

Future direction

Our results indicate that for cerebellar tDCS to become an effective tool, technical advances must be identified that improve the strength and consistency of its effect on functional tasks. For example, the common assumption is to that currents of 1-2mA are effective (Woods et al., 2016). However, previous work has used currents of up to 5mA on other brain areas (Furubayashi et al., 2008, Hammerer et al., 2016, Bonaiuto and Bestmann, 2015), suggesting greater current intensities are possible with cerebellar tDCS. Alternatively, there is exciting work suggesting high-definition tDCS combined with computational modelling of the brain's impedances can lead to exact predictions regarding the behavioural results associated with tDCS (Furubayashi et al., 2008, Hammerer et al., 2016, Bonaiuto and Bestmann, 2015). It is possible that using high-definition tDCS along with computational modelling to optimise electrode placement could enhance the magnitude and reliability of the tDCS effect on the cerebellum (Kuo et al., 2013).

Conclusion

In conclusion, we failed to find a consistent effect of cerebellar tDCS on visuomotor adaptation. Although initially replicating previous reports of cerebellar tDCS enhancing visuomotor adaptation, we found this not to be consistent across varying task parameters, nor reproducible in a new group of participants. We believe these results highlight the need for substantially larger group sizes for tDCS studies, and may call into question the validity of using cerebellar tDCS within a clinical context where a robust effect across behaviours would be required.

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Disclosures

Authors have no conflict of interest, financial or otherwise.

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Figure captions

Fig. 1(A) Vertical screen set up; participants sat behind a table facing a vertically- orientated screen placed 105 cm in front of them **(B)** Horizontal screen set up; participants sat in front of a horizontally suspended mirror. The mirror prevented direct vision of the hand and arm, but showed a reflection of a computer monitor mounted above that appeared to be in the same plane as the hand. **(C)** Finger; Initial experiment started with the Polhemus sensor attached to the right index finger. **(D)** Pen tool**;** Sensor was attached to a pen-shape tool. Participants were asked to hold the top part of the pen. **(E)** Abrupt 30˚ visual rotation (VR) protocol: Following 2 baseline blocks (96 trials: pre 1-2), an abrupt 30˚ VR was applied to the screen cursor and was maintained across 3 blocks (adapt 1-3). ctDCS (anodal/sham) was applied from pre 2 until adapt 3 (pink area). Following this, retention was examined by removing visual feedback (grey) for the final 3 blocks (post 1-3). **(F)** Offline ctDCS protocol: ctDCS (anodal/sham) was applied for 25 minutes during rest between pre2 and adapt 1. Due to the length of the experiment, retention (no visual feedback blocks) was not examined. **(G)** Step adaptation protocol: Following 2 baseline blocks (64 trials: pre 1-2), a 30˚ VR was applied to the cursor in steps of 10˚ per block (96 trials: adapt 1-3). A short block (16 trials; explicit) followed this in which participants verbally reported their planned aiming direction. This is thought to measure the participant's level of cognitive strategy (Taylor et al., 2014). Finally, retention was examined through one long block (192 trials) with no visual feedback. **(H)** Gradual adaptation protocol: A 30˚ VR was applied to the cursor gradually (0.156˚ per trial) across 192 trials. It was then maintained at 30˚ for 96 trials (Adapt). A short block (16 trials; explicit) followed this in which participants verbally reported their planned aiming direction. Finally, retention was examined through one long block (192 trials) with no visual feedback.

Fig 2. Kinematic data for two sample participants in experiment 1 (blue = anodal; red = sham). Both participants performed similarly during pre 1 (left). In addition, they showed similar initial error when exposed to the 30 degree CCW visual rotation (middle). However, by the end of adaptation the participant in the anodal group displayed a reduced amount of error in their movement trajectories (right).

Fig. 3 Experiment 1: Vertical screen. Epoch (average across 8 trials) uncorrected angular hand direction (˚) data for the anodal (blue) and sham (red) ctDCS groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3) and retention (post 1-3). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Solid lines, mean; shaded areas/error bars, S.E.M. There was significant difference between the anodal and sham ctDCS groups (14 in each group) during adaptation ($t_{(26)}$= 2.9, p=0.007, *d*=1.17).

Fig. 4 Experiment 2: Horizontal screen. Epoch (average across 8 trials) uncorrected angular hand direction (⁰) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3) and retention (post 1-3). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Performance of both groups was identical. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (10 in each group) during adaptation ($t_{(18)}$=-0.005, p=0.9, d=0.00).

Fig. 5 Experiment 3: tool. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3) and retention (post 1-3). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (14 anodal/13 sham) during adaptation ($t_{(25)}$=- 0.28, p=0.78, d=0.09).

Fig. 6 Experiment 4: offline cerebellar tDCS. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3). This was determined for each participant by averaging consecutive epochs. Independent t-tests compared these values between groups. There was a clear difference between groups during pre 1. However, there were no significant differences between groups during adaptation when using either hand direction. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (12 anodal/ 11 sham) during adaptation ($t_{(21)}$=0.37, p=0.71, d=0.15).

Fig. 7 Experiment 5: step perturbation schedule. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation (adapt 1-3) and retention. This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Performance of the anodal and sham groups was identical throughout the experiment. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (18 in each group) during adaptation ($t_{(34)}$=-0.35, p=0.72, d=0.1).

Fig. 8 Experiment 6: gradual perturbation schedule. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation blocks and retention (post). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Performance of the anodal and sham groups was identical throughout the experiment. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (16 in each group) during adaptation ($t_{(30)}$=0.1, p=0.9, *d*=0.00).

Fig. 9 Experiment 7: experiment 1 validation. Epoch (average across 8 trials) uncorrected angular hand direction (°) data for the anodal (blue) and sham (red) groups. Positive values indicate CW hand direction. Bar graphs inset indicate mean hand direction for the anodal and sham groups during adaptation blocks and retention (post). This was determined for each participant by averaging consecutive epochs (see Methods). Independent t-tests compared these values between groups. Performance of the anodal and sham groups was identical throughout the experiment. Solid lines, mean; shaded areas/error bars, S.E.M. There was no significant difference between the anodal and sham ctDCS groups (13 in each group) during adaptation ($t_{(24)}$=-2.5, p=0.8, d=0.1).

Tables

Table 1 Self-reported rate of attention, fatigue, quality of sleep (1 is poorest and 7 is the maximal), perceived tDCS as active (1) or placebo (0) and sleep hours. All the values are averaged and compared using independent t-test across the whole experiments and presented as mean ± standard deviation (SD).

Experiment 1	attention	Fatigue	Sleeping hours	Quality of sleep	Active or placebo
Anodal	5.3 ± 1.2	4.1 ± 1.4	7.3 ± 1.6	4.6 ± 1.8	0.9 ± 0.3
Sham	4.6 ± 1.1	3.7 ± 1.5	7.2 ± 1.6	4.7 ± 1.7	0.7 ± 0.5
T-test	$t_{(25)}$= 1.5, p = 0.1	$t_{(25)}$= 0.8, p = 0.5	$t_{(25)}$= 0.2, p = 0.8	$t_{(25)}$= 0.1, p= 0.9	$t_{(25)}$ = 1.4, p= 0.2
Experiment 2					
Anodal	5.9 ± 1	3.3 ± 1.6	7.7 ± 1.6	5.3 ± 1.1	0.9 ± 0.3
Sham	5.2 ± 1.2	3.8 ± 1.7	7.4 ± 2.8	5.4 ± 0.5	1 ± 0
T-test	$t_{(18)}$= 1.3, p = 0.2	$t_{(18)}$= 0.6, p = 0.5	$t_{(18)}$= 0.4, p = 0.7	$t_{(18)}$= 0.4, p = 0.7	$t_{(18)}$= 0.9, p = 0.4
Experiment 3					
Anodal	5.0 ± 1.1	3.9 ± 1.6	8.0 ± 1.0	5.3 ± 1.0	0.8 ± 0.4
Sham	5.4 ± 1.3	4.0 ± 1.5	7.4 ± 1.4	5.3 ± 1.1	0.7 ± 0.5
T-test	$t_{(22)}$= 0.6, p = 0.5	$t_{(22)}$= 0.6, p = 0.8	$t_{(22)}$= 0.4, p = 0.1	$t_{(22)}$= 0.4, p = 0.8	$t_{(22)}$= 0, p = 1.0
Experiment 4					
Anodal	5.6 ± 1	2.7 ± 1	6.9 ± 1.2	5.1 ± 1.2	0.9 ± 0.3
Sham	5.8 ± 1	2.8 ± 1	7.0 ± 1.3	5.0 ± 1.8	0.8 ± 0.4
T-test	$t_{(19)}$= 0.5, p = 0.6	$t_{(19)}$= 0.04, p = 0.9	$t_{(19)}$= 0.2, p = 0.8	$t_{(19)}$= 0.1, p = 0.9	$t_{(19)}$= 0.9, p = 0.4
Experiment 5					
Anodal	5.0 ± 0.9	3.0 ± 1.4	7.6 ± 1.0	5.3 ± 1.0	0.7 ± 0.5
Sham	5.32 ± 1.3	3.4 ± 1.5	7.3 ± 1.4	5.3 ± 1.1	0.4 ± 0.5
T-test	$t_{(21)}$= 0.4, p = 0.7	$t_{(21)}$= 0.6, p = 0.5	$t_{(21)}$= 0.6, p = 0.6	$t_{(21)}$= 0.8, p = 0.4	$t_{(21)}$= 1.4, p = 0.2
Experiment 6					
Anodal	5.0 ± 1.2	4.2 ± 1.6	7.8 ± 1.0	5.1 ± 1.0	0.7 ± 0.5
Sham	5.4 ± 1.0	3.5 ± 1.6	7.1 ± 1.3	5.1 ± 1.4	0.6 ± 0.5
T-test	$t_{(30)}$= 0.8, p = 0.4	$t_{(30)}$= 1.2, p = 0.2	$t_{(30)}$= 1.6, p = 0.1	$t_{(30)}$= 0, p = 1.0	$t_{(30)}$= 0.7, p = 0.5

Table 2 Hand direction in both baselines and ∆ hand direction (corrected to baseline) in the first trial of adapt1 are shown across the whole experiments and independent t-test between two groups of anodal and sham. Values are mean ± SD.

Experiment 1	Pre 1	Pre 2	1st trial of adapt1
Anodal	0.98 ± 0.97	2.03 ± 2.06	0.3±3.7
Sham	1.91 ± 1.7	1.96 ± 1.8	1.7±7.1
T-Test	$t_{(26)}$= -1.7, p=0.1	$t_{(26)}$=1.01, p=0.3	$t_{(26)}$= -0.7, p=0.5
Experiment 2			
Anodal	-0.74 ± 0.71	-1.18 ±1.04	-2.3± -2.2
Sham	-0.88 ± 1.06	-1.18 ±1.04	0.3±3.1
T-Test	$t_{(18)}$=.34, p=0.7	$t_{(18)}$=1.05, p=0.3	$t_{(18)}$= -1.9 , p= 0.07
Experiment 3			
Anodal	1.07 ± .85	2.1± 1.52	-0.02±4.2
Sham	1.8 ± 1.8	1.3 ± 1.95	-1.07±4.5
T-Test	$t_{(25)}$= -1.3, p=0.20	$t_{(25)}$=1.15, p=0.26	$t_{(25)}$= 0.7, p=0.5
Experiment 4			
Anodal	2.4 ± 1.02	1.9 ± 1.03	2.6 ± 5.1
Sham	1.4 ± .95	.39 ± 1.2	-0.3 ± 5.3
T-Test	$t_{(21)}$=2. 4, *p=0.03	$t_{(21)}$=3.2, **p=0.003	$t_{(21)}$ =1.05, p=0.3
Experiment 5			
Anodal	0.96 ± .91	1.5± 1.6	7.4±5.4
Sham	1.2 ± 1.1	2.1 ± 1.9	5.7±5.5
T-Test	$t_{(34)}$= -.73, p=0.47	$t_{(34)}$=-.86, p=0.39	$t_{(34)}$= 0.9, p=0.4
Experiment 6			
Anodal	2.04 ± 1.4	1.7±1.6	0.6 ± 5.1
Sham	0.89 ± 1.4	1.5±2.3	3.9 ± 5.0
T-Test	$t_{(30)}$= 2.3, *p=0.03	$t_{(30)}$=-.40, p=0.87	$t_{(30)}$=-1.8, p=0.07
Experiment 7			
Anodal	1.01 ± 0 9	2.1 ± 1.8	5.1±3.8
Sham	1.4 ± 1.2	2.36 ± 2.1	3.3±3.6
T-Test	$t_{(24)}$= -0.87, p=0.39	$t_{(24)}$=-0.25, p=0.80	$t_{(24)}$= 0.1, p=0.9

Table 3 Reaction time and movement time across all experiments. Values are mean ± SD.

	Reaction Time (sec)			Movement time (sec)		
	Anodal	Sham	t-test	Anodal	Sham	t-test
Experiment 1						
adapt	0.38 ± 0.04	0.37 ± 0.05	$t_{(26)}$=0.24, p= 0.8	0.38 ± 0.04	0.38 ± 0.05	$t_{(26)}$= 0.24, p= 0.8
retention	0.37 ± 0.05	0.37 ± 0.05	$t_{(26)}$=0.08, p= 0.9	0.23 ± 0.04	0.22 ± 0.05	$t_{(26)}$=-0.05, p= 0.9
Experiment 2						
adapt	0.49 ± 0.04	0.45 ± 0.02	$t_{(18)}$=0.8, p= 0.4	0.25±0.02	0.25 ± 0.01	$t_{(18)}$=0.1, p= 0.9
retention	0.44± 0.04	0.42 ± 0.02	$t_{(18)}$=0.5, p= 0.6	0.23±0.01	0.23 ± 0.01	$t_{(18)}$=0.8, p= 0.8
Experiment 3						
adapt	0.39 ± 0.03	0.39 ±0.04	$t_{(25)}$=-0.19, p= 0.8	0.22 ± 0.02	0.22 ± 0.07	$t_{(25)}$= -0.36, p= 0.7
retention	0.39 ± 0.04	0.38 ± 0.04	$t_{(25)}$= 0.43, p= 0.7	0.19 ± 0.02	0.21 ± 0.06	$t_{(25)}$ = -1.34, p= 0.2
Experiment 4						
adapt	0.45 ± 0.02	0.47 ± 0.02	$t_{(21)}$=-0.5, p= 0.6	0.20 ± 0.01	0.20 ± 0.01	$t_{(21)}$=-0.2, p= 0.8
Experiment 5						
adapt	0.40 ± 0.02	0.41 ±0.02	$t_{(34)}$= -0.3, p= 0.7	0.26 ± 0.01	0.27 ± 0.01	$t_{(34)}$= -0.4, p= 0.7
retention	0.39 ± 0.02	0.40 ± 0.01	$t_{(34)}$= -0.6, p= 0.5	0.23 ± 0.01	0.23 ± 0.02	$t_{(34)}$= -0.1, p= 0.9
Experiment 6						
adapt	0.35 ± 0.02	0.38 ±0.02	$t_{(30)}$= -0.7, p= 0.5	0.28 ± 0.02	0.30 ± 0.02	$t_{(30)}$= -0.6, p= 0.6
retention	0.34 ± 0.03	0.39 ± 0.02	$t_{(30)}$= -1.4, p= 0.2	0.28 ± 0.04	0.22 ± 0.01	$t_{(30)}$= 1.5, p= 0.1
Experiment 7						
adapt	0.44 ± 0.08	0.40 ± 0.05	$t_{(36)}$=0.9, p= 0.1	0.22 ± 0.04	0.23 ± 0.03	$t_{(36)}$= -0.36, p= 0.7
retention	0.42 ± 0.07	0.39 ± 0.04	$t_{(36)}$=0.4, p= 0.2	0.20 ± 0.04	0.21 ± 0.04	$t_{(36)}$=-1.34, p= 0.2