Transcranial Electrical Stimulation (TES)

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tES Workshop, NIMH, Sept 29-30, 2016
Outline

- The Problem
- The Promise
- The Pitfalls
- The Priorities
The Problem

- Brain-based disorders are leading drivers of preventable deaths

**Suicide Rates Climbing: CDC Report**

<table>
<thead>
<tr>
<th>Rate per 100,000</th>
<th>Female</th>
<th>Male</th>
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<tbody>
<tr>
<td></td>
<td>1999</td>
<td>2014</td>
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<td>10-14</td>
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<td>15-24</td>
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<td>25-44</td>
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<td>45-64</td>
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<tr>
<td>65-74</td>
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<tr>
<td>75+</td>
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All differences significant

CDC National Center for Health Statistics April 2016
The Problem

- Brain-based disorders are leading drivers of disability worldwide

The single best way to improve overall health is to improve brain health

Source: WHO 2008
The Problem

- Brain-based disorders are leading drivers of disability worldwide
- Gaps in knowledge of the causes of many brain-based disorders
  - No biomarkers yet found to aid individual diagnosis
  - Impedes diagnosis and stymies treatment development

Healthy volunteer  Patient with Schizophrenia

Where’s the lesion?
Outline

- The Problem
- The Promise
- The Pitfalls
- The Priorities
The Promise

- Emerging brain science
  - shedding light on the circuits and dynamics underlying brain-based disorders
The Promise

- Emerging brain science
- Emerging targets for therapeutic intervention

Circuits

Anxious avoidance

Dorsal and rostral nodes have been noted in depression, social anxiety disorder, and cognitive control.

Activation

- Hyper
- Typical
- Hypo

Connectivity

- Hyperconnectivity
- Typical connectivity
- Hypoconnectivity

Williams, Lancet Psychiatry 2016
The Promise

- Emerging brain science
- Emerging targets for therapeutic intervention
  - Circuits
  - Dynamics

Lustenberger et al Current Biology 2016
The Promise

- Emerging brain science
- Emerging targets for therapeutic intervention
- Emerging brain tools
  - Measure brain structure & function

Source: Human Connectome Project
The Promise

- Emerging brain science
- Emerging targets for therapeutic intervention
- Emerging brain tools
  - Measure brain structure & function
  - Modulate brain structure & function Noninvasively

Transcranial Magnetic Stimulation

TDCS/TACS

Magnetic Seizure Therapy

ECT

Deep Brain Stimulation

TMS

MST

DBS
The Promise

- Emerging brain science
- Emerging targets for therapeutic intervention
- Emerging brain tools
  - Measure brain structure & function
  - Modulate brain structure & function Noninvasively

Transcranial Magnetic Stimulation
TMS

Transcranial Direct or Alternating Current Stim.
TDCS/TACS

Magnetic Seizure Therapy
MST

Electro-convulsive Therapy
ECT

Noninvasive Transcranial electric

NIH National Institute of Mental Health
The Promise

- Emerging brain science
- Emerging targets for therapeutic intervention
- Emerging brain tools
  - Measure brain structure & function
  - Modulate brain structure & function Noninvasively

TDCS/TACS
Transcranial Direct or Alternating Current Stim.

ECT
Electro-convulsive Therapy

Transcranial electric
Sub-convulsive

NIH National Institute of Mental Health
Emerging brain science
Emerging targets for therapeutic intervention
Emerging brain tools
Next Generation brain tools on the way

– Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative

Source Human Connectome Project

Next-gen tools to probe neural control of thoughts, feelings, movements

Brainbow transgenes.
Credit: Joshua Sanes, Ph.D.
The Promise

- Emerging brain science
- Emerging targets for therapeutic intervention
- Emerging brain tools
- Next Generation brain tools on the way
  - Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative
  - **Goal:** to revolutionize understanding of the human brain by accelerating development and application of innovative technologies
• Noninvasive NeuroMod Tool Development and Optimization
Outline

- The Problem
- The Promise
- **The Pitfalls**
- The Priorities
The Pitfalls

- Optimal dosing unknown, infinite parameter space
  - Conventional “Dosing dogma” is misleading

<table>
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<tr>
<th></th>
<th>High freq</th>
<th>Low freq</th>
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<tr>
<td>rTMS</td>
<td>Continuous</td>
<td>Intermittent</td>
</tr>
<tr>
<td>TBS</td>
<td>Anodal</td>
<td>Cathodal</td>
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Excitatory | Inhibitory
The Pitfalls

- Optimal dosing unknown, infinite parameter space
  - Conventional “Dosing dogma” is misleading

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**Excitatory & Inhibitory**
The Pitfalls

- Optimal dosing unknown, infinite parameter space
  - Spatial targeting – where to put it
  - Temporal targeting – how to tune it
  - Controlling context – state of brain at time of stim

Interactions of all of the above

Delivered Dose

- E-field distribution
- Frequency, train duration, pulse shape

Context of Use

- Endogenous & task-related activity, oscillatory phase, sleep/wake cycle, meds, social context
Outline

- The Problem
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- The Priorities
Are we asking the right question?

Does TDCS/TACS work for ___?

Depression, Anxiety, Psychosis, Addictions, Traumatic Brain Injury, Autism, Pain, Dementia
Are we asking the right question?

**How does it work?**

Extracellular Currents

- Endogenously Generated
- Exogenously Applied

Emerging role of abnormal neural oscillations in psychiatric disorders