Effects of transvertebral direct current stimulation in healthy humans: Results from an ongoing randomized cross over study

Radha Korupolu, MBBS, MS (PGY4)
Physical Medicine & Rehabilitation
University of Kentucky

Mentor: Lumy Sawaki, MD, PhD

Team Members:
Elizabeth Salmon, BE, MS; Cheryl Carrico, MS,OT/L; Lakshmi Reddy, MBBS
Transcranial direct current stimulation

- Modulates cortical excitability
  - Anodal stimulation increases cortical excitability
  - Cathodal stimulation decreases cortical excitability
- Effects may last for >1 hr after single stimulation
- Longer & stronger the stimulus the stronger the aftereffects

(Nitsche and Paulus, 2001; Nitsche et al., 2003)
Transcranial direct current stimulation

Possible Mechanism:

- Changes the resting membrane potential of the neurons in cortex
  (Bikson et al. 2004; Ruffini et al. 2013)

- Changes local concentration of GABA & glutamate
  (Stagg et al. 2009; Clark et al. 2011)

Positive effects in variety of clinical conditions

- Stroke
- Chronic pain
- Depression
- Cognitive deficits
- Movement disorders
- Schizophrenia

(Fregni et al., 2006; Song et al., 2012; David et al., 2013; Khedr et al., 2013; Moreno-Duarte et al., 2013)
Transvertebral direct current stimulation (tvDCS)

Preliminary studies in healthy subjects suggest possibility of similar modulation in spinal neurons. However, data in this regard is very limited & inconsistent.
F. Cogiamanian et al. (2008)

- **Sample size**: 12 healthy subjects

- **Intervention**:
  - tvDCS over T10 spinous process (anodal or cathodal)
  - 2.5 mA for 15 mins, current density of 0.071 mA/cm²

- **Outcome Measures**:
  - Post. Tibial N & Median N SEPs were recorded
  - Before, at current offset & 20 mins after tvDCS

- **Results**:
  - Anodal tvDCS decreased PTN SEPs (P33) amp. by 25%
  - Serum *neuron specific enolase*, a marker of neuronal damage, was not elevated 1 hr after tvDCS
Sample size: 10 healthy subjects

Intervention:

- tvDCS at T11 level 2 cm paravertebrally (Cathodal, anodal or sham)
- 2.5 mA applied for 15 min, current density of 0.063 mA/cm²

Outcome measures:

- $H_{\text{max}}/M_{\text{max}}$ ratio & H-reflex post activation depression
- Before, at current offset, & 15 min after tvDCS

Results

- No change in $H_{\text{max}}/M_{\text{max}}$ ratio
- Anodal tvDCS decreased H-reflex post-activation depression
- Cathodal tvDCS increased H-reflex post-activation depression
Lamy et al. (2012)

- **Sample size**: 17 healthy subjects

- **Intervention**:
  - tvDCS at T11 level over spinous process (Cathodal, anodal or sham)
  - 2.5 mA applied for 15 min, current density of 0.071 mA/cm²

- **Outcome measures**:
  - Stimulus-response curves of the soleus H reflex
  - Before, at current offset, & 15 min after tvDCS

- **Results**
  - Anodal tvDCS induced a leftward shift of the recruitment curve of the H reflex
Research Study

- **Aim to study** the effects of tvDCS in healthy subjects to establish a reliable & reproducible tvDCS methodology to modulate spinal excitability in subjects with SCI
Methods

- **Design:** Randomized crossover study

- **Participants:** 5 healthy subjects (Target 10, ongoing study)

- **Intervention:**
  - Each subject randomly received anodal, cathodal, or sham tvDCS
  - Active electrode (10 x 4.5 cm) over T10-T11 spinous process
  - Reference electrode (10 x 4.5 cm) over left shoulder
  - 2.0 mA for 20 minutes, current density of 0.04 mA/cm²
  - For sham tvDCS, current was ramped up to 2.5 mA then ramped down over a 30 secs window
Active electrode T11 2 cm from spinous process
Reference electrode over left shoulder
Direct current stimulator

Active electrode over T10-T11
Reference electrode over left shoulder
Direct current stimulator
Outcome Measure: 1

- To evaluate corticospinal excitability, we measured bilateral triceps surae motor evoked potentials (MEP) elicited by transcranial magnetic stimulation.

- We delivered transcranial magnetic stimulation (TMS) using a Magstim 2002 stimulator fitted with a double-cone coil (Magstim, Whitland, Dyfed, UK) over motor cortex.

- We measured five MEPs at intensities ranging from 100% to 180% of resting motor threshold.
Transcranial Magnetic Stimulation
To assess spinal cord excitability, bilat. Soleus $H_{\text{max}}/M_{\text{max}}$ ratio was obtained.

For $H_{\text{max}}$, we started at 30% of $M_{\text{max}}$ intensity & recorded H wave at 5% intensity increments until $H_{\text{max}}$ was identified.

LabVIEW (National Instruments, Austin, TX) data collection program was used to record M wave & H wave.
- Active Electrode: b/w medial malleolus & popliteal fossa
- Reference electrode: Achilles tendon
- Ground electrode: b/w popliteal fossa & active electrode
- Tibial nerve was stimulated in popliteal fossa
H_{max}/M_{max} ratio

- Common method of H-reflex normalization
- H_{max} is an indirect estimate of the number of MNs being recruited
- M_{max} represents the entire MN pool
- H_{max}/M_{max} ratio can be interpreted as the proportion of the entire MN pool capable of being recruited
- H-reflex amplitude increases after SCI

(Ratto et al., 1986; Nielsen 2004)
<table>
<thead>
<tr>
<th>Intervention flow sheet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre MEPs</td>
</tr>
<tr>
<td>Pre $H_{\text{max}}/M_{\text{max}}$ ratio</td>
</tr>
<tr>
<td>Intervention: tvDCS</td>
</tr>
<tr>
<td>Post $H_{\text{max}}/M_{\text{max}}$ ratio</td>
</tr>
<tr>
<td>Post MEPs</td>
</tr>
</tbody>
</table>
# Demographics

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 1</td>
<td>49</td>
<td>25</td>
</tr>
<tr>
<td>Subject 2</td>
<td>22</td>
<td>21</td>
</tr>
<tr>
<td>Subject 3</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>Subject 4</td>
<td>34</td>
<td>25</td>
</tr>
<tr>
<td>Subject 5</td>
<td>32</td>
<td>22</td>
</tr>
</tbody>
</table>
Mean amplitude of MEPs recorded at 100-180% rMT of left brain-right leg
$H_{\text{max}}/M_{\text{max}}$ ratio obtained from right leg
Discussion

• MEPs elicited by TMS as an outcome measure in healthy subjects?

• Other outcome measures: H-reflex post activation depression

• tvDCS electrode size and positioning

• Duration and intensity of tvDCS

• May be no effects in healthy humans after single tvDCS session
Conclusion

• Too early to make any conclusions at this time

• Small sample size

• Appropriate statistical analysis after completion of the study

• Further research is required to refine tvDCS methodology
Future Plan

- Further work is needed on healthy subjects to refine tvDCS methodology.
- Apply the tvDCS methodology developed in healthy humans to subjects with incomplete SCI.
- Our long term objective is to evaluate the effects of tvDCS on functional motor recovery, paired with robot-assisted treadmill training in subjects with SCI.
Questions