Symptom management in adults with knee osteoarthritis using transcranial direct current stimulation: A pilot study

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Education/Training

- BE in Electrical Engineering, Seoul, 1997
- MS in Electrical and Computer Engineering, UF, 2004
- BS in Nursing, UF, 2007
- MS in Adult and Elderly Nursing, UF, 2009
  - Board-Certified Adult Nurse Practitioner, 2009
- PhD in Nursing Science, UF, 2012
- Postgraduate training, UF CTSI, 2013 - 2015
- Certificate in Brain Stimulation (tDCS), Neuromodec, 2014
- MS in Clinical and Translational Science, UF, 2015
- Graduate Certificate in Aging/Geriatric Practice, UF, 2016
- Certificate in Multimodal Brain Imaging Program, Harvard/MIT Martinos Center for Biomedical Imaging, 2017
Background and Significance
Prevalence and Costs of Several Chronic Diseases in the United States

- **Cancer**
  - Point Prevalence (in millions): 40
  - 2010 Annual Costs (in billions): 0

- **HIV/AIDS**
  - Point Prevalence (in millions): 0
  - 2010 Annual Costs (in billions): 0

- **Heart Disease**
  - Point Prevalence (in millions): 20
  - 2010 Annual Costs (in billions): 100

- **Diabetes**
  - Point Prevalence (in millions): 40
  - 2010 Annual Costs (in billions): 300

- **Alzheimer's**
  - Point Prevalence (in millions): 10
  - 2010 Annual Costs (in billions): 60

- **Chronic Pain**
  - Point Prevalence (in millions): 100
  - 2010 Annual Costs (in billions): 600

**Legend**:
- **Blue** - Prevalence
- **Red** - Annual Costs
Knee Osteoarthritis (OA) Pain

- Arthritis is one of the leading causes of pain, impairments of activities in daily life, and disability in people aged 45 and above.
- Osteoarthritis (OA) is the most common of the arthritic conditions, with the knee being the most commonly affected joint.
- Patients with chronic pain, such as knee OA pain, often have insufficient pain relief.
- Pharmacologic treatments are often inadequate and can lead to adverse events among older adults.
Transcranial Direct Current Stimulation (tDCS)

- 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.

- tDCS with anode over the M1 is believed to produce analgesic effects by modulating pain processing pathways (European Chapter of the International Federation of Clinical Neurophysiology).

- Recent brain imaging studies report a reliable cortical and subcortical neurophysiologic response to tDCS with anode over M1 and cathode over SO.
Specific Aims

- To evaluate the preliminary efficacy on pain symptoms of tDCS over contralateral primary motor cortex (M1) and ipsilateral supraorbital region (SO), as compared with sham tDCS, in older adults with knee OA
- To evaluate safety of tDCS in older adults with knee OA
Design

- Single-center, double-blind, randomized, sham-controlled clinical study
- 6 study visits and 3 phone interviews
  - Baseline evaluation
  - Five consecutive daily sessions of tDCS
  - Three weekly follow-up assessments
- 40 older adults with knee osteoarthritis
  - randomly assigned to receive five daily sessions of 2mA tDCS for 20 minutes (n=20) or sham tDCS (n=20).
Randomization and Blinding

- Participants will be randomly assigned at a ratio of 1 to 1 to either the active tDCS (n=20) or sham tDCS group (n=20).
- The experimenter will be blind to the condition and enter a 6-digit code into the device to deliver stimulation.
Participants

- Participants who were aged 50-70 years old were considered eligible if they: (1) had knee OA pain according to American College of Rheumatology criteria; (2) had no plan to change medication regimens for pain throughout the trial.

- 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 (e.g., peripheral neuropathy, systemic rheumatic disorders)
For sham stimulation, the electrodes were placed in the same positions as for active stimulation, but the stimulator only delivered 2 mA of current for 30 seconds, with the same ramp up and down period of ten seconds.

- 2 mA constant current for 20 minutes once a day for 5 consecutive days
Measurements: WOMAC

- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): OA-related pain symptoms
  - 3 subscales: pain during activities (5 items), stiffness during the day (2 items), and impairments of physical function (17 items)
  - higher scores indicating worse pain, stiffness, and impairments of physical function.
Measurements: Safety

- Safety
  - Safety questionnaire: tingling, itching sensation, burning sensation, pain, fatigue, nervousness, headache, difficulty concentrating, mood change, and change in the vision or visual perception
  - All the side effects were recorded from 0 (not at all) to 10 (highest degree). The safety questionnaire was administered after each session of stimulation.
Assessment for eligibility (n=43)

Not meeting selection criteria: uncontrolled hypertension (n=2)

Randomized (n=41)

Allocated to active group (n=21)
- Withdraw (n=1)
- Analyzed (n=20)

Allocated to sham group (n=20)
- Withdraw (n=0)
- Analyzed (n=20)
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sham (n=20)</th>
<th>Active (n=20)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, M (SD)</td>
<td>59.30 ± 8.60</td>
<td>60.60 ± 9.80</td>
<td>0.67</td>
</tr>
<tr>
<td>Male, n(%)</td>
<td>9(45%)</td>
<td>10(50%)</td>
<td>0.75</td>
</tr>
<tr>
<td>White, n(%)</td>
<td>10 (50%)</td>
<td>10 (50%)</td>
<td>1.00</td>
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<tr>
<td>K/L radiographic score</td>
<td></td>
<td></td>
<td>0.70</td>
</tr>
<tr>
<td>Grade 0</td>
<td>8 (40.0%)</td>
<td>5 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>3 (15.0%)</td>
<td>5 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>5 (25.0%)</td>
<td>5 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>4 (20.0%)</td>
<td>4 (20.0%)</td>
<td></td>
</tr>
</tbody>
</table>
### WOMAC Subscale

<table>
<thead>
<tr>
<th>WOMAC Subscale</th>
<th>sham</th>
<th>active</th>
<th>Cohen’s d</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Pain</td>
<td>-0.60 ± 2.10</td>
<td>-1.30 ± 3.10</td>
<td>-0.26</td>
<td>0.45</td>
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<tr>
<td>Stiffness</td>
<td>-0.20 ± 0.80</td>
<td>-0.60 ± 1.40</td>
<td>-0.35</td>
<td>0.33</td>
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<tr>
<td>Functional impairment</td>
<td>0.10 ± 7.30</td>
<td>-2.40 ± 10.40</td>
<td>-0.28</td>
<td>0.39</td>
</tr>
</tbody>
</table>

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index
No serious adverse effects

- No participants complained of fatigue, nervousness, headache, difficulty concentrating, mood change, or vision changes during tDCS sessions.

Twenty-seven incidents occurred during tDCS session

- Pain at the stimulation site (6 incidents: 2 in the sham versus 4 in the active; \( P=0.66 \))
- Change in visual perception (1 in the active group, \( P=1.00 \))
- The severity of these symptoms were less than or equal to 2 out of 10, and participants wanted to complete the tDCS session and did not complain these symptoms after completing the tDCS sessions.
Discussion and Implications
Discussion

- One of the first to test the efficacy tDCS in older adults with knee OA using a double-blind, randomized, sham-controlled design
- Marginally greater reduction in WOMAC in active group
- No significant adverse effects
Limitations

- Small sample of adults with knee OA
- Long-term efficacy of tDCS cannot be established.
Future Research

- Different parameters of brain stimulation as well as combined therapy with other interventions
- Larger samples and longer-term follow-up
- Brain Imaging Measures to understand the underlying mechanisms of tDCS
Conclusion

- Although our primary results were nonsignificant, there is a preliminary suggestion that tDCS targeting primary motor cortex may reduce osteoarthritis-related pain symptoms in adults with knee OA without any significant adverse effects. Future studies are needed to refine this novel approach for pain neuromodulation.
Acknowledgements

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Questions