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

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Background

- **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; Ruffinietal.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

T. Winkler et al. (2010)

- **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_{max}/M_{max} ratio & H-reflex post activation depression
  - Before, at current offset, & 15 min after tvDCS
- **Results**
  - No change in H_{max}/M_{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 0.04mA/cm^2
  - For sham tvDCS, current was ramped up to 2.5 mA then ramped down over a 30 secs window

Active electrode over
T10-T11

Reference electrode
over left shoulder

Direct current stimulator

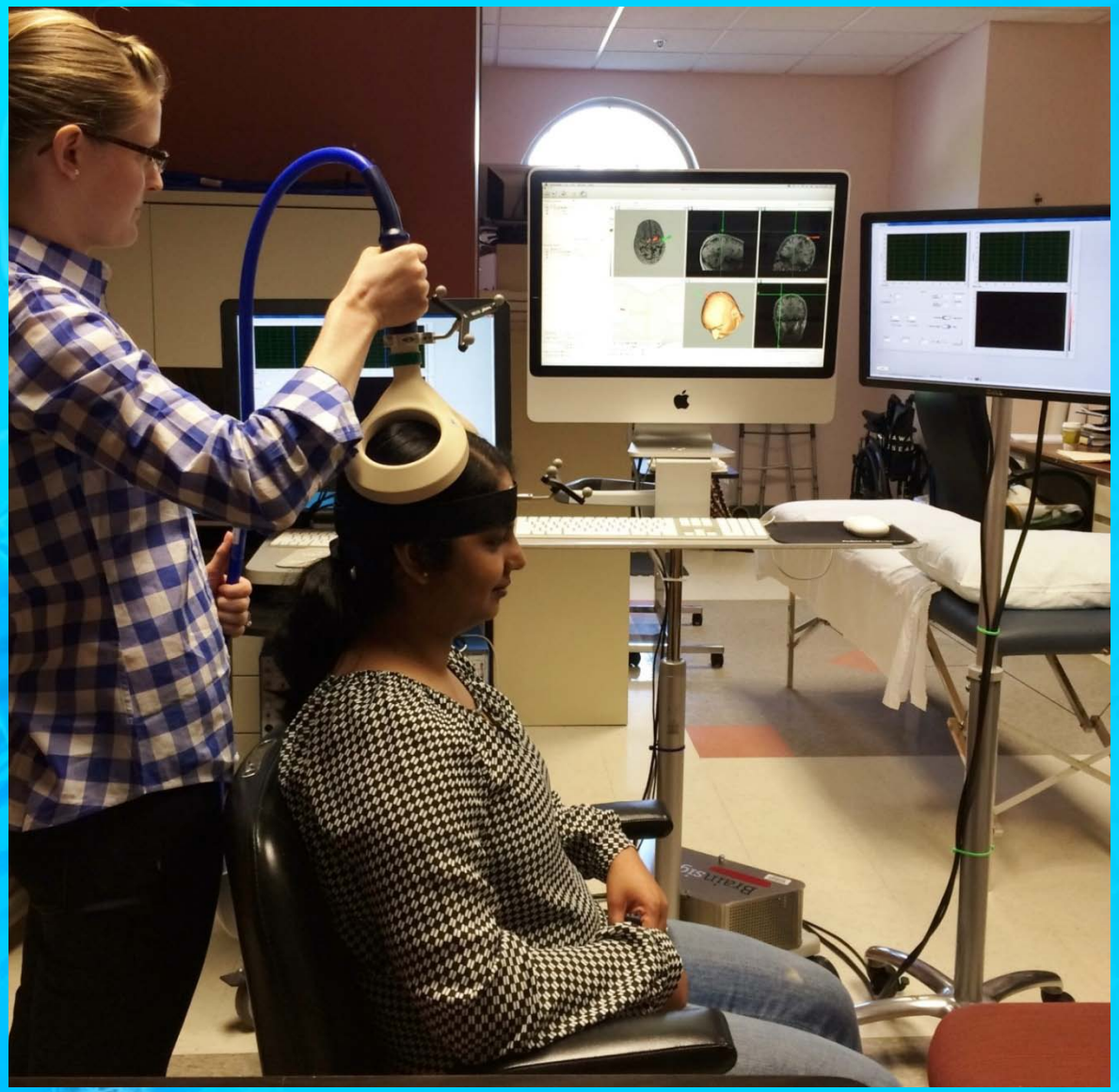
Outcome Measure: 1

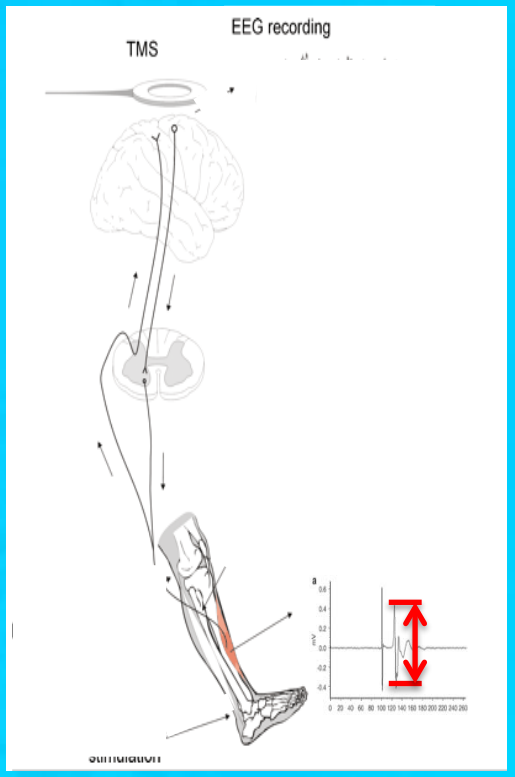
- To evaluate corticospinal excitability, we measured **bilateral triceps surae motor evoked potentials** (MEP) elicited by transcranial magnetic stimulation

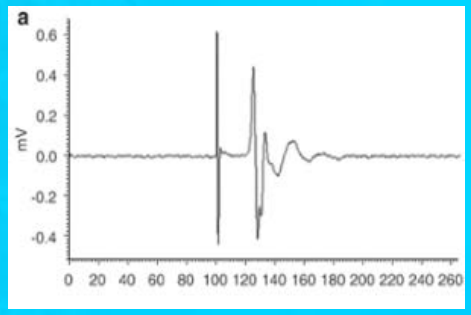
- We delivered transcranial magnetic stimulation (TMS) using a Magstim 2002 stimulator fitted with a double-cone coil (Magstim, Whitland, Dyfed, UK) over motor cortex

- We measured five MEPs at intensities ranging from 100% to 180% of resting motor threshold

Transcranial Magnetic Stimulation





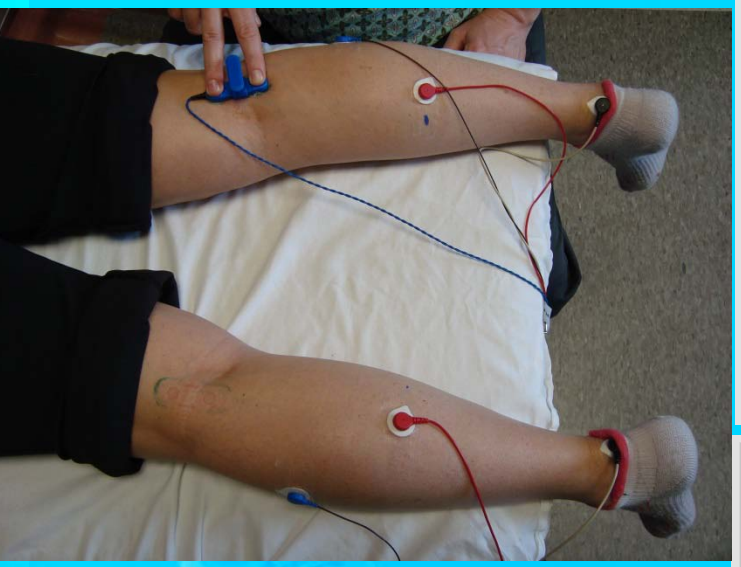


Outcome Measure: 2

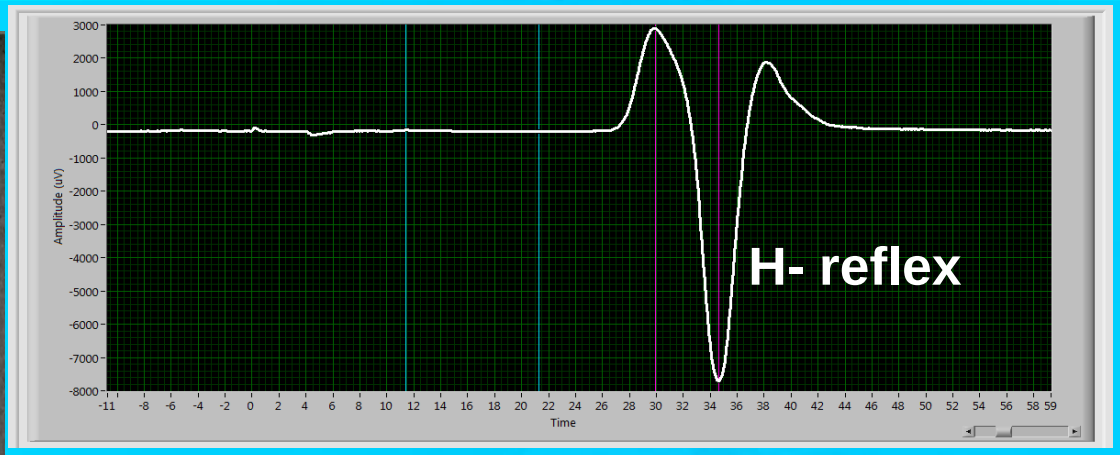
- To assess spinal cord excitability, bilat.Soleus **H_{max}/M_{max} ratio** was obtained

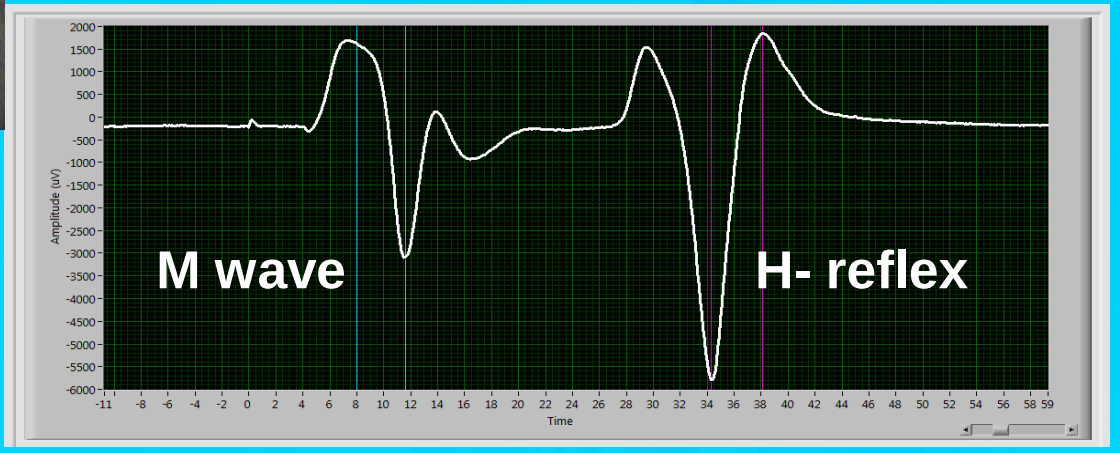
- For H_{max}, we started at 30% of M_{max} intensity & recorded H wave at 5 % intensity increments until H_{max} was identified

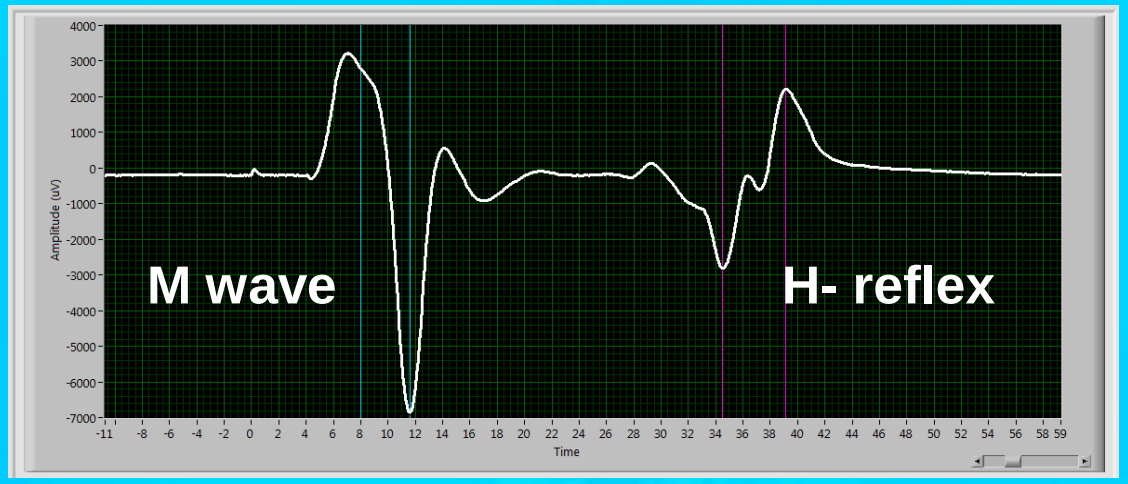
- LabVIEW (National Instruments, Austin, TX) data collection program was used to record M wave & H wave



- 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)

Intervention flow sheet

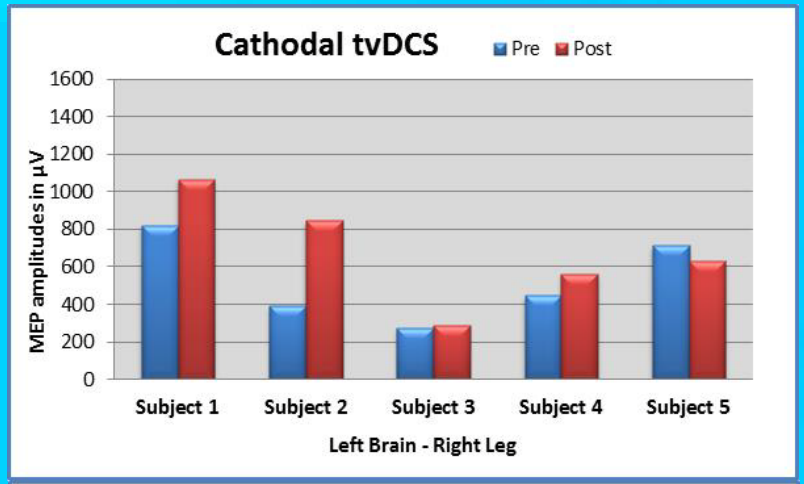
Pre MEPs
Pre H_{max}/M_{max} ratio
Intervention: tvDCS
Post H_{max}/M_{max} ratio
Post MEPs

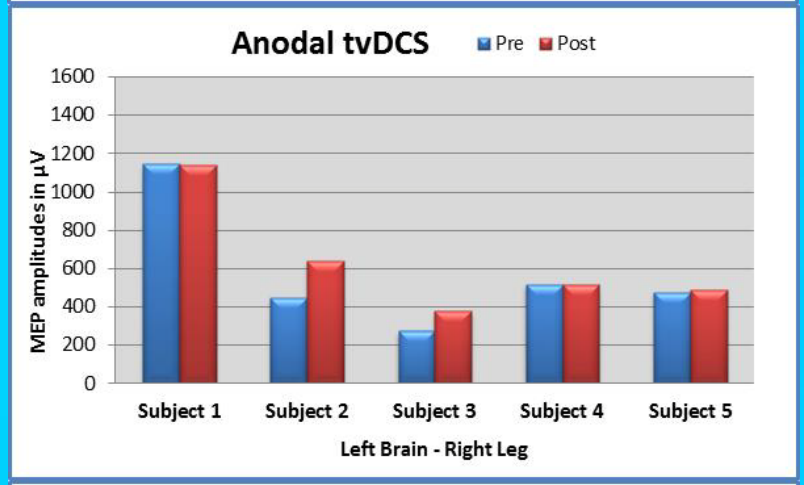
Demographics

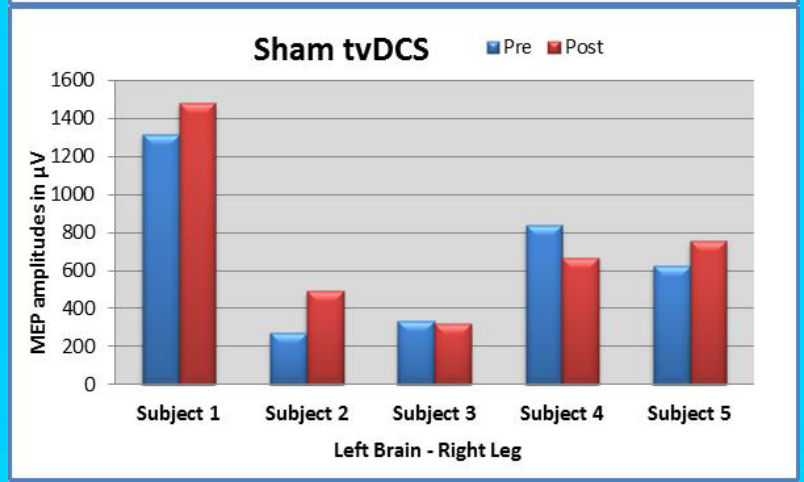
	Age (years)	BMI (kg/m^2)
Subject 1	49	25
Subject 2	22	21
Subject 3	27	23
Subject 4	34	25
Subject 5	32	22

Preliminary Results

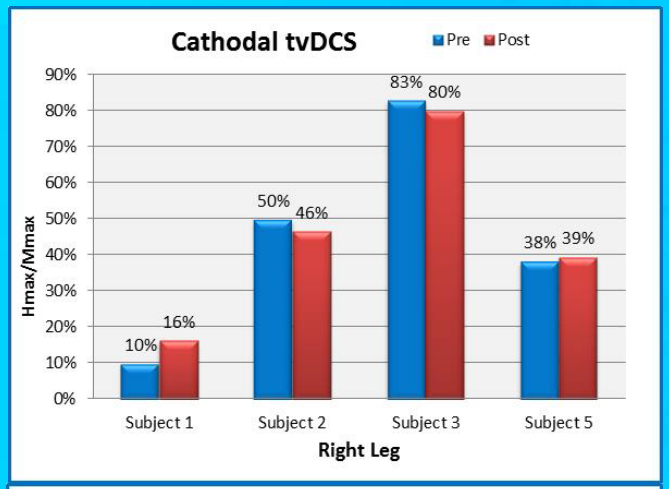
Mean amplitude of MEPs recorded at 100-180% rMT of left brain- right leg

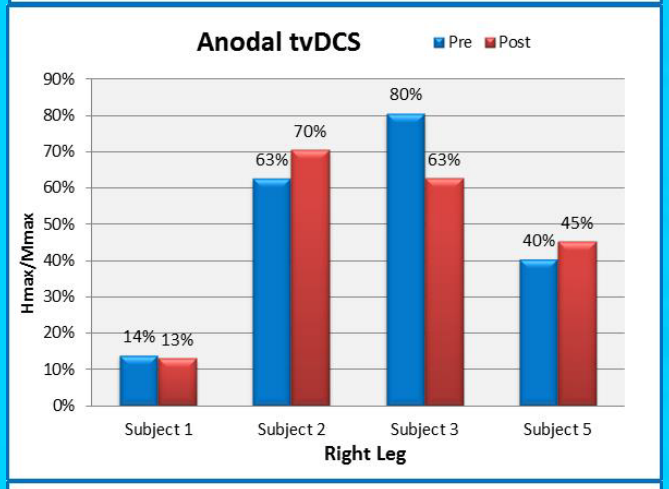


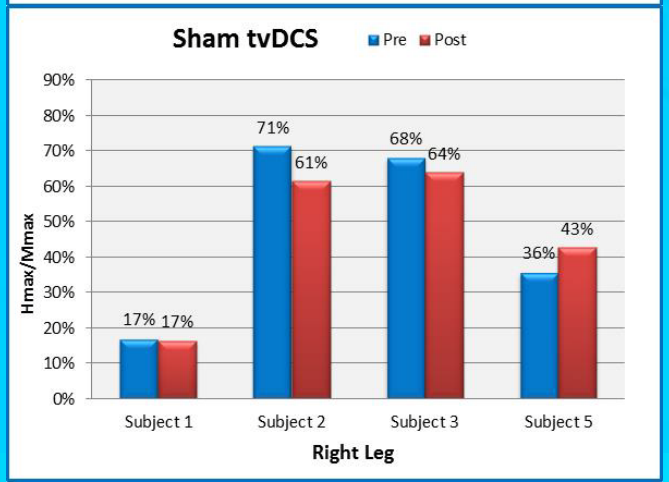




H_{max}/M_{max} ratio obtained from right leg







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