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Targeting Chronic Recurrent Low Back Pain From the Top-down and the Bottom-up: A Combined Transcranial Direct Current Stimulation and Peripheral Electrical Stimulation Intervention

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ABSTRACT

Background: Mechanisms such as neural sensitization and maladaptive cortical organization provide novel targets for therapy in chronic recurrent low back pain (CLBP).
Objective: We investigated the effect of a transcranial direct current stimulation (tDCS) and peripheral electrical stimulation (PES) treatment on pain, cortical organization, sensitization and sensory function in CLBP.
Methods: Using a placebo-controlled crossover design, 16 individuals received four treatments in separate sessions: i) anodal tDCS/PES; ii) anodal tDCS/sham PES; iii) sham tDCS/PES; or iv) sham tDCS/sham PES. Pain was assessed at baseline, immediately following, and at 1 and 3 days after treatment. Motor cortical organization, sensitization and sensory function were measured before and immediately after treatment.
Results: Combined tDCS/PES reduced pain and sensitization, normalized motor cortical organization and improved sensory function. The reduction in pain was greater in individuals with more pronounced sensitization. Applied alone, tDCS or PES also reduced pain. However, with the exception of improved sensory function and reduced map volume following PES, clinical and neurophysiological outcomes were unaltered by tDCS or PES applied separately. No changes were observed following sham treatment.
Conclusion: Our data suggest a combined tDCS/PES intervention more effectively improves CLBP symptoms and mechanisms of cortical organization and sensitization, than either intervention applied alone or a sham control.

Introduction

Termed a 'Western epidemic,' chronic recurrent low back pain (CLBP) is a leading cause of disability in the developed world. Lifetime prevalence is as high as 79% in adults [1] and 84% in adolescents [2]. Significant social and economic costs are associated with poor rates of recovery (58% at 1 month) and high rates of recurrence (73% in 12 months) [3]. Despite the tremendous scale of the problem, CLBP remains challenging to treat. Systematic reviews of existing therapies report, at best, small effects [4,5]. There is a critical need for innovative therapies that improve recovery and reduce symptom recurrence in LBP.

Advances in understanding CLBP have revealed new biological targets for therapy. Mechanisms such as increased sensitivity of cortical and spinal neurons to sensory stimuli ('central sensitization'), and maladaptive reorganization of the complex network of brain regions involved in the experience of pain (i.e. 'pain neuromatrix'), are thought to contribute to persistent pain [6–9]. Yet, few non-pharmacological interventions have been trialed that target these mechanisms. Transcranial direct current stimulation (tDCS) and peripheral electrical stimulation (PES) are two interventions with the potential to desensitize the nervous system and regulate brain organization via complementary 'top-down' and 'bottom-up' effects [10–18]. The combined application of these techniques provides a novel opportunity to bombard multiple pain systems, across multiple levels of the nervous system, simultaneously and

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may improve clinical outcomes. Further, there is the possibility of synergistic effects when tDCS and PES are combined. For example, PES is known to reduce cortical excitability [19], potentially shifting the synaptic threshold toward long-term depression (LTD) and favoring the increased cortical excitability induced by anodal tDCS. This phenomenon, whereby one intervention can increase the brain's receptiveness to another, is known as 'priming' [20].

If the combined mechanisms of tDCS/PES can be harnessed, this intervention may provide clinical benefits for people with CLBP. However, it is unknown how a combined intervention affects organization of the motor regions of the brain, sensitization of the nervous system or higher sensory functions, each of which is known to be modified in CLBP, or how changes to these mechanisms may relate to clinical outcomes.

This study aimed to investigate the immediate effect of a combined tDCS/PES intervention on: i) pain, ii) organization of the motor cortex, iii) sensitization (central and peripheral), and iv) higher sensory function in people with recurring episodes of LBP and to compare this effect with tDCS and PES applied alone and a sham treatment control. We also aimed to undertake additional exploratory analysis to consider whether the response to each treatment differed between individuals based on signs of primary and secondary hyperalgesia or features of motor cortex organization. We hypothesized that the combined intervention would reduce pain and sensitization, normalize cortical organization and improve higher sensory function, to a greater extent than each intervention applied alone or a sham intervention control.

Materials and methods

Study design

A placebo-controlled crossover design with participant blinding was used. Individuals with CLBP received four interventions, across separate sessions, in random order: i) anodal tDCS/PES ('tDCS/PES'); ii) anodal tDCS/sham PES ('tDCS alone'); iii) sham tDCS/PES ('PES alone'); or iv) sham tDCS/sham PES ('sham'). Subsequent interventions were applied no less than 7 days apart. All outcome measures were performed immediately before and after application of each intervention. Pain severity was further assessed at day 1 and 3 following each intervention.

All procedures were approved by the institutional Medical Research Ethics Committee and conformed to the Declaration of Helsinki. Participants provided written, informed consent and were free to withdraw from the study at any time.

Participants

Sixteen right-handed individuals with recurring episodes of non-specific LBP, defined as at least 2 episodes in the last 12 months [21], participated. Individuals were included if they experienced episodic pain in their low back (with or without buttock pain), sufficient to limit function, with a current pain intensity greater than 3 on an 11-point numerical rating scale (NRS) anchored with "no pain" at zero and "worst pain imaginable" at 10. Participant characteristics are provided in Table 1. Individuals were excluded from participation if they had a history of major circulatory, neurological or psychiatric conditions, previous spinal surgery, recent or current pregnancy, analgesic or anti-inflammatory medication in the last month or had received treatment from a health professional in the last month. No participant reported beginning a new treatment during the course of the study.

Table 1
Participant characteristics.

Characteristic	Mean ± standard error
Age (years)	30 ± 2.0
Gender (female:male)	7:9
Weight	73.6 ± 6.0
Height	175.4 ± 3.9
Baseline pain NRS (0–10 cm)	5.3 ± 0.4
Pain duration (years)	4.2 ± 0.7
Side of worst pain (right:left)	11:5

Electromyography (EMG)

Surface EMG was recorded from the back muscles at two sites: 3 cm lateral to the spinous process of L3, and 1 cm lateral to the spinous process of L5. Recordings were made on the side of worst pain using silver–silver chloride disposable electrodes (Noraxon USA Inc, AZ, USA). These sites are appropriate for recording general EMG from the back muscles [22] and are appropriate for evaluation of features of the motor cortical map of the paraspinal muscles [3,23]. The ground electrode was positioned over the anterior superior iliac spine. EMG data were amplified 1000×, filtered 20–1000 Hz and sampled at 2000 Hz using a Micro1401 data acquisition system and Spike2 software (Cambridge Electronic Design, Cambridge, UK).

Interventions

Interventions were applied for 30 min. This is based on previous research that demonstrates reduced cortical excitability after 30 min of PES applied at noxious intensity [19] and tDCS literature that uses common application times of between 20 and 40 min [24].

Transcranial direct current stimulation (tDCS)

Delivered using a direct current stimulator (constant current of 1 mA; DC stimulator plus; Magstim UK) via two 35 cm^2 (5 × 7 cm) saline-soaked surface sponge electrodes. Based on previous studies of the motor cortical representation of the back muscles [23,25], the center of the active electrode was positioned over the approximate location of the motor cortical representation of the back muscles (1 cm anterior and 4 cm lateral to the vertex) contralateral to the side of worst pain and the reference electrode over the contralateral supraorbital region. Current intensity was ramped up (0–1 mA) and down (1–0 mA) over 10 s at the beginning and end of the 30-min stimulation period. The sham tDCS condition involved electrodes placed in an identical position to that used for active stimulation. In this condition the stimulation was turned on for 15 s and then off to provide participants with the initial "itching" sensation but without current for the remainder of the "stimulation" period. This procedure has been shown to effectively blind participants to the stimulation condition [26].

Peripheral electrical stimulation (PES)

Applied to the area of worst pain using a Chattanooga Intelect Advanced therapy system (Chattanooga Group, Vista, USA). Stimulation was delivered using the same electrodes used for recording EMG. A biphasic waveform (0.1 ms pulse duration) was delivered at a frequency of 2 Hz. Stimulation intensity was set at 2–3× perceptual threshold to produce a strong, tingling sensation that was just below pain threshold. These parameters are commonly used in rehabilitation settings for the treatment of chronic pain [19,27–29]. Habituation to the stimulus was monitored verbally every 5 min. If the participant indicated a reduced sensation, current intensity was increased until the subject indicated a consistent