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Original Article

Does transcranial direct current stimulation enhance the hypoalgesic effect of exercise?

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ABSTRACT

Exercise produces a decrease in pain sensitivity via an effect called exercise-induced hypoalgesia (EIH). Transcranial direct current stimulation (tDCS), acting on similar analgesic mechanisms as EIH, represents a potential complementary intervention that may amplify the effects of exercise on pain. This study aimed to explore if anodal tDCS could enhance the effect of exercise on pain compared to exercise alone. A total of 35 healthy participants aged 19–37 years completed a familiarisation session followed by two separate sessions where active and sham tDCS was applied in a randomised cross-over design. The familiarisation session involved familiarisation to the pain assessment and exercise tasks, while the subsequent tDCS sessions involved pain sensitivity assessment, exercise and either anodal tDCS or sham tDCS. tDCS doses were applied at 2 mA over the primary motor cortex for 10 min, with the reference electrode placed over the contralateral supraorbital area. The exercise task involved a sustained isometric grip strength contraction at 35% of maximal voluntary contraction (MVC) until volitional exhaustion. Pain sensitivity was evaluated as pressure pain threshold before tDCS, after tDCS, and after exercise. Across both tDCS conditions, pain threshold was higher after exercise when compared to pre- and post-tDCS measurement. This increase in pain threshold did not differ between active and sham tDCS conditions. Our findings suggest that the hypoalgesic effects of active anodal tDCS over the motor cortex prior to exercise are no greater than the effects of sham tDCS prior to exercise.

1. Introduction

In healthy adults, it is widely reported that acute exercise can transiently reduce pain; an effect commonly referred to as exercise induced hypoalgesia.[1] Reduced pain sensitivity following exercise has been observed across an array of pain sensitivity measures including pain threshold, tolerance, and suprathreshold intensity ratings.[2] Operationalised as a decrease in pain sensitivity from pre-to post-exercise, a greater reduction in sensitivity suggests a stronger hypoalgesic response.[3] Due in part to this observed hypoalgesic response, exercise has been prescribed as a conservative treatment for many chronic pain conditions, including chronic neck pain,[4] osteoarthritis,[5] and fibromyalgia.[6] The hypoalgesic effect is also seen in healthy individuals after exercise, with reductions in pain sensitivity after a wide range of exercise tasks, including running,[7] cycling,[8] and isometric tasks.[9] Despite the potential of exercise to induce this hypoalgesic effect, recent findings have produced weak or inconsistent effects.[10] To better understand and optimise the hypoalgesic effect of exercise, dual interventions have been considered. To examine the role of opioid systems in the modulation of exercise induced hypoalgesia, a number of studies in both animals and humans have administered an opioid antagonist (naltrexone or naloxone) before exercise.[11,12] In mice, Terman et al.[12] report that naltrexone significantly reduced the analgesic response induced by a 3 and 5 minute (min) swim. In humans, Crombie et al.[11] performed a randomised, double-blinded, counterbalanced trial where participants received either naltrexone or a placebo prior to an isometric handgrip task at 25% of maximal voluntary contraction (MVC). It was reported that exercise induced a significant reduction in pain sensitivity, however this was not attenuated by the opioid antagonist.

While opioid antagonists have been investigated for their potential to reduce the hypoalgesic effect of exercise, little research has considered interventions that may enhance the hypoalgesic response. One intervention that may enhance the hypoalgesic response to exercise is transcranial direct current stimulation (tDCS). tDCS is a form of non-invasive brain stimulation that is increasingly being investigated for its effect on top-down pain modulatory networks.[13] tDCS delivers a weak electrical current to the brain, modulating the excitability of cortical neurons in the

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Abbreviation

Adult pre-screening system APSS
Analysis of variance ANOVA
Electromyography EMG
Exercise induced hypoalgesia EIH
First dorsal interosseous FDI
Maximal voluntary contraction MVC
Motor evoked potentials MEPs
Pain pressure thresholds PPTs
Time to exhaustion TTE
Transcranial direct current stimulation tDCS
Transcranial magnetic stimulation TMS

underlying brain regions.[14] The direct current applied through the surface electrodes stimulates both temporary and enduring changes in the excitability of cortical neurons.[14] This change in excitability, when targeted at the motor cortex,[15] has been shown to activate descending pain modulatory pathways and induce hypoalgesic effects.[16] Further, tDCS has been shown to be an effective adjunct to more established approaches to chronic pain treatments,[17] including exercise.[18] These findings indicate the potential for tDCS to complement other hypoalgesic interventions, such as exercise, by priming pain-related brain regions.[19] Specifically, tDCS may facilitate the hypoalgesic effects of subsequent exercise by acting on common nociceptive inhibitory pathways.[10,20]

Previous research provides partial support for the potential for tDCS to enhance the hypoalgesic effects of exercise. Borovskis et al.[21] examined the effect of tDCS and exercise on pain resulting from intramuscular injection of nerve growth factor into the extensor carpi radialis brevis. Anodal tDCS combined with exercise resulted in lower pain ratings during muscle extension and flexion when compared to exercise paired with sham tDCS. These findings offer preliminary support for tDCS-induced enhancement of the EIH response. However, further research is needed to support and clarify these findings. In particular, it is unclear whether the "augmentation" of the EIH effect reported by Borovskis et al.[21] extends to changes in pain sensitivity in those not experiencing acute experimental muscle pain.

The present study aimed to investigate whether the effects of exercise on pain sensitivity are influenced by prior administration of anodal tDCS to the motor cortex. It was hypothesised that pain thresholds would be higher following an isometric grip strength task that was preceded by anodal tDCS when compared to sham tDCS. A secondary aim of this study was to assess the independent effect of tDCS on pain sensitivity. It was hypothesised that anodal tDCS would induce a significant decrease in pain sensitivity when compared to sham stimulation immediately after stimulation.

2. Materials and methods

2.1. Design

The current study implemented a within-subjects, single-blinded, sham-controlled, randomised block design. Participants were required to attend the laboratory on three separate occasions; a familiarisation session and two experimental sessions corresponding to two different experimental conditions (anodal tDCS, sham tDCS).

2.2. Ethical approval

All participants signed an informed consent document before starting the study. All experimental procedures were approved by the University of Canberra's Human Research Ethics Committee (Project ID: 11882) and conformed to the principles outlined in the Declaration of Helsinki.

2.3. Participants

Participant recruitment utilised online advertisements in January 2023 and experimentation began in March 2023. A total of 37 healthy, recreationally active participants aged between 19 and 37 years were recruited from both a local university student population and from the larger local population. Due to the known influences of age on pain sensitivity,[22] those younger than 18 and older than 40 years were excluded from participation. Participants were required to report the frequency and duration of their regular exercise habits by completing Stage 1 of the Adult Pre-Screening System (APSS).[23] The APSS was used to characterise the exercise habits of the sample and exclude those who exercised for ten or more hours of moderate and/or high intensity exercise per week, as previous studies suggest that these individuals possess a more efficient endogenous modulatory system,[24] and consequently may have impacted the results. Additionally, individuals were excluded if they were taking medication that could influence the autonomic nervous system, or if they reported any contraindication to the grip strength task (i.e., hand or forearm muscular pain),[25] transcranial magnetic stimulation (TMS) or tDCS (see Taylor et al.[26] and Villamar et al.[27] for complete list of TMS and tDCS contraindications).

2.3.1. Sample size calculation

The lack of research investigating whether tDCS can enhance the hypoalgesic potential of exercise made estimation of an expected effect difficult. To indicate a reasonable, but conservative estimate of the effect of the combined intervention, we referred to the commonly reported independent effect of exercise on pain sensitivity. Koltyn and Umeda[1] in their investigation of hypoalgesia following a submaximal isometric grip strength task, reported a very large effect size of $d = 1.46$ (equivalent to $f = 0.73$). Similarly, the mean difference between pain sensitivity post active tDCS and sham tDCS was of a large effect size in the study conducted by Borovskis et al.[21] To provide a more conservative estimate of our expected effect, we instead used a medium effect size ($f = 0.25$) in our a priori power analysis calculation using G*Power (Version 3.1.9.6).[28,29] For the aims of comparing pain sensitivity before and after tDCS, and after an exercise task across the two stimulation conditions (active tDCS, sham tDCS), the following input parameters were used: α (two-sided) = 0.05, power = 0.90, allocation ratio = 1:1, number of groups = 2, number of measurements = 3. The power analysis suggested that 36 participants would be required in this study to detect a statistically significant difference in pain perception across the three time points (pre-tDCS, post-tDCS, post-time to exhaustion [TTE]) and two experimental conditions.

From the recruited sample ($n = 37$), two participants withdrew because of discomfort with TMS stimulation. The experimental procedure was otherwise well tolerated by participants with no other reports of negative side effects from the experimental methods employed. The total number of participants that completed all sessions was 35. The final sample consisted of 14 males (40%) and 21 females (60%), with 31 (89%) participants being right-hand dominant. Data relating to the characteristics of the sample are provided in Table 1.

Table 1
Characteristics of the sample.

Variable	Mean (*SD*)
Age (years)	25 (4)
Height (cm)	171.10 (7.70)
Weight (kg)	77.76 (14.59)
Body mass index (kg/m^2)	26 (4)
Exercise (min/week)	302 (126)

Abbreviations: *SD* = standard deviation.

2.4. Procedure

Each participant visited the laboratory on three separate occasions, with the two experimental conditions presented in a randomised order. Before each session, participants refrained from consuming caffeine or analgesic medications or engaging in vigorous exercise for at least 24 hour (h). All experimental protocols were conducted in the same temperature controlled (~23 °C, 33% humidity) laboratory. All conditions were separated by at least 72 h to ensure recovery from the exercise task[30] and to minimise carry-over effects of the stimulation.[31]

2.4.1. Familiarisation session

Participants attended the first session, where assessments of baseline physical characteristics, familiarisation to the exercise tasks and pain procedures took place. Demographic and anthropometric data (i.e., weight, height, gender) were first collected. Hand dominance was also assessed using the Edinburgh Handedness Inventory (Short Form).[32] Participants were then introduced to the pain assessment protocol, which included a demonstration of the testing procedure to ensure recognition of a noxious pressure stimulus.[33] Participants then proceeded to complete the exercise tasks involving grip force MVC and time to exhaustion (TTE). A consistent 2 min break was implemented between the TTE task and the final assessment of pressure pain thresholds (PPTs). Throughout the familiarisation session, participants were encouraged to ask questions about the procedure to ensure familiarity was achieved prior to the subsequent experimental sessions.

2.4.2. Experimental sessions

The experimental sessions commenced with baseline assessment of participants' PPTs. The hand motor hotspot was then located using TMS and electromyography (EMG). Following hotspot identification, tDCS was delivered for 10 min according to the assigned condition (anodal tDCS, sham tDCS). Post-tDCS PPT measurements were then collected immediately after the tDCS treatment. Participants then completed the exercise tasks involving both MVC and TTE grip strength tasks. Post-TTE PPT assessments were then conducted immediately following the completion of the grip strength TTE protocol. A diagram of the procedure is provided in Fig. 1.

2.5. Materials and measures

2.5.1. Pain sensitivity

Pain sensitivity was assessed as participants' pain threshold at the index finger of the non-dominant hand. Participants were seated at a table and instructed to place their non-dominant hand flat on the surface of the table, with their palm facing down. Pressure was applied perpendicular to the surface of the skin using a handheld algometer (Wagner Force Dial FDK 20, Wagner Instruments, Greenwich, CT) and gradually increased at a rate of approximately 1 kg/s. The PPT was defined as the point at which the participant verbally reported that the sensation of pressure first changed to a perception of pain. At the onset of pain, pressure was released and PPT was recorded in kilograms of force. Three measurements were taken at the same site, with a 30-second (s)

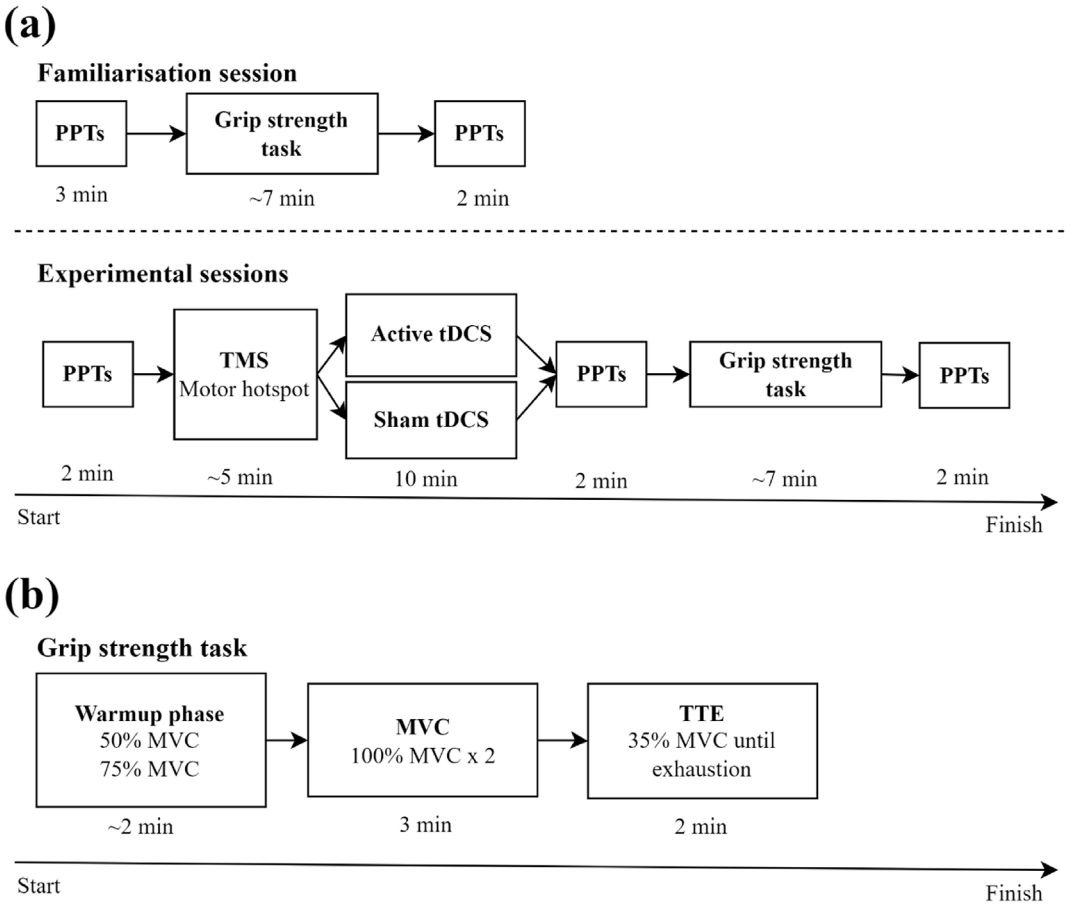

Fig. 1. Panel **A** presents the experimental protocol that occurred during the familiarisation and subsequent intervention sessions. Panel **B** presents the experimental protocol for the grip strength TTE task. Out of the initial cohort of 37 participants, 35 individuals successfully completed all three sessions. **Abbreviations:** tDCS = transcranial direct current stimulation, TTE = time to exhaustion, MVC = maximal voluntary contraction, PPTs = pain pressure thresholds, TMS = transcranial magnetic stimulation.

interval separating each. PPT was calculated as the mean of these three trials. To ensure understanding of the measure, participants were initially provided with a familiarisation trial on their ring finger. One minute separated this familiarisation trial and the first of three experimental trials.

2.5.2. Identification of motor hotspot

In each experimental session, single-pulse TMS was used in conjunction with EMG to locate the hand motor hotspot before the application of tDCS. The hand representation was identified by measuring motor evoked potentials (MEPs) from the first dorsal interosseous (FDI) muscle, resulting from biphasic TMS pulses (Neurosoft, Ivanovo, Russia) delivered to the primary motor cortex contralateral to the dominant hand. MEPs were calculated from EMG activity, recorded at 5 000 Hz using self-adhesive disposable silver/silver chloride surface electrodes (23 mm width, 2 cm interelectrode distance). Electrode placement and skin preparation adhered to accepted protocols.[34] These electrodes were connected to a Neuro-EMG-MS 2-channel EMG amplifier, and the data were recorded using the Neuro-MEP.NET software.

Stimulation at the motor cortex region was initiated at an intensity of 35% maximum stimulator output and adjusted for each participant until EMG activity at the FDI was observed. The optimal scalp site ('hotspot') to evoke responses in FDI was then established by systematically delivering TMS in 1 cm increments over the scalp.[35] The site that evoked the largest EMG amplitude at a given stimulator intensity was considered the hotspot,[35] over which the middle of the anode tDCS electrode was positioned.

2.5.3. Transcranial direct current stimulation (tDCS)

A 1 × 1 low-intensity direct current stimulator (Model 1300, Soterix Medical) connected to a pair of saline soaked electrodes (35 cm^2) was used to deliver the electrical current. A primary motor cortex supraorbital montage was selected as it is a commonly used montage in investigations of analgesic effects of tDCS.[36,37] Specifically, in the experimental sessions, the anode electrode was centred over the motor hotspot of the contralateral FDI as identified by TMS. The cathode electrode was positioned over the contralateral supraorbital area. tDCS application was completed approximately 5 min prior to the start of the grip strength TTE task. This "offline" administration of tDCS was selected as it has been shown to produce significant effects on pain outcomes assessed post-stimulation.[38,39]

Active stimulation was applied at an intensity of 2 mA for a period of 10 min.[40] This duration of stimulation has previously been shown to reduce exercise-induced pain intensity[40] and produce changes in corticospinal excitability that last 120 min after the completion of stimulation.[41] After an initial 30 s ramping up period, where stimulation intensity was gradually increased from 0 mA to the target intensity of 2 mA (~0.1 A/m^2, see Fig. 2), the current remained at 2 mA for 10 min, followed by a 30 s ramping down to 0 mA. tDCS was started only after the impedance was < 30 kΩ. For sham stimulation, the current intensity ramped up to 2 mA over 30 s before ramping immediately back down to 0 mA at the start, and again at the end of the 10 min period as per standard protocol.[42,43] Protocols for the delivery of active and sham stimulation, including ramping periods, were automated by the stimulation device, ensuring consistency throughout the experiment. Participants sat quietly for the duration of the stimulation protocol.

2.5.4. Isometric exercise

The exercise task used in the current study involved participants performing an isometric grip strength contraction with their dominant hand, exerting 35% of MVC until volitional exhaustion. Previous research has reported consistent hypoalgesic responses to similar isometric grip strength tasks.[1,45–47] Grip strength MVC and TTE was measured with an electronic grip force transducer (Model MLT004/ST, ADInstruments,

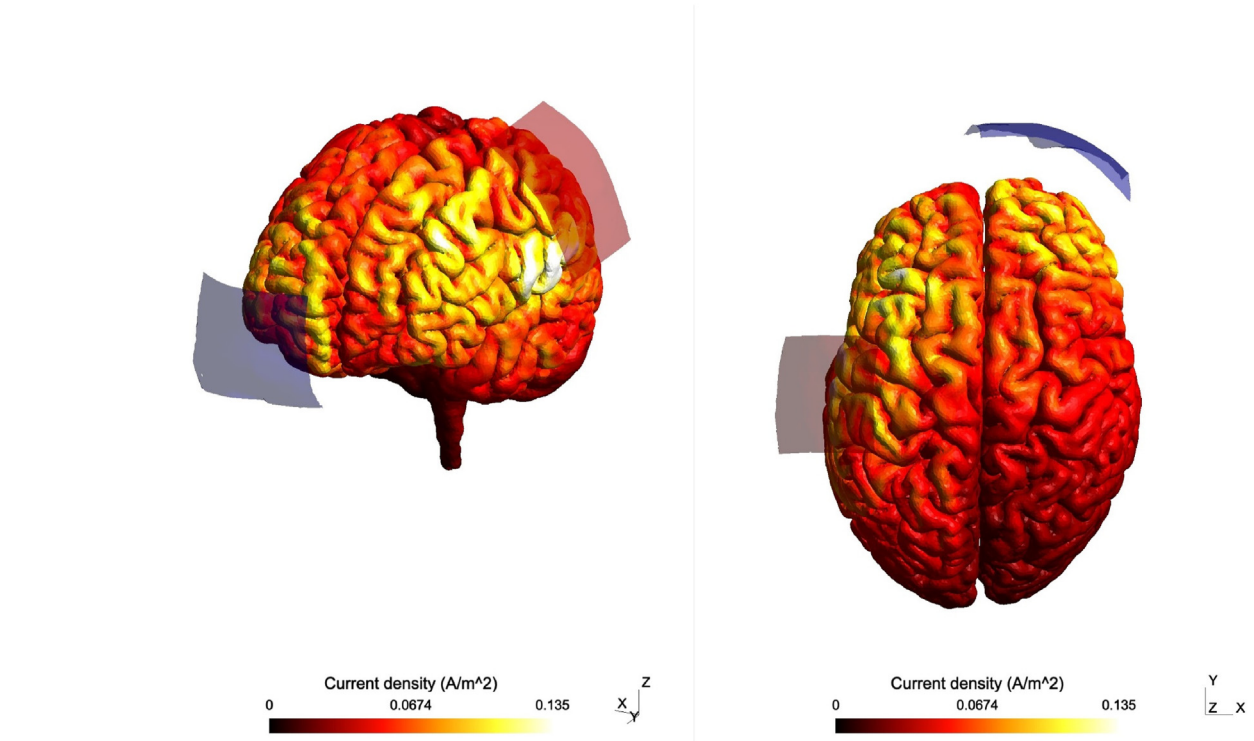

Fig. 2. SimNIBS (v3.2.5, Danish Research Centre for Magnetic Resonance, Copenhagen, Denmark)[44] was used to simulate electric field strength induced by tDCS. Parameters of the tDCS modelling were set according to the protocol defined in text. The following describes the set of parameters used in the computational model: two 4.5 cm × 4.5 cm electrodes of 1.0 mm thickness and two 5 cm × 7 cm 8.0 mm sponge were used. The electrodes were located according to a right-hand dominant participant. The anode was centred at the coordinates corresponding to C3, and the cathode located at the contralateral supraorbital area. Note the anode positioning is an approximation of the TMS guided positioning used in the current study.

Dunedin, NZ). The transducer was sampled at 2 000 Hz via a PowerLab data acquisition unit (ADInstruments, Dunedin, NZ) and was recorded using LabChart software (version 8.1.13, ADInstruments, Dunedin, NZ).

2.5.4.1. Maximal voluntary contraction. Prior to completing the TTE task, maximal grip strength was assessed for the quantification of the TTE target force. Participants were seated in an upright position in front of a table with their dominant forearm rested on the table while holding the transducer in their dominant hand in a neutral position. This positioning allowed the upper arm to be aligned with the trunk (shoulder abduction and elevation angles at 0°) and elbow flexed at 90°. Warm-up trials included two 5-s submaximal isometric contractions at gradually increasing intensities (50%, 75%), separated by a 30 s rest. Participants were instructed to squeeze the transducer maximally for 5 s. Real-time force production was displayed on a laptop monitor, with participants receiving verbal encouragement for maximal effort. A 1 min rest period preceded the second MVC, and the trial with the highest value was considered the true maximum contraction, and recorded as the participants' MVC.

2.5.4.2. Time to exhaustion task. After the MVC task, participants rested for 2 min, during which the target force for the TTE task was calculated as 35% of the participant's MVC. During the TTE task, participants were instructed to maintain an isometric contraction between 35% and 45% of their MVC for as long as possible, without altering the forearm positioning used for the MVC trials. The laptop monitor displayed the track lines at 35% and 45% of MVC, and the TTE duration was defined as the time elapsed from reaching the target force until the last second at or above 35% of MVC. Throughout the test, participants received verbal encouragement. Time measurements were recorded using a digital stopwatch and reported in seconds.

2.5.5. Statistical analysis

Data were analysed using SPSS statistical software (Version 28, IBM Corp, Armonk, NY) and R Statistical Software (Version 4.3.0).[48] A visual inspection of *Z*-score distributions of all variables revealed no univariate outliers greater than 3.29 standard deviations from the mean. Visual inspection of relevant histograms supported the assumption of normality. Prior to analysis, assumptions for parametric tests were assessed and confirmed. Normal distribution was assessed with the Kolmogorov-Smirnov Test, and non-sphericity was corrected using the Greenhouse-Geisser Correction.

The primary analysis compared PPTs at pre-tDCS, post-tDCS, and post-TTE across the two tDCS conditions using a repeated measures analysis of variance (ANOVA) with factors of condition (anodal tDCS, sham tDCS) and time (pre-tDCS, post-tDCS, post-TTE). Mauchly's test of sphericity was not violated for the ANOVA. Bonferroni's post hoc test was used whenever a significant main effect was observed. In cases of significant interactions, simple effects analyses using one-way ANOVA's and Bonferroni's correction were used. Partial eta squared (η_p^2) was reported as a measure of the effect size. For all analyses, $p < 0.05$ was considered statistically significant.

3. Results

3.1. Pain sensitivity

The analysis of PPT data revealed a significant main effect of time; $F_{(1.73,\ 58.89)} = 36.36$, $p < 0.001$, $\eta_p^2 = 0.52$. Results also revealed a non-significant main effect of condition; $F_{(1,\ 34)} = 1.11$, $p = 0.30$, $\eta_p^2 = 0.03$. Further, a non-significant condition by time interaction effect was also observed; $F_{(2,\ 63.80)} = 2.93$, $p = 0.06$, $\eta_p^2 = 0.08$. To further investigate the main effect of time, post-hoc analysis with a Bonferroni adjustment revealed that, irrespective of condition, post-TTE PPT was significantly higher from pre-tDCS PPT (MD, 0.55, 95% confidence interval [*CI*], 0.35 to 0.76; $p < 0.001$) and post-tDCS PPT (MD, 0.47, 95% *CI*, 0.32 to 0.61; $p < 0.001$). Means, standard error, and 95% *CIs* are presented in Table 2. See Fig. 3 for a visual representation of PPTs across condition and time.

4. Discussion

The current study aimed to investigate whether the effects of exercise on pain sensitivity are influenced by prior administration of anodal tDCS. It was hypothesised that pain thresholds would be higher following an isometric grip strength task that was preceded by anodal tDCS when compared to sham tDCS. An additional aim of this study was to assess the independent effect of tDCS on pain sensitivity. It was hypothesised that anodal tDCS would produce a greater increase in pain thresholds when compared to sham stimulation. The findings of this study do not support either hypothesis. Pain thresholds following the combined active tDCS and exercise intervention were not significantly different to pain thresholds following sham tDCS and exercise. With regards to the hypothesised analgesic effect of tDCS alone, there was no difference in the effect of anodal and sham stimulation on pain threshold.

The primary finding of the current study is that anodal tDCS does not appear to enhance the acute hypoalgesic effect of an isometric grip strength task. Only one study has previously examined the potential for tDCS to augment the hypoalgesic effects of tDCS.[21] In this study, pain attributed to intramuscular injection of nerve growth factor was lower post-exercise in the active tDCS condition compared to the sham condition. While this finding suggests that anodal tDCS may have enhanced EIH, baseline differences limit the clarity of the findings. The current findings also contradict research examining the potential for tDCS to complement longer-term behavioural interventions, including exercise, for pain relief in chronic pain populations[49]; however, it should be noted that the nature of these longer term interventions and the samples examined differ markedly from that examined in the current study. Given the limited and inconsistent data, further research is needed to examine the potential for tDCS to enhance the acute hypoalgesic effects of exercise.

It is acknowledged that any explanation for the lack of complementary analgesic effects of tDCS and exercise is beyond the scope of this study. However, one possible explanation is that these findings indicate a ceiling effect for hypoalgesic effects of exercise, that limits the capacity of a second intervention to enhance the response. Indeed, this ceiling effect of EIH has been reported in previous research.[50] Notably, using a

Table 2
Summary of ANOVA results for pain pressure thresholds.

	Condition	Time	Mean	*SE*	Lower bound 95% *CI*	Upper bound 95% *CI*
Time		Pre-tDCS	6.80	0.18	6.43	7.16
		Post-tDCS	6.88	0.17	6.54	7.23
		Post-TTE	7.35	0.19	6.97	7.73
Time × Condition	**Active tDCS**	Pre-tDCS	6.69	0.22	6.24	7.14
		Post-tDCS	6.89	0.20	6.45	7.29
		Post-TTE	7.17	0.22	6.73	7.61
	Sham tDCS	Pre-tDCS	6.91	0.19	6.53	7.28
		Post-tDCS	6.88	0.19	6.50	7.25
		Post-TTE	7.53	0.22	7.08	7.97

$n = 35$. **Abbreviations:** tDCS = transcranial direct current stimulation, *SE* = standard error, TTE = time to exhaustion, *CI* = confidence interval.

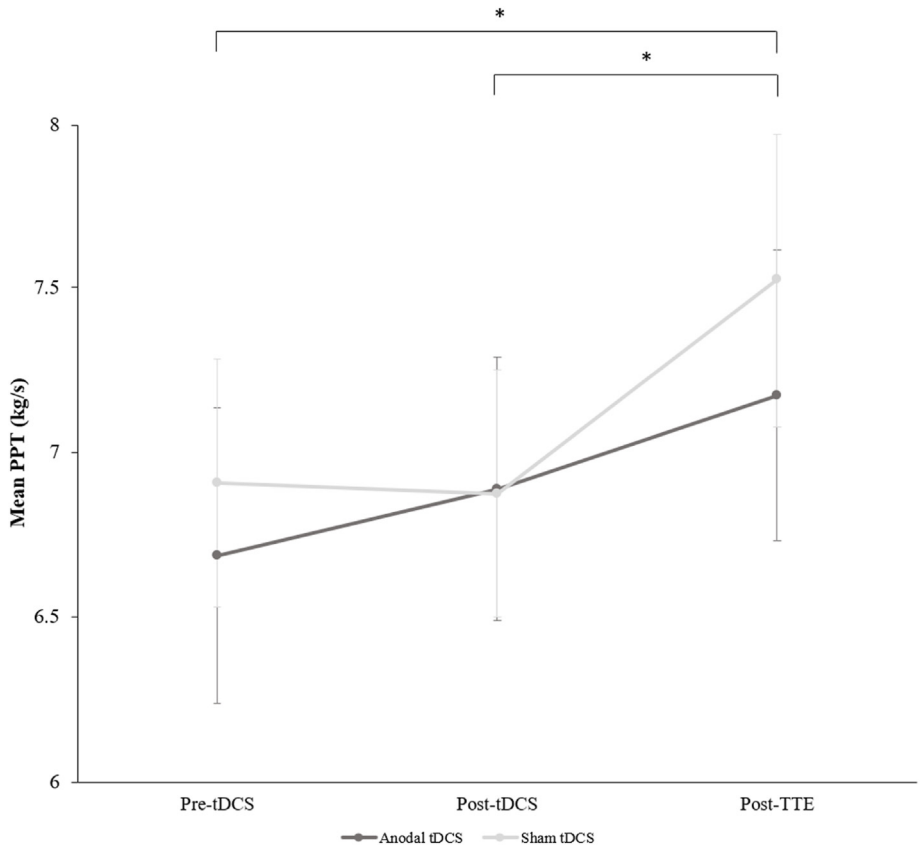

Fig. 3. Pre-tDCS, post-tDCS, and post-TTE PPT values across conditions. Error bars are standard error. $n = 35$. * = $p < 0.05$ **Abbreviations:** PPT = pain pressure threshold, tDCS = transcranial direct current stimulation, TTE = time to exhaustion.

conditioned pain modulation assessment post-exercise, it was observed that the exercise had already elicited the maximum hypoalgesic effect, precluding any additional hypoalgesia induced by a second noxious stimulus.[50] In the context of the present study, it is plausible that the isometric exercise task performed may have already induced the maximum hypoalgesic response achievable, leaving minimal room for tDCS to further enhance this effect. While plausible, such a suggestion remains speculative and requires further investigation.

Contrary to our hypothesis, anodal tDCS over the motor cortex did not produce a hypoalgesic effect independent of exercise. This finding is inconsistent with the result of a recent meta-analysis by Giannoni-Luza et al.[51] who reported that anodal tDCS over the motor cortex had an overall small to medium effect on pain thresholds in both healthy and chronic pain populations. However, a separate meta-analysis conducted by Li et al.[38] found that anodal tDCS over several sites including the motor cortex did not have a significant influence on pain thresholds or pain tolerance in healthy populations. Anodal tDCS did however appear to produce a significant reduction in pain-intensity ratings to supra-threshold noxious stimuli.[38] These findings suggest that the effects of tDCS on pain processing are complex, likely involving sensory, affective and cognitive components that cannot be evaluated through pain threshold measurement. While such a suggestion is not new,[38] further research is required to understand the hypoalgesic potential of tDCS and the underlying mechanisms of action.

Interpreting the outcomes of our study necessitates a recognition of several limitations. Primarily, our methodology did not employ a no-exercise control condition. As a result, we cannot confirm that the observed increase in pain thresholds post-exercise was indicative of an exercise induced hypoalgesic response. For example, it is possible that the observed increase in pain thresholds was due to repeated assessment within-session. Despite the lack of a no-exercise control condition, the study design did allow for an investigation of whether pain sensitivity post-exercise is influenced by prior administration of active tDCS. Further, the lack of a no-exercise control condition aligns with existing research examining the potential for preceding interventions to affect exercise induced hypoalgesia. For example, in previous research examining whether an opioid antagonist affects exercise-induced hypoalgesia,[11,12] exercise interventions have been included in active and placebo arms of the trials without the inclusion of a no-exercise control. A second potential limitation of the current study relates to the timing of pain assessment. Our evaluation of pain threshold was confined to immediate post-tDCS and post-TTE measurements, limiting our opportunity to examine the potential enduring effects of the combined intervention on pain sensitivity. Although it is possible that we missed the peak hypoalgesic response, PPTs were assessed immediately post-exercise based on research showing that hypoalgesic responses decay linearly post-exercise.[52] Lastly, we acknowledge the use of a single-blind design as a limitation of this study. While participants were blinded to their experimental conditions, researchers were aware of the stimulation conditions, which may have introduced potential bias in the data collection. Future studies should aim to implement double-blinding to further reduce the risk of bias.

Our findings revealed that pain sensitivity after a grip strength exercise task were not affected by preceding tDCS. Further, tDCS alone did not produce any significant effect on pressure pain threshold. Future research should replicate and extend on the currently limited research examining the potential for tDCS to complement the hypoalgesic effects of exercise. Consideration should be given to the inclusion of a no-exercise control condition to support the delineation of the independent and combined effects of exercise and tDCS on pain. Follow-up pain assessment is also recommended as a means of exploring time-course effects of the EIH phenomenon.

CRediT authorship contribution statement

Aidan Lewis: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Ben Rattray:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Constantino Toufexis:** Writing – review & editing, Writing – original draft. **Andrew Flood:** Writing – review & editing, Validation, Supervision, Project administration, Conceptualization.

Data availability

The datasets generated and analysed during the current study are available in the Digital Commons Data repository: https://doi.org/10.17632/g94823v5vw.1.

Ethical approval statement

All participants signed an informed consent document before starting the study. All experimental procedures were approved by the University of Canberra's Human Research Ethics Committee (Project ID: 11882) and conformed to the principles outlined in the Declaration of Helsinki.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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