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Original publication available at:
https://doi.org/10.1152/jn.00926.2017

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Dose-response of somatosensory cortex repeated anodal transcranial direct current stimulation on vibrotactile detection. A randomized sham-controlled trial

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Running Head: RCT of repeated a-tDCS of S1 on vibrotactile detection.

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ABSTRACT

This randomized sham-controlled trial investigated anodal transcranial direct current stimulation (tDCS) over the somatosensory cortex contralateral to hand dominance for dose-response (1mA-20 minutes x 5 days) effects on vibrotactile detection thresholds (VDT). VDT was measured before and after tDCS on days 1,3&5 for low (30hz) and high (200hz) frequency vibrations on the dominant and non-dominant hands in 29 healthy adults (mean age = 22.86; 15 males, 14 females). Only the dominant hand 200Hz VDT displayed statistically significant medium effect size improvement for mixed model analysis of variance time x group interaction for active tDCS compared to sham. Post Hoc contrasts were statistically significant for dominant hand 200Hz VDT on day 5 after tDCS compared to day 1 before tDCS, day 1 after tDCS and day 3 before tDCS. There was a linear dose-response improvement with dominant hand 200Hz VDT mean difference decreasing from day 1 before tDCS peaking at -15.5% (SD=34.9%) on day 5 after tDCS. Both groups showed learning effect trends over time for all VDT test conditions but only the non-dominant hand 30Hz VDT was statistically significant (p=0.03) though Post Hoc contrasts were non-significant after Sidak adjustment. No adverse effects for tDCS were reported. In conclusion, anodal tDCS 1mA-20 minutes x 5 days on the dominant sensory cortex can modulate a linear improvement of dominant hand high frequency VDT but not for low frequency or non-dominant hand VDT.

Keywords: Transcranial direct current stimulation, primary somatosensory cortex, vibrotactile detection threshold.

New & Noteworthy:
Repeated weak anodal transcranial direct current stimulation (1mA-20min) on the dominant sensory cortex provides linear improvement in dominant hand high frequency vibration detection thresholds. No effects were observed for low frequency or non-dominant hand vibration detection thresholds.

INTRODUCTION
Hand function is essential in many activities of daily living that require tactile detection, discrimination and object manipulation. Neurophysiological and psychophysical studies have provided an understanding of the tactile sensibility of the glabrous skin of the hands and fingers (Vallbo et al. 1984; Gescheider et al. 2010). Low-threshold mechanoreceptors rapidly adapting to low frequency vibration/flutter (Meissner’s corpuscles) and high frequency vibration (Pacinian corpuscles) respond to the initial contact, lifting, replacing and final contact of mechanical stimuli. In contrast, slowly adapting Merkel’s disks and Ruffini endings fire during continued mechanical stimuli (Gescheider et al. 2010). Independent afferent relay through the Pacinian and non-Pacinian channels and eventual somatosensory cortex integration of low (30Hz) and high frequency (200Hz) vibrotactile signals subsequently results in a vibrotactile sensory perception (Tommerdahl et al. 2010; Carter et al. 2014). Furthermore, evidence suggests that there is both a contralateral and ipsilateral influence in somatosensory processing of vibrotactile sensory stimuli (Tommerdahl et al. 2010; Tamè et al. 2016). Somatosensory stimulation contributes also to corticomotoneuronal excitability aiding the execution of dexterous object manipulation in activities of daily living (Kaelin-Lang et al. 2002; Johansson and Flanagan 2008).

There is increasing research interest in exploring the use of non-invasive brain stimulation techniques to induce neuroplasticity for meaningful purposes. One such meaningful purpose is in the rehabilitation of acquired or age related somatosensory dysfunction where deficits in vibrotactile sensory perception may influence quality of life (Klingner et al. 2012; Stuart et al. 2003). Transcranial direct current stimulation (tDCS) is a brain stimulatory technique which involves delivering low amplitude direct current (1-2mA) to the brain via scalp electrodes (Nitsche et al. 2008). Scoping reviews of the literature suggest that tDCS may modulate the excitability of the somatosensory pathways as well as having long-term potentiating effects on behavioral aspects of nervous system function in healthy humans and clinical populations (Nitsche et al. 2008; Costa et al. 2015). With the application of an anodal current polarity over the primary sensory cortex, tDCS has been displayed to modulate an increase in somatosensory cortical excitability, while cathodal polarity modulates a decrease in somatosensory cortical excitability (Rehmann et al. 2016).

A systematic review by Vaseghi et al. (2014) identified that only a few studies with blinded sham-controlled methodology have investigated the effects of anodal somatosensory cortex tDCS on sensory function of the hand in healthy individuals. These studies had however displayed inconsistent findings that a single session of sensory cortex tDCS can induce minimal percentage change from baseline values when testing contralateral hand thermal sensory detection and tactile discrimination during tDCS and up to 40 minutes post-stimulation (Rogalewski et al. 2004; Ragert et al. 2008; Grundmann et al. 2011). Similar inconsistencies have been reported for transcranial magnetic stimulation (Tamè & Holmes 2016; Convento et al. 2018). However, more recent high-quality studies by Fujimoto et al. (2014) assessing sensory discrimination and Labbé et al. (2016) assessing low frequency vibrotactile detection (VDT) and discrimination have supported the hypothesis that anodal tDCS decreases contralateral hand thresholds in a healthy human population. Lenoir et al. (2017) provided similar evidence of tDCS modulatory effects on early-latency S1 response after high frequency vibrotactile stimuli. One study has investigated potential tDCS related changes of excitability in tDCS stimulated versus non-stimulated S1 cerebral hemispheres. Sensory evoked potentials performed at the dominant and non-dominant hands found tDCS induced effects only in the tDCS stimulated dominant side and not in the non-dominant S1 cortex suggesting no significant effect on interhemispheric inhibition (Rehmann et al. 2016).
Understanding the dose-response relationship of tDCS has recently been expressed as a research priority (Giordano et al. 2017). The dosing of tDCS can be controlled by factors such as electrode size, stimulation site, polarity, as well as duration, frequency and strength of stimulation. Horneric dose response models adapted from toxicology have been used to explain the biphasic therapeutic effects of low doses of tDCS and increased side effects of higher doses (Giordano et al. 2017). A safe and therapeutic strength of anodal polarity current has been shown to range between 1-2mA for up to 30 minutes (Poreisz et al. 2007). However, up to 18% of subjects found the stimulation procedure unpleasant (Poreisz et al. 2007). With regards to the frequency of stimulation, repeated sessions are thought to enhance the reinforcement of the tDCS modulated neural activity. These adaptive processes following additional disruptions of homeostasis after repeated sessions likely explain immediate, shortterm and long-term responses of tDCS. One pseudorandomized sham-controlled study on healthy individuals has investigated the repeated session (1 session x 5 days) dose-response of primary sensory cortex anodal tDCS (2mA – 20 minutes). Within this therapeutic window a linear improvement in performance of sensory discrimination testing was displayed with a learning effect largely maintained 4 weeks later (Hilgenstock et al. 2016). It is however unknown if the same dose response relationship is evident at the lower end of the therapeutic strength and duration spectrum of 1mA – 20-minute stimulation with potentially lower reports of unpleasant adverse effects.

Based on the limited number of high quality studies and inconsistent findings, the current quality of evidence is low and warranting further investigation. The aim of this study is therefore to explore the dose-response effects of five consecutive daily sessions (1 session / treatment day) of anodal tDCS (1mA-20min) applied over the sensory cortex side contralateral to hand dominance when testing low and high frequency VDT in dominant and non-dominant hands of a healthy human population compared to sham tDCS. It is hypothesized that consecutive daily sessions of anodal sensory cortex tDCS to the side contralateral to hand dominance may linearly decrease low frequency and high frequency VDT for the dominant hand rather than non-dominant hand compared to sham over time.

MATERIALS AND METHODS

Participants

Twenty-nine healthy adult volunteers were consecutively recruited between July 2012 and May 2013 from staff and students responding to advertisements at Bond University, Australia. Subjects were cleared for tDCS contraindications such as cranial/brain metal implants or electronic devices; history of epilepsy, convulsion or seizure; first degree relatives with epilepsy; consumption of >4 standard drinks alcohol/day; cardiac conditions; current pregnancy; hearing problems or tinnitus. Volunteers had a mean age of 22.86 (SD=6.78) years and consisted of n=15 males and n=14 females, 24 with right handed writing dominance. The study was approved by the Bond University Human Research Ethics Committee (RO1439) and carried out in accordance with the 2008 version of the Declaration of Helsinki.

Study design

A prospective randomized single blinded controlled trial was instituted involving one experimental tDCS group and one sham control tDCS group. After volunteering and providing written informed consent to participate in the study, subjects were allocated to their respective groups through random concealed allocation using opaque envelopes containing a noted intervention (i.e. active or sham). Randomization resulted in 14 subjects allocated to the experimental group and 15 subjects to the control group. With respect to blinding, participants
were not told what intervention group they belonged to. The investigator could not be blinded
due to limitations in resources to finance equipment or additional personnel to enable blinding
of the investigator.

Transcranial direct current stimulation
tDCS was applied using a low intensity direct current stimulator (Chattanooga Ionto,
Tennessee, USA) and delivered via scalp electrodes prepared as follows: Household sponges
(thickness = 10mm, contact area = 35cm²) were soaked in electrolyte solution (NaCl
=154mM) and attached to each side of an aluminum foil sheet (area = 35 cm²) with a rubber
band. The anode was positioned over the sensory cortex at either the C3’ or C4’ position,
which correlated to 2 cm posterior to the C3 or C4 position (10-20 EEG system) of the
subject’s dominant cortex (Ragert et al. 2008). Therefore, the contact area of the anode
stimulates these S1 areas but also potentially stimulates the parietal lobe, post central gyrus,
S2 and M1. The cathode was placed over the contralateral supra-orbital region (Ragert et al.
2008). The electrodes were maintained in position by a non-conducting elastic strap, which
was strapped firmly around the subject’s head (Norris et al. 2010). For each session, tDCS
was delivered at a current intensity of 1mA (current density of .02857 mA/cm²) for 20
minutes. The current density, polarity, and duration of tDCS that was applied in this study
have all previously been shown to influence somatosensory processing in a healthy population
(Boggio et al. 2008).

To quantify any placebo effect there was a control group, which received sham stimulation
only. This involved activating the tDCS device at a current intensity of 1mA but turning the
tDCS device off slowly, out of the subject’s field of view, after ~30 seconds (Gandiga et al.
2006). The sham procedure chosen was based on research that demonstrated that ≤ two
minutes of tDCS at a current intensity of .02857 mA/cm2 delivered to the motor cortex was
insufficient to induce alterations post-stimulation to motor pathway excitability (Nitsche and
Paulus 2000). This approach has previously been proven to be reliable at 1 mA for both naive
and experienced subjects (Ambrus et al. 2012). Stimulation followed the current published
guidelines for safe use (Nitsche et al. 2008).

Vibration detection threshold testing
This study specifically looked at the ability to detect sinusoidal vibrations, which were
vertical uni-planar, periodical oscillations applied to the skin surface. A signal generator
software program (AD Instruments, LabChart 7, Australia) generated the sinusoidal
waveforms, which were then passed to a linear power amplifier (Gearing and Watson, PA30,
UK) before being delivered to the skin surface via a perspex probe (6-mm-diameter) attached
to the shaft of a mechanical vibrator (Gearing and Watson, GWV4, UK). The mechanical
vibrator was mounted on an isolated rigid trunnion (Gearing and Watson, T4, UK). The
software-controlled alterations to both the frequency and voltage amplitude of the sinusoid
waveforms. This type of vibration system has been used in similar research to the present
study (Morley et al. 2007). As the mechanical vibrator system is not feedback controlled,
offline calibrations were made using a hydraulic micromanipulator (Narishige, MHW-103,
Japan) to identify the amplitude of vibration that is produced (in microns) with known settings
on the signal generator/amplifier system.

The testing was carried out in a quiet, temperature controlled (21 degrees Celsius) university
research laboratory. The subjects were seated upright in a chair and in parallel to the length of
a rectangular table, which stationed the mechanical vibrator. Foam blocks on the table
stabilized the subject’s upper limb and helped to keep the hand in a pronated position. A
measuring tape was used to ensure the same distance between foam block and mechanical
vibrator for each VDT assessment. The investigator then lined the center of the subject’s
distal pad of the third digit on the vibrator’s probe tip, which was flush with a 6mm hole in a
rigid perspex plate (surface area = 30 cm2) suspended from the rigid trunnion. The plate
limits the spread of surface waves across the skin and helped to maintain a constant
indentation of the probe in the skin of the testing site (Stuart et al. 2003). The probe and the
rigid surround were separated by a gap of 2mm. A measuring tape was used to ensure that the
same site of stimulation was used between sessions. The subject was instructed to keep their
finger in soft contact with the stimulating probe for the testing. Subjects also wore earmuffs to
avoid any potential auditory cues from the vibration device.

Vibrations were delivered specifically to the distal pad of the third digit of both hands at two
different frequencies (30 & 200Hz). Both upper limbs were assessed to measure both the
patient reported dominant and non-dominant sides. VDT was assessed using the following
method of limits technique described in a previous study by the research group (Stuart et al.
2003). For each frequency, subjects initially experienced a randomly chosen supra-threshold
vibratory stimulus. The stimulus amplitude was then gradually decreased (descending mode)
at a constant rate (~1s / stimulus amplitude) until the subject verbally indicated that they could
confidently no longer detect it. After this, the vibratory stimulus was then gradually increased
at a constant rate (~1s / stimulus amplitude) from a randomly chosen sub threshold level
(ascending mode) until the subject verbally indicated that they could confidently detect the
vibration stimulus. The stimulus amplitude in ascending or descending mode occurred in steps
of 0.17 μm for 200 Hz vibration and 1.05 μm for 30 Hz vibration where three step changes in
amplitude were made during each second. The mean of a minimum of 10 detection thresholds
(five ascending and descending) for each frequency and upper limb was calculated for each
subject. The method of limits procedure was selected for measuring VDT as it has previously
been shown to be more reliable and time efficient than the forced choice procedure (Gerr and
Letz 1988). Furthermore Stuart et al. (2003) showed no significant differences between VDT
measures.

With respect to timing, VDT was objectively measured both before and after tDCS during the
1st, 3rd and 5th day sessions. A questionnaire investigating incidence of adverse effects was
completed after each stimulation session. Baseline (i.e. pre-tDCS) VDT were measured only
at time point 1. The sequence of VDT testing was dominant hand 30Hz (D30), dominant hand
200Hz (D200), non-dominant hand 30Hz (ND30) and non-dominant 200Hz (ND200). A
practice session was also conducted on day 1. All the measurements were performed between
7:45am and 5:30pm. The experimental procedure is shown diagrammatically in figure 1.

Sample size power calculation
An a priori sample size power analysis was used to calculate required sample size to test
analysis of variance (ANOVA) within-subjects factor (6x time-points) and between-subjects
factor (2x treatment group) interactions. Using G*Power software, eta-squared can be used to
calculate effect size (f) for ANOVA (Prajapati et al. 2010). Aslaksen et al. (2014) previously
reported eta-squared values in the range of 0.07 to 0.33 for significant tDCS induced effects
on experimental pain in a healthy human population. Considering 95% statistical power, a
two-sided α = .05 and a ‘moderate’ effect size = 0.27 a total of n=24 were required (Faul et al.

Data analysis
In the presence of a significant interaction, the analysis would be refined by using the syntax features of SPSS to allow a simple main effects analysis with Sidak Post Hoc test for the interaction effect (Peat and Barton 2014). Sidak adjustment was used for Post hoc tests because it is not affected as much by loss of statistical power compared with Bonferroni adjustments (Dmitrienko and D’Agostino 2013). If the interaction effect between the within-subjects and between-subjects factor was not significant, the interpretation of the analysis would be reverted to interpreting the main effects for both factors (i.e., the “within-subjects” factor and “between-subjects” factor). In addition, if the main effect of time was statistically significant, output from Sidak Post Hoc tests would be interpreted to understand where the differences between factors lie.

The standardized residuals were checked to determine if they were approximately normally distributed, through Shapiro–Wilk’s test for normality and visually through histograms. The homogeneity of variance assumption was assumed if Fmax was less than 10 or Levene’s test of equality of error variances was p > 0.05 (Tabachnick and Fidell 2007). Huyn-Feldt or Greenhouse-Geisser Epsilon corrections were used if Mauchly’s test for sphericity was significant. Greenhouse-Geisser Epsilon correction was used if the estimated epsilon was < 0.75 whereas Huyn-Feldt Epsilon correction was used if the estimated epsilon was > 0.75. Partial eta-squared ($\eta^2_p$) was used as an estimated measure of effect size where $\eta^2_p = 0.02 \sim$ small effect, $\eta^2_p = 0.13 \sim$ medium effect and $\eta^2_p = 0.26 \sim$ large effect (Peat and Barton 2014). An independent samples t-test was used to compare mean VDT between groups at baseline to ensure equivalent baseline characteristic between groups after randomization had occurred. Percentage change from baseline following 1 and 5 tDCS sessions within groups was also assessed. A percentage change from baseline value assessment was performed to enable comparisons in findings with recent systematic reviews (Vaseghi et al. 2014). A p-value of ≤ 0.05 was considered significant for significance tests. For each analysis, IBM SPSS 20.0 for Windows was used.

RESULTS

All subjects completed the study and tolerated the tDCS procedure well reporting no side-effects. One subject displayed extremely outlying VDT values (skewness/standard error = > 1.96) from baseline and over time compared to the rest of the subjects, so these values were excluded leaving data from N=28 subjects for further analyses. Furthermore, distributions of standardized residuals after fitting separate mixed model ANOVAs for D30, D200, ND200 violated the assumption of normality and were therefore transformed at all time points (i.e. reciprocally for D30 & D200 and logarithmically for ND200) to meet the normality assumption. An independent samples t-test displayed that there were no statistically significant differences between groups in mean VDT at baseline. Pooled mean VDTs and standard deviations at each time point for D30, D200, ND30 and ND200 are displayed in figure 2.
ANOVA analyses demonstrated a statistically significant time x group interaction indicating improved VDT for active tDCS over time compared to sham tDCS for the D200 test condition (p = .01) but not for D30, ND200 or ND30 (Table 1). Post hoc comparisons for the D200 time x group interaction was significant from time points 1-3 compared to time point 6 demonstrating that there was a significant lower VDT in D200 at time point 6 compared to time point 1 (p = .03; 95% CI = -0.20 to -0.01; Mean difference = 0.21), time point 2 (p = 0.03; 95% CI = -0.17 to -0.01; Mean difference = 0.17) and time point 3 (p = 0.01; -0.13 to -0.01; Mean difference = 0.13) for active tDCS. A medium effect size (η² = 0.14) for the interaction effect for D200 was observed. There was a linear dose-response relationship (y = -0.0411x + 1.563, R² = 0.91) with the mean difference in VDT decrease from baseline peaking at -15.5% (SD=34.9%) after the final tDCS session. When reverting to main effects analysis for the other test conditions, no statistically significant between group differences were seen for group as a factor (Table 1). In contrast, the ANOVA demonstrated statistically significant within-subjects differences for time as a factor for ND30 (p = .03). A small effect size (η² = 0.09) was observed for time as a factor for ND30. However, post hoc pairwise comparisons for ND30 were not significant following Sidak adjustment. Both groups showed learning effect trends over time for all VDT test conditions (figure 2).

DISCUSSION
The study results support our initial hypothesis that tDCS modulates a statistically significant moderate level linear decrease of high frequency VDT for the dominant hand compared to sham. The study results however do not support a similar tDCS modulatory effect for low frequency VDT for the dominant hand or ipsilateral low and high frequency VDT (Stagg et al., 2009). The findings therefore provide new knowledge of enduring high frequency VDT specific effects of repeated S1 anodal tDCS (1mA-20 minutes), building upon the previous research suggesting a modulatory effect on vibrotactile sensory function compared to sham (Rogalewski et al. 2004; Ragert et al. 2008; Fujimoto et al. 2014; Labbé et al. 2016; Hilgenstock et al. 2016; Lenoir et al. 2017).

A possible neurophysiological explanation for the preferential modulation of high frequency VDT may be due to the ventral posterior inferior nucleus (VPI) which receives Pacinian channel afferents, projects thalamocortical axons that terminate in the superficial layers of the primary sensory cortex with potentially closer proximity to the anode depending on the individuals anatomy regarding the folding of the postcentral gyrus (Jones, 1998; Tommerdahl et al., 2005a; Tommerdahl et al., 2010). In contrast, ventral posterolateral nucleus (VPL) and the ventral postero medial nucleus (VPM) which receives non-Pacinian channel afferents, projects thalamocortical axons that terminate in the middle cortical layers (Jones, 1998; Tommerdahl etal., 2005a; Tommerdahl et al., 2010). Anodal tDCS studies on rodents support this notion of increased neuronal activity in outer cortical layers and decreased activity in deeper layers (Stagg and Nitsche, 2011; Purpura and Mcmurtry, 1965). The EEG based cortical current source density depth in humans display outward current in the outer cortical layers and an inward current in deeper layers suggesting a dipole that anodal tDCS may potentially be able to modulate (Csercsa et al., 2010). This may potentially even modulate Pacinian channel input to S2 which has higher levels of activation during high-frequency vibrotactile stimulation compared with SI neurons (Rowe et al., 1996). Furthermore, Tommerdahl et al. (2005b) has shown that increased activity in Pacinian channels may even decrease the low frequency discriminative capacity of non-Pacinian channels which is in line with the results observed in the current study. The amplitude thresholds for detecting a 30Hz vibration are however much higher than for 200Hz, where the Pacinian channels could...
influence detection of the 30Hz stimuli since the threshold functions of different channels are
quite close at this frequency (Gescheider et al. 2002). Fujimoto et al. (2017) however
displayed through electric field monitoring of tDCS over the S2 with 25cm² electrodes that a
corresponding stimulation of S1 could not be ruled out. It is therefore likely that our use of
35cm² electrodes over the S1 also contributed to stimulation of the S2 and possibly
influencing both low and high frequency VDT processing.

A possible explanation for the lack of tDCS effects on the opposite side sensory cortex
processing of low and high frequency VDT may be due to interhemispheric inhibition
(Rehmann et al. 2016). This suggests an increased inhibition of sensory processing from the
opposite side of the body in preference for efficient processing of sensory inputs on the tDCS
stimulated side. Recent studies investigating unilateral and dual-hemisphere tDCS effects on
the S1 and S2 further support this notion of opposite side interhemispheric inhibition of tactile
processing (Fujimoto et al. 2014, 2017).

With respect to sensory detection threshold levels, the mean detection thresholds obtained in
this study for both high and low frequency vibrations were comparable to results reported by
Morley and Rowe (1990) that had an identical VDT testing procedure. Comparison with other
studies measuring VDTs for vibrations delivered at both high and low frequencies to the
finger using differing contact conditions such as the stimulation probe size and the size of the
gap between contactor and rigid surround can provided varying results (Morioka et al. 2008).
For example, Stuart et al. (2003) displayed smaller VDTs for vibrations delivered at both high
and low frequencies to the finger where the stimulation probe size was bigger and the size of
the gap between contactor and rigid surround was smaller.

When interpreting the results of the study, there are a number of methodological strengths and
weaknesses that need to be considered. In line with a repeated sessions design, the participant
performed several VDT measurements with the same standardized procedure. However, the
repeated sessions design can be susceptible to test-retest bias (e.g. retest performances
influenced by previous sessions). Test-retest bias with psychophysical measures has
previously been reported (Teepker et al. 2010). In the present study, all VDT test conditions
for both active tDCS and sham tDCS groups showed steady reductions in the same direction
throughout the sessions. These findings suggest that learning or training effect trends may
have been present especially in the statistical significant main effect for the non-
dominant hand 30Hz VDT test condition. Factoring session-to-session effects into the
analyses would have required repeated VDT tests before start of the trial. This would have
required more resources (i.e. project finances, participant time) to do so.

Despite the methodological strength of a randomized sham controlled and patient blinded
design used, limitations in resources to finance additional personnel resulted in the researcher
not being blinded to the test condition. In the interpretation of the results, a strength is that no
statistically significant baseline differences where observed between the intervention and
sham controlled groups and the study was well powered. It can be argued that the 4 test
conditions can be considered as separate entities and therefore may not require restrictive
multiplicity penalization of the model (Dmitrienko, D’Agostino 2013). Sidak adjustment was
however used for repeated measures of separate test conditions and was chosen because it is
not affected as much by loss of statistical power for which Bonferroni adjustments are
affected. With regards to generalizability of results, the study was conducted on
predominantly a young university student population. Hence, the results from this study may
not necessarily translate to other age groups. Furthermore, the outcome measures were also
performed only at one anatomical location (i.e., glabrous skin of the finger). The results from this study may therefore also not necessarily translate to other body parts.

From the dose response relationship observed in this study and the lack of adverse effects reported by subjects, it can be motivated to investigate the modulatory effects of low therapeutic amplitude and duration repeated tDCS (1mA–20 minutes) in the rehabilitation of clinical conditions displaying sensory dysfunction for high frequency vibrations especially during initial contact, lifting, replacing and final contact of mechanical stimuli tasks.

CONCLUSION
In summary, this is the first study that has demonstrated that consecutive daily sessions of low dose tDCS on the sensory cortex contralateral to hand dominance can modulate a linear lowering of high frequency VDT without adverse effects in a healthy human population compared to sham tDCS.

REFERENCES


Competing interests
The authors have no competing interests to declare.

Authors’ contributions
BT, AA conceived the project. BT, PJ, AA assisted with the protocol design. BF, BT, PJ, AA lead, the co-ordination of the trial. All authors provided feedback on drafts of this manuscript and have read and approved the final paper.

Figure 1: Study design, showing the time course of transcranial direct current stimulation (tDCS) treatments and vibration detection threshold (VDT) measurements. tDCS treatments (20 mins) were delivered once per day for 5 consecutive days. VDT were measured before and after tDCS on days 1, 3 and 5. Baseline (i.e. pre-tDCS) VDT were measured only at time point 1.

Figure 2: Pooled mean vibration detection thresholds (VDT) before and after transcranial direct current stimulation (tDCS) on day 1 (time points 1&2), day 3 (time points 3&4), and day 5 (time points 5&6) for vibrations delivered at frequencies of 30Hz or 200Hz to the dominant and non-dominant hands.

Table 1: Mixed model analysis of variance (ANOVA) statistics for 4 vibration detection threshold (VDT) test conditions: Dominant hand 30Hz (D30), Non-dominant hand 30Hz (ND30), Dominant hand 200Hz (D200), Non-dominant hand 200Hz (ND200) over 6 time-points (Factor = Time) in response to either active or sham tDCS (Factor = Group).
<table>
<thead>
<tr>
<th>VDT condition</th>
<th>Test</th>
<th>F</th>
<th>Sig.</th>
<th>$\eta_p^2$</th>
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<td>Group</td>
<td>&gt;0.01</td>
<td>0.98</td>
<td>&gt;0.01</td>
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<td></td>
<td>Time</td>
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<td>0.07</td>
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<td></td>
<td>Time x Group</td>
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<td>Group</td>
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<td>&gt;0.01</td>
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<td>Time</td>
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<td>0.03</td>
<td>&gt;0.01</td>
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<td></td>
<td>Time x Group</td>
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<td>0.79</td>
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<tr>
<td>D200&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Group</td>
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<td></td>
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<td>ND200&lt;sup&gt;b&lt;/sup&gt;</td>
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<td></td>
<td>Time x Group</td>
<td>2.00</td>
<td>0.11</td>
<td>0.07</td>
</tr>
</tbody>
</table>

<sup>a</sup> = reciprocally transformed  
<sup>b</sup> = logarithmically transformed  
**Bold text p<0.05**