PAIN, THE BRAIN AND NEUROSTIMULATION TECHNOLOGY

Jeff Borckardt, Ph.D.
Dept. of Psychiatry and Behavioral Sciences
Dept. of Anesthesia and Perioperative Medicine
Three Dimensions of Pain

- **Sensory-Discriminatory**
  - Location, quality, intensity
  - *Primary and Secondary Somatosensory Cortices*

- **Motivational-Affective**
  - Emotional Valence, Depression, Anxiety
  - *Insular, Anterior Cingulate Cortices*

- **Cognitive-Evaluative**
  - Thoughts about the cause and significance of the pain
  - *Prefrontal cortex*
Neurostimulation

- Transcutaneous Electrical Nerve Stimulation (TENS)
- Spinal Cord Stimulation (SCS)
- Motor Cortex Stimulation; MCS
- Transcranial Magnetic Stimulation (TMS)
- Transcranial Direct Current Stimulation (tDCS)
TMS is a minimally invasive brain stimulation technology that can focally stimulate the brain of an awake individual.

A localized pulsed magnetic field transmitted through a figure-8 coil (lasting only microseconds) is able to focally stimulate the cortex by depolarizing superficial neurons inducing electrical currents in the brain.

TMS can induce varying brain effects depending on:
- 1) the cortical region stimulated,
- 2) the activity that the brain is engaged in
- 3) the TMS device parameters (particularly frequency and intensity).
Change in Thermal Threshold (°C) from Mean Baseline Threshold

Thermal Threshold Trial Following rTMS

(Borckardt et al., 2007)
Most clinical studies have examined motor cortex rTMS for neuropathic pain.

We conducted a small cross-over-controlled trial of fast rTMS (10Hz 100%rMT) over left DLPFC for neuropathy.

3 treatments were conducted of both real and sham rTMS.

Daily pain-diaries were collected.
20 TMS-naïve subjects with FMS for >1 year
10 Sessions of real (n=10) or sham (n=10) 10Hz prefrontal rTMS of Left DLPFC (over 2-weeks)
Daily pain diaries were completed
Perioperative TMS

Supporting wrist for APB movement monitoring

Laptop running PEST software

TMS Coil

TMS Machine
Perioperative TMS
Mean cumulative patient-delivered morphine

- Active TMS
- Sham TMS

Hour after Surgery

(Borckardt et al., 2006)
20 TMS-naïve healthy volunteers
Pain threshold testing conducted using thermal stimulator on the arm
Block-design implemented in 3T Siemens MRI scanner (pain-rest)
Participants received 20-minutes of 10Hz rTMS over the left DLPFC outside of scanner
The pain-rest block paradigm was repeated
fMRI pre-treatment pain signal
Real > Sham, Post > Pre
24 Healthy volunteers

Real (n=12) or Sham (n=12) rTMS 10Hz 110%rMT of left DLPFC

2 visits… one involved IV naloxone bolus (0.1mg/kg); one involved IV saline bolus

Thermal pain thresholds measured via method of limits using Pathway thermode
Transcranial Direct Current Stimulation (tDCS)
tDSC-ERCP Pilot Study

- 21 Females (Mean age = 37.2; SE=2.4)
- ERCP for pancreatitis-related pain
- Randomly assigned to receive 20-mins of REAL or SHAM tDCS (2.0 mA) immediately after ERCP
- Anode over left prefrontal cortex
- Cathode over gut-representation of the sensory cortex
- Pain ratings and PCA usage tracked
Endoscopic Retrograde Cholangiopancreatography (ERCP)

Anode - left dlPFC; Cathode - Gut representation of sensory cortex

22% Reduction
tDCS for Total Knee Arthroplasty Pain

• 40 patients undergoing unilateral TKA
• Randomly assigned to receive a total of 80 minutes of real (n=20) or sham tDCS (n=20)
• Anode placed over the knee representation of the motor strip
• Cathode placed over the right dorsolateral prefrontal cortex
• Patient controlled analgesia (PCA; hydromorphone) use was tracked during the ~48-hours post-surgery.
Cumulative PCA (mg dilaudid) Dose vs. Hour Post-Op

- Sham tDCS
- Real tDCS

43% Reduction
Regardless of screen-color and participant performance, the thermal stimuli are all random and the durations are balanced between green and red screen conditions.
41 Healthy Adults
Underwent pain perceived controllability task
20 mins of anodal (n=21) or cathodal (n=20) tDCS at 2mA over left DLPFC during pain controllability task
Other electrode was attached to right shoulder
The graph shows the mean (StdErr) NRS Control Ratings for different conditions:

- **Perceived Control Trials**
  - Cathode
  - Anode

- **No Perceived Control Trials**
  - Cathode

- **Overall**
  - Cathode

The graph indicates a comparison between the Cathode and Anode conditions under perceived control trials and overall conditions.
Pilot study (n=8) of healthy volunteer participants

Thermal pain tolerance assessed pre-, during, and post- a laboratory CBT intervention

tDCS applied to the left DLPFC (anodal versus cathodal) during the CBT intervention

Post-task retrospective assessment administered to evaluate subjective perspectives
Laboratory CBT plus Anodal versus Cathodal tDCS of the left DLPFC
Minimally invasive neurostimulation technologies such as TMS and tDCS have shown analgesic promise.

The mechanisms of action are becoming clearer but we still do not know much about optimal cortical targets or dosing strategies.

Combining these technologies with other rehabilitative therapies may offer valuable synergistic effects.

There is a need for more well-controlled clinical trials in numerous patient populations in order to determine specific utility of the interventions.
QUESTIONS/COMMENTS?
HOW DO WE REDUCE THE DISCOMFORT ASSOCIATED WITH RTMS?
Voxel map of sensation location between real and eSham TMS
Average Pain Ratings → 2-Days → Average Mood Ratings
R = -.492 SE = .243

Activity Ratings → 6-Days → Average Pain Ratings
R = .551 SE = .277

Average Mood Ratings → 2-Days → Pain Medication Use
R = -.498 SE = .243
TMS Effects on Pain Ratings

![Graph showing percent change in pain ratings following TMS. The graph compares Post Real TMS and Post Sham TMS conditions. The graphs show a decrease in pain ratings, with Post Real TMS showing a decrease of 12.39 and Post Sham TMS showing a decrease of 7.18.](image-url)