



THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL



UNC
SCHOOL OF MEDICINE

Clinical Trials of tACS in Psychiatry

Flavio Frohlich

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Department of Psychiatry

Department of Cell Biology and Physiology

Department of Biomedical Engineering

Department of Neurology

Neuroscience Center



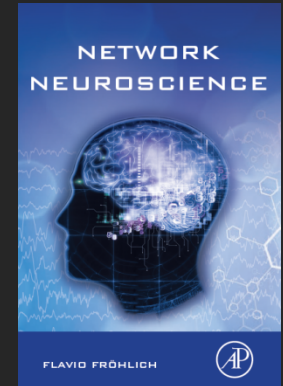
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Conflicts of Interest

- 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

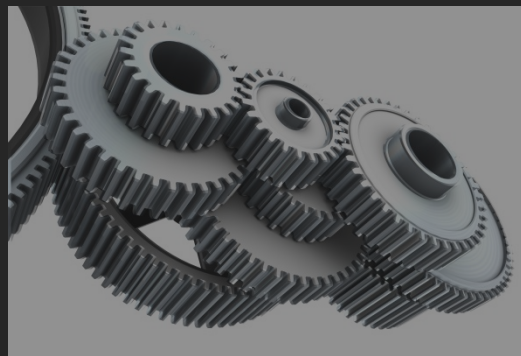
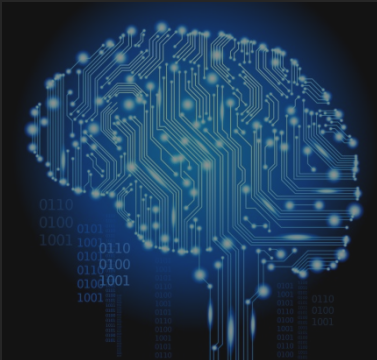
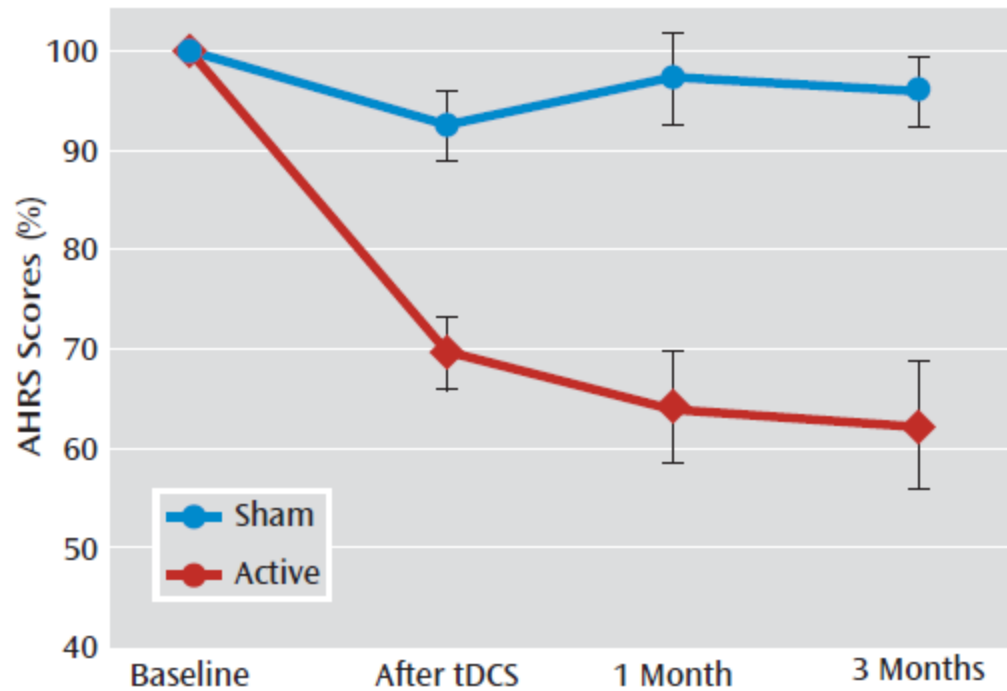
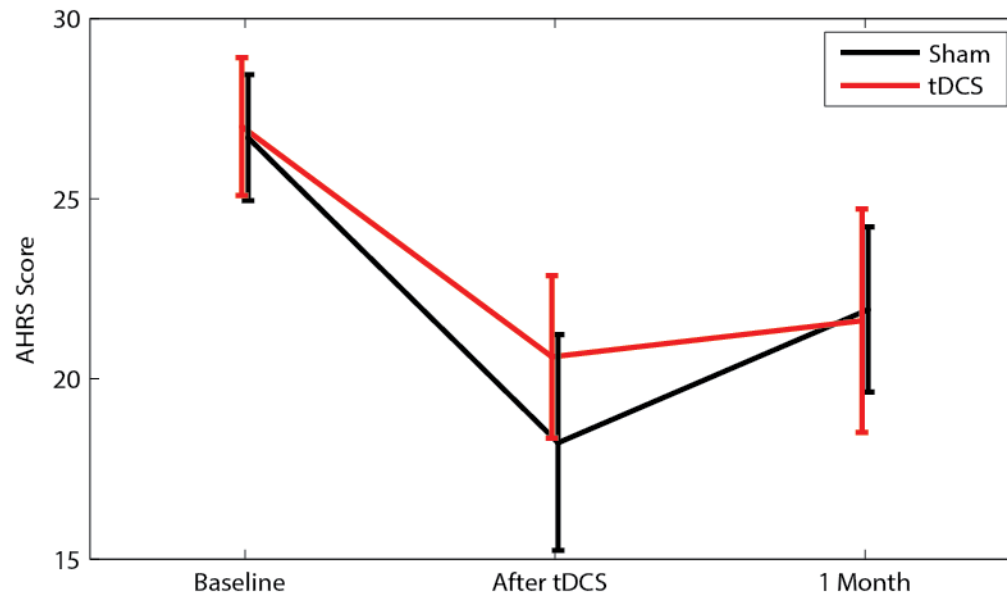


FIGURE 1. Effect of Active and Sham Transcranial Direct-Current Stimulation (tDCS) on the Severity of Auditory Verbal Hallucinations^a





Neuronal Dynamics and Neuropsychiatric Disorders: Toward a Translational Paradigm for Dysfunctional Large-Scale Networks

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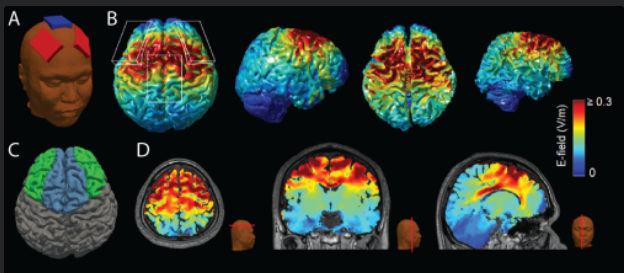
<http://dx.doi.org/10.1016/j.neuron.2012.09.004>



- 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



Angel Peterchev

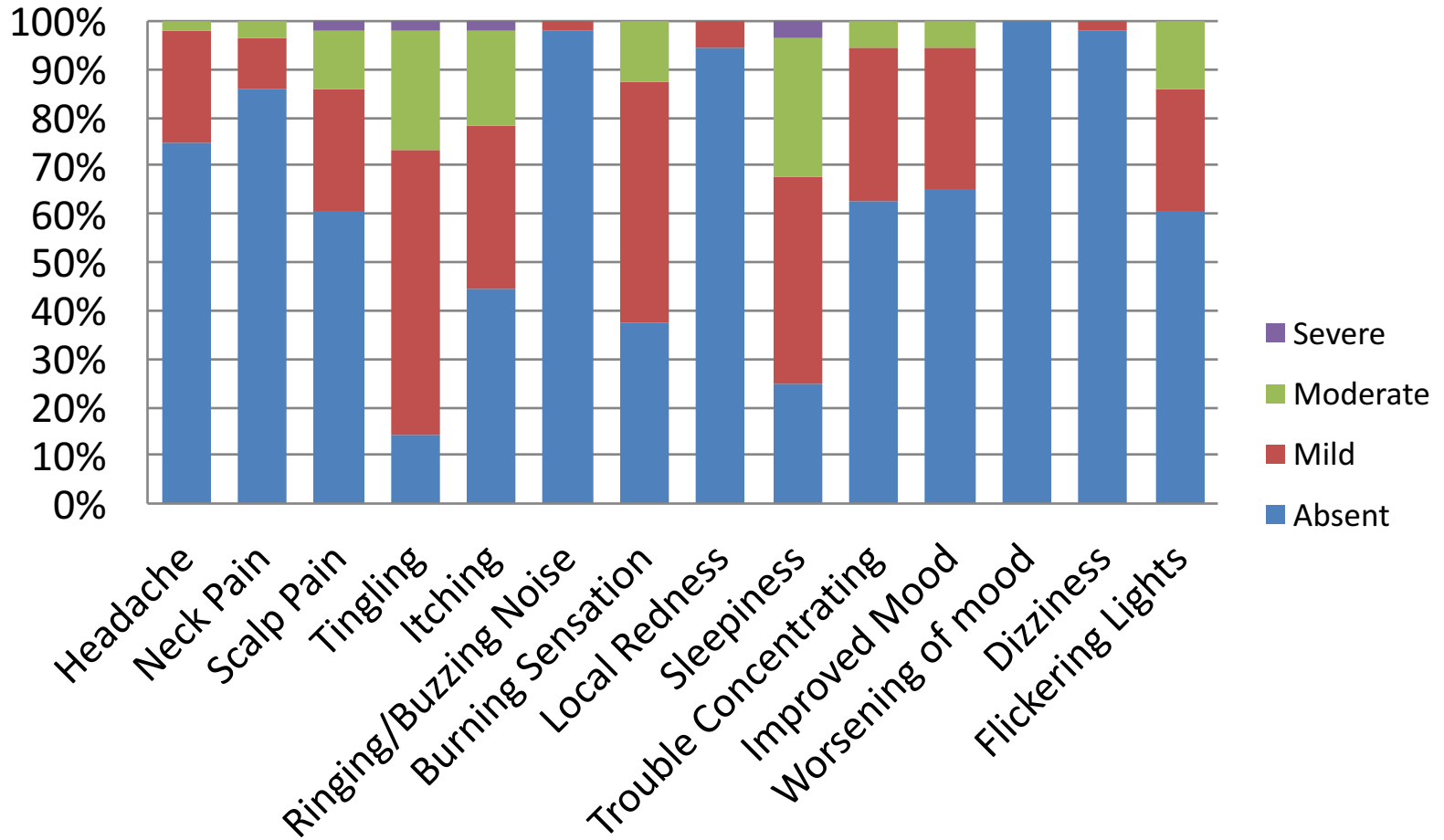
Our Experience

Safety

Feasibility

Technology

Stimulation Questionnaire Results



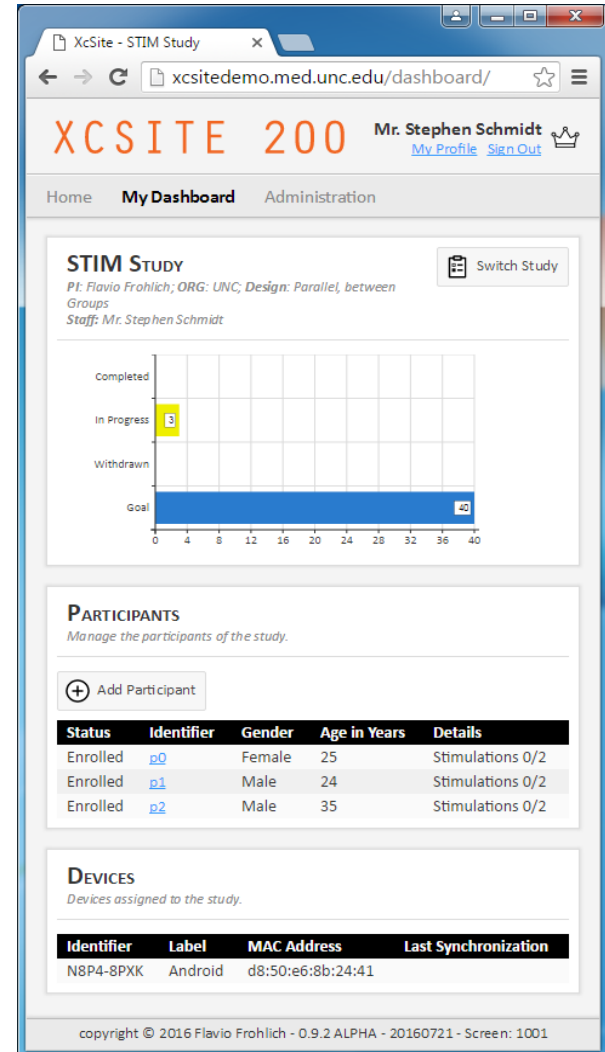
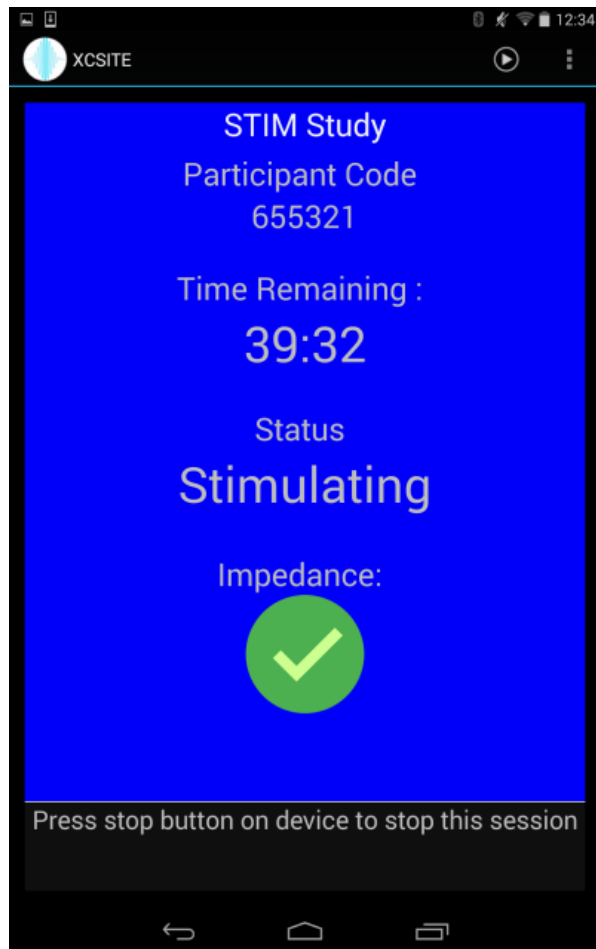
Device Technology

Safety

Placebo Stimulation

Effective Blinding

Quality Control



The Future?

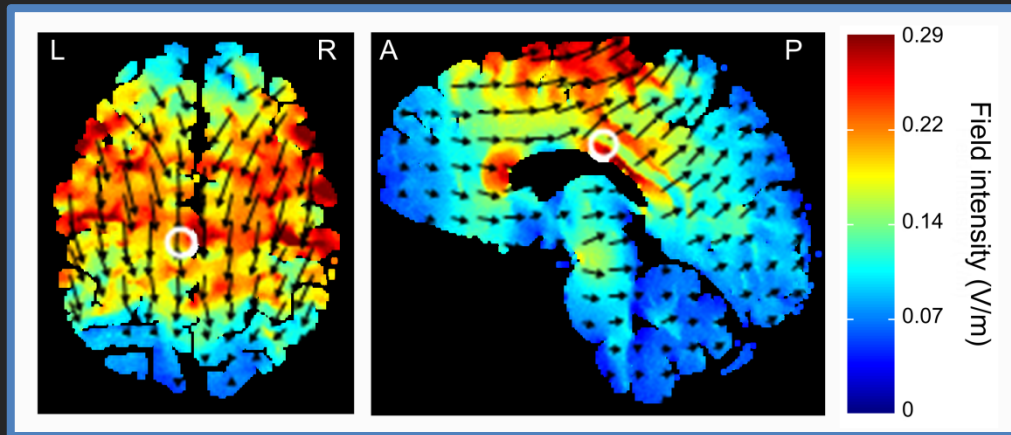
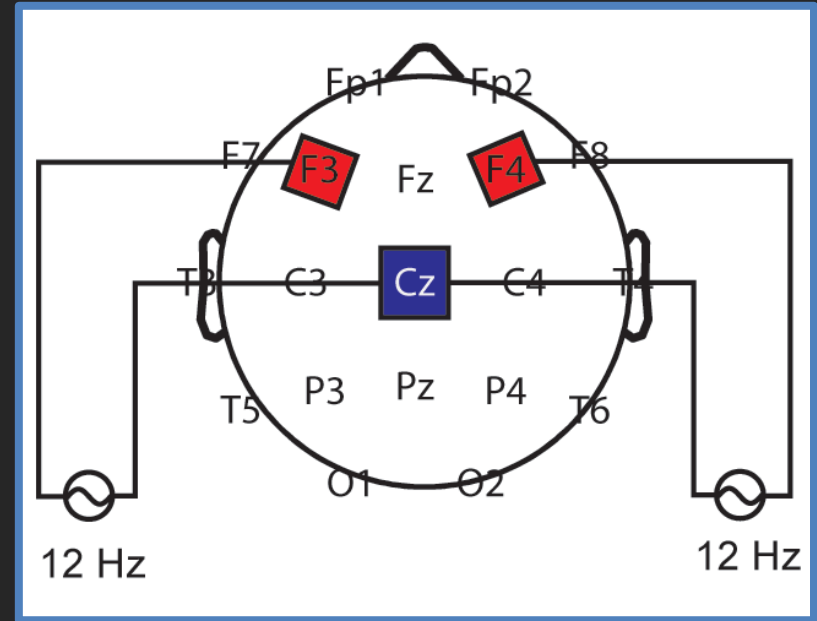
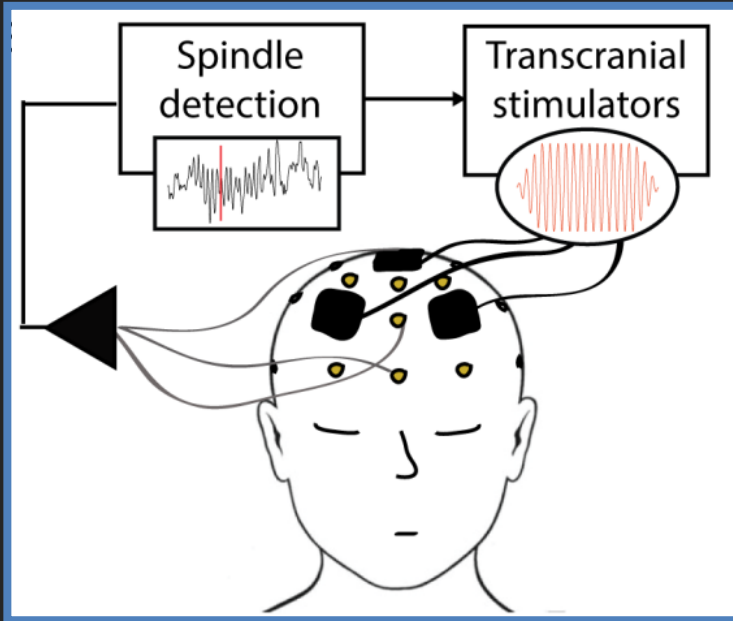
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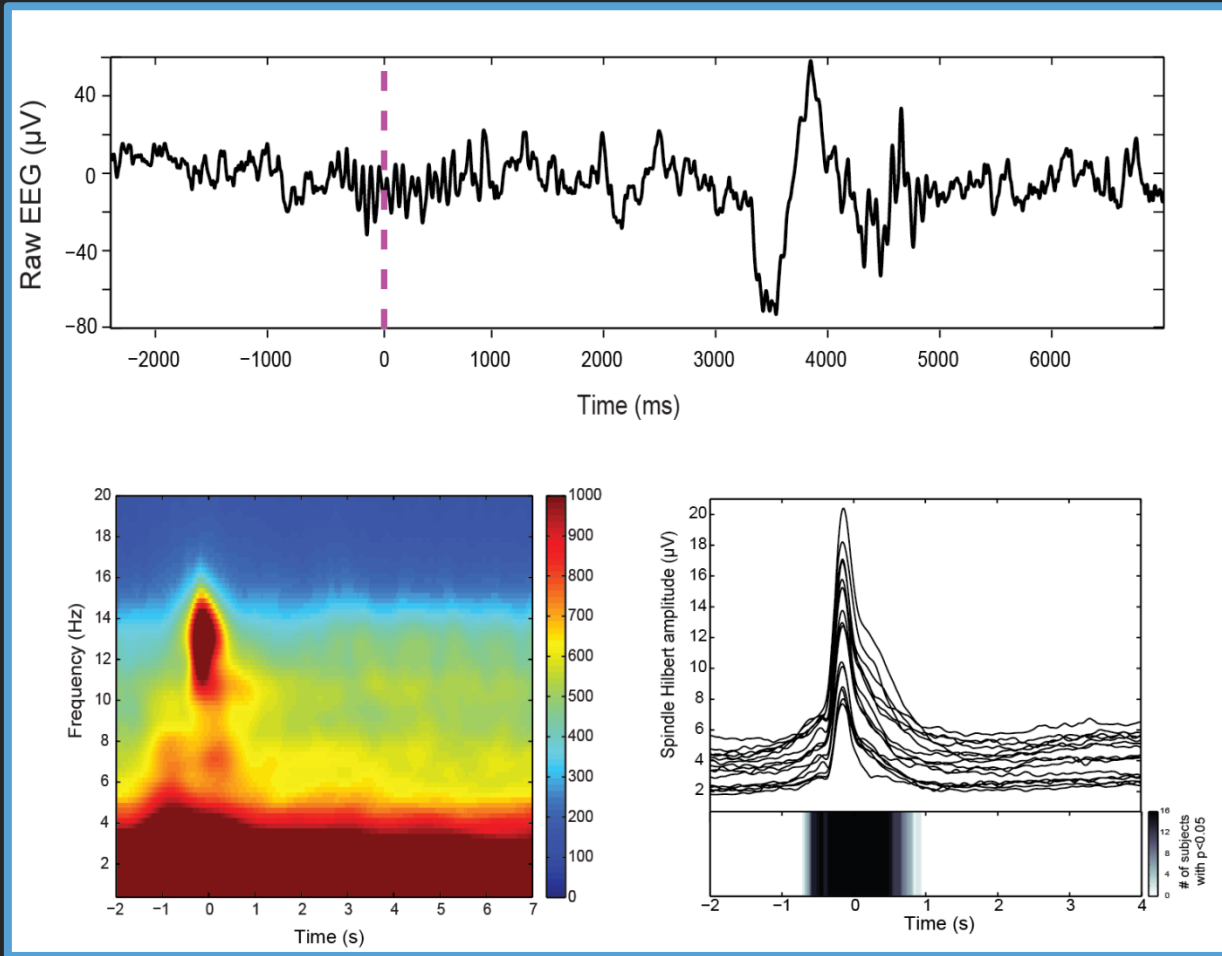


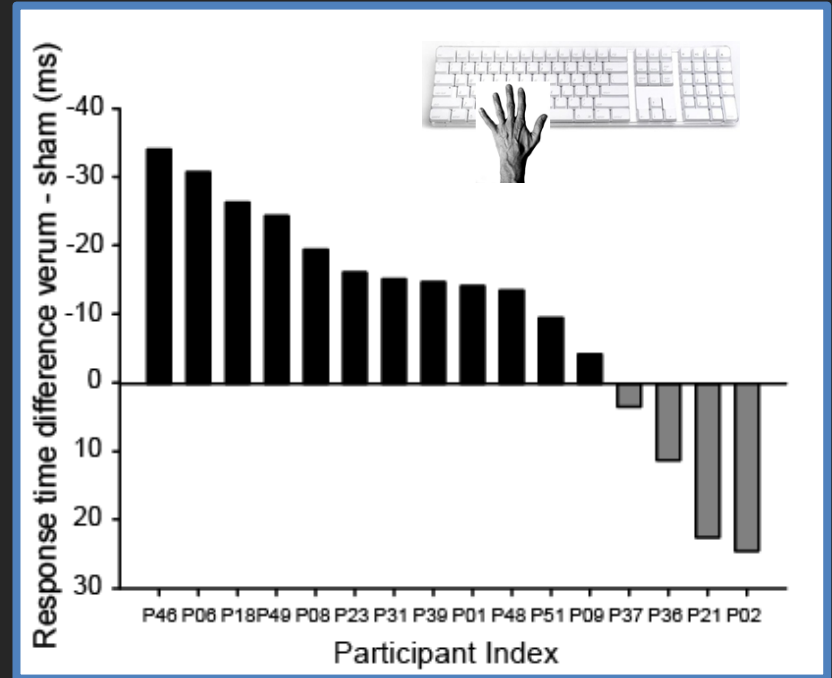
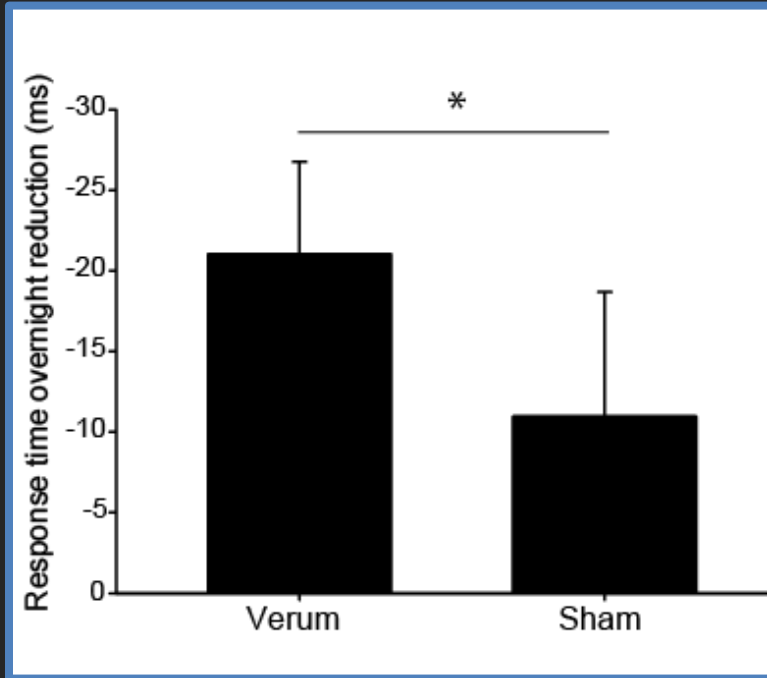
Premenstrual dysphoric disorder (crossover, 10Hz tACS, placebo).

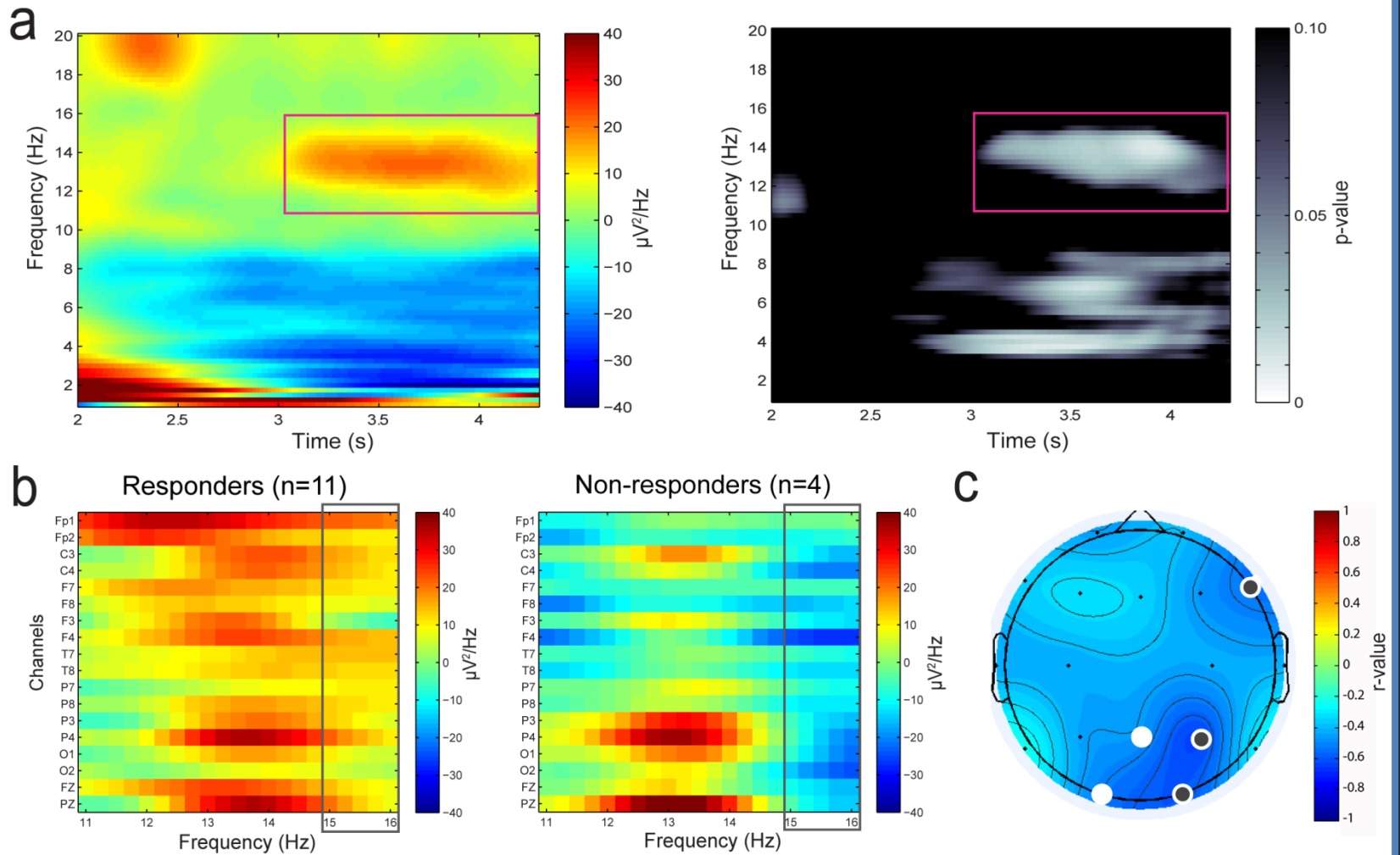


Post-traumatic stress disorder (10Hz tACS, placebo).









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

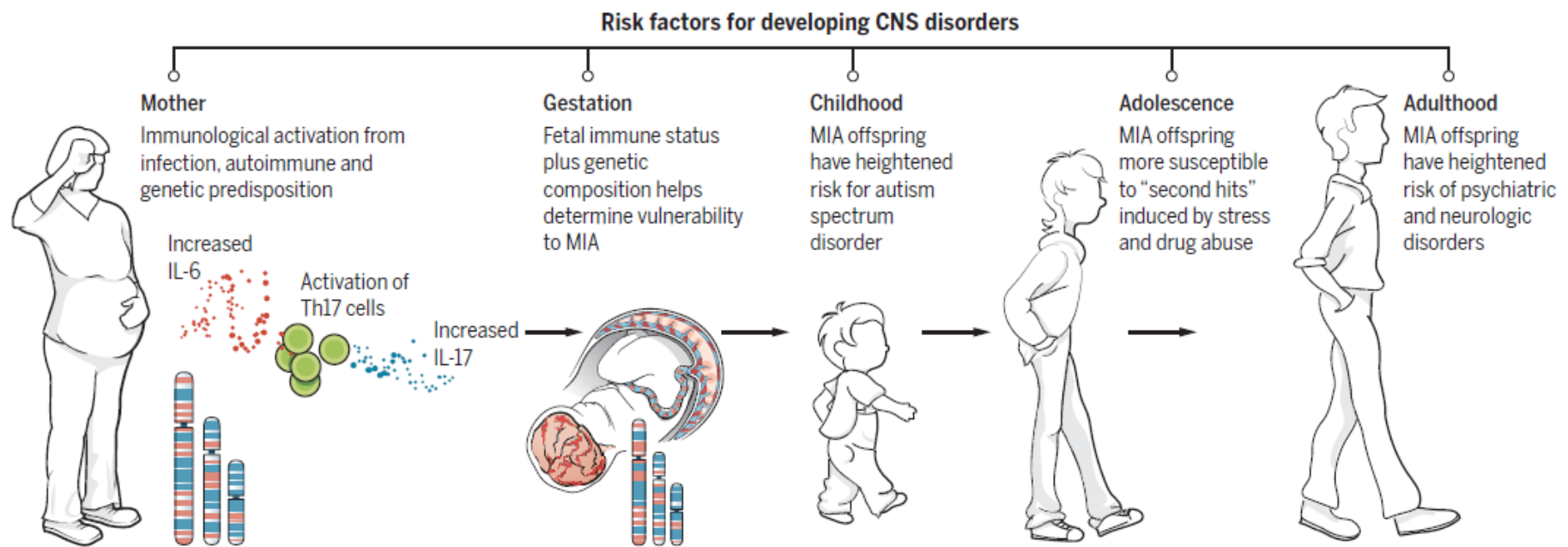
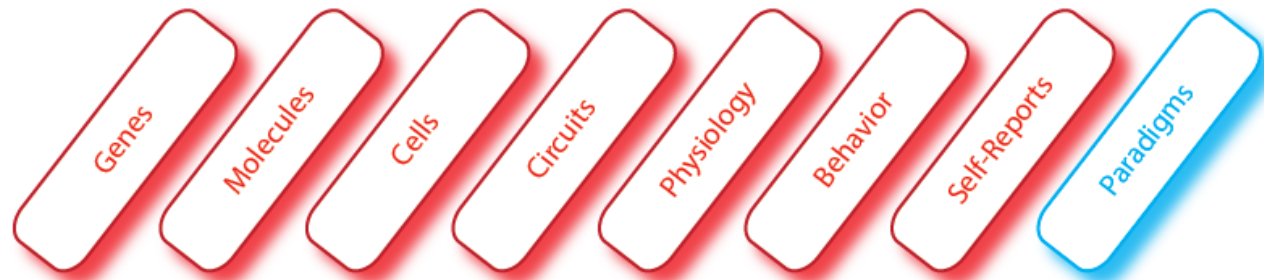


Fig. 1. MIA as a disease primer. This schematic depicts the current model for how MIA leads to psychiatric disorders in offspring. Infection leads to release of pro-inflammatory cytokines and activation of T_H17 cells in the mother's bloodstream (6, 19). A combination of genetic background, autoimmune 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).



Negative Valence
Systems

Positive Valence
Systems

Cognitive
Systems

Social Processes
Systems

Arousal & Regulatory
Systems

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.

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SCZ Clinical Trial: Dr. Fred Jarskog, Dr. John Gilmore
Mood Disorders Clinical Trials: Dr. David Rubinow

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