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Efficacy of transcranial direct current stimulation over primary motor cortex (anode) and contralateral supraorbital area (cathode) on clinical pain severity and mobility performance in persons with knee osteoarthritis: An experimenter- and participant-blinded, randomized, sham-controlled pilot clinical study☆

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ABSTRACT

Background: Previous studies indicate that transcranial direct current stimulation (tDCS) with anode over motor cortex (M1) and cathode over contralateral supraorbital region (SO) may be effective in reducing pain, but these studies are limited in number and have not focused on older adults with osteoarthritis (OA).
Objective: To evaluate the preliminary efficacy and safety of M1-SO applied tDCS on clinical pain severity and mobility performance in adults with knee OA pain.
Methods: Forty 50- to 70-year-old community-dwelling participants with knee OA were randomly assigned to receive five daily sessions of 2 mA tDCS for 20 min (n = 20) or sham tDCS (n = 20). We measured clinical pain severity via Numeric Rating Scale, Western Ontario and McMaster Universities Osteoarthritis Index, and Short-Form McGill Pain Questionnaire. In addition, we measured mobility performance using the 6-Minute Walk Test and the Short Physical Performance Battery. Moreover, we obtained a sensation/safety questionnaire and measured cognition changes using the PROMIS-Applied Cognition-Abilities-Short Form 8a.
Results: Active tDCS over M1-SO significantly reduced Numeric Rating Scale of pain compared to sham tDCS after completion of the five daily sessions, and remained up to three weeks. No other measures were significantly different from sham. Participants tolerated tDCS over M1-SO well without serious adverse effects or cognition changes.
Conclusion: Although not consistent in all pain measurements, our findings demonstrate promising clinical efficacy for reduction in pain perception for older adults with knee OA.
Trial registration: ClinicalTrials.gov Identifier NCT02512393.

Abbreviations: tDCS, transcranial direct current stimulation; OA, osteoarthritis; M1, primary motor cortex; SO, supraorbital region; NRS, Numeric Rating Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; SF-MPQ-2, Short-Form McGill Pain Questionnaire-2; 6MWT, 6-Minute Walk Test; SPPB, Short Physical Performance Battery.

☆ Some results were presented at the NYC Neuromodulation 2017 Conference, New York, NY.

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Introduction

Arthritis is a leading cause of pain, impairment of activities in daily life, and disability in people aged 45 years and above [1,2]. Of the 53 million adults diagnosed with arthritis, more than 22 million (42%) struggle with activities of daily living due to arthritis pain [3]. Osteoarthritis (OA) is the most common of the arthritic conditions, with the knee being the most commonly affected joint [2,4,5]. Patients with chronic pain, such as knee OA pain, often have insufficient pain relief [6]. Recent evidence suggests that OA pain may be characterized by generalized changes in pain and sensory processing in the central nervous system, similar to other chronic pain syndromes [7,8]. Because pharmacologic treatments are often inadequate and can lead to adverse events among older adults [9–11], there is a growing interest in non-pharmacologic interventions targeting central nervous system pain processing.

Specifically, noninvasive brain stimulation, such as transcranial direct current stimulation (tDCS), has received significant attention for the treatment of pain in chronic conditions owing to its neuromodulatory effect [12–15]. tDCS involves the application of weak direct electric current to the head in a noninvasive and painless manner, leading to the modulation of the resting membrane potentials of neurons and alteration of the endogenous excitability of the targeted brain tissue [16–18]. For pain, stimulation is typically delivered with the anode electrode placed over the primary motor cortex (M1) of the hemisphere contralateral to the pain-affected area of the body and with the cathode electrode placed over the supraorbital region (SO) ipsilateral to the affected area [15,19]. In particular, the European Chapter of the International Federation of Clinical Neurophysiology recommended that stimulation with anode over the M1 contralateral to pain side and cathode over SO contralateral to M1 placement for possible efficacy among populations with chronic pain [20]. This stimulation with anode over the M1 is believed to produce analgesic effects by modulating pain processing pathways [21,22], and recent brain imaging studies report a reliable cortical and subcortical neurophysiologic response to tDCS with anode over M1 and cathode over SO, referred to hereafter simply as M1-SO applied tDCS [23,24]. Previous studies indicated that M1-SO applied tDCS is effective in reducing pain in patients with fibromyalgia, multiple sclerosis, and traumatic spinal cord injury [12,14,25], but these studies are limited in number and have not focused on older adults or those with arthritis.

The efficacy of M1-SO applied tDCS, for the treatment of pain in older adults remains an open question. Increased atrophy of brain gray and white matter is a hallmark of the aging process in the human brain [26–28]. Computational models suggest that differences in the cerebrospinal fluid space between the location of the electrodes on the scalp and the gray matter alters the intensity of current delivered to brain tissue [29,30]. Furthermore, changes in the structural and functional integrity of white and gray matter in aging may also affect the overall efficacy of electrical neuromodulation in older adults [31]. In addition, functional connectivity of brain networks is also thought to change with age [32–34]. These pose the possibility that M1-SO applied tDCS effects previously shown effective in younger populations may not translate to older adults. Thus, studies investigating the efficacy of M1-SO applied tDCS in older populations are needed. In the current study, we sought to evaluate the preliminary efficacy and safety of M1-SO applied tDCS to reduce clinical pain severity and improve mobility performance in older adults with knee OA.

Methods

Design

We conducted a single-center, experimenter- and participant-blinded, randomized, sham-controlled pilot clinical study at the University of Florida Institute on Aging to evaluate the efficacy of five daily sessions of M1-SO applied tDCS on clinical pain severity and mobility performance in older persons with knee OA. The study included a total of 6 study visits (baseline evaluation and 5 consecutive daily sessions) and 3 weekly follow-up assessments. After undergoing a telephone screening for eligibility assessment, participants were scheduled for a baseline evaluation, which included the following: acquisition of written informed consent; determination of OA using the American College of Rheumatology criteria [35,36]; and a baseline evaluation of demographic and clinical characteristics including medications. Weight-bearing radiographs of both knees were taken for all participants, and the OA severity was determined using the Kellgren-Lawrence grading system [37] (Fig. 1). We chose a 3-week follow-up because M1-SO applied tDCS has been shown to induce modulatory effects for up to 3 weeks after the end of five daily stimulation sessions [12]. All procedures were approved by the Institutional Review Board of the affiliated university, and written informed consent was obtained from all participants before participation.

Randomization and blinding

Participants who met eligibility criteria were randomly assigned with a ratio of 1 to 1 to either the active tDCS ($n = 20$) or sham tDCS group ($n = 20$) using a covariate adaptive randomization procedure so that the two groups had approximately equal distribution regarding age, gender and race. Allocation concealment was ensured as the randomization codes were released only after all the interventions and assessments were completed.

We used a Soterix CT direct current stimulator (Soterix Medical Inc., NY) to deliver experimenter- and participant-blinded tDCS. The experimenter was blind to the condition, and entered a 6-digit code into the device to deliver stimulation. The participants were blinded with regard to the type of tDCS and they were aware of the fact that they could receive either sham or active stimulation. Only the statistician with no clinical involvement in this trial was able to unblind data at the completion of the study.

Study participants

Participants with knee OA pain were recruited in North Central Florida between September 2015 and August 2016 using advertisements in local institutions and communities. Participants who were 50–70 years old were considered eligible if they had self-reported unilateral or bilateral knee OA pain, according to American College of Rheumatology criteria [35,36]; could speak and read English; were willing to be randomly assigned to either the intervention or control group; were available for five consecutive daily sessions and for a follow-up phone assessment each week for three weeks; had no plan to change medication regimens for pain throughout the trial; and were willing and able to provide written informed consent prior to enrollment. Participants were excluded if they had concurrent medical conditions that could confound symptomatic OA-related outcome measures or coexisting diseases that could hinder the completion of the protocol, including: (1) prosthetic knee replacement or non-arthroscopic surgery to the affected knee, (2) serious medical illness, such as uncontrolled