Clinical Trials of tACS in Psychiatry

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Follow us on Twitter:
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www.facebook.com/FrohlichLabUNC
Conflicts of Interest

- UNC owns IP related with FF as the lead inventor.
- UNC has determined the absence of a conflict of interest (COI) for the majority of work presented here and has determined a “COI with administrative considerations” for the clinical trials in the Frohlich Lab.
- FF is the founder, chief scientific officer, and majority owner of Pulvinar Neuro LLC. We provide solutions for transcranial current stimulation research.
- I speak with many companies and have received industry funding from Tal Medical (travel + research).
- I frequently travel and give presentations. I typically receive reimbursement and a stipend.
RATIONAL DESIGN

Target Identification

Target Engagement

Target Validation
FIGURE 1. Effect of Active and Sham Transcranial Direct-Current Stimulation (tDCS) on the Severity of Auditory Verbal Hallucinations

Brunelin et al. 2012
Frohlich et al. 2016

![Graph showing changes in AHRS Score over time with baseline, after tDCS, and 1 month post-tDCS data points for Sham and tDCS conditions.](image)
Neuronal Dynamics and Neuropsychiatric Disorders: Toward a Translational Paradigm for Dysfunctional Large-Scale Networks

Peter J. Uhlhaas1,2,3,* and Wolf Singer1,2,4
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http://dx.doi.org/10.1016/j.neuron.2012.09.004
• Auditory Hallucinations in SCZ
• 10Hz-tACS/tDCS/placebo (double blind)
• 20 min bid / 5 days
• 24 pts
• Primary: AHRS
• Target Engagement: hdEEG
• Major depressive disorder
• 10Hz-tACS/40Hz-tACS/placebo (double blind)
• 40 min qd / 5 days
• 30 pts
• Primary: MADRS (4 week follow up)
• Target Engagement: hdEEG
Our Experience

Safety
Feasibility
Technology
Stimulation Questionnaire Results

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

Severe
Moderate
Mild
Absent

- Headache
- Neck Pain
- Scalp Pain
- Pain
- Tingling
- Itching
- Burning
- Noise
- Sensation
- Local Redness
- Sleepiness
- Concentrating
- Improved Mood
- Worsening of mood
- Dizziness
- Flickering Lights

Legend:
- Severe
- Moderate
- Mild
- Absent
Device Technology

Safety
Placebo Stimulation
Effective Blinding
Quality Control
STIM Study
Participant Code
655321
Time Remaining:
39:32
Status
Stimulating
Impedance:
Press stop button on device to stop this session

STIM STUDY
Pt: Flavio Frohlich; ORG: UNC; Design: Parallel, between Groups
Study: Mr. Stephen Schmidt

PARTICIPANTS
Manage the participants of the study.

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DEVICES
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The Future?

...is here?
Premenstrual dysphoric disorder (crossover, 10Hz tACS, placebo).

Post-traumatic stress disorder (10Hz tACS, placebo).
Lustenberger et al. 2016
Maternal immune activation: Implications for neuropsychiatric disorders

Myka L. Estes and A. Kimberley McAllister*

Epidemiological evidence implicates maternal infection as a risk factor for autism spectrum disorder and schizophrenia. Animal models corroborate this link and demonstrate that maternal immune activation (MIA) alone is sufficient to impart lifelong neuropathology and altered behaviors.

Risk factors for developing CNS disorders

Mother
- Immunological activation from infection, autoimmune and genetic predisposition
  - Increased IL-6
  - Activation of Th17 cells

Gestation
- Fetal immune status plus genetic composition helps determine vulnerability to MIA
  - Increased IL-17

Childhood
- MIA offspring have heightened risk for autism spectrum disorder

Adolescence
- MIA offspring more susceptible to "second hits" induced by stress and drug abuse

Adulthood
- MIA offspring have heightened risk of psychiatric and neurologic disorders

Fig. 1. MIA as a disease primer. This schematic depicts the current model for how MIA leads to psychiatric disorders in offspring. Infection leads to release of pro-inflammatory cytokines and activation of Th17 cells in the mother's bloodstream (6, 19). A combination of genetic background, autoimmune status, and second hits during childhood and adolescence (including stress and drug abuse) combines with the consequences of maternal infection to increase the likelihood of offspring developing psychiatric disorders as adults (3, 6, 14, 37).
Example:
Construct: Acute Threat (Fear)
Domain: Negative Valence Systems
Molecules: Glutamate, Dopamine, Serotonin etc.
Cells: Neurons, Glia, etc.
Circuits: Amygdala, Hippocampus, Hypothalamus, etc.
Physiology: Skin Conductance, Heart Rate, Respiration, etc.
Behavior: Freezing, Avoidance, Response Inhibition etc.
Self-Reports: Fear Questionnaire, Trait Fear Inventory, etc.
Paradigms: Fear conditioning, viewing aversive pictures, etc.
Alumni Lab Members
Mohsin Ali
Kristin Sellers
Katrina Kutchko
Stephen Schmidt
Chunxiu Yu
Carrington Merritt

Collaborators
ECOG: Dr. Haewon Shin
Sleep Spindles: Dr. Bradley Vaughn
Modeling ECOG: Dr. Jeremy Lefebvre
Electric Field Spatial Targeting: Dr. Angel Peterchev
SCZ Clinical Trial: Dr. Fred Jarskog, Dr. John Gilmore
Mood Disorders Clinical Trials: Dr. David Rubinow

Funding
NIMH BRAINS R01 MH101547, NIMH R21MH105557, NIMH R21MH105574, Human Frontier Science Program, UNC School of Medicine, Department of Psychiatry, NCTraCS (CTSA #1UL1TR001111), Foundation of Hope, UNC SOM TTSA, NARSAD, Tal Medical, Patient Donations.