

Noninvasive Neuromodulation in Psychiatric Treatment: *Current and Developing*

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DukePsychiatry & Behavioral Sciences





Non-Invasive Neuromodulation Devices FDA Approved for Therapeutic Use in Psychiatry

ECT



TMS



dTMS



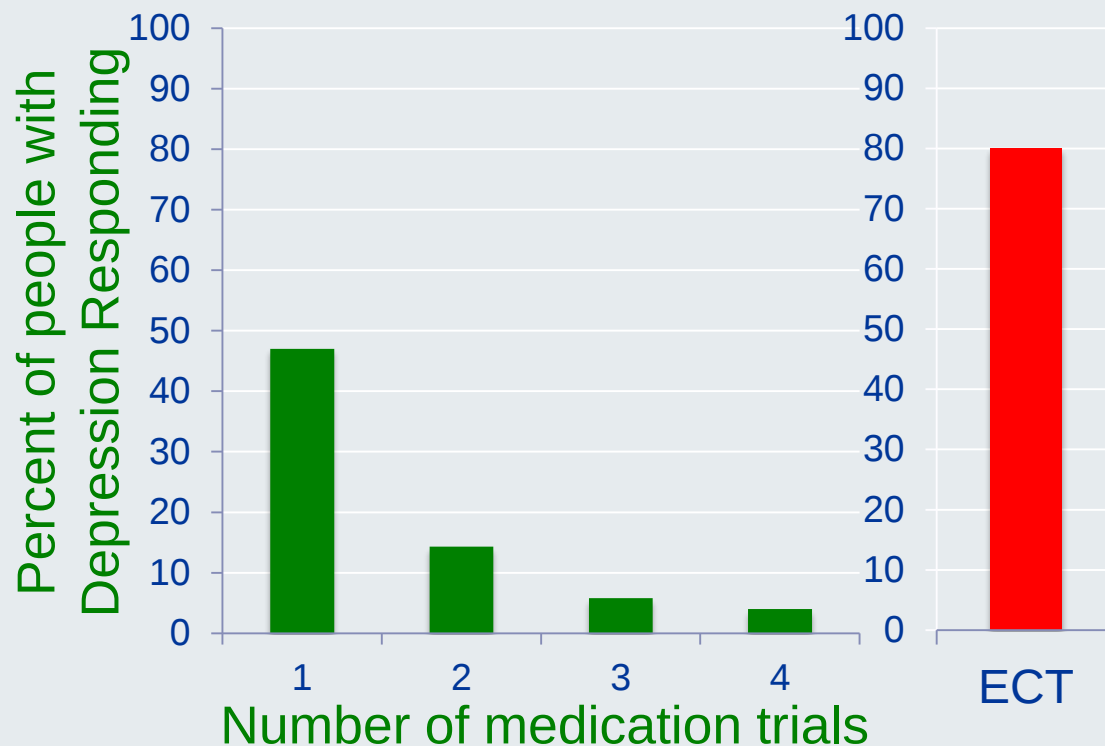
- Benefits
- Risks
- Critical knowledge gaps and needs for future work



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- Benefits
 - Unparalleled efficacy



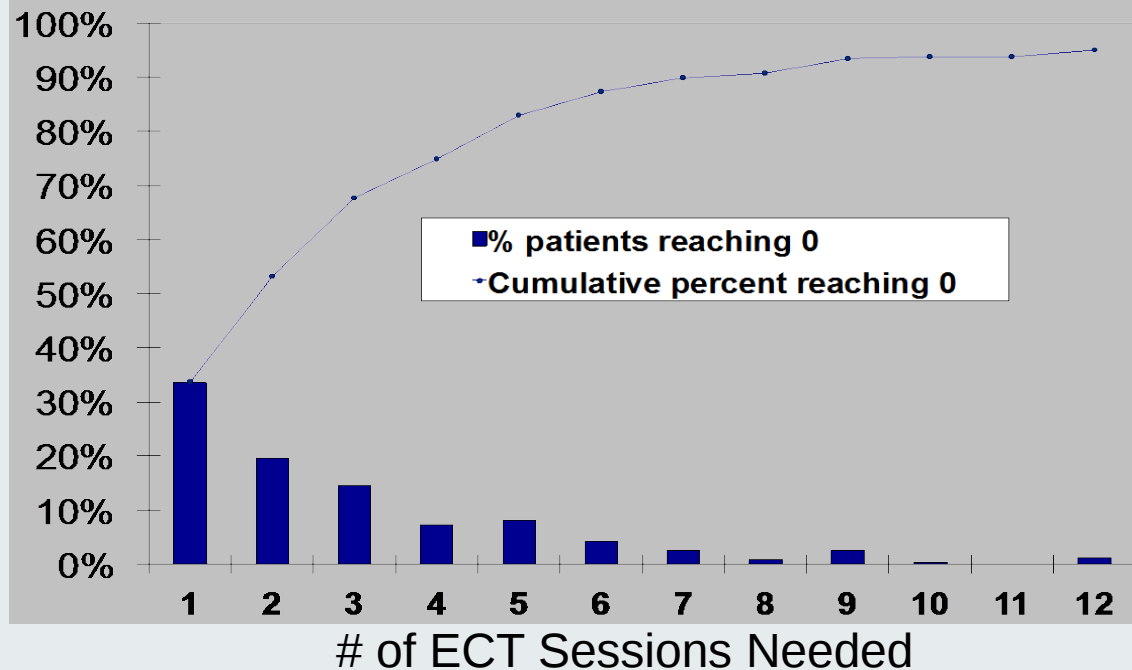


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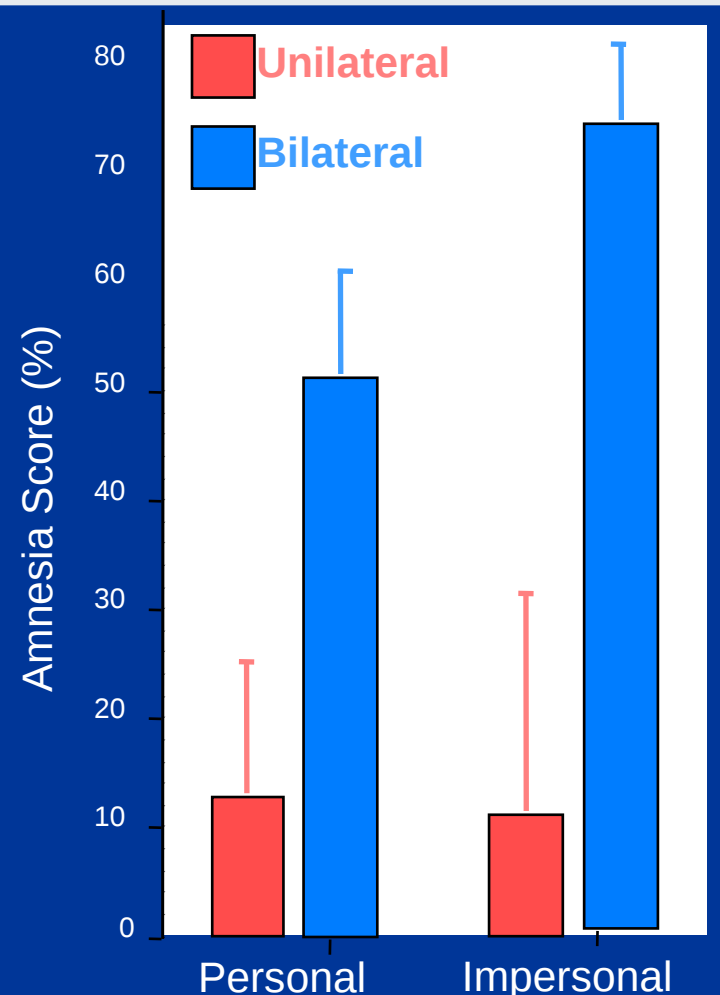
- Benefits

- Unparalleled efficacy
- Rapidly resolves suicide risk

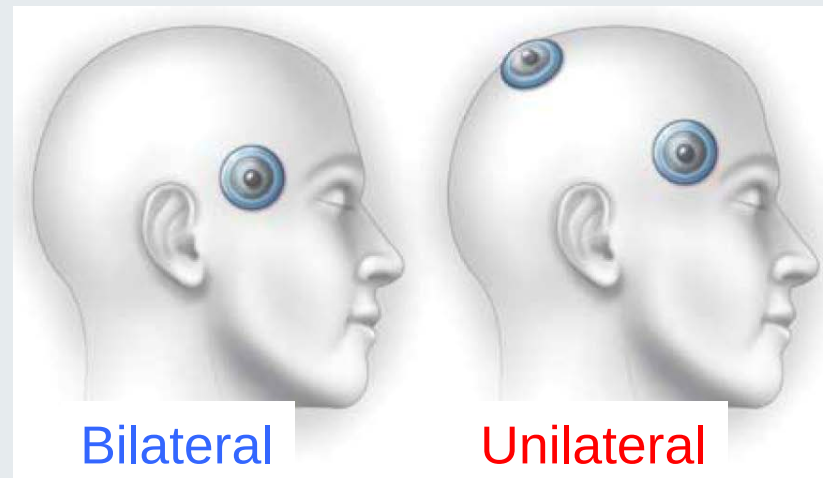




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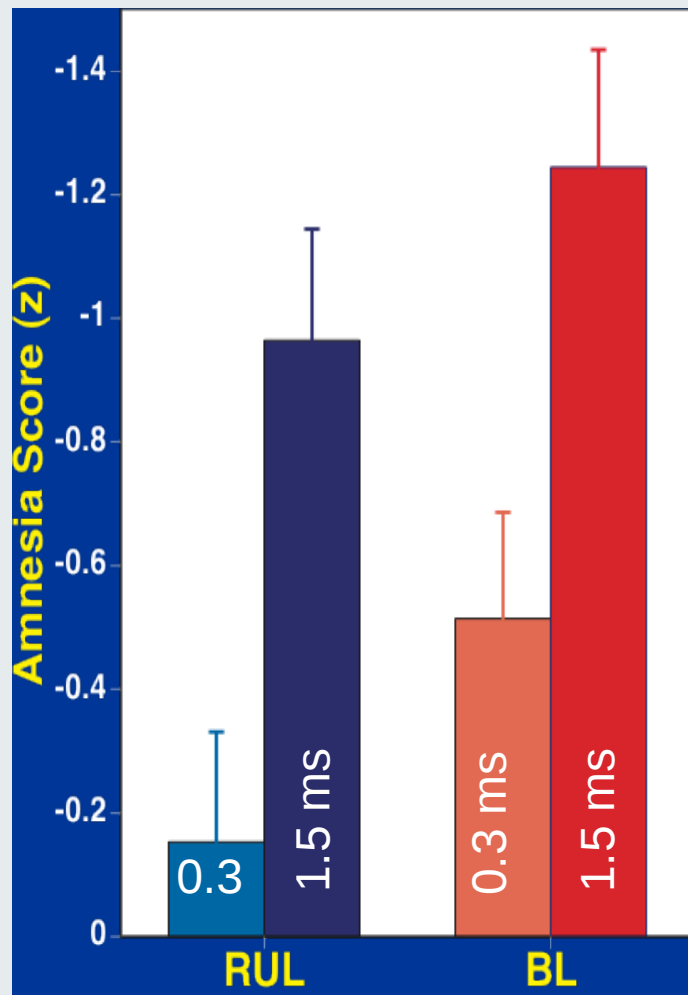


- Benefits
- Risks
 - Memory loss
 - Reduced with unilateral electrode placement



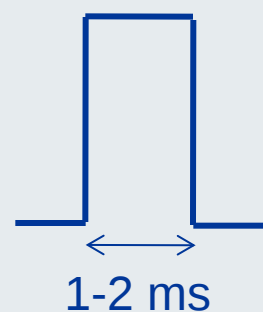


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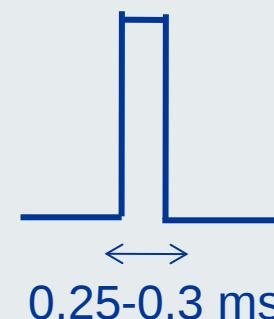


- Benefits
- Risks
 - Memory loss
 - Reduced with unilateral electrode placement, and
 - Ultrabrief pulse width

Standard Pulse

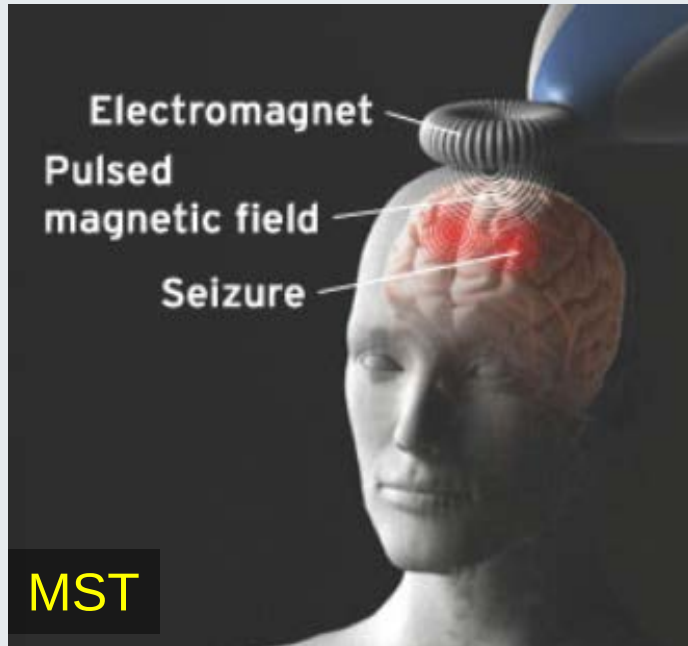


Ultra-Brief Pulse





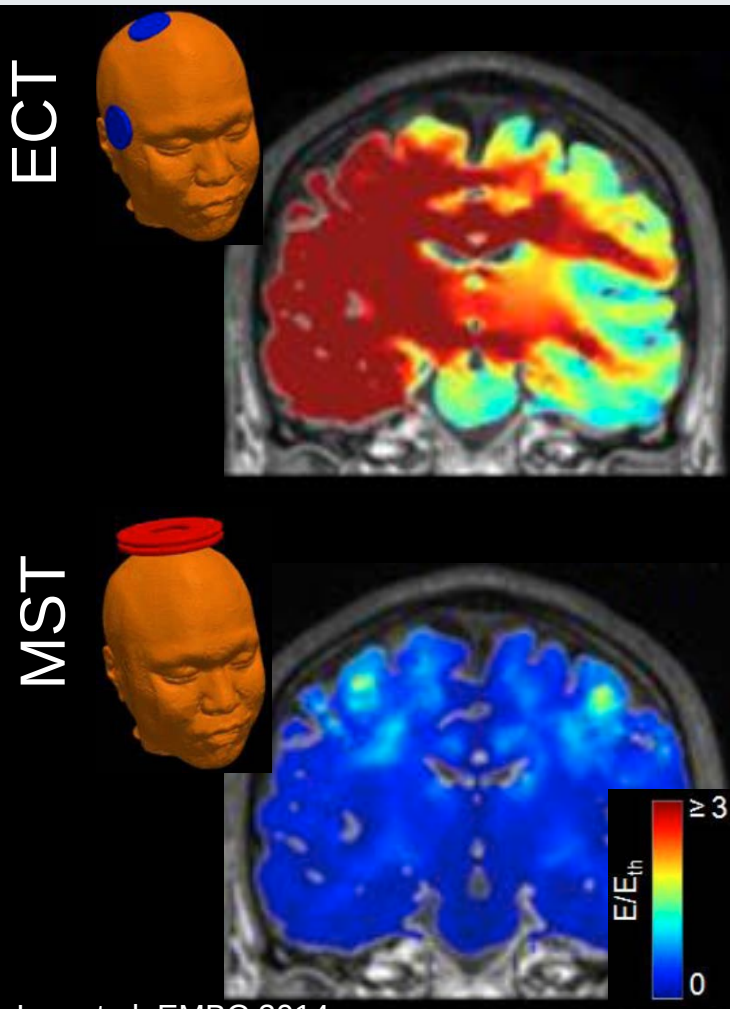
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- Benefits
- Risks
- Critical knowledge gaps and needs for future work
 - Novel strategies to protect memory
 - Magnetic Seizure Therapy



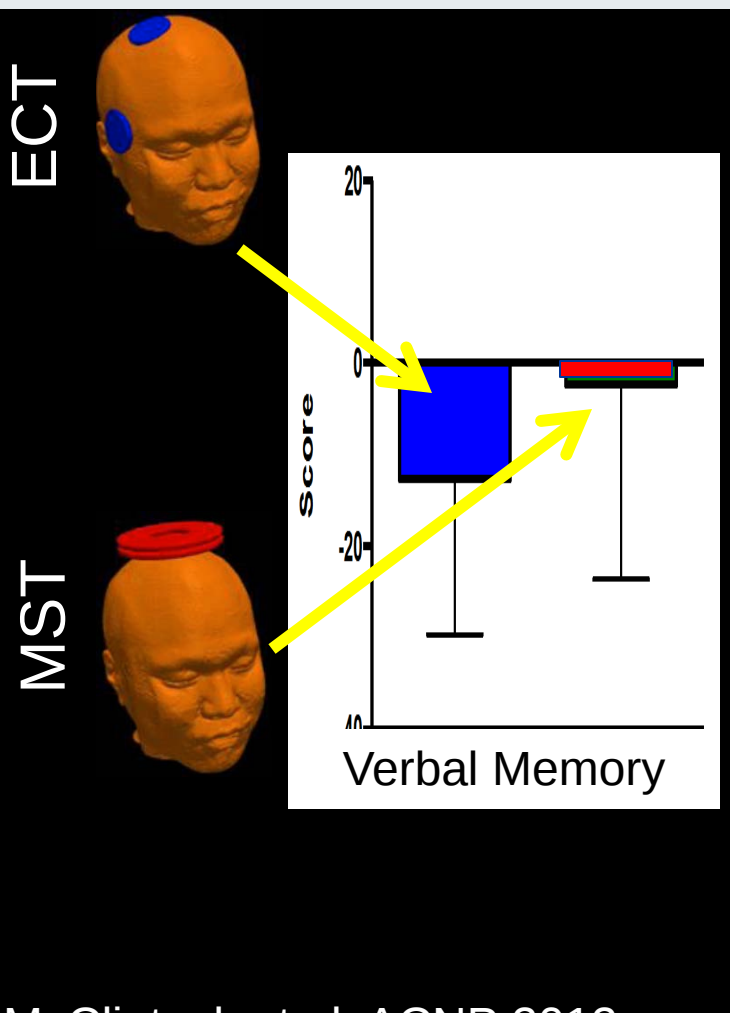
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- Benefits
- Risks
- Critical knowledge gaps and needs for future work
 - Novel strategies to protect memory
 - Magnetic Seizure Therapy
 - More focal Electric fields in brain



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- Benefits
- Risks
- Critical knowledge gaps and needs for future work
 - Novel strategies to protect memory
 - **Magnetic Seizure Therapy**
 - More focal Electric fields in brain
 - Superior cognitive outcomes



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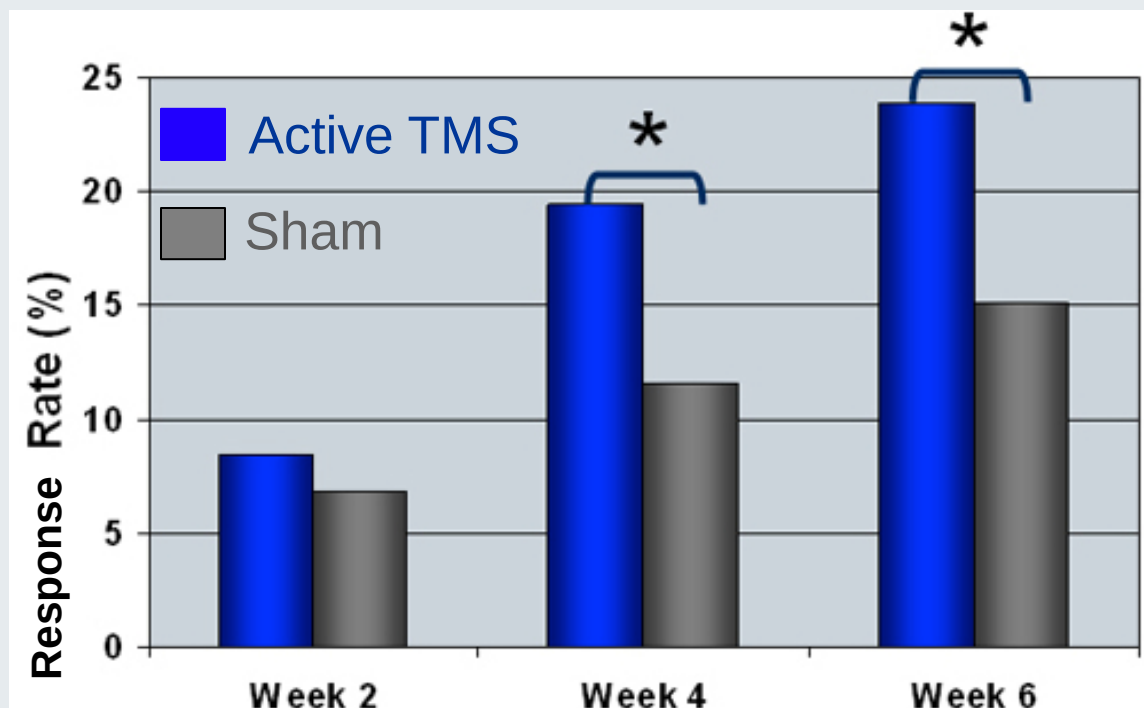
- Benefits
- Risks
- Critical knowledge gaps and needs for future work
 - Novel strategies to protect memory
 - Deeper understanding of mechanisms of action of seizures
 - Remains the most potent antidepressant and suicide prevention strategy currently FDA approved



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- Benefits
 - Antidepressant efficacy

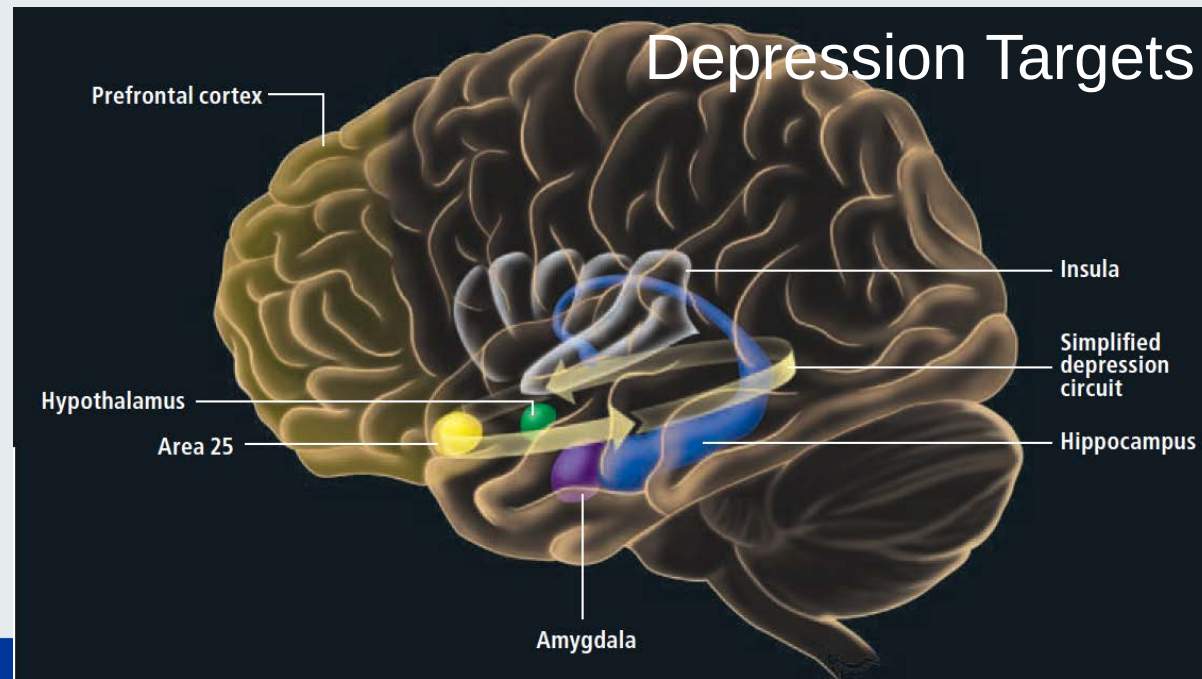




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- Benefits
 - Antidepressant efficacy
 - Tool to target illness-related circuits





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- **Benefits**
 - Antidepressant efficacy
 - Tool to target illness-related circuits
 - Lacks amnesia seen with ECT



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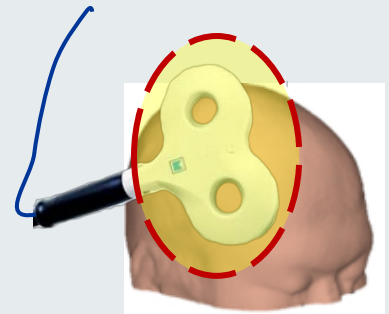
- Benefits
- Risks
 - Hearing loss / tinnitus
 - Seizure
 - Role of concomitant medications
 - Medical comorbidities
 - Substance use disorders
 - Vulnerable populations
 - seizure threshold lower in children, seizure risk higher in autism and after traumatic brain injury



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- Benefits
- Risks
- Critical knowledge gaps and needs for future work
 - Optimal dosage
 - Spatial distribution

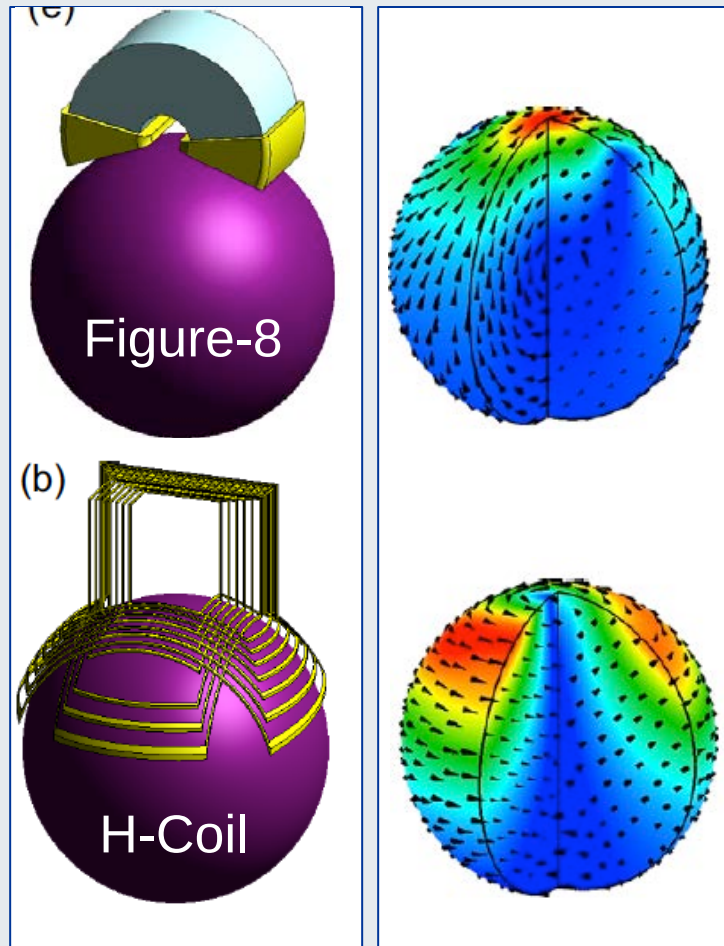




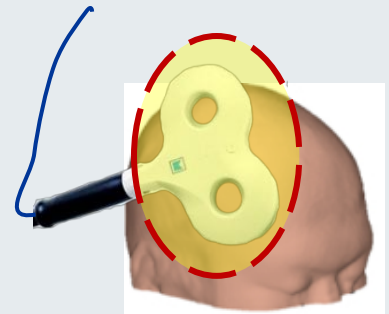
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Coil

E field



- Benefits
- Risks
- Critical knowledge gaps and needs for future work
 - Optimal dosage
 - Spatial distribution

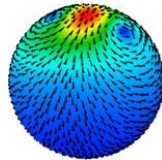


Wide Variety of Coil Designs

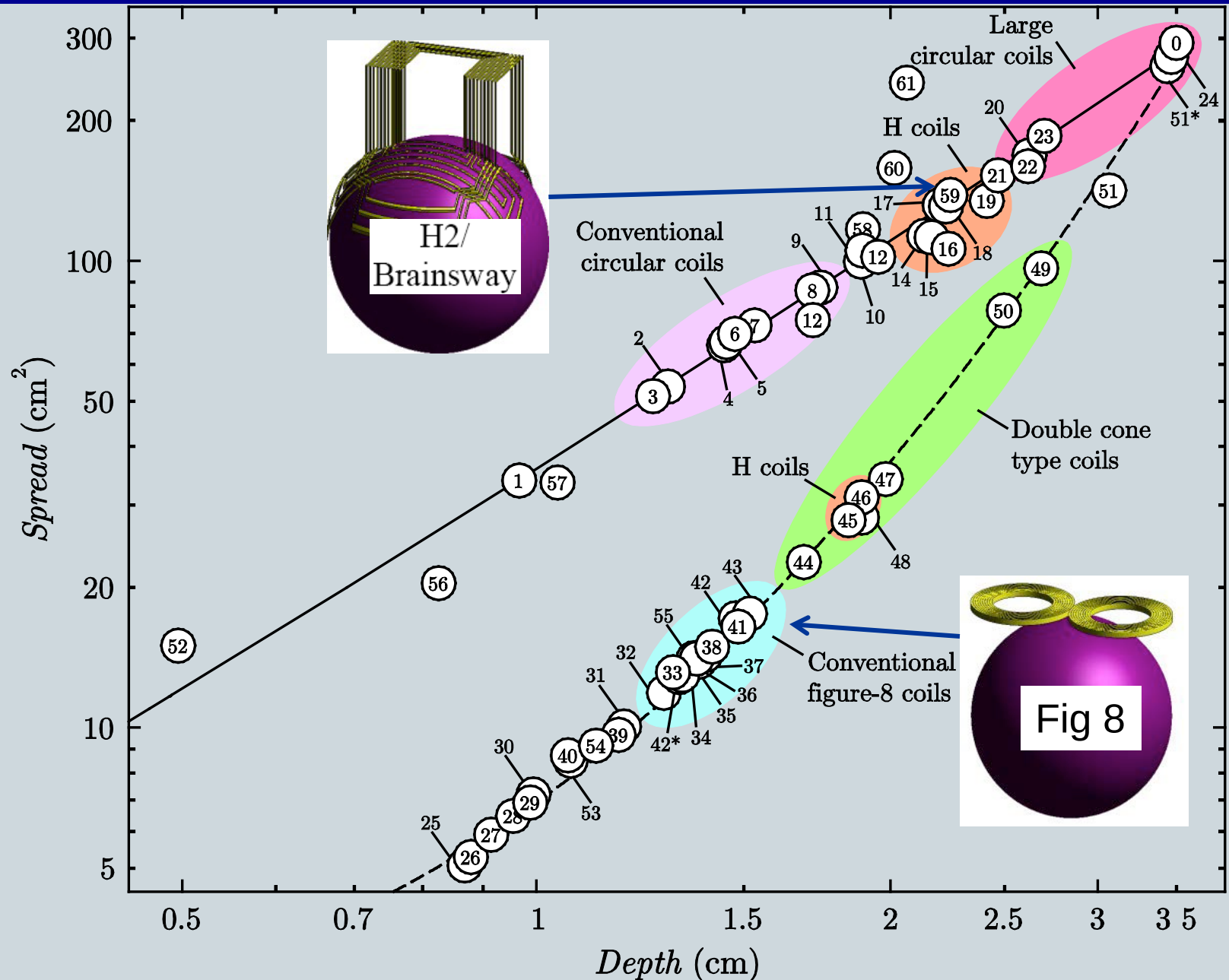


Wide
Variety of
Coil
Designs

Wide
Variety of
E-field
Spatial
Spread



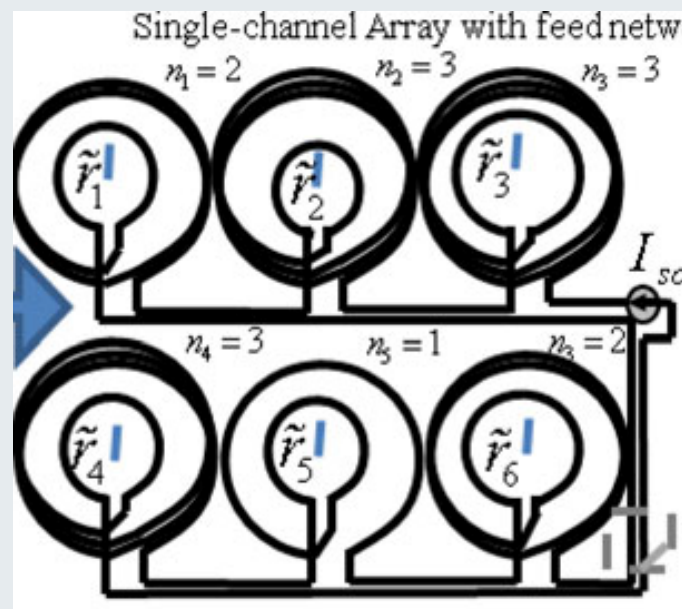
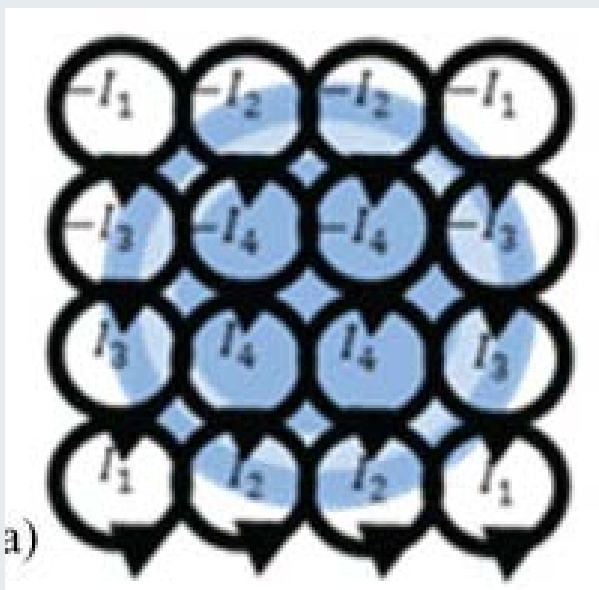
Focality/Depth Tradeoff of 61 Coils



[Mod. from Deng, Lisanby & Peterchev, Brain Stim. 2013]



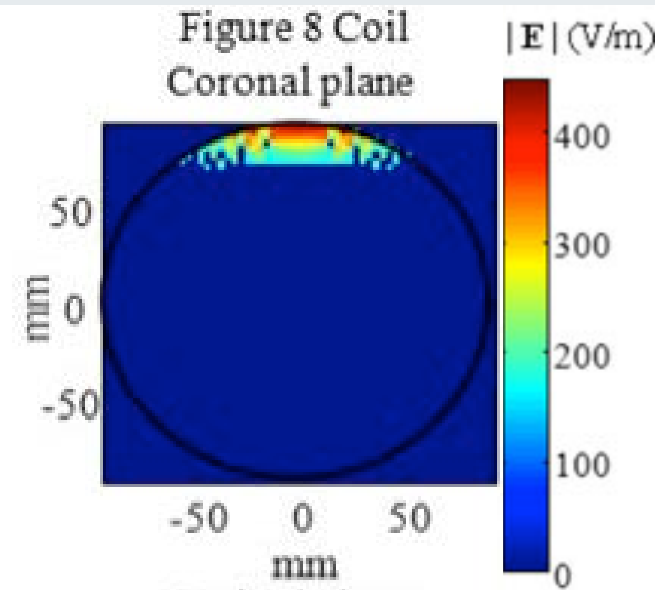
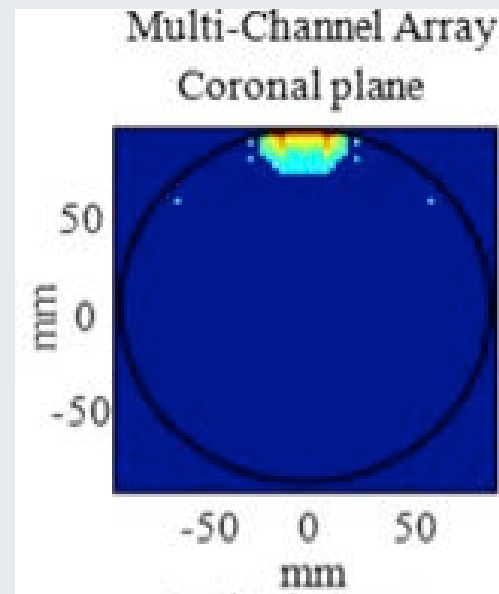
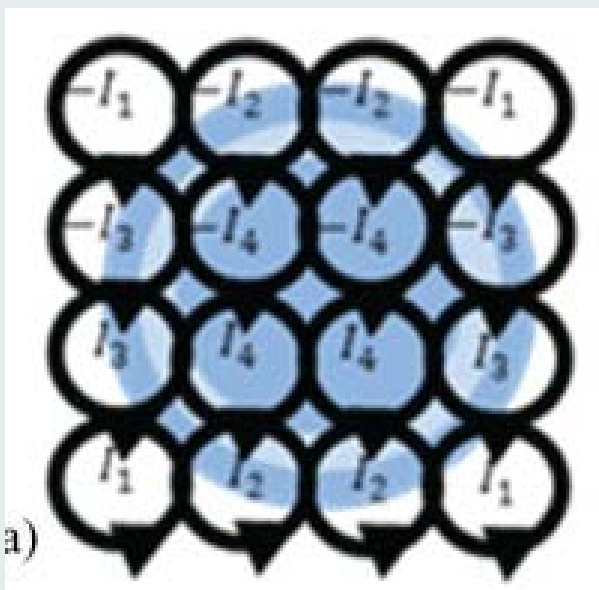
New approaches to shape field through coil design



- Single source multi-coil array
- Each loop is neighbored by a loop with current in the opposite direction, permitting field cancellation



New approaches to shape field through coil design



- Single source multi-coil array
- Each loop is neighbored by a loop with current in the opposite direction, permitting field cancellation
- Engineering challenges in implementation



New approaches to shape field through coil design



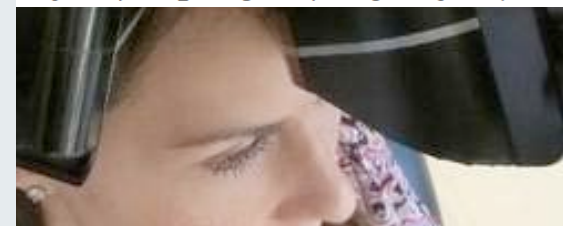
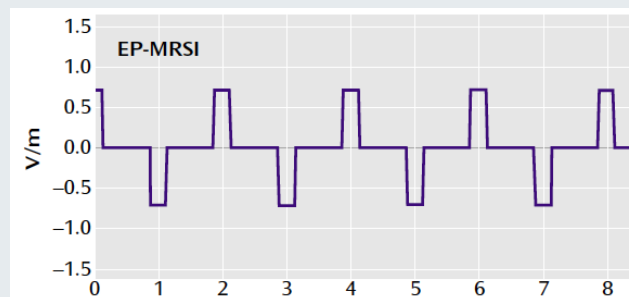
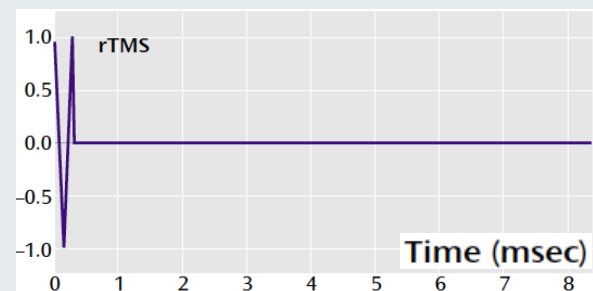
- Cervel Neurotech
Deep Shaped-Field
repetitive
transcranial
magnetic stimulator
(DSF-rTMS)
 - **NCT01431001**



- Tal Low Field Magnetic
Stimulation (LFMS)
 - **NIMH-RAPID, NCT01654796**



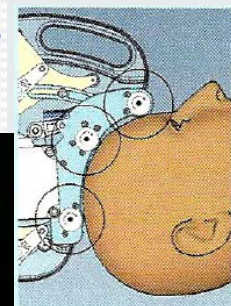
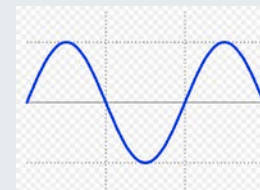
New approaches to shape field through coil design



- Cervel Neurotech Deep Shaped-Field repetitive transcranial magnetic stimulator (DSF-rTMS)
 - NCT01431001



- Tal Low Field Magnetic Stimulation (LFMS)
 - NIMH-RAPID, NCT01654796

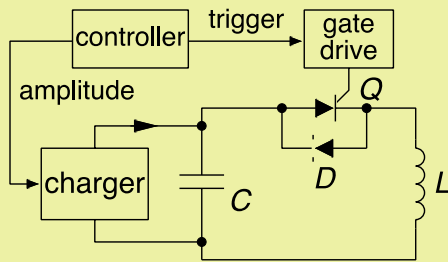


- NeoSync EEG Synchronized TMS
 - NCT01370733



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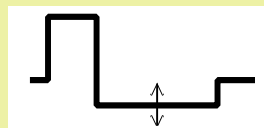
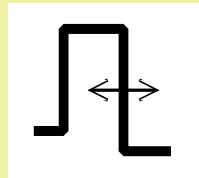
Conventional TMS



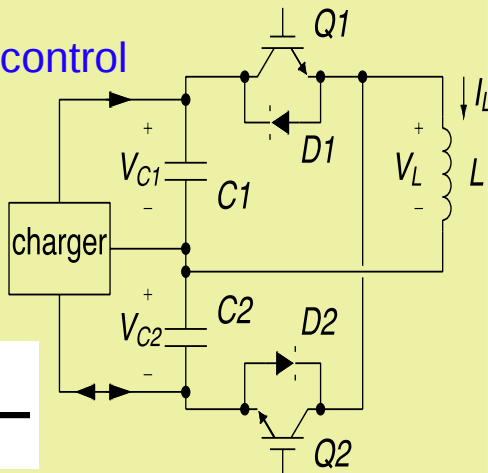
- Benefits
- Risks
- Critical knowledge gaps and needs for future work

cTMS

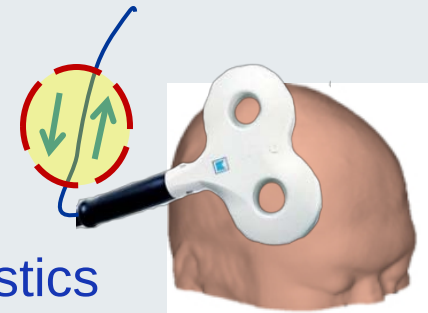
Pulse width control



Directionality control



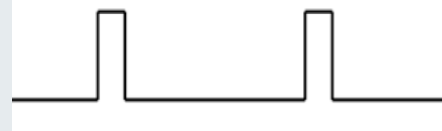
- Optimal dosage
 - Spatial distribution
 - Temporal characteristics
 - Pulse shape



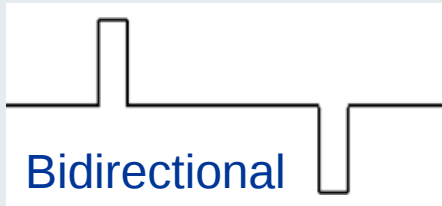


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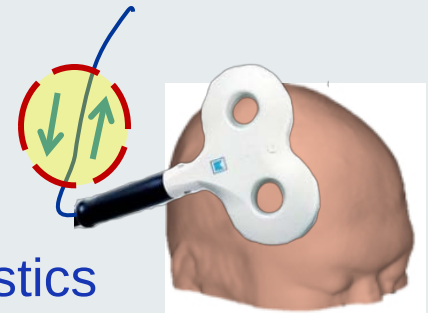
Unidirectional



Bidirectional

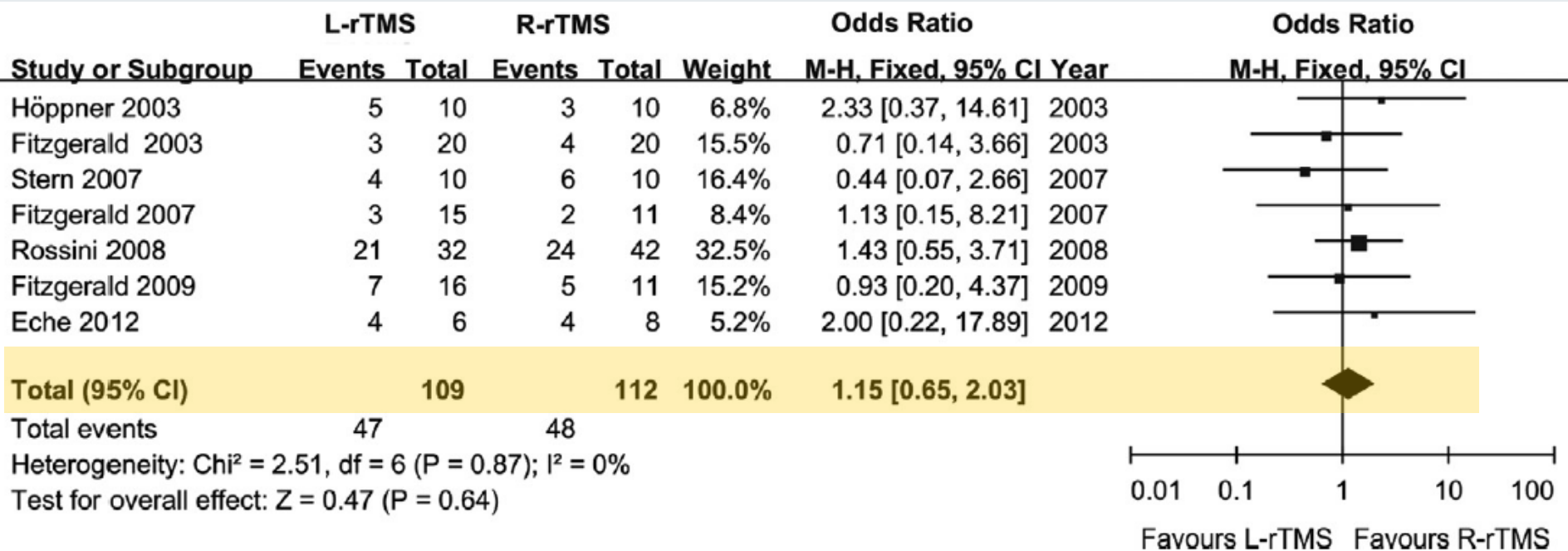


- Benefits
- Risks
- Critical knowledge gaps and needs for future work
 - Optimal dosage
 - Spatial distribution
 - Temporal characteristics
 - Pulse shape
 - Train parameters
 - » Frequency, duration, directionality





Low Frequency Right versus High Frequency Left for Depression



- 8 Randomized Controlled Trial, 249 patients
- No detectable difference between low or high frequency
- Implications for practice as low frequency has lower seizure risk than high frequency



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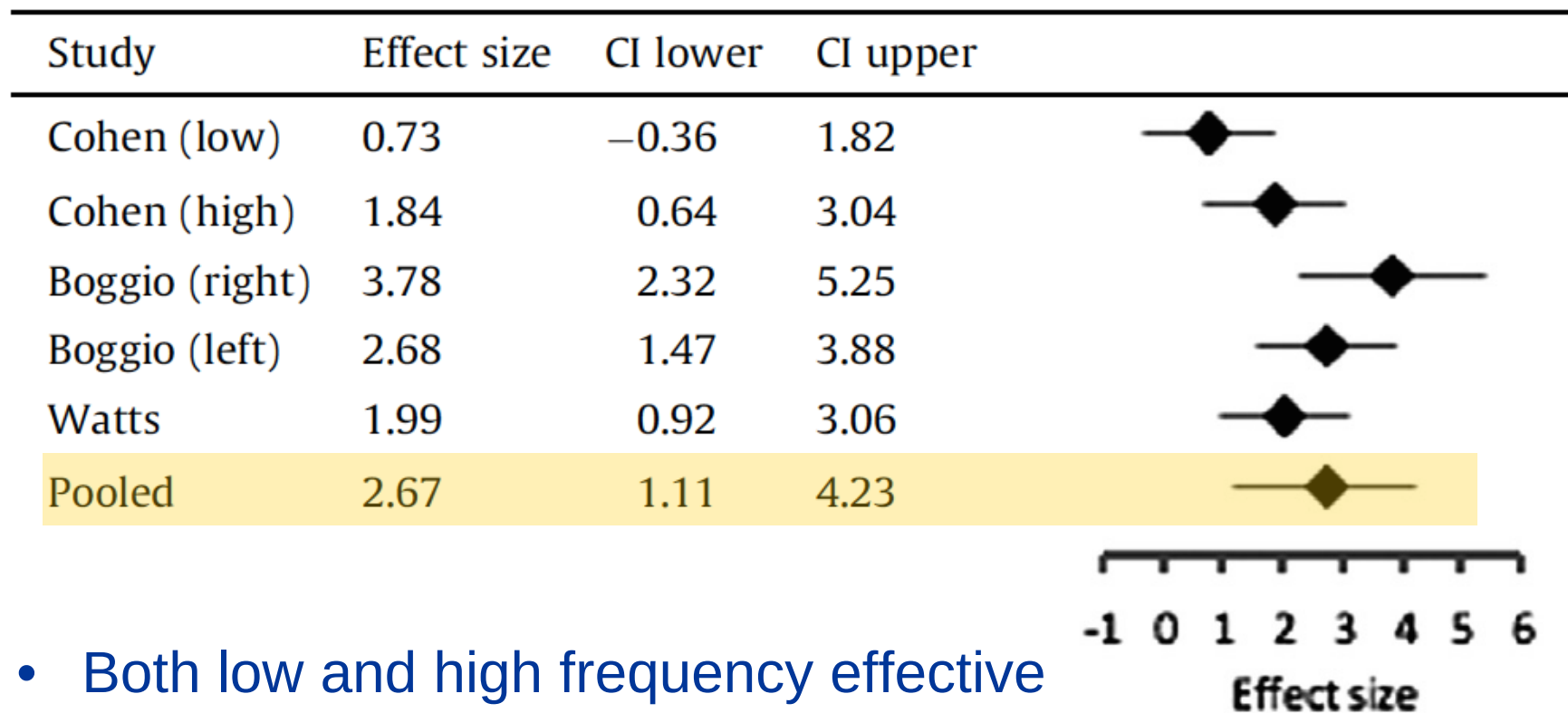


- Benefits
- Risks
- Critical knowledge gaps and needs for future work
 - Optimal dosage
 - Optimal patient selection
 - Other indications
 - Anxiety Disorders
 - » OCD, PTSD
 - Addictions
 - Cognitive enhancement
 - » TBI



Future Indications Under Investigation: PTSD

Forest plot showing effect size calculated as Hedges g for TMS on PTSD symptom scales.



- Both low and high frequency effective

CI = confidence interval.



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- Benefits
- Risks
- Critical knowledge gaps and needs for future work
 - Optimal dosage
 - Optimal patient selection
 - Concomitant therapies
 - Pharmacological
 - Nonpharmacological/behavioral



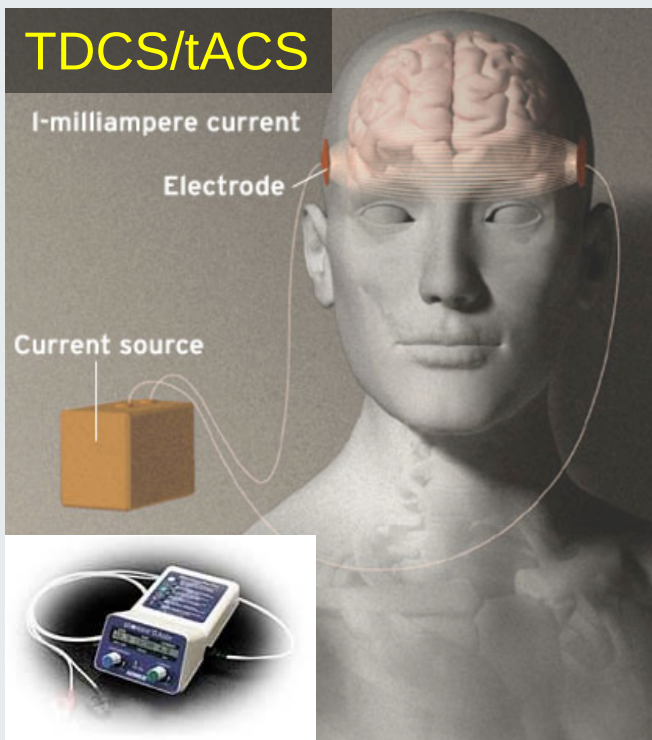
Non-Invasive Neuromodulation in Development for Psychiatric Treatment

TDCS/tACS

1-milliampere current

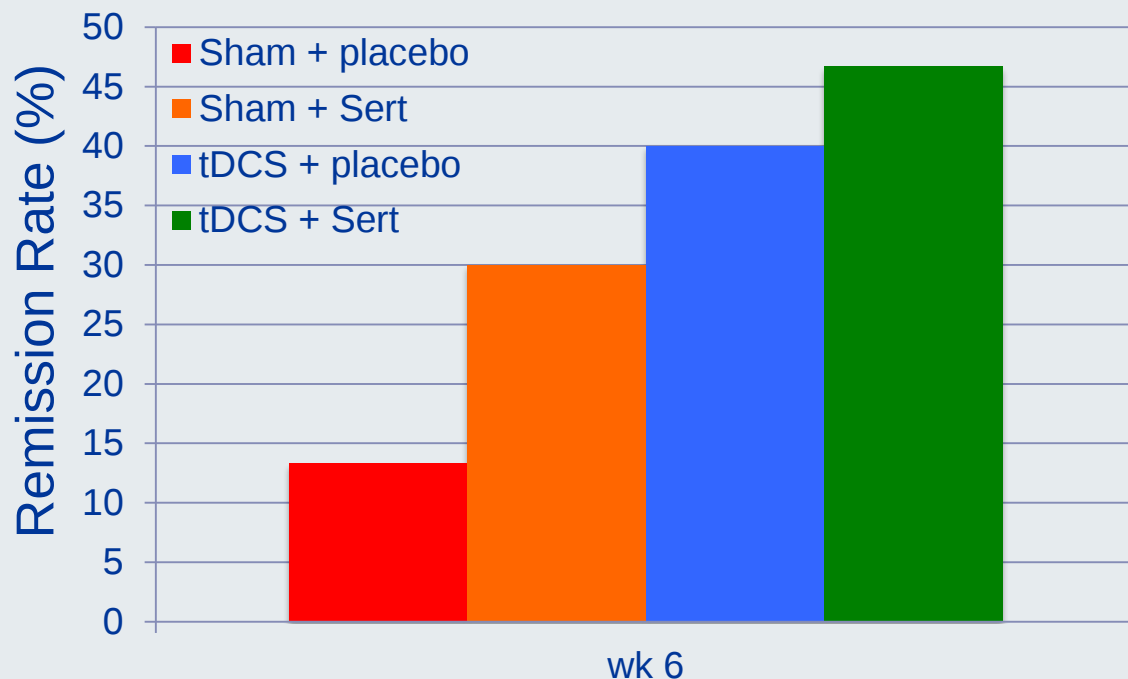
Electrode

Current source



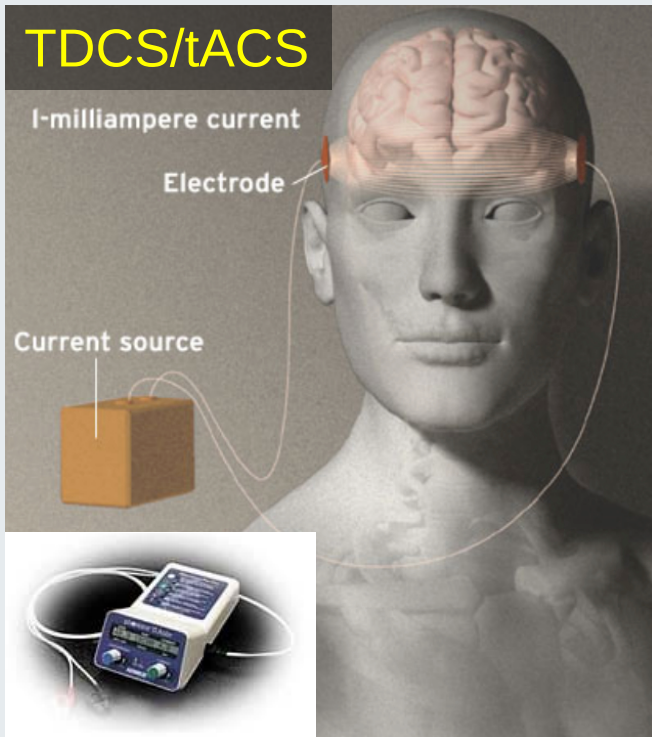
- Benefits

- Evidence for antidepressant effects





Non-Invasive Neuromodulation in Development for Psychiatric Treatment



- Benefits
- Risks
 - Excellent safety profile
- Critical knowledge gaps and needs for future work
 - Mechanisms of action and optimizing dosimetry in space and time



Are we asking the right question?

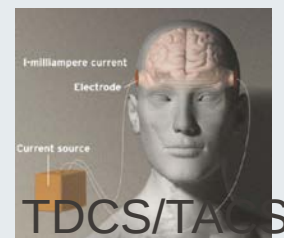
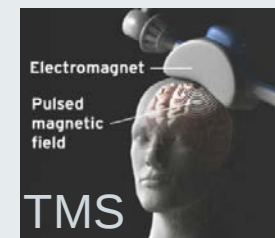
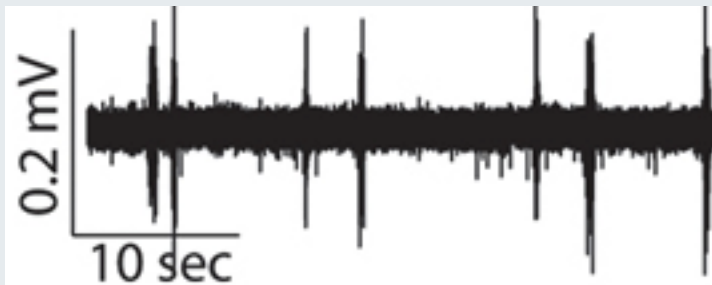
HOW DOES **IT** WORK ?

Extracellular Currents



Endogenously Generated

Exogenously Applied



Neural oscillations – epiphenomenon or signal?

Emerging role of abnormal neural oscillations in psychiatric disorders

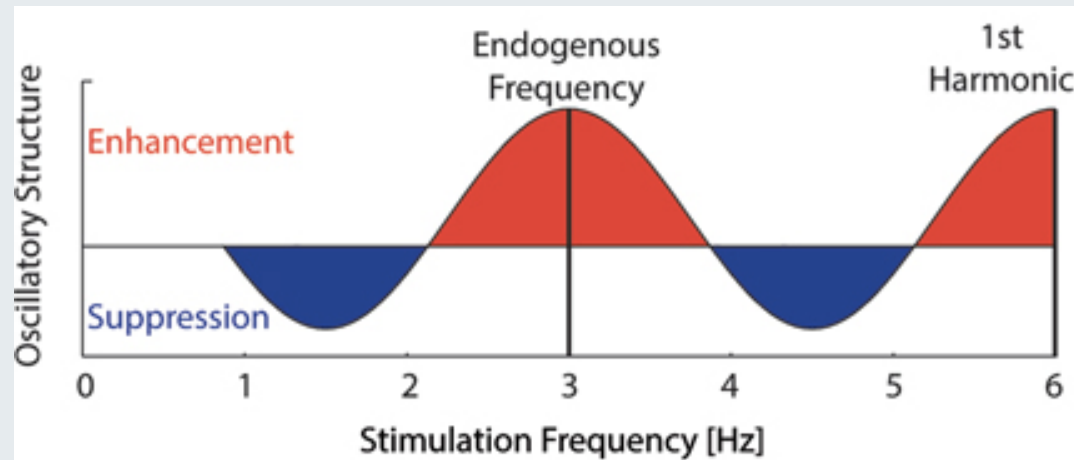


Are we asking the right question?

HOW DOES **IT** WORK ?

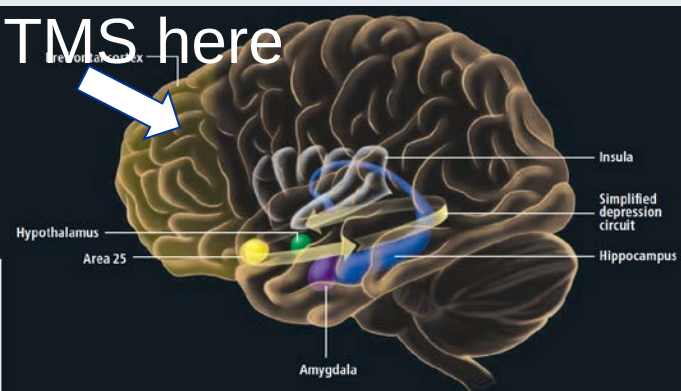
Extracellular Currents

Endogenously Generated $\longleftrightarrow$ Exogenously Applied

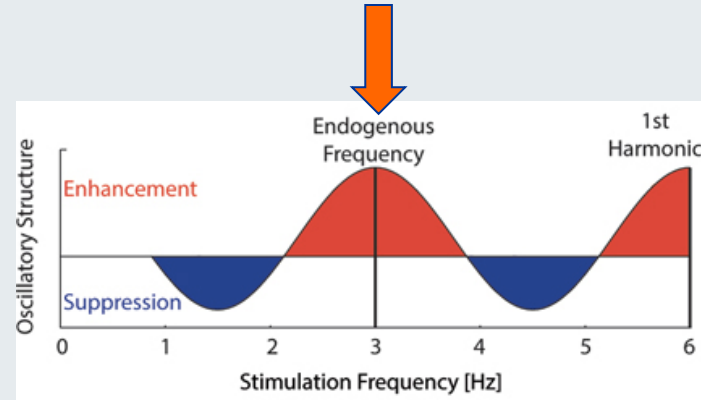




Conclusions



TMS now



- **Spatial** maps of neurocircuitry underlying disorders have guided spatial targeting for depression, but
- **Temporal** targeting is presently lacking, but of great potential impact
- Understanding the interaction between **endogenous** neural dynamics underlying psychiatric disorders and **exogenously** applied electrical currents represents a key knowledge gap in the development noninvasive neuromodulation for psychiatric disorders.



The Future for Devices in Psychiatry

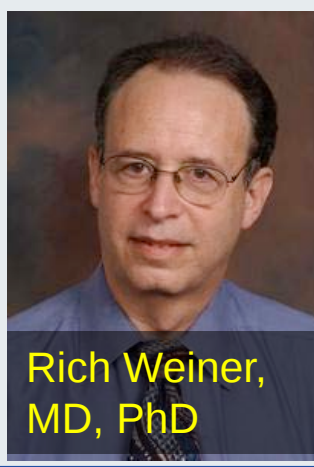


*“Now this is not the end.
It is not even the
beginning of the end.
But it is, perhaps, the
end of the beginning.”*

Winston S. Churchill, The Bright Gleam of Victory
November, 10, 1942. Mansion House, London.

Acknowledgements

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Stanley Foundation (Lisanby/Husain)