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Efficacy of tDCS and EEG Neurofeedback, individually and combined, on Neuropathic Pain following spinal cord injury: Protocol for a Randomised Controlled Trial

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Article

Keywords:

Posted Date: April 9th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9142924/v1

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Additional Declarations: There is no duality of interest

Efficacy of tDCS and EEG Neurofeedback, individually and combined, on Neuropathic Pain following spinal cord injury: Protocol for a Randomised Controlled Trial

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Title	Efficacy of tDCS and EEG Neurofeedback, individually and combined, on Neuropathic Pain following spinal cord injury: Protocol for a Randomised Controlled Trial
Trial registration	ANZCTR identifier: ACTRN12625000737437p

Protocol version	1
Ethics Approval	iRECS9099, Ethics approval date: 29/01/2026
Funding	Medical Research Future Fund
Author details	[1]Centre for Pain IMPACT, Neuroscience Research Australia, Sydney, New South Wales, Australia [2] NeuroRecovery Research Hub, School of Psychology, University of New South Wales, Sydney, New South Wales, Australia [3]Faculty of Health, University of Technology Sydney, Australia [4]John Walsh Centre for Rehabilitation Research, The Kolling Institute, Faculty of Medicine and Health, University of Sydney, Sydney, Australia [5]Department of Rehabilitation Medicine, University of Washington, Seattle, USA [6] The Kolling Institute, Faculty of Medicine and Health, University of Sydney, Sydney, Australia [7]Statistical Consulting Unit, University of New South Wales, Australia [8]School of Health Science, University of New South Wales, Australia
Name and contact information for the trial sponsor	The University of New South Wales
Role of sponsor	Holds accountability for trial governance and compliance, and delegates day-to-day conduct and oversight to the Coordinating Principal Investigator under defined conditions and reporting requirements.

Abstract

Study Design: Randomised controlled trial (RCT) Protocol

Objectives: Neuropathic pain (NP) affects approximately 60% of individuals with spinal cord injury (SCI). Existing pharmacological treatments provide modest relief and are often limited by adverse

effects, while non-pharmacological options show small effects at best. Thus, there remains a need for accessible, mechanism-informed treatments for SCI-NP. This protocol describes an RCT evaluating the efficacy of two promising home-based neuromodulatory interventions for SCI-NP - electroencephalography neurofeedback (EEG-NF) and transcranial direct current stimulation (tDCS) - tested both independently and in combination.

Setting: Australia-wide

Methods: A partially double-blinded (i.e. 1 treatment blinded, the other not), 2×2 factorial RCT will be implemented. Adults with SCI-NP (N=192) will be randomised to one of four groups: EEG-NF + active tDCS, EEG-NF + sham tDCS, active tDCS, or sham tDCS. Participants will complete 20 home-based sessions over 5 weeks. The primary outcome is pain severity at 6 weeks post-randomisation. Secondary outcomes include pain severity at 16, 26 and 52 weeks, and worst pain intensity, pain interference, sleep disturbance, depressive symptoms, and health-related quality of life at 6, 16, 26 and 52 weeks post-randomisation.

Results: The trial has been prospectively registered and approved by the University of New South Wales Human Research Ethics Committee.

Conclusion: This trial will provide the first large-scale evaluation of home-based EEG-NF and tDCS, delivered individually and in combination, for SCI-NP. If effective, these scalable interventions may support integration of home-based neuromodulation into routine care for this population.

Funding: Medical Research Future Fund (MRFF) Clinical Trials Activity

Introduction

Neuropathic pain (NP) affects approximately 60% of individuals with spinal cord injury (SCI) and is often rated by these individuals as more disabling than loss of mobility[1]. It typically occurs at or below the injury level, and is described as burning, shock-like, tingling, stabbing sharp and persistent, and substantially impairs mood, sleep and social functioning[2]. Moreover, SCI-NP is often resistant to treatment and tends to worsen over time[3]. Current evidence-based pharmacological treatments for central neuropathic pain (tricyclic antidepressants, SNRIs, gabapentin and pregabalin) provide only modest pain relief on average and are frequently limited by adverse effects; opioids are generally discouraged, with tramadol reserved for short episodes of severe pain[4]. Non-pharmacological approaches, such as cognitive behavioural therapy, physical therapies, acupuncture, and therapeutic hypnosis generally show at best small effects, and, for central neuropathic pain specifically, there exists insufficient evidence[2-6]. The lack of effective treatments highlights the need for new treatments to address SCI-NP and improve patients' pain outcomes. Here we present a protocol for a trial aiming to evaluate two promising home-based neuromodulation treatments for SCI-NP. Home-based treatments are gaining traction due to their potential to accommodate mobility limitations in individuals with SCI-NP.

Electroencephalography (EEG) Neurofeedback (NF). The development and maintenance of chronic neuropathic pain following SCI is hypothesized to be associated with thalamocortical dysrhythmia[7]. This problem can be detected using surface electroencephalography (EEG)[8]. In SCI-NP, this dysrhythmia has been characterised by increased resting state theta (4–7 Hz) and high beta (20–30 Hz) power and reduced sensorimotor rhythm (10–15 Hz) power compared with healthy controls[8-10]. EEG-NF trains individuals to self-regulate these rhythms.[11,12] EEG is recorded (e.g., over sensorimotor cortex), relevant frequency bands are extracted in real time, and their power is translated into game-like or audio-visual feedback that reinforces desired brain activity[13-16]. This may enable individuals with SCI-NP to normalise dysrhythmic activity and reduce pain[8,17]. EEG-NF has shown promising effects for SCI-NP with a favourable adverse-effect profile compared to pharmacological therapies[8,12]. However, large, well-controlled randomised controlled trials (RCTs) in SCI-NP are lacking. A recent RCT in 116 individuals with chronic pain compared active EEG-NF to a sham

82 "yoked feedback" condition where participants viewed another individual's feedback; 44–46% of
83 participants in both groups achieved moderate pain relief, with no between-group difference[18].
84 However, as the authors note, the sham condition likely acted as an active intervention, because ~25%
85 of the replayed feedback still coincided with desirable EEG patterns. Consistent with broader critiques
86 of sham neurofeedback[19], such designs may underestimate true treatment effects. To minimise this
87 issue, the current trial evaluates EEG-NF in addition to treatment as usual, rather than against an
88 active sham.

89 **Transcranial Direct Current Stimulation (tDCS).** Chronic neuropathic pain is often
90 associated with an increase in activity in central pain pathways (central sensitisation[20]) motivating
91 treatments that directly target the central nervous system. tDCS involves delivery of an electrical
92 current through scalp electrodes, resulting in modulation of cortical excitability[21], and activation of
93 descending anti-nociceptive pathways[22] with relatively few side effects compared with
94 pharmacological or surgical options. In a 2018 Cochrane review of RCTs for chronic pain[23] and 2025
95 Lancet review of RCTs for neuropathic pain[24], while tDCS was found to elicit small to moderate
96 reductions in pain intensity, the certainty of evidence was rated very low. As discussed in our recent
97 perspective piece[25], two factors for this inconclusive evidence are (1) underpowered sample sizes
98 across trials and (2) a strong reliance on a generic tDCS montage (placement of electrodes) involving
99 the anode placed on left M1 and cathode placed on the right supraorbital (SO) region[26], rather than
100 tailoring the montage towards the mechanisms underlying pain. Because SCI-NP is commonly
101 dominated by bilateral and lower extremity pain, a montage that preferentially modulates the bilateral
102 lower extremity motor areas in M1 may be a more appropriate mechanistic target[27]. Thus, in addition
103 to adequate statistical power, the present trial will, for the first time, test a novel montage for SCI-NP
104 with the anode positioned over the vertex and the return electrode on the shoulder. Modelling suggests
105 that this configuration engages bilateral lower-extremity motor cortical representations, while the
106 extracephalic cathode may reduce confounding cortical effects associated with a cephalic return
107 electrode.

108 **Combined EEG-NF and tDCS.** The combination of EEG-NF and tDCS may also yield
109 therapeutic benefits. tDCS has been hypothesised to "prime" cortical networks by increasing cortical

excitability and promoting plasticity, thereby enhancing the effects of concurrent therapies[28]. In SCI-NP, a study of 39 participants found that tDCS augmented the pain-relieving effects of a visual illusion gait intervention compared with either treatment alone[29]. A larger RCT of 130 participants reported greater pain reduction when tDCS was combined with visual illusions when compared to a control group, although it did not compare the combination to sham tDCS (i.e. placebo)[30]. These findings suggest that pairing tDCS with an EEG-NF may also yield therapeutic benefits, however no large-scale trial has yet tested this in SCI-NP.

Aims of the Current Trial. The primary aim of the study described herein is to conduct an RCT that addresses the methodological limitations of prior research, described previously. Specifically, we plan to conduct a 2×2 factorial RCT that will evaluate the independent and combined efficacy of home-based EEG-NF and tDCS for SCI-NP. This will be the first large-scale trial of these home-based interventions in SCI-NP and will provide critical evidence to guide future clinical implementation.

Methods

Trial Design

The trial will use a partially double-blinded, 2 × 2 factorial randomised controlled design. Participants will be allocated to one of the four groups shown in Table 1.

The trial has been prospectively registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12625000737437p) and this protocol adheres to the Standard Protocol Items: Recommendations for Interventional Trials Guidelines[31]. Findings from this study will be reported according to the Consolidated Standards of Reporting Trials statement[32]. Figure 1 shows the CONSORT flow diagram.

Objectives

Primary Objectives

1. To test the causal effect of EEG-NF compared to no EEG-NF on pain severity at 6 weeks post-randomisation (primary endpoint), in individuals not given active tDCS.
2. To test the causal effect of active tDCS compared to sham tDCS on pain severity at 6 weeks post-randomisation, in individuals not given EEG-NF.

3. To test the causal effect of combined EEG-NF and active tDCS compared to sham tDCS on pain severity at 6 weeks post-randomisation.

Secondary Objectives

1. To describe, in individuals not given active tDCS, the possible causal effect of EEG-NF compared to no-EEG-NF on:
    a. Pain severity at 16, 26, and 52 weeks post-randomisation.
    b. Worst pain severity, pain interference, sleep problems, depressive symptoms and health-related quality of life at 6, 16, 26, and 52 weeks post-randomisation.
2. To describe, in individuals not given EEG-NF, the possible causal effect of active tDCS compared to sham tDCS on:
    a. Pain severity at 16, 26, and 52 weeks post-randomisation.
    b. Worst pain severity, pain interference, sleep problems, depressive symptoms and health-related quality of life at 6, 16, 26, and 52 weeks post-randomisation.
3. To describe the possible causal effect of combined EEG-NF and active tDCS compared to sham tDCS, on:
    a. Pain severity at 16, 26, and 52 weeks post-randomisation.
    b. Worst pain severity, pain interference, sleep problems, depressive symptoms and health-related quality of life at 6, 16, 26, and 52 weeks post-randomisation.

Sample Size

The sample size calculation was conducted by Dr Robert Herbert, an independent biostatistician. The sample size required to provide nominal power for null hypothesis tests corresponding to each of the trial's primary objectives was determined analytically and using Monte Carlo simulations (5,000 simulated trials). The trial is powered to detect a 1-point difference on the primary outcome (pain severity), consistent with the OMERACT-recommended minimal clinically important difference (MCID) of 1 point on a 0–10 scale[33]. The SD (1.9) was taken from a previous SCI neuropathic pain trial (HC210932, VRWalk[34]) and conservatively rounded to 2.0. The baseline–post correlation of the measure of pain severity in that trial was 0.76; here, correlations between adjacent timepoints were assumed to be 0.75, decaying by 0.05 for each increasingly distant timepoint. Baseline (pre-treatment) pain severity score was included as a covariate. The nominal Type I error rate (two-sided) was set at 0.05, and allowance was made for a worst-case loss to follow-up of 20%. These calculations indicated that a total sample size of 192 participants (48 per group) would

provide 90% power for each of the three primary objectives (main effect of tDCS vs sham tDCS; main effect of EEG neurofeedback vs control; and their combined effect).

Study setting and eligibility

Participants will complete the intervention at home anywhere in Australia; all equipment and procedure manuals will be mailed to their address. The study will recruit adults (≥18 years) with a complete or incomplete cervical, thoracic or lumbar spinal cord injury ≥6 months post-injury, with ongoing neuropathic pain at or below the injury level for >3 months and average pain ≥4/10 over the past week. Eligibility requires endorsement of ≥2 items on the 4-item Screening for SCI-NP Instrument (SCIPI)[35], independent breathing, ability to read and understand English, and capacity to complete the intervention (self-administering tDCS/EEG-NF or with caregiver assistance), including one session per day for 20 days over 5 weeks. Exclusion criteria include contraindications to brain stimulation (e.g., cardiac pacemaker, cochlear implant, deep brain stimulator, metal in the head, history of serious head injury or stroke, personal or first-degree family history of seizures, pregnancy or lactation), neurological or psychiatric disorders with cognitive impairment (e.g., dementia, schizophrenia), and residence outside Australia.

Recruitment and consent

Participants will be recruited using existing databases at Neuroscience Research Australia, NeuroRecovery Research Hub, UNSW, the George Institute's Join Us register, as well as using community flyers, social media, and national SCI/NP organisations and support groups. Prospective participants will receive a Participant Information Statement, have time to consider participation, and provide electronic consent via REDCap with support from a research assistant trained in Good Clinical Practice. They may optionally provide consent for the release of Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) data from Services Australia for health economic analyses.

Randomisation

Following eligibility screening, informed consent, and baseline questionnaires, participants will be randomised to one of four groups (Groups 1–4) in a 1:1:1:1 ratio. The randomisation sequence will be in permuted blocks of size 4, 8 or 12. An independent statistician, not involved in recruitment

or assessment, will use a random number generator to create a schedule assigning each participant ID to a group. After consent and baseline assessment, allocations will be revealed (on REDCap) only to a team member not involved in recruitment or assessment, who will then mail the relevant equipment and manuals to participants' home addresses. The first intervention session will commence 1 week later to allow for delivery. The allocation schedule will remain inaccessible to other trial staff until study completion to ensure allocation concealment.

Blinding

Participants and assessors will be blinded to tDCS allocation; however, blinding will not be feasible for EEG-NF. An investigator independent of outcome assessment will pre-program the device to deliver active or sham tDCS. Sham involves a 20s ramp-up to 2 mA, a 17 s ramp-down to 0 mA, and brief 0.1 mA pulses every 5 minutes to monitor impedance, mimicking active sensations without ongoing current. Participants in all groups will be informed they may experience mild scalp sensations (e.g. tingling/itching) that may diminish over time. Participants will not be told their allocation and will be debriefed at study completion. Blinding integrity will be assessed via end-of-trial questionnaires in which participants guess their tDCS allocation and rate confidence, and assessors guess group allocation. All analyses will use de-identified, coded data, and the allocation schedule will remain inaccessible to other staff until trial completion to preserve concealment.

Overview of Intervention

All participants will complete 20 home-based sessions over five weeks (four sessions per week), commencing no earlier than one-week post-randomisation. Groups 1 and 2 will complete 60-minute sessions combining tDCS and EEG-NF; Groups 3 and 4 will complete 30-minute tDCS-only sessions. For all groups, a study tablet will guide each session with step-by-step setup instructions, and for Groups 1 and 2, serve as the EEG-NF interface. Each session will include 10 minutes of tDCS setup followed by 20 minutes of stimulation. Groups 3 and 4 then conclude, whereas Groups 1 and 2 complete an additional 10-minute EEG-NF setup and 20 minutes of neurofeedback. To verify adherence and montage accuracy, the tablet will prompt all participants to upload a photo of their tDCS and EEG-NF setup before the intervention. Images will be uploaded in real time to a secure AWS Cloud dashboard for monitoring and quality assurance.

tDCS Intervention

Overview. Active tDCS or Sham will be delivered at 2mA for 20 min via a Sooma stimulator (ARTG ID 278349, Sooma, Finland) using 5 cm circular rubber electrodes with saline-soaked sponge pads. Stimulation will commence only once electrode impedance is sufficiently low. If impedance is too high, the tablet interface will instruct participants to apply additional saline.

tDCS Montage. Existing RCTs for SCI-NP have placed the anode over C3 (hand motor cortex) and the cathode over the right supraorbital region[23]. However, systematic reviews have reported inconclusive evidence for neuropathic pain using this montage[24,36], possibly because it does not specifically target neural mechanisms and body regions most relevant to SCI-NP. Converging evidence indicates that cortical excitability is a key mechanistic target for neuromodulation. Low corticomotor excitability has been proposed as a biomarker for chronic pain development[37], and individuals with SCI-NP exhibit reduced motor cortex excitability compared with those without NP[38]. Furthermore, high-frequency rTMS, which increases cortical excitability[39], has been shown to produce analgesic effects in neuropathic pain[40]. Because SCI-NP is commonly dominated by bilateral and lower-extremity pain, an optimal montage may be one that preferentially modulates the bilateral and lower-extremity motor cortical representations.

A review of tDCS montages[41] highlighted work by Kasi et al.[42] , showing that a Cz–Inion montage significantly increased motor-evoked potential amplitudes in bilateral tibialis anterior. Electrical field modelling further demonstrated that Cz–Inion tDCS aligns current flow parallel to pyramidal tract fibres projecting to the lower extremities, enhancing stimulation efficiency [43] and subsequent work in 31 participants confirmed more pronounced reductions in lower limb motor thresholds with Cz–Inion than with C3–C4 or C1–C2 montages. These data support Cz–Inion as a promising approach for increasing excitability in lower extremity representations.

However, montage selection must also avoid unwanted inhibitory effects at the cathode, which may attenuate or reverse anodal benefits[44]. Placing the cathode at the Inion delivers cathodal (inhibitory) stimulation over cerebellar regions, which may be suboptimal for pain modulation[45]. A recent synthesis of brain stimulation targets for chronic pain, combining a meta-analysis of 92 neuroimaging studies with resting-state fMRI in 90 patients, identified the cerebellum as a promising

site for excitatory neuromodulation. Consistent with this, anodal cerebellar tDCS has reduced pain intensity during experimental pain in healthy volunteers and in individuals with peripheral neuropathic pain [46,47]. Cathodal cerebellar stimulation, as in Cz–Inion, could therefore undermine analgesic aims.

To address this, extra-cephalic montages placing the return electrode on the shoulder have been proposed. Modelling studies indicate that extra-cephalic placements can generate more focused current under the anode and allow greater depth of penetration to reach deeper structures. Experimental work applying anodal tDCS over the vertex with a shoulder return electrode has shown significant increases in quadriceps motor cortex excitability and improved cycling performance[44,48-50], suggesting a vertex–shoulder montage can effectively modulate lower extremity motor areas while avoiding cortical inhibition at the cathode.

For the present trial, we modelled a Cz–shoulder montage using SIMNIBS Ernie Extended[51], with 5 cm electrodes and default tissue conductivities (Figure 2). Electrical field modelling indicated robust fields in both the leg motor area (maximal 0.80, mean 0.46 volts/m) and cerebellum (maximal 1.24, mean 0.86), supporting the Cz–shoulder configuration as a biologically plausible approach for targeting lower extremity motor cortex and cerebellar pain networks in SCI-NP. It is also important to note that this montage would direct current closer to the EEG-NF electrode sites (C1 and C2), which may be preferable to a standard montage in which current enters predominantly through one side of the motor cortex (e.g., C3) but not the other.

In this trial, the anode at the vertex will be secured with a 3D-printed headset (Figure 3) and the shoulder cathode with a band, both designed for home use. Detailed instructions are provided through printed manuals, step-by-step guidance in the tablet app, and a supervised initial online session.

Time window between tDCS and EEG-NF (Groups 1 and 2 only). Once the tDCS is complete, participants will be instructed to clean residual tDCS saline (comb out crystals, rinse and wipe with water, gauze, cotton swabs, then dry with gauze and alcohol wipes). tDCS is thought to prime the brain by increasing cortical excitability and enhancing plasticity in neural circuits engaged by concurrent therapies[52]. However, our system cannot deliver EEG-NF and tDCS simultaneously because tDCS introduces electrical artefacts that disrupt the neurofeedback algorithm, so EEG-NF must follow tDCS. To determine how long motor cortical excitability remains elevated after 2mA anodal motor cortex tDCS, we collected pilot data from 20 individuals with an SCI (13 of whom had neuropathic pain), measuring motor evoked potentials (MEPs) every 5 minutes for 60 minutes. Figure 4 shows the mean MEP amplitude at each timepoint, normalised to the pre-tDCS MEP amplitude; error bars indicate 95% confidence intervals. The confidence intervals remained consistently above the pre-tDCS reference (i.e., 1.0) until at least 45 minutes post-tDCS, suggesting a sustained period of heightened corticomotor excitability. To ensure EEG-NF is administered within this window, we will commence approximately 10 minutes after tDCS, with this interval used for EEG-NF setup.

EEG Neurofeedback Intervention (Groups 1 and 2 Only)

A wireless EEG headset was custom-designed for this trial using a variant of the OpenBCI Ganglion board (openbci.com). Several 3D-printed prototypes were iteratively tested in several able-bodied participants to optimise comfort, usability, and signal quality [53]. The final one-size-fits-all design includes adjustable sliding earpieces and two saline-soaked sponge electrodes at C1 and C2 (10–20 system) targeting sensorimotor cortex, with two ear-clip reference electrodes.

A tablet app guides participants through headset setup, impedance checks, resting-state EEG, and neurofeedback (Figure 5). Before each session, switch on the headset, connect via Bluetooth, insert pre-soaked electrodes at C1/C2, and attach ear-clips. Impedance is checked automatically; if >50 kΩ, on-screen troubleshooting is provided.

Each session will start with 2 minutes of eyes-open resting-state EEG to establish individual alpha, theta, and beta baselines. Participants will then complete five 2.5-minute neurofeedback game rounds, with short breaks. Four games (Jellyfish, Bird, Plane, Rocket) will be introduced sequentially

to maintain engagement. The protocol trains suppression of theta (4–7 Hz) and high-beta (20–30 Hz), and enhancement of sensorimotor rhythms (SMR, 10–15 Hz, constituting high alpha and low beta). When all three bands move in the desired direction, the games provide real-time visual feedback via character motion and background changes; scores at the end of each round track progress. Participants will be encouraged to develop their own mental strategies (e.g., positive thinking, focus on game elements, pleasant imagery, breathing techniques). Relaxing background music can be adjusted or muted. Post-intervention interviews will explore strategies perceived as most effective.

Summary of the Interventions

A summary of each intervention session is provided in Figure 6.

Outcome Measures

Table 2 shows the schedule of enrolment, interventions and assessments. Responses to all outcome measures will be self-entered and recorded online directly through REDCap[54]. At baseline, an online questionnaire will be sent to participants requesting demographics (age, birth sex, gender identity, marital status, education, employment, household income, and country of birth) and injury information (time since injury, injury level, aetiology of injury).

Primary Outcome: Pain Severity

The primary outcome is the pain severity assessed 6 weeks post-randomisation (primary endpoint). Pain severity will be assessed using the Brief Pain Inventory (BPI) - Pain Severity scale. Participants will be asked to rate their worst and least over the last 7 days in addition to their average and current pain, on a scale from 0 (no pain) to 10 (worst imaginable pain). Pain severity will be operationalised as the average of these four items.

Secondary Outcomes

- **Pain Severity**: BPI Pain Severity assessed at 16 weeks, 26 weeks, and 52 weeks post-randomisation

Other secondary outcomes (listed below) will be measured at baseline, 6 weeks, 16 weeks, 26 weeks, and 52 weeks post-randomisation.

- **Worst Pain: '**Pain at its worst' item from BPI-Pain Severity
- **Pain Interference:** BPI Pain Interference, modified for SCI
- **Sleep Disturbance:** PROMIS Sleep Disturbance 8b Short Form + 2 items of Medical Outcomes Study Sleep Scale (MOS-SS)
- **Mood:** Patient Health Questionnaire (PHQ-9)
- **Health-related quality of life:** Short-Form Survey (SF-36), modified for SCI

Statistical Analyses

A detailed, date-stamped Statistical Analysis Plan (SAP) will be uploaded to the Open Science Framework. Key elements are summarised here.

General principles. Analyses will emphasise estimation of causal effects with point estimates and confidence intervals, supplemented by two-sided tests[55,56]. A blinded "dummy" analysis (artificial re-randomisation) will be used to finalise modelling choices. Reporting will follow CONSORT (including non-pharmacological/sham extensions) [57]. All randomised participants will be analysed under an intention-to-treat framework.

Estimands. Primary estimands are the average causal effects of (1) the effect of EEG-NF compared to no EEG-NF when given sham tDCS, (2) the effect of tDCS compared to sham tDCS when not given EEG-NF, and (3) the effect of combined tDCS + EEG-NF together compared to no intervention (sham tDCS), on BPI–Pain Severity at 6 weeks.

Multiplicity. Each of the three primary objectives (EEG-NF, tDCS, combined) will use $\alpha = 0.05$ (two-sided) without formal multiplicity adjustment, consistent with a "three-trials-in-one" design.

Primary analysis of effectiveness. For the primary endpoint (pain severity at 6 weeks), the primary analysis will use an optimally efficient factorial regression model with BPI–Pain Severity as the dependent variable, baseline BPI–Pain Severity as a covariate, and fixed indicators for EEG-NF (yes/no), tDCS (active/sham), and their interaction (EEG-NF×tDCS). This model provides estimates of each intervention's effect and their combination, adjusted for baseline values. From this model,

three pre-specified pairwise comparisons will be estimated using linear contrasts: (1) EEG-NF vs no EEG-NF within sham tDCS, (2) active vs sham tDCS within no EEG-NF, and (3) combined EEG-NF + active tDCS vs sham tDCS. These contrasts will be estimated within a single factorial model, enabling interpretation of each intervention's effect conditional on the absence of the other. Results will be reported as mean differences (negative favouring active), with 95% confidence intervals and two-sided p-values, focusing on estimation.

Missing data. Primary analyses will use all available data assuming missing at random[58]. We will report missingness by arm/timepoint. If 5–40% of 6-week outcomes are missing, a sensitivity analysis using multiple imputation (Bayesian MCMC under a multivariate normal model; 50 imputations; Rubin's rules) will be conducted [59]:

Ethics and Dissemination

The protocol has been approved by the University of New South Wales Human Research Ethics Committee (iRECS9099). Any protocol deviations will require ethics amendments and registry updates. Identifying information will be replaced with unique IDs, and personal data will be kept confidential in line with NHMRC guidelines and stored in a secure, password-protected database accessible only to the research team for 15 years. Findings will be disseminated via peer-reviewed publications and conference presentations.

Trial Status

The trial is scheduled to begin in June 2026 and end in December 2029.

Discussion

This trial addresses a major unmet need for addressing neuropathic pain after SCI, a common, highly disabling secondary condition, which is often refractory to existing pharmacological and non-pharmacological treatments[1-6]. By targeting thalamocortical dysrhythmia and aberrant sensorimotor rhythms using EEG-NF and cortical excitability with a mechanistically informed tDCS montage, the trial directly tests promising, low-risk neuromodulatory approaches that can be delivered at home, reducing access barriers for people with significant mobility limitations. The trial is powered based on

an established MCID for pain and incorporates long-term follow-up to assess durability of benefit. Rigorous methods, including prospective registration, SPIRIT- and CONSORT-consistent reporting, pre-specified estimands and a detailed SAP are designed to maximise robustness and interpretability. If EEG-NF and/or tDCS prove effective, alone or in combination, the findings will provide a strong evidential and mechanistic basis for integrating home-based neuromodulatory therapies into routine care pathways for SCI-NP.

Conflict of Interest

The authors declare that they have no competing interests

Funding

This work was supported by the Medical Research Future Fund Clinical Trails Activity Grant awarded to Sylvia M Gustin

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Figure Legends

Figure 1. CONSORT flow diagram.

Figure 2. Results of Electrical field modelling using a novel Montage with the anode positioned on Cz and return electrode placed on the right shoulder. E fields are generated in both the leg motor area and cerebellum.

Figure 3. Photographs of the building blocks of the montage, including a 3D printed headset that will contain the anodal electrode, and right shoulder armband that will contain with cathodal electrode

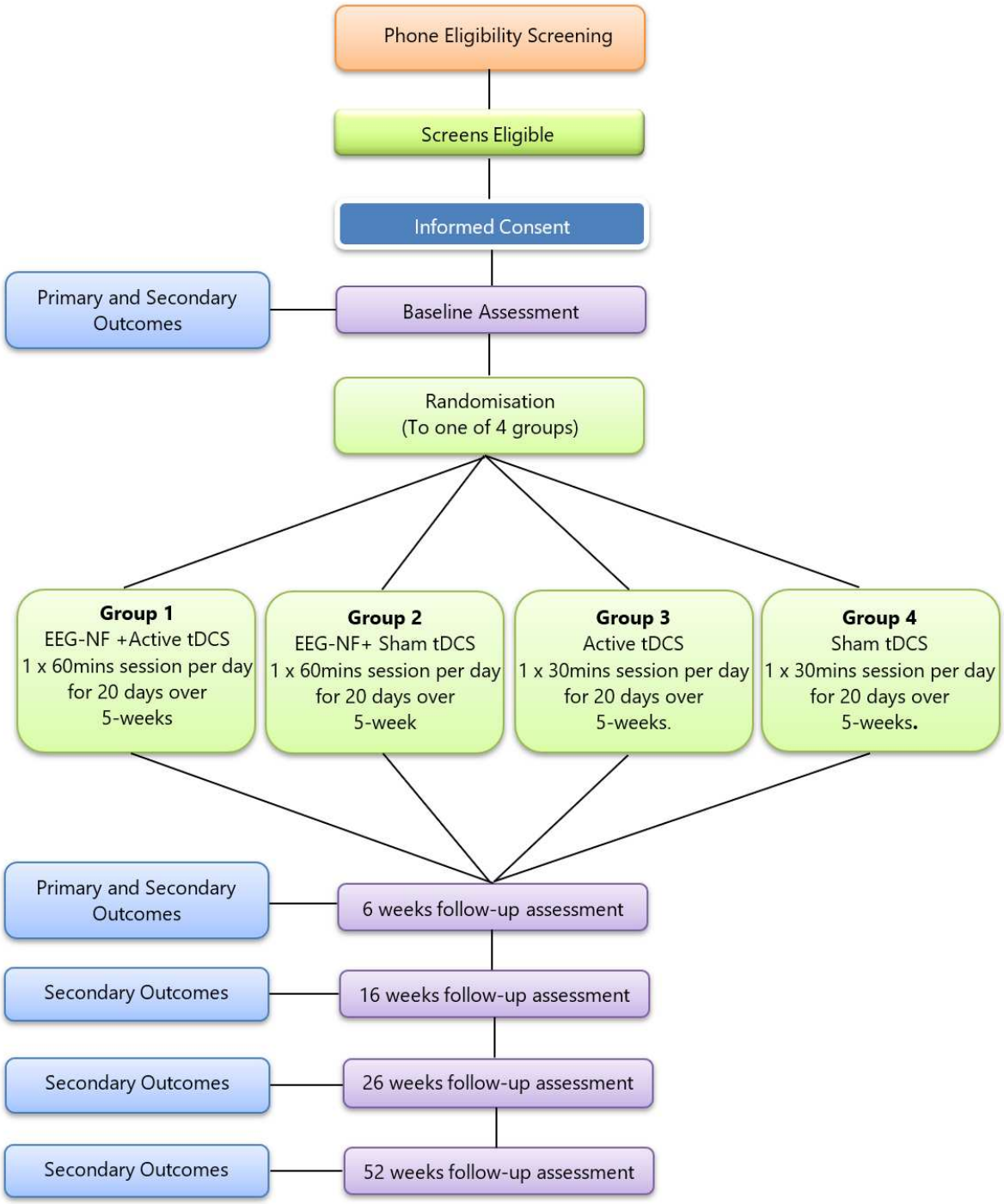
Figure 4. Changes in corticomotor excitability within a 60-minute period following 10 minutes of 2mA anodal tDCS to the left primary motor cortex in 20 individuals with an SCI. The error bars represent the 95% confidence interval.

Figure 5. Upper Panel: Jellyfish Game - The jellyfish swims through the bright blue ocean as participants successfully regulate the targeted frequency bands. Lower Panel: Bird game - the Bird flies through the blue sky in response to participants' regulation of the targeted frequency bands.

Figure 6. Overview of the Intervention in each of the 4 groups. All groups will begin with the setup of transcranial direct current stimulation (tDCS), which takes approximately 10 minutes. This involves placing a headset and a shoulder armband, which respectively contain the anode (positioned over Cz) and the cathode (positioned over the right shoulder). Further justification for this electrode montage is provided in the main text. Both electrodes are prepared by applying saline to a foam pad located within the electrode casing. Once the setup is complete and impedance levels are confirmed to be acceptable, participants will undergo a 20-minute tDCS session. During stimulation, participants will remain seated and relaxed. Participants in Groups 1 and 3 will receive active tDCS (i.e., 2mA constant current), while those in Groups 2 and 4 will receive sham tDCS (i.e., a brief ramp-up to 2 mA followed by a constant current of 0 mA to mimic the sensation of stimulation without the neuromodulatory effects). Following tDCS, participants in Groups 1 and 2 will proceed to setup for the EEG-NF session, which also takes approximately 10 minutes. This setup involves placing pre-soaked sponges over electrodes C1 and C2 of the EEG-NF headset. Once impedance levels are confirmed to be below 50kΩ, participants will begin a 20-minute EEG-NF session.

609 **Figures**

610 Figure 1



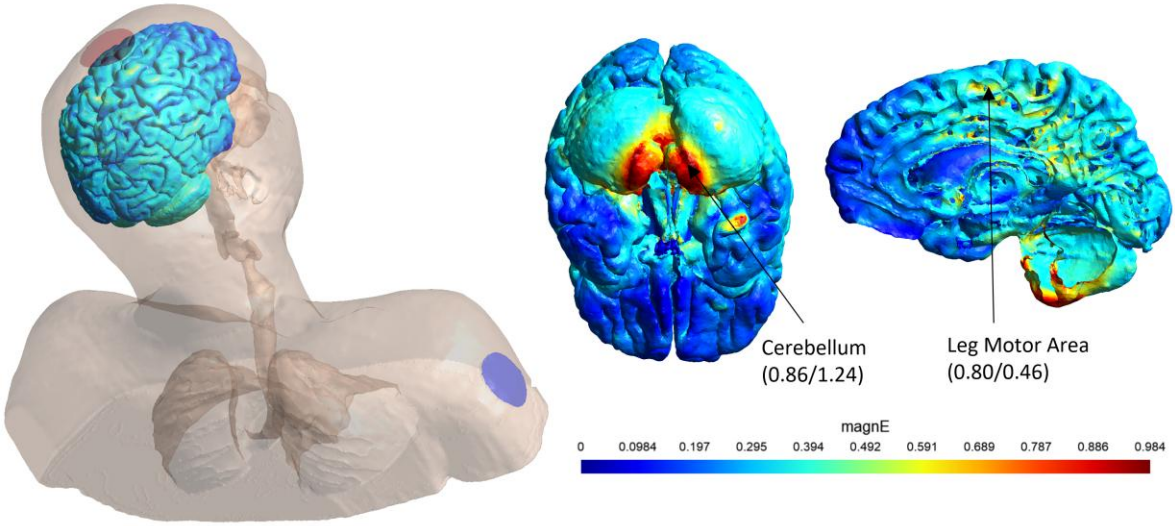
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615 Figure 2



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Figure 3



Figure 4

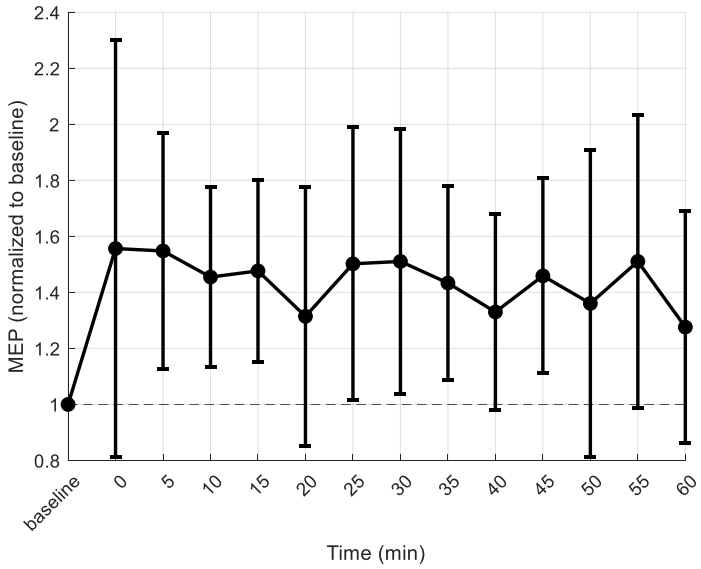
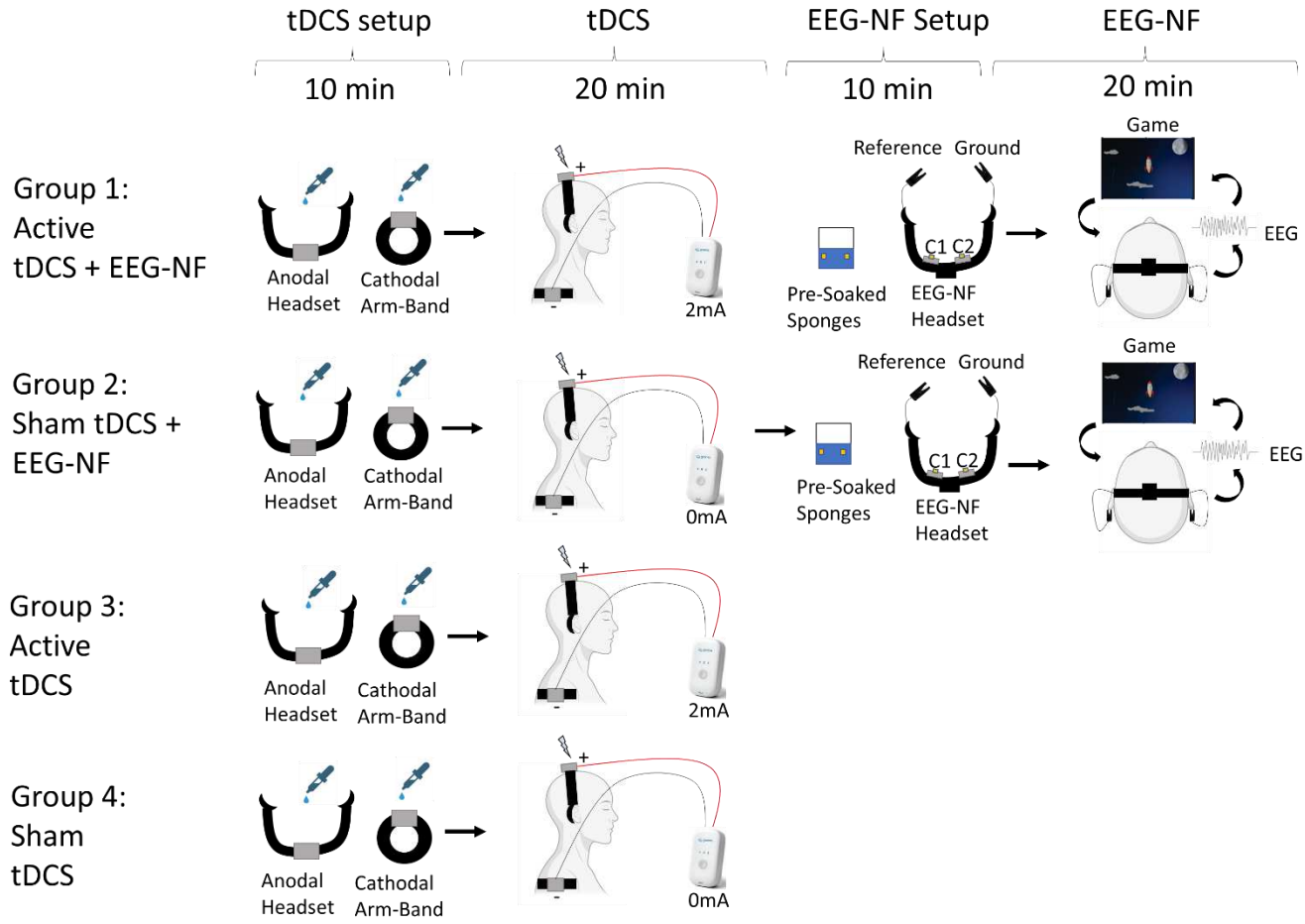

MEP (normalized to baseline)
2.4
2.2
2
1.8
1.6
1.4
1.2
1
0.8
baseline
0
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Time (min)

Figure 5



687 Figure 6



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Tables

Table 1. Group Allocation

	Receives active tDCS	**Receives sham tDCS**
Receives EEG NF	Group 1: EEG-NF + Active tDCS	Group 2: EEG-NF + Sham tDCS
Does not Receive EEG -NF	Group 3: Active tDCS	Group 4: Sham tDCS

Participants in all groups will continue to receive their usual treatments and care throughout the study, as clinically indicated. This may include, but is not limited to, pharmacological, psychological and rehabilitative treatments. The interventions tested in this trial will be provided in addition to, not instead of, their current treatment

725 *Table 2. Schedule of enrolment, interventions and assessments*

Timepoint	Enrolment	Baseline	Randomisation	20 Sessions within 5 weeks	6 weeks	16 weeks	26 weeks	52 weeks
PRE-INTERVENTION								
Eligibility Screening	X							
Informed Consent	X							
Baseline Questionnaires		X						
Randomisation Module			X					
INTERVENTIONS:								
Active tDCS				X				
Sham tDCS				X				
EEG-NF + Active tDCS				X				
EEG-NF + Sham tDCS				X				
ASSESSMENTS:								
BPI-Pain Severity		X			X	X	X	X
BPI-Pain Interference		X			X	X	X	X
BPI-Worst Pain		X			X	X	X	X
Sleep assessment		X			X	X	X	X
PHQ-9		X			X	X	X	X
SF-36		X			X	X	X	X

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