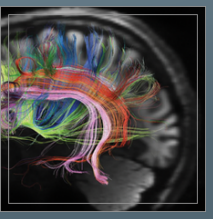



Transcranial Electrical Stimulation (TES)

Sarah Hollingsworth Lisanby, MD

Director, Translational Research Division

Team B Lead – BRAIN Initiative

Chief, Noninvasive Neuromodulation Unit

Experimental Therapeutics & Pathophysiology Branch

National Institute of Mental Health (NIMH)

tES Workshop, NIMH, Sept 29-30, 2016

NIH National Institute of Mental Health

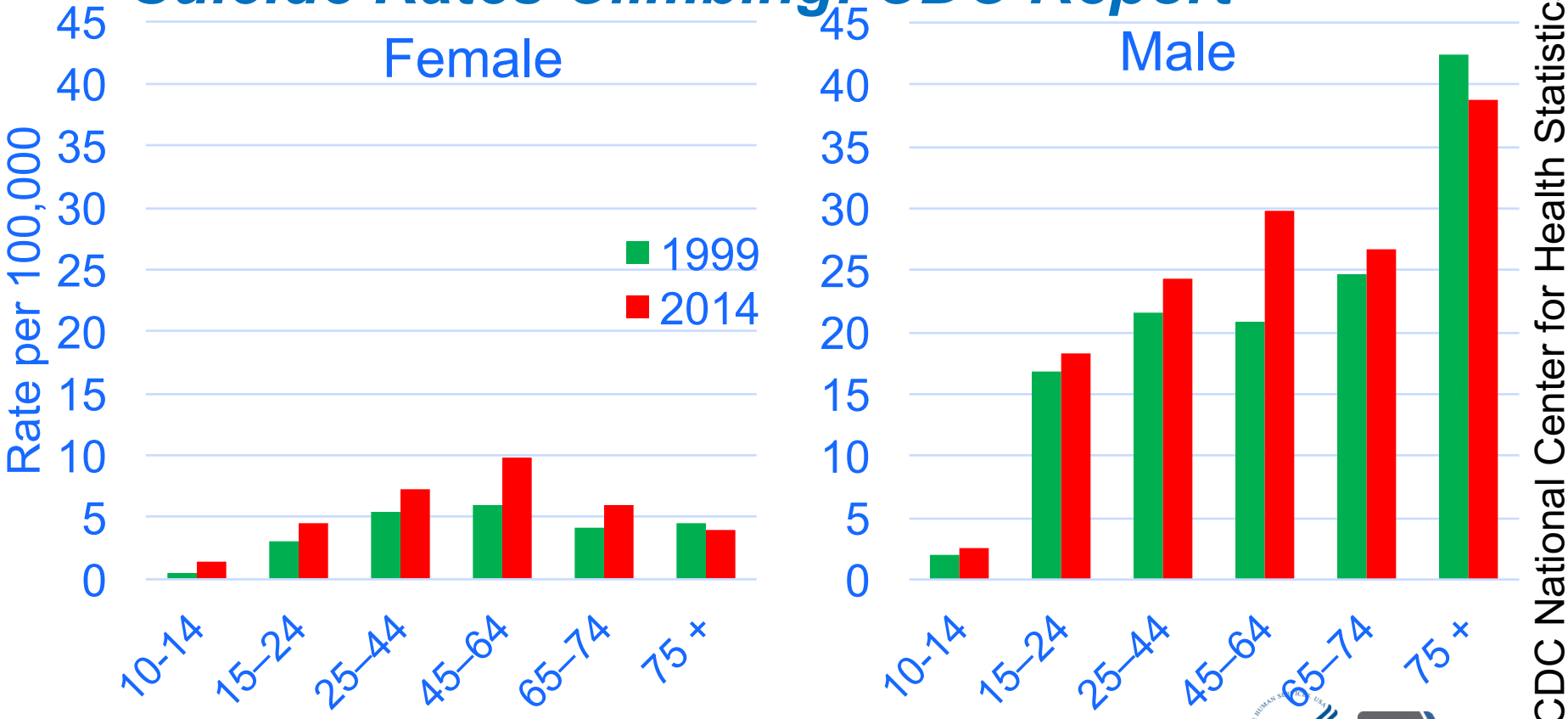
Outline

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

The Problem

- Brain-based disorders are leading drivers of preventable deaths

Suicide Rates Climbing: CDC Report



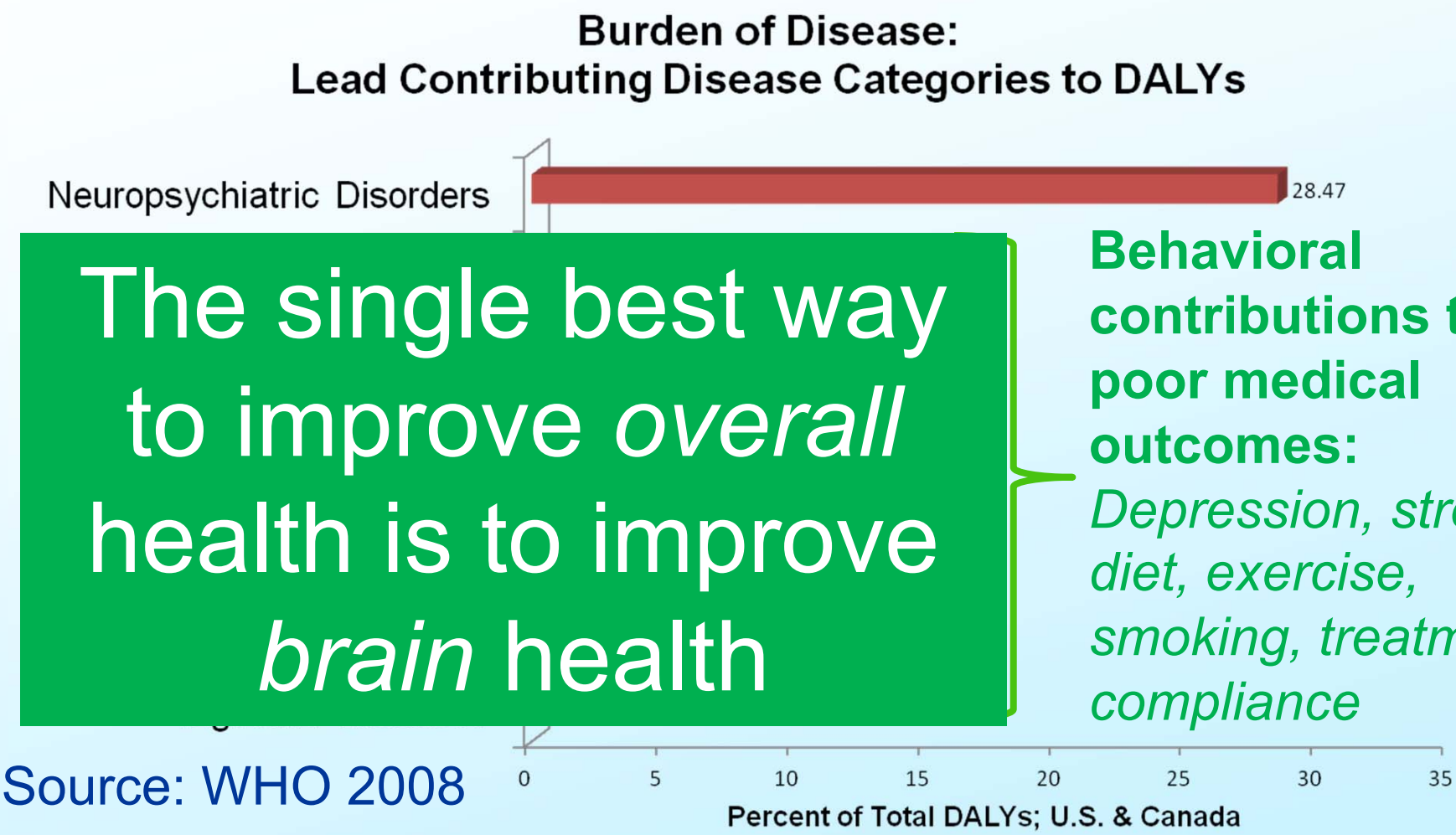
All differences significant

CDC National Center for Health Statistics April 2016

National Institute of Mental Health

The Problem

- Brain-based disorders are leading drivers of disability worldwide



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

Behavioral contributions to poor medical outcomes:
Depression, stress, diet, exercise, smoking, treatment compliance

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

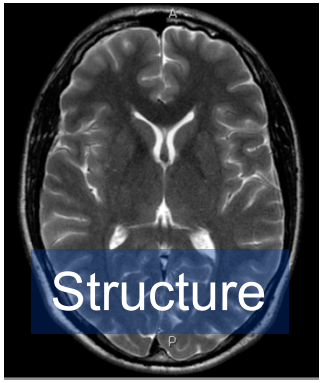
Patient with Schizophrenia

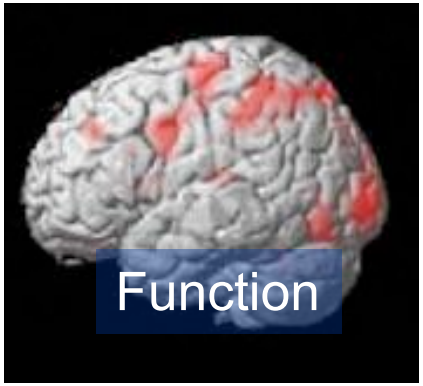
Outline

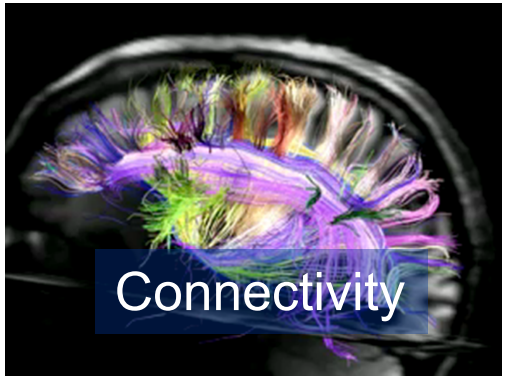
- The Problem
- The Promise
- The Pitfalls
- The Priorities

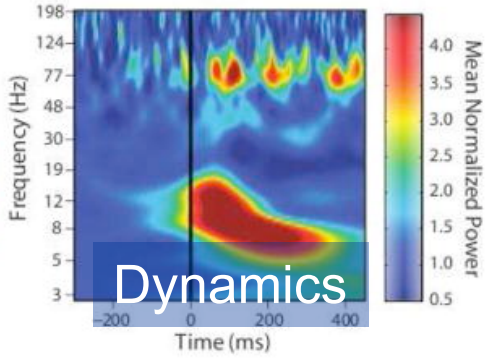
The Promise

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





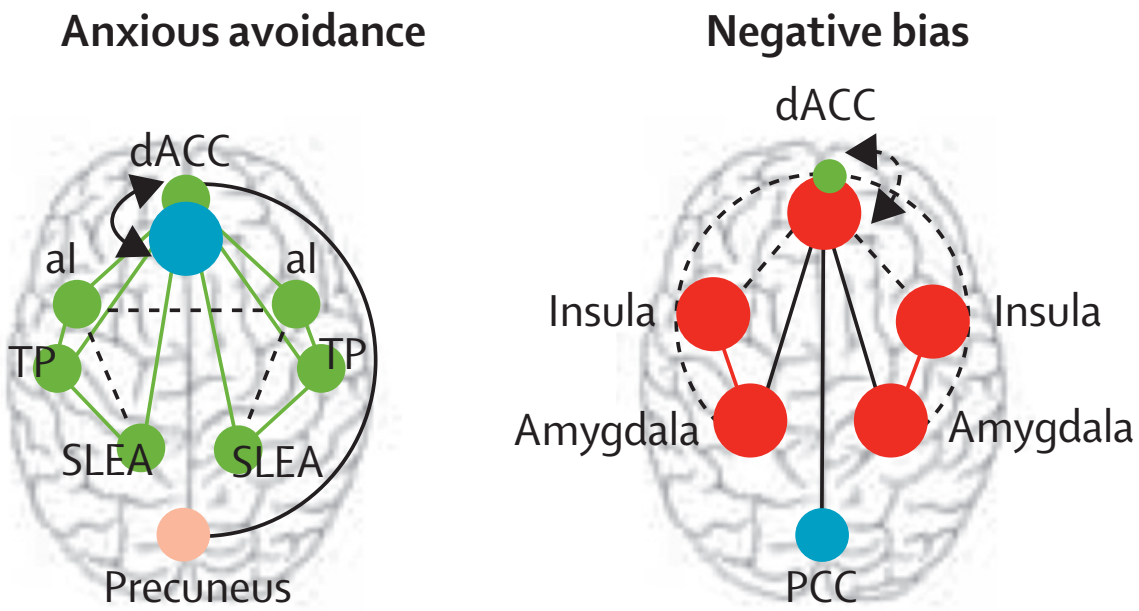




National Institute of Mental Health

The Promise

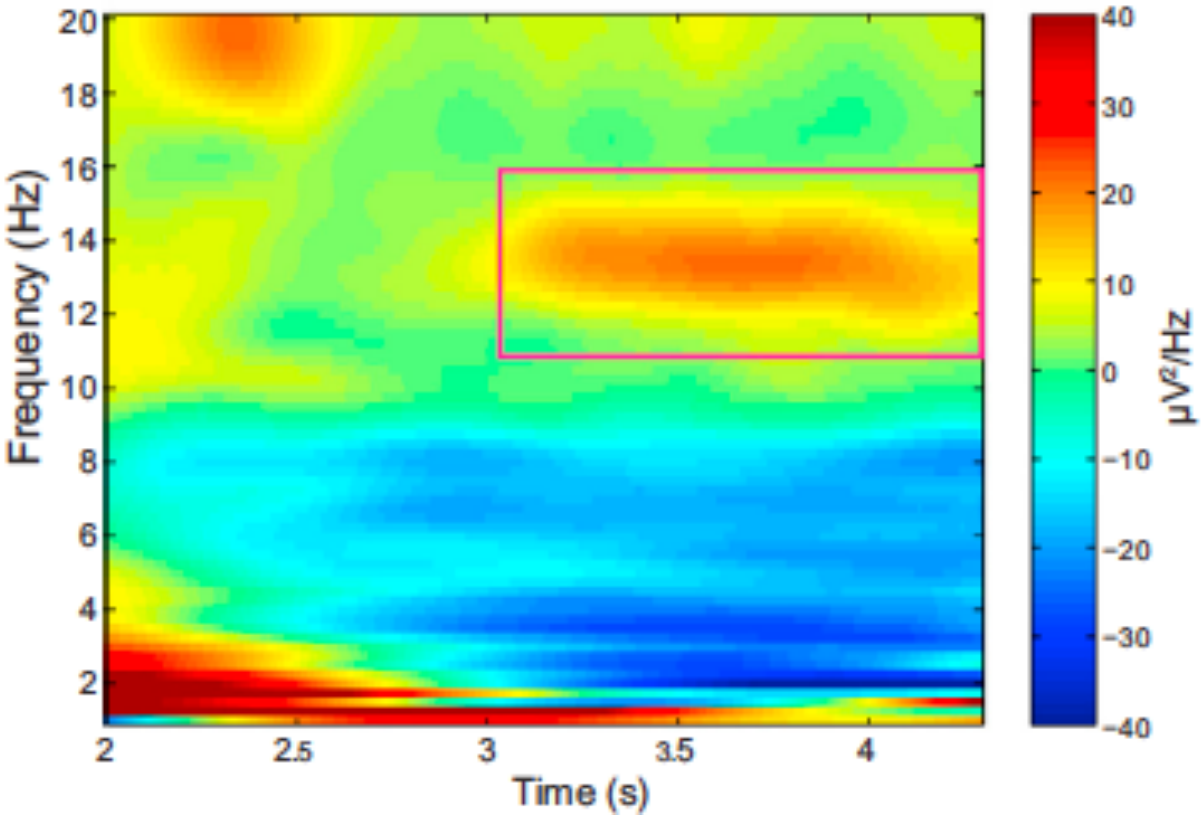
- Emerging brain science
- Emerging targets for therapeutic intervention
  - Circuits



Williams, Lancet Psychiatry 2016

The Promise

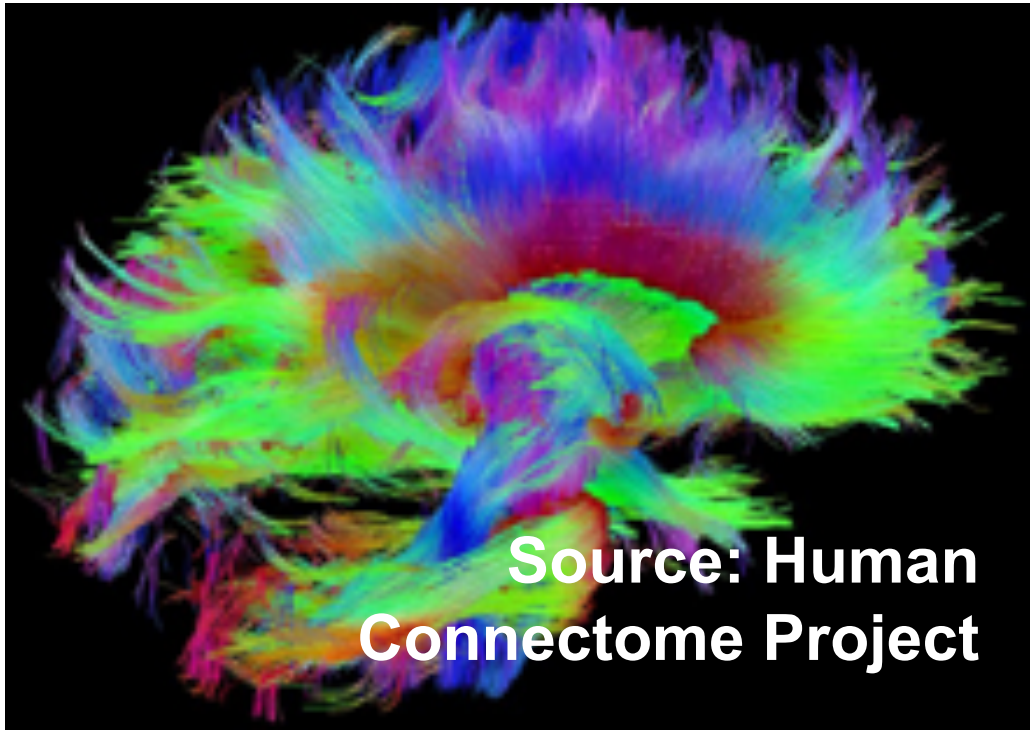
- Emerging brain science
- Emerging targets for therapeutic intervention
  - Circuits
  - Dynamics



Lustenberger et al Current Biology 2016

The Promise

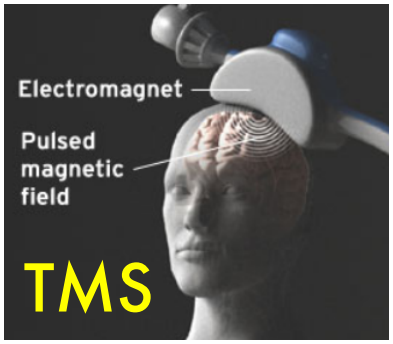
- Emerging brain science
- Emerging targets for therapeutic intervention
- Emerging brain tools
  - Measure brain structure & function

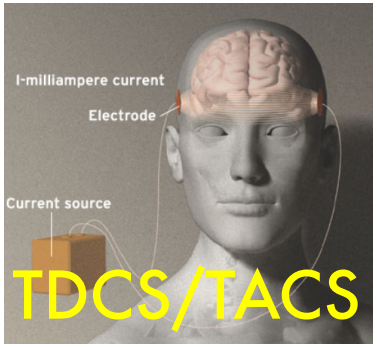


The Promise

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

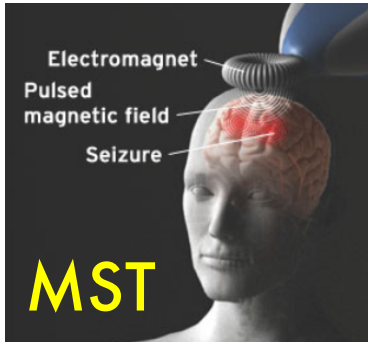
Transcranial Magnetic Stimulation

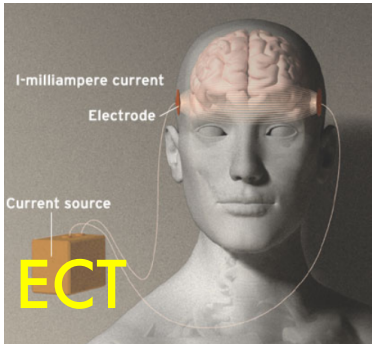




Transcranial Direct or Alternating Current Stim.

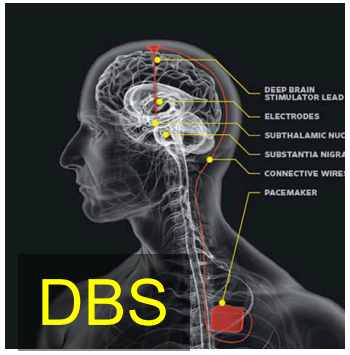
Magnetic Seizure Therapy





Electro-convulsive Therapy

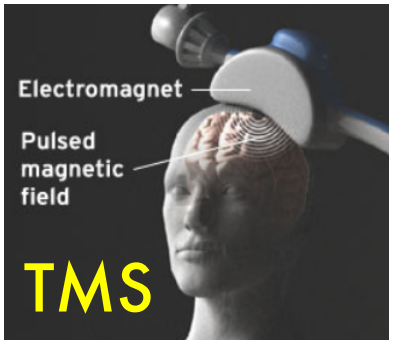
Deep Brain Stimulation

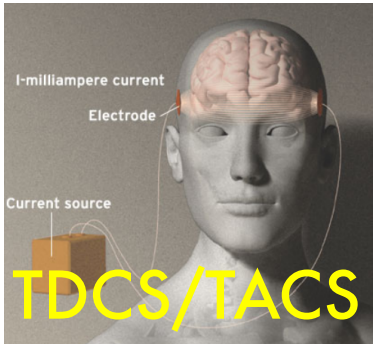


The Promise

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

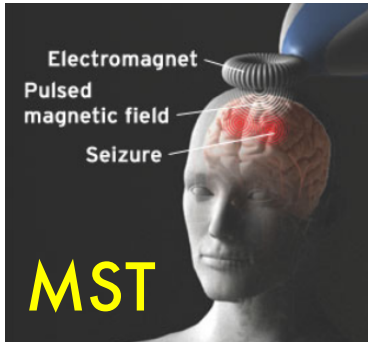
Transcranial Magnetic Stimulation

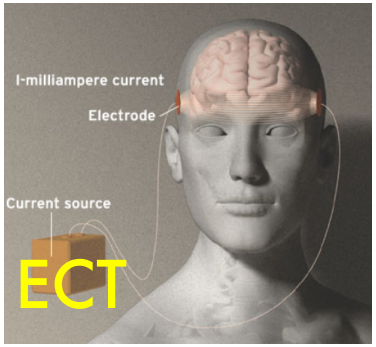




Transcranial Direct or Alternating Current Stim.

Magnetic Seizure Therapy





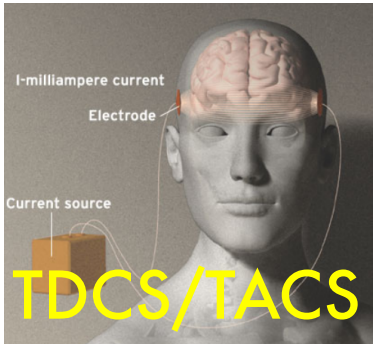
Electro-convulsive Therapy

Trans-cranial electric

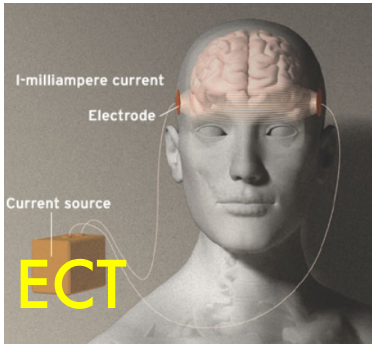
NIH National Institute of Mental Health

The Promise

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



Transcranial Direct or Alternating Current Stim.



Electro-convulsive Therapy

Trans-cranial electric

Sub-convulsive

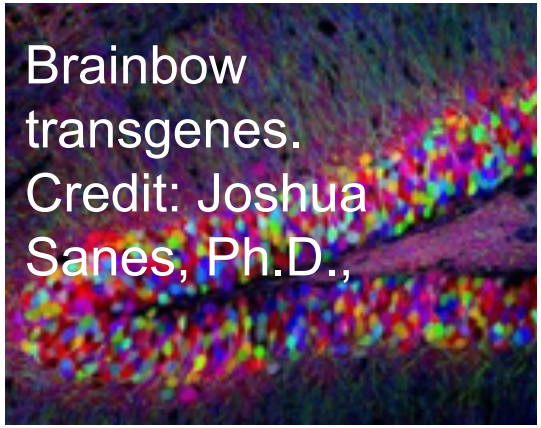
NIH National Institute of Mental Health

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*


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

NextGen Tools

THE BRAIN INITIATIVE®

- **Noninvasive NeuroMod Tool Development and Optimization**
  - RFA-MH-17-240: BRAIN Initiative: Non-Invasive Neuromodulation - **New Tools** and Techniques for Spatiotemporal Precision
  - RFA-MH-17-245: BRAIN Initiative: Non-Invasive Neuromodulation - **Mechanisms and Dose/Response** Relationships for Targeted CNS Effects (R01)

Outline

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

The Pitfalls

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

rTMS	High freq	Low freq
TBS	Continuous	Intermittent
tDCS	Anodal	Cathodal
	Excitatory	**Inhibitory**

The Pitfalls

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

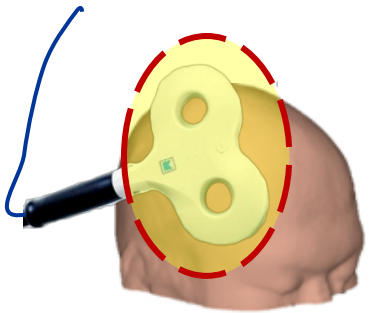
rTMS	High freq	Low freq
TBS	Continuous	Intermittent
tDCS	Anodal	Cathodal

Excitatory & **Inhibitory**

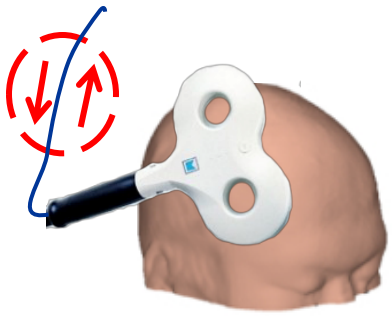
The Pitfalls

- 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

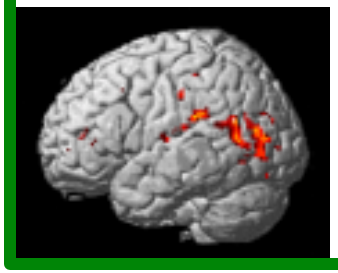


E-field distribution



Frequency, train duration, pulse shape

Context of Use



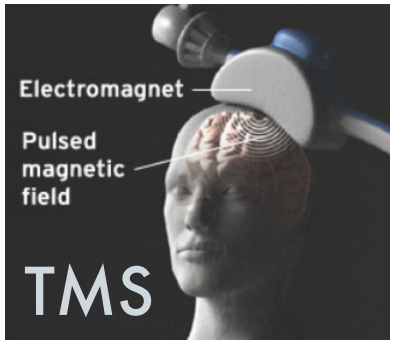
Endogenous & task-related activity, oscillatory phase, sleep/wake cycle, meds, social context

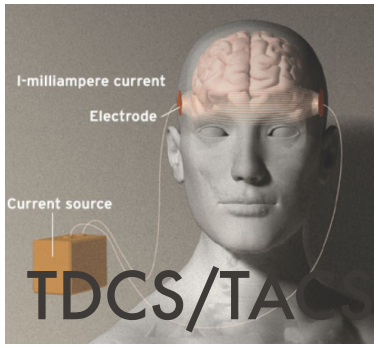
Outline

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

Are we asking the right question?

DOES TMS WORK FOR ___?





Depression, Anxiety, Psychosis, Addictions, Traumatic Brain Injury, Autism, Pain, Dementia

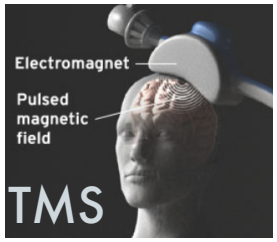
Are we asking the right question?

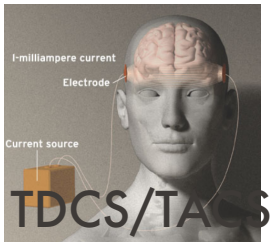
HOW DOES IT WORK ?

Extracellular Currents

Endogenously Generated

Exogenously Applied





Emerging role of abnormal neural oscillations in psychiatric disorders

National Institute of Mental Health