



UNIVERSITY OF CALGARY
CUMMING SCHOOL OF MEDICINE



**HOTCHKISS
BRAIN INSTITUTE**

Non-Invasive Brain Stimulation for OCD.

Alexander McGirr, MD PhD FRCPC
June 22nd, 2022



Disclosures

I am a founder of MCGRx Corp and Salvostim Development Corp, and have filed provisional patent filings related to rTMS for depression and OCD.

Objectives

1. Understand the basic mechanisms of repetitive transcranial magnetic stimulation.
2. Identify the primary safety considerations for repetitive transcranial magnetic stimulation.
3. Know how to coordinate care during repetitive transcranial magnetic stimulation.

Disclaimer

- The mandate for the AHS rTMS program is major depressive disorder.
- I am not aware of private clinics or other resources that are providing TMS for OCD
 - The McGirr lab at the University of Calgary is running a clinical trial of TMS for OCD.

Obsessive Compulsive Disorder

- 3% population
- Obsessions
 - Intrusive thoughts, urges or mental images
- Compulsions
- 40-60% of patients do not fully respond to available treatments

Repetitive Transcranial Magnetic Stimulation for OCD

- In August 2018, the FDA approves repetitive transcranial magnetic stimulation (TMS) for OCD

FDA NEWS RELEASE

FDA permits marketing of transcranial magnetic stimulation for treatment of obsessive compulsive disorder

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For Immediate Release: August 17, 2018

[Español](#)

Today, the U.S. Food and Drug Administration permitted marketing of the Brainsway Deep Transcranial Magnetic Stimulation System for treatment of obsessive compulsive disorder (OCD).

“Transcranial magnetic stimulation has shown its potential to help patients suffering from depression and headaches,” said Carlos Peña, Ph.D., M.S., director of the Division of Neurological and Physical Medicine Devices in the FDA’s Center for Devices and Radiological Health. “With today’s marketing authorization, patients with OCD who have not responded to traditional treatments now have another option.”

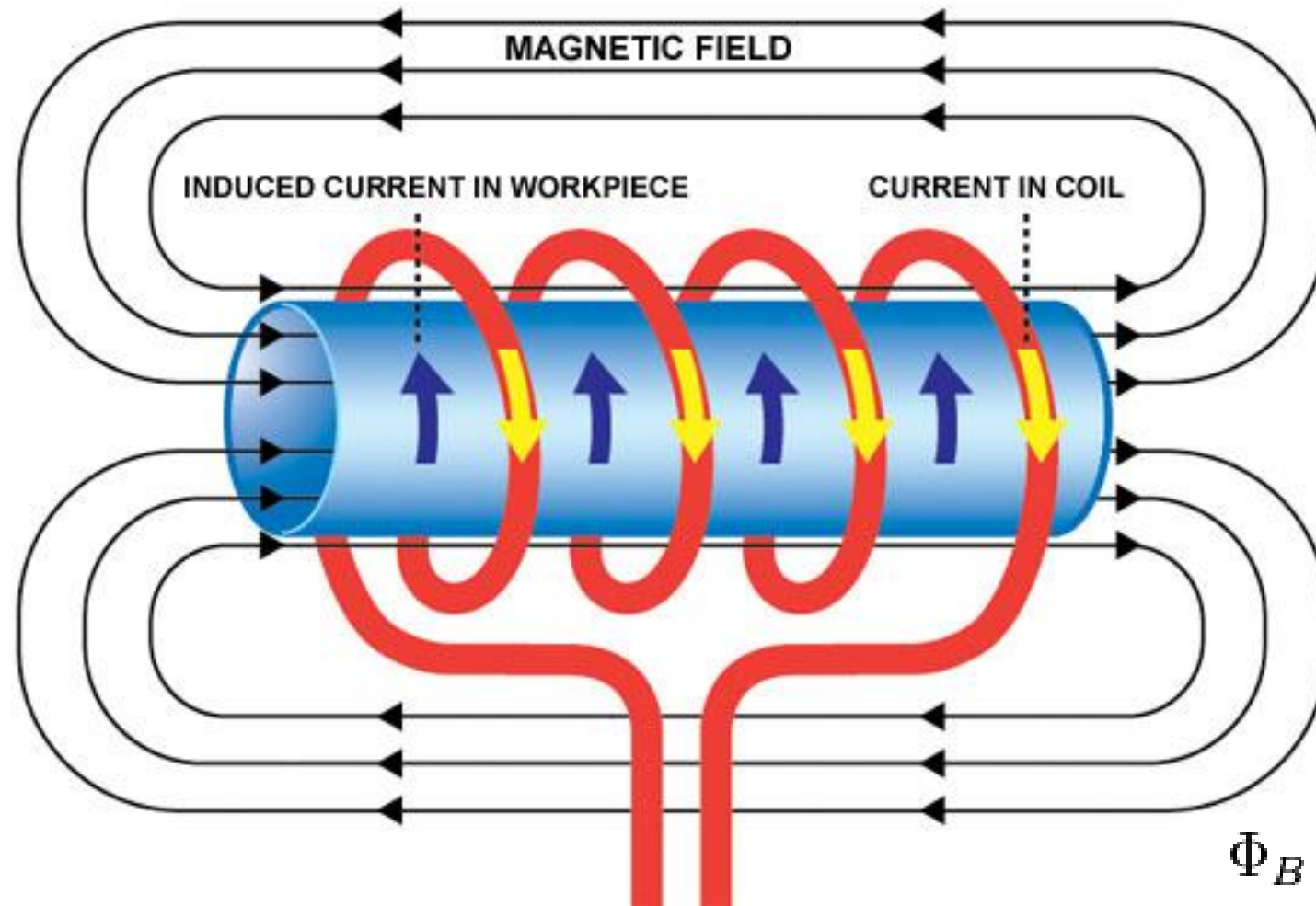
What is Transcranial Magnetic Stimulation?

Transcranial Magnetic Stimulation

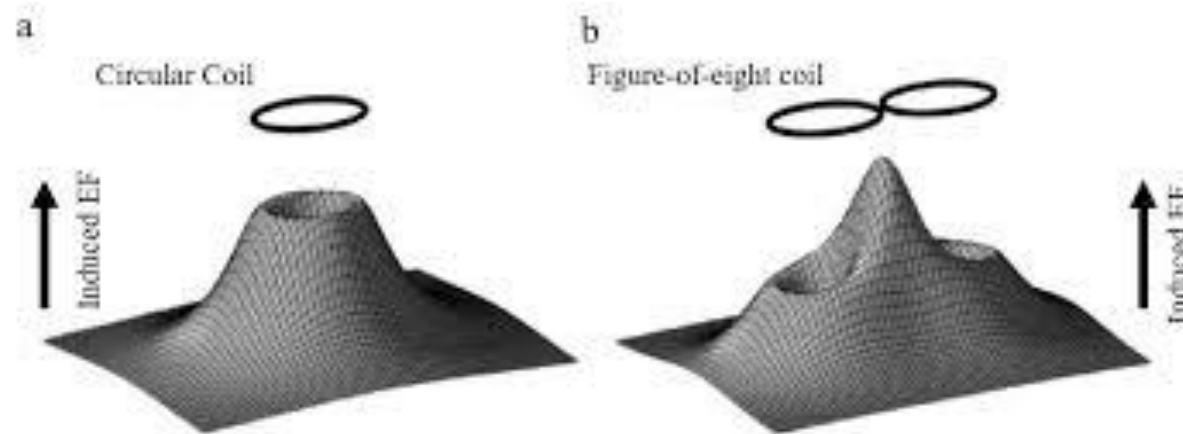
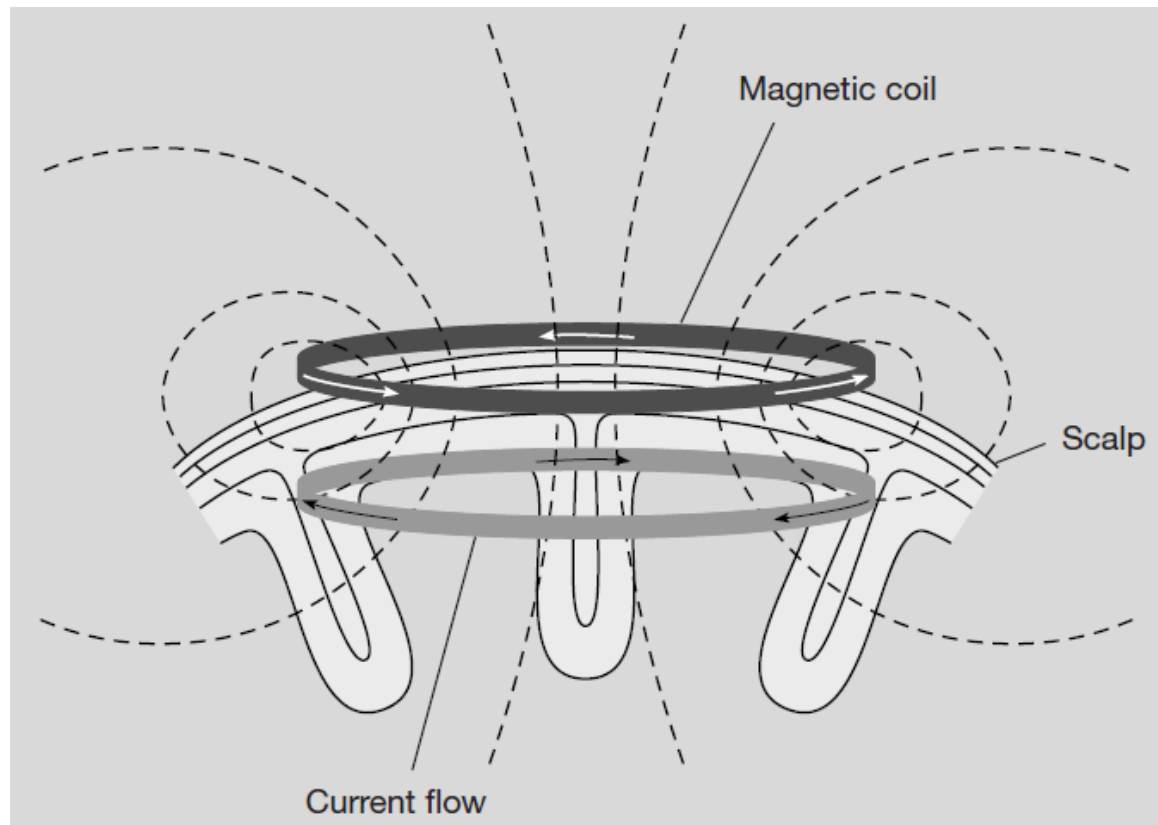
A method of:

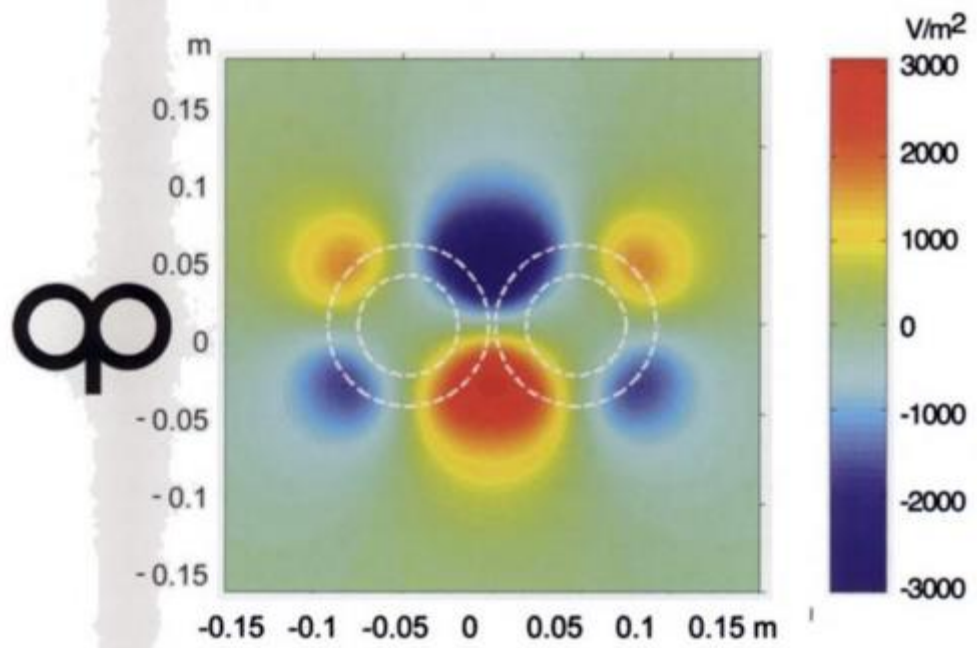
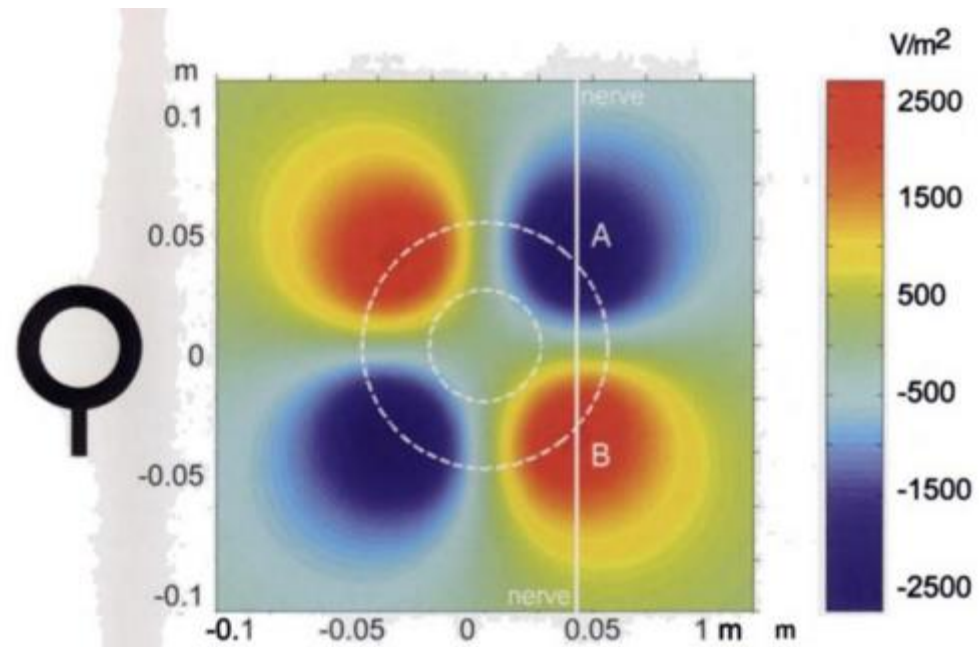
- Delivering electromagnetic pulses
- These have a corresponding electrical field

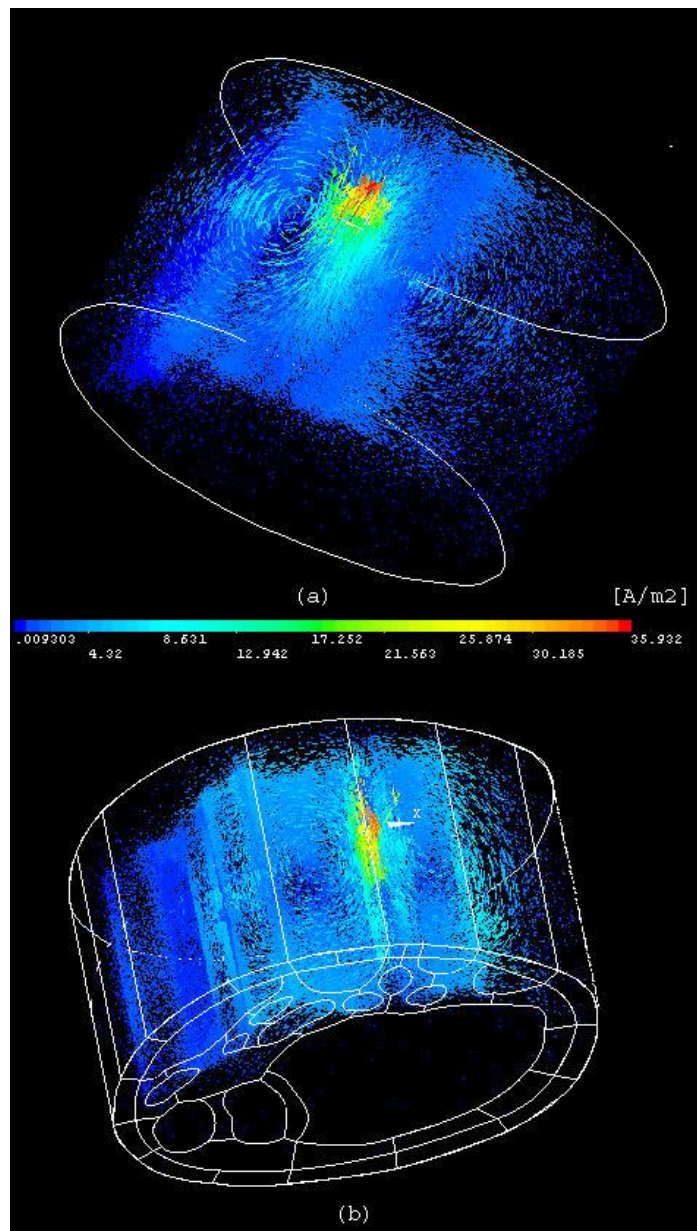
Electromagnetism

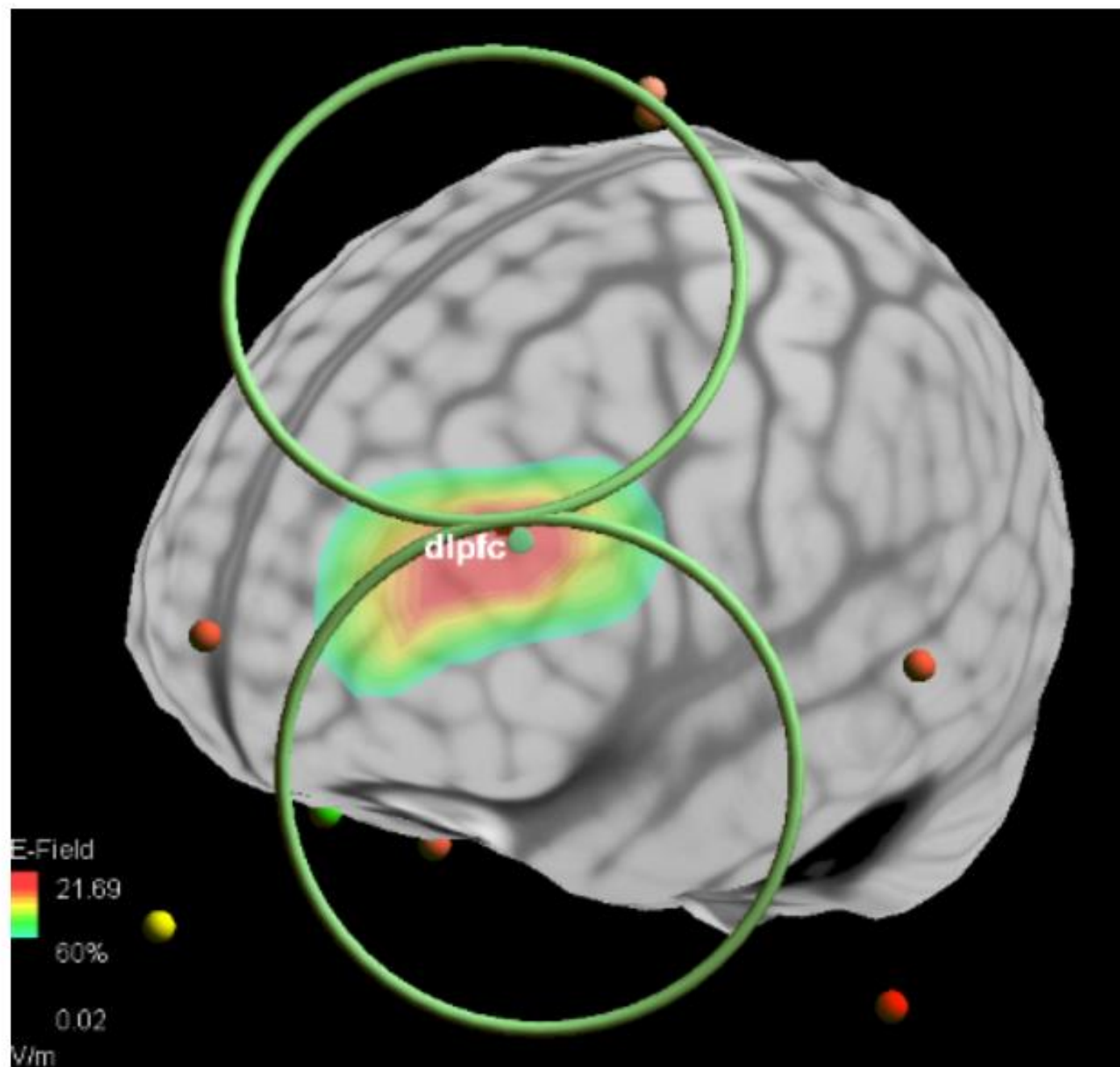


$$\Phi_B = \iint_{\Sigma(t)} \mathbf{B}(\mathbf{r}, t) \cdot d\mathbf{A} ,$$







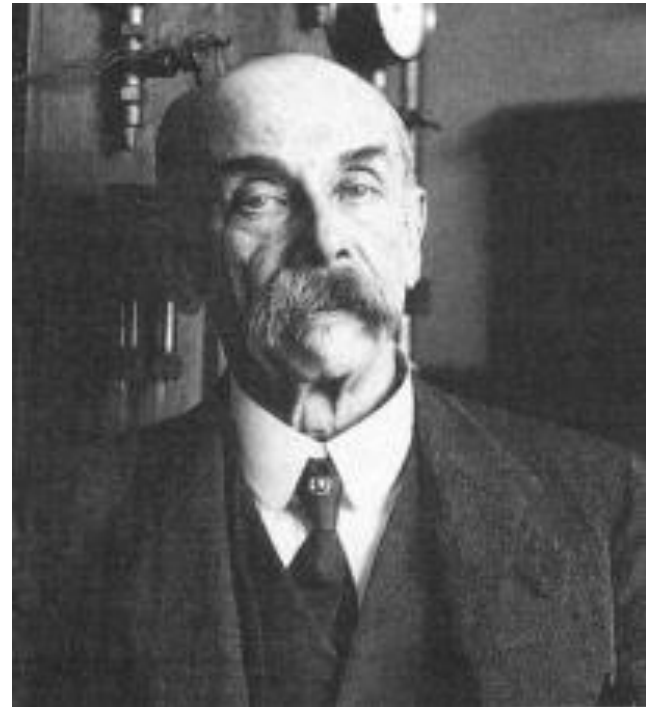


A Long History

- Silvanus P Thompson
(1851-1916)
- Mathematics &
electromagnetism
- 1910
 - Flickering lights even with
eyes closed



- Jacques-Arsene d'Arsonval
(1851-1940)
- Study of alternating currents
- 1936:
 - Magneto phosphenes



Stimulation of the cerebral cortex in the intact human subject

P. A. Merton & H. B. Morton

The National Hospital, Queen Square, London WC1N 3BG, UK

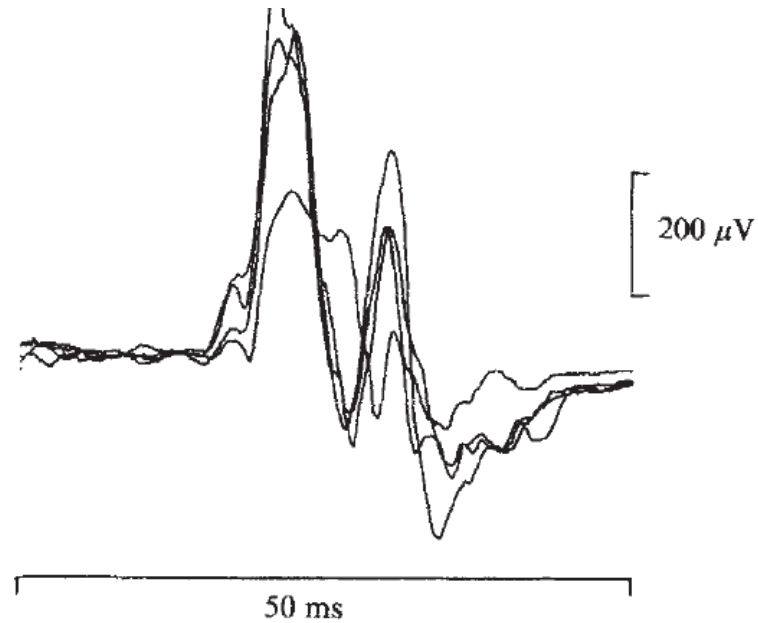


Fig. 1 Stimulation of the arm area of the motor cortex. The records shown are of action potentials from the contracting muscles in the forearm. Stimulation is at the start of the sweep. Four records are superimposed. The latency of responses was 16 ms. (Subject P.A.M.)

The First TMS Machine

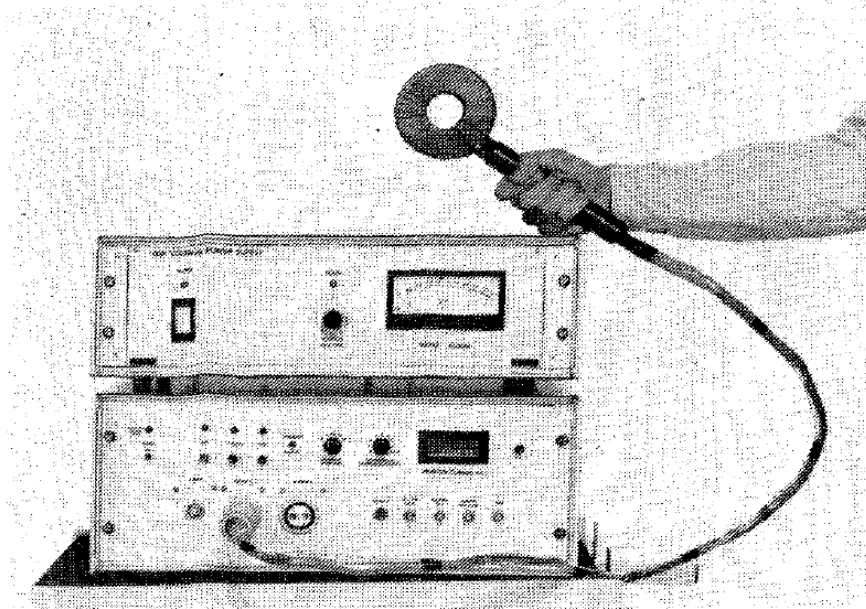


Fig 1—Magnetic stimulator and coil.

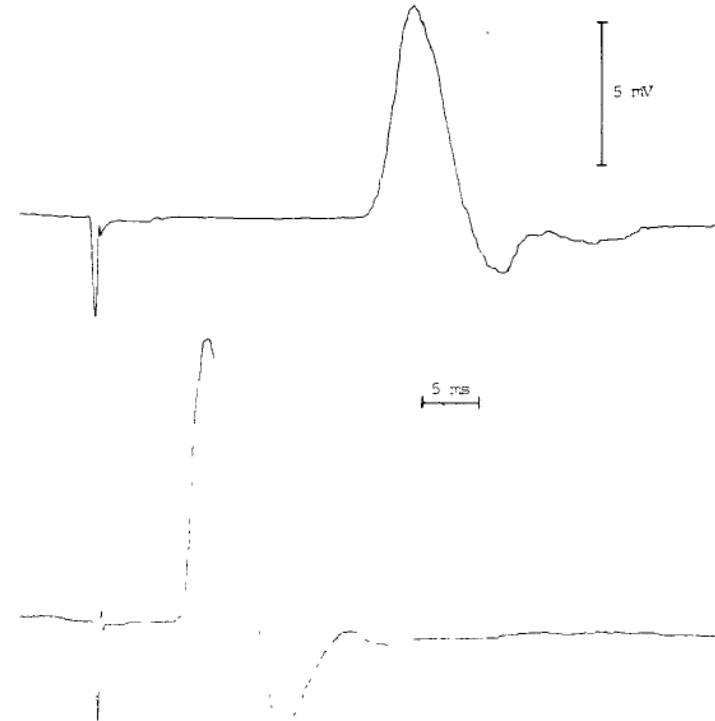
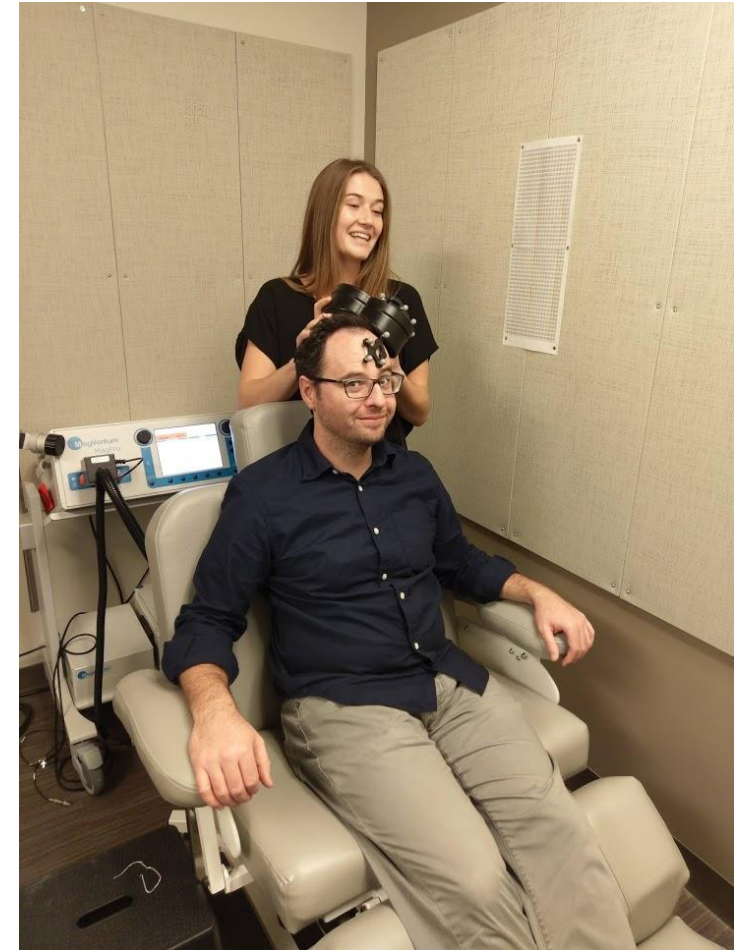


Fig 2—Muscle action potentials recorded from surface electrodes over abductor digiti minimi resulting from magnetic stimulus applied to opposite motor cortex (latency of response 23 ms) (upper) and to ulnar nerve at elbow (latency of response 7 ms) (lower).

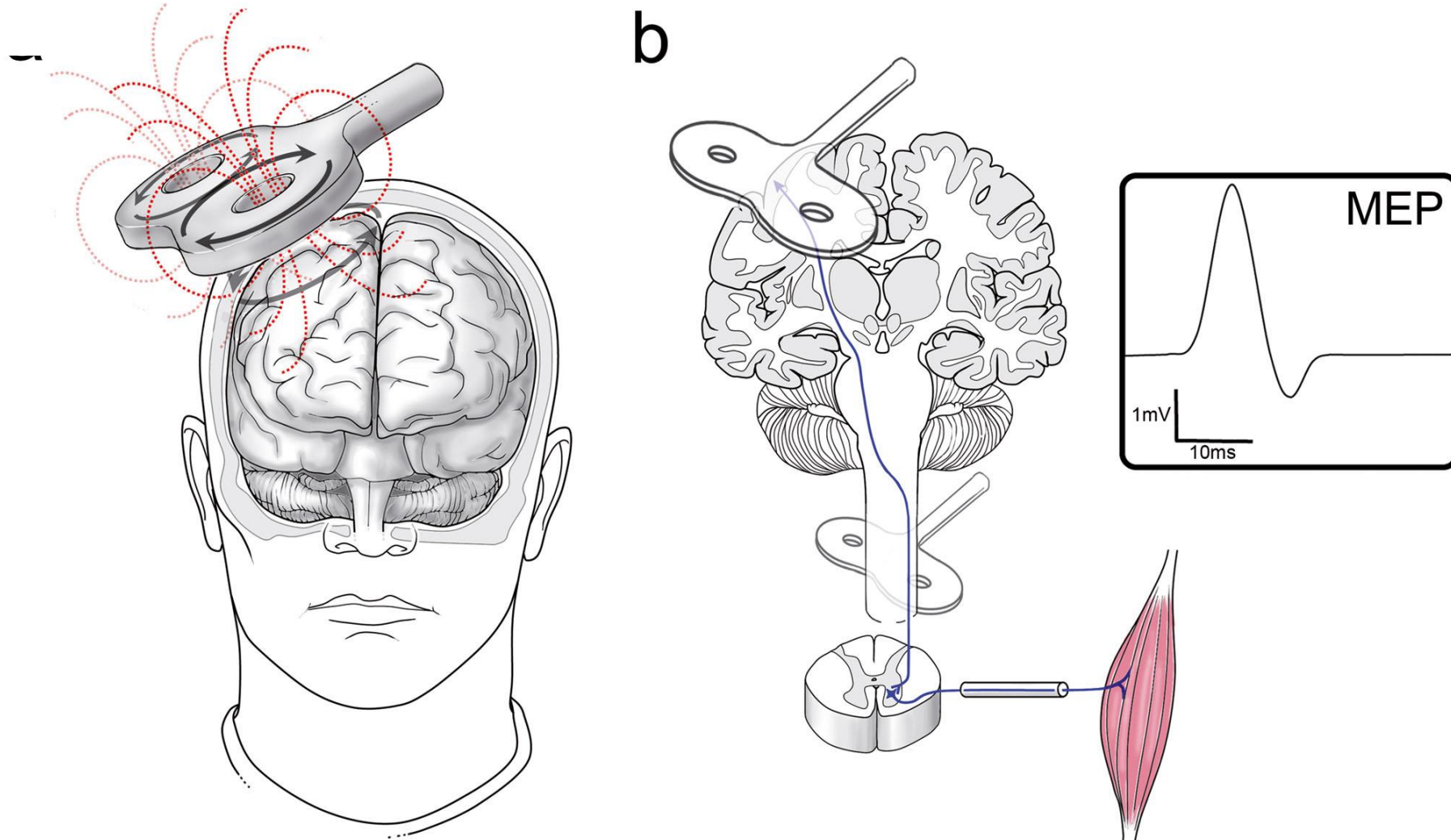
Basic Mechanisms of Repetitive Transcranial Magnetic Stimulation

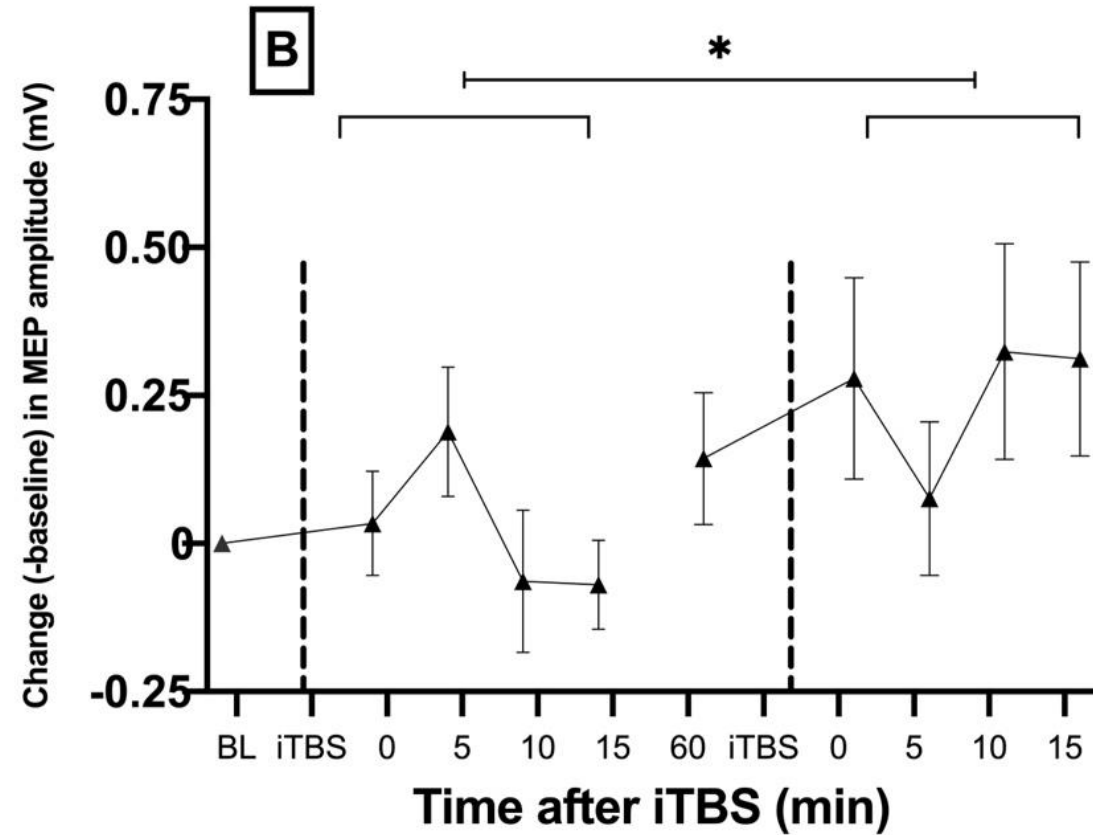
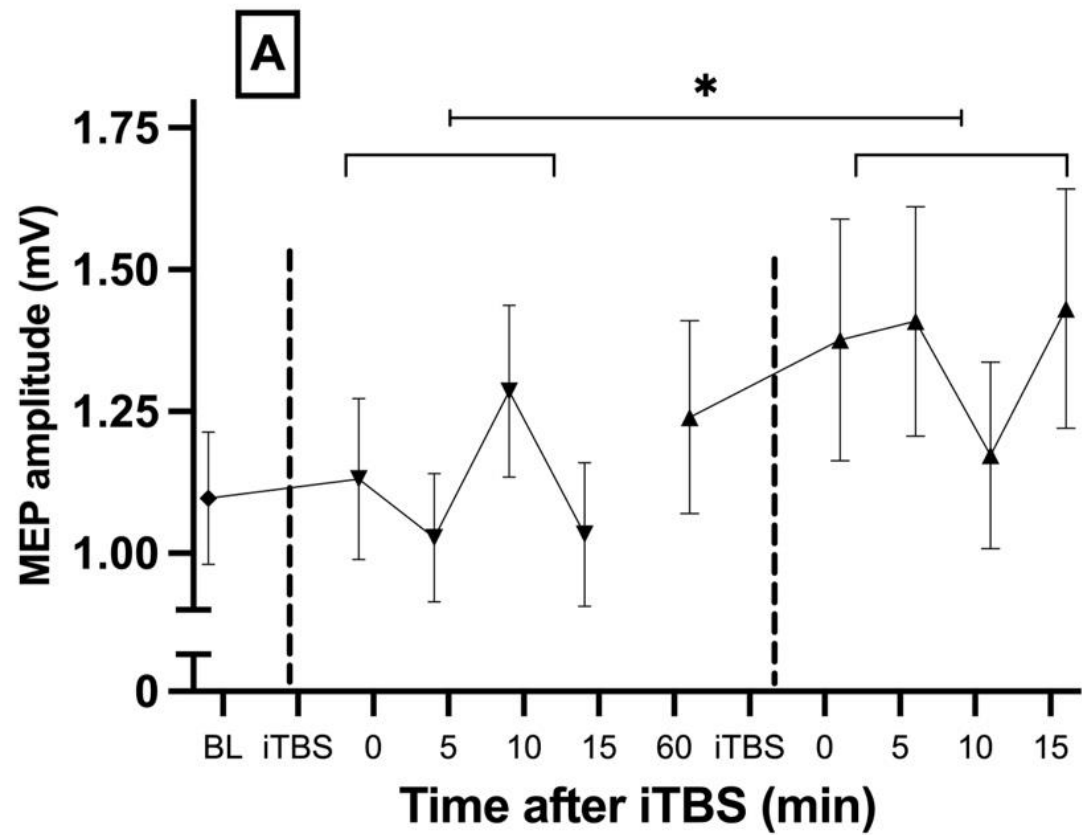
Repetitive Transcranial Magnetic Stimulation (rTMS) and Theta-Burst Stimulation (TBS)

- Most established evidence base for non-invasive neurostimulation treatment for OCD.
- Protocols of patterned pulses drive **synaptic plasticity** at cortical targets.
- Leverage reciprocal connections with cortical and subcortical regions.



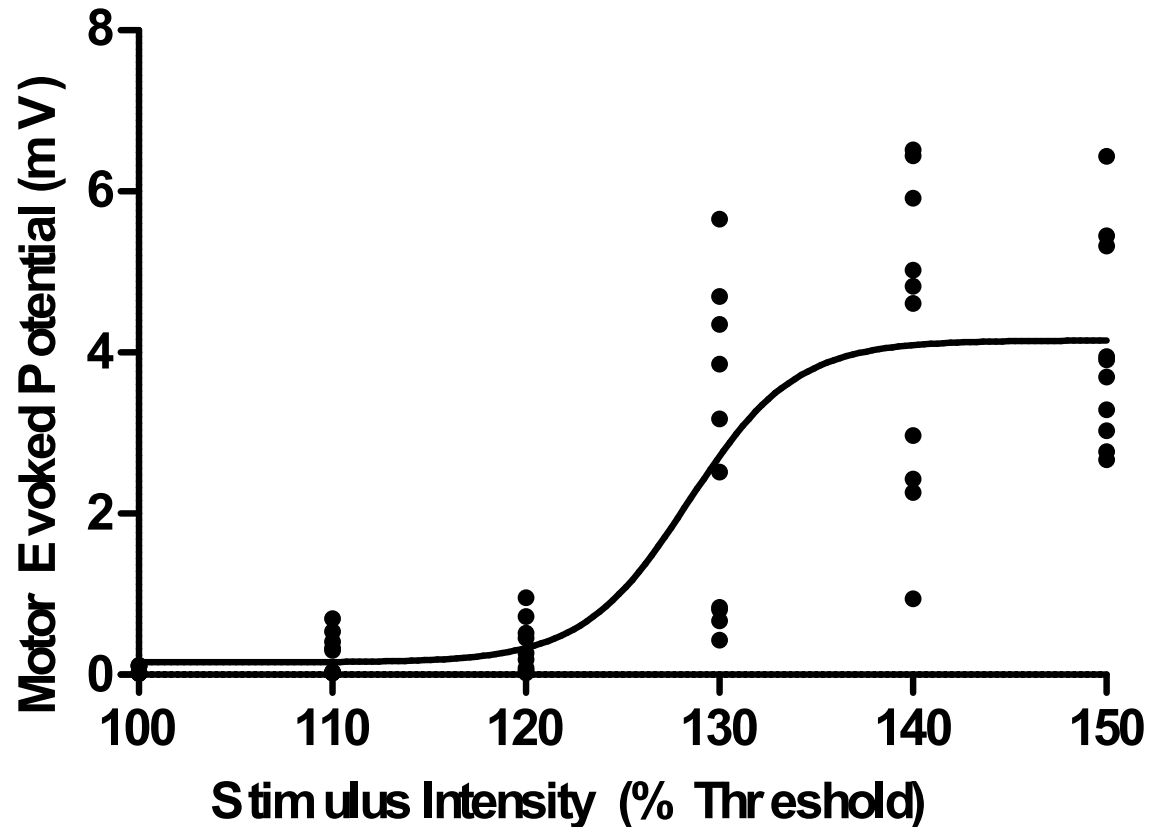
Modelling plasticity with TMS



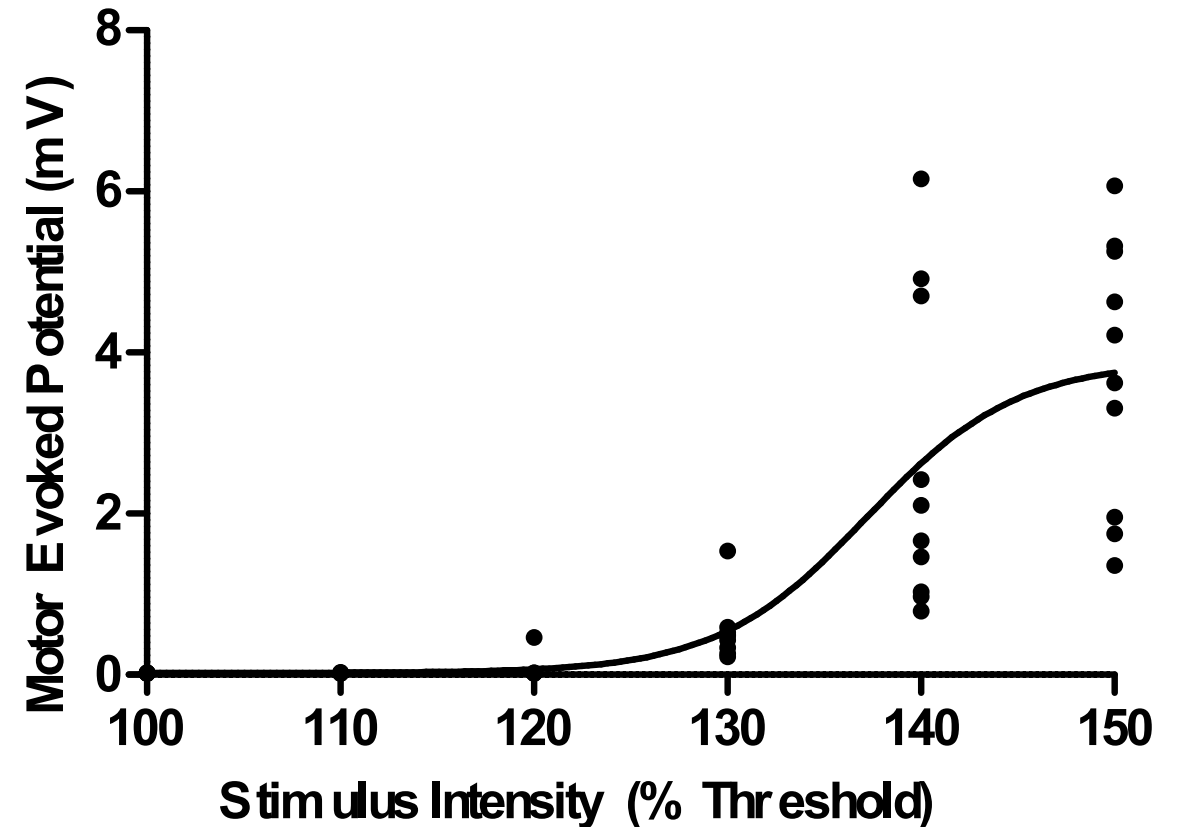


Recruitment Curves and TMS Plasticity

PRE-iTBS

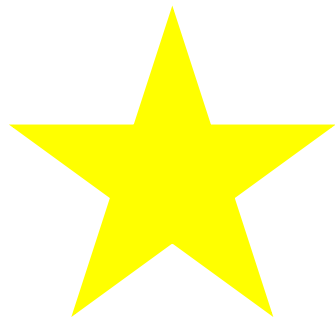


POST-iTBS



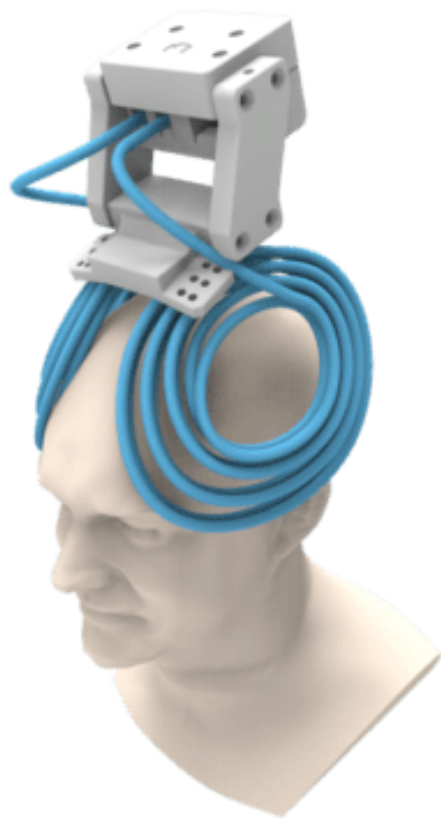
What is rTMS indicated for?

- Major Depressive Disorder
- Migraine
- Obsessive Compulsive Disorder
- Smoking Cessation





H1-Coil
for Major Depressive
Disorder (MDD)



H7-Coil
for Obsessive-Compulsive
Disorder (OCD)



H4-Coil
for Smoking
Cessation



Traditional TMS Coil
for Major Depressive
Disorder (MDD)



Nexstim



CLOUDTMS™

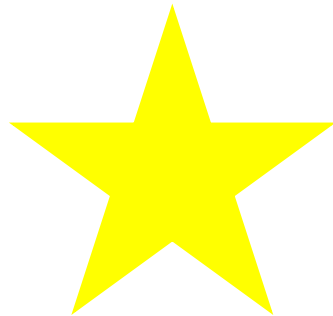


eNeura®



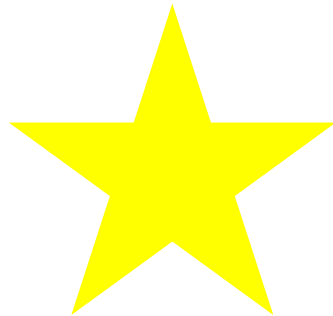
Risks of rTMS

- Seizure
 - 1:1,000-1:10,000
 - Previous seizures
 - Intracranial lesion
 - Traumatic brain injury
 - Alcohol use disorder
- Magnetic fields
 - Heat or move metal
 - Metal workers
 - Aneurysm clips
 - Cochlear implants
- Dental hardware is OK



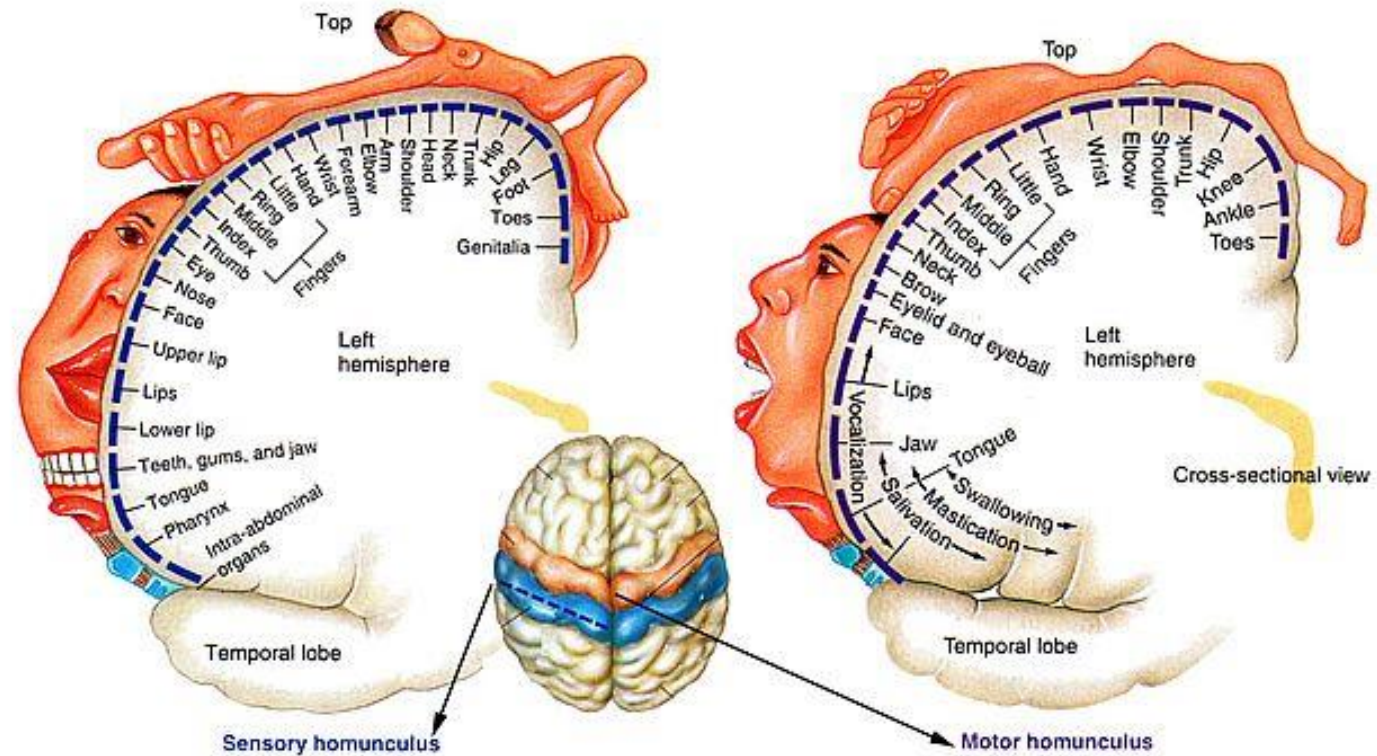
Side Effects

- Common
 - Headaches 65%
 - Scalp tingling discomfort 60%
- Less common (<10%)
 - Nausea
 - Vertigo
 - Worsening insomnia
 - Fatigue



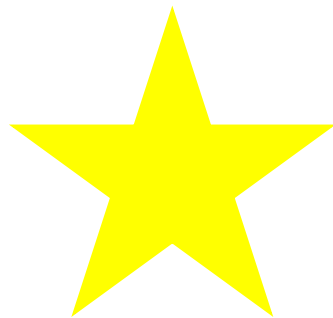
rTMS Safety

- Pulses are delivered relative to a personalized threshold
- Motor cortex
- Active and resting motor threshold (aMT and rMT)



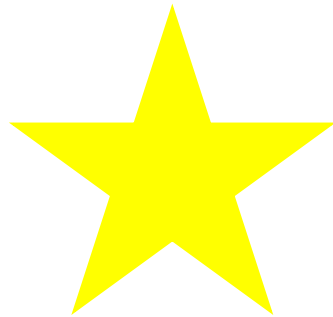
rTMS Safety

- Motor threshold is a metric of cortical excitability
- Things that change cortical excitability:
 - Medications
 - Substances
 - Sleep
- Things that do not change cortical excitability:
 - Psychotherapy
 - Mood
 - Symptom changes

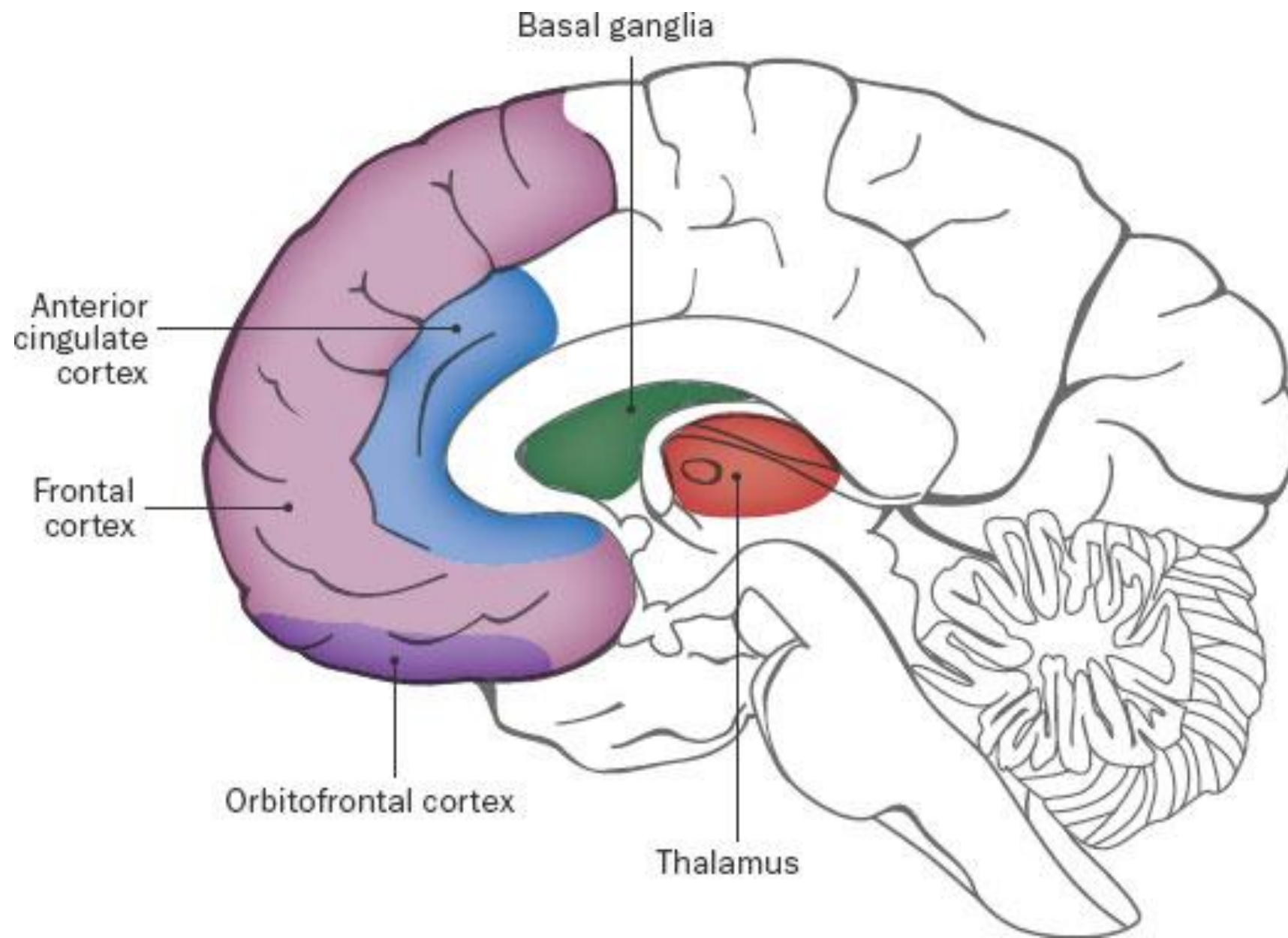


What makes rTMS work better or worse?

- Better:
 - Not clear
 - Likely dependent on the disorder
- Worse:
 - Benzodiazepines
 - Gabapentin/pregabalin
 - Anticonvulsants

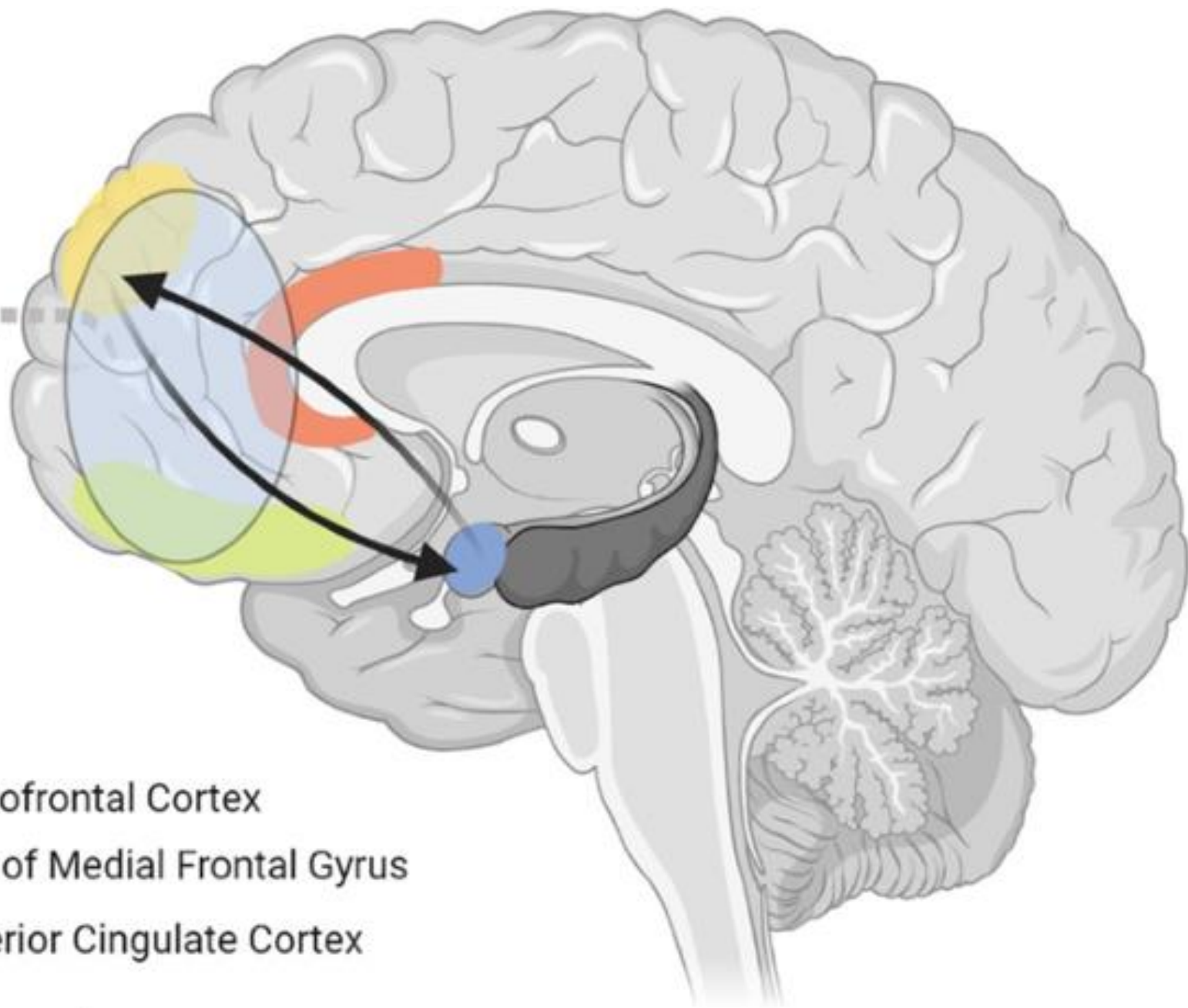


A Circuit Level Treatment for OCD



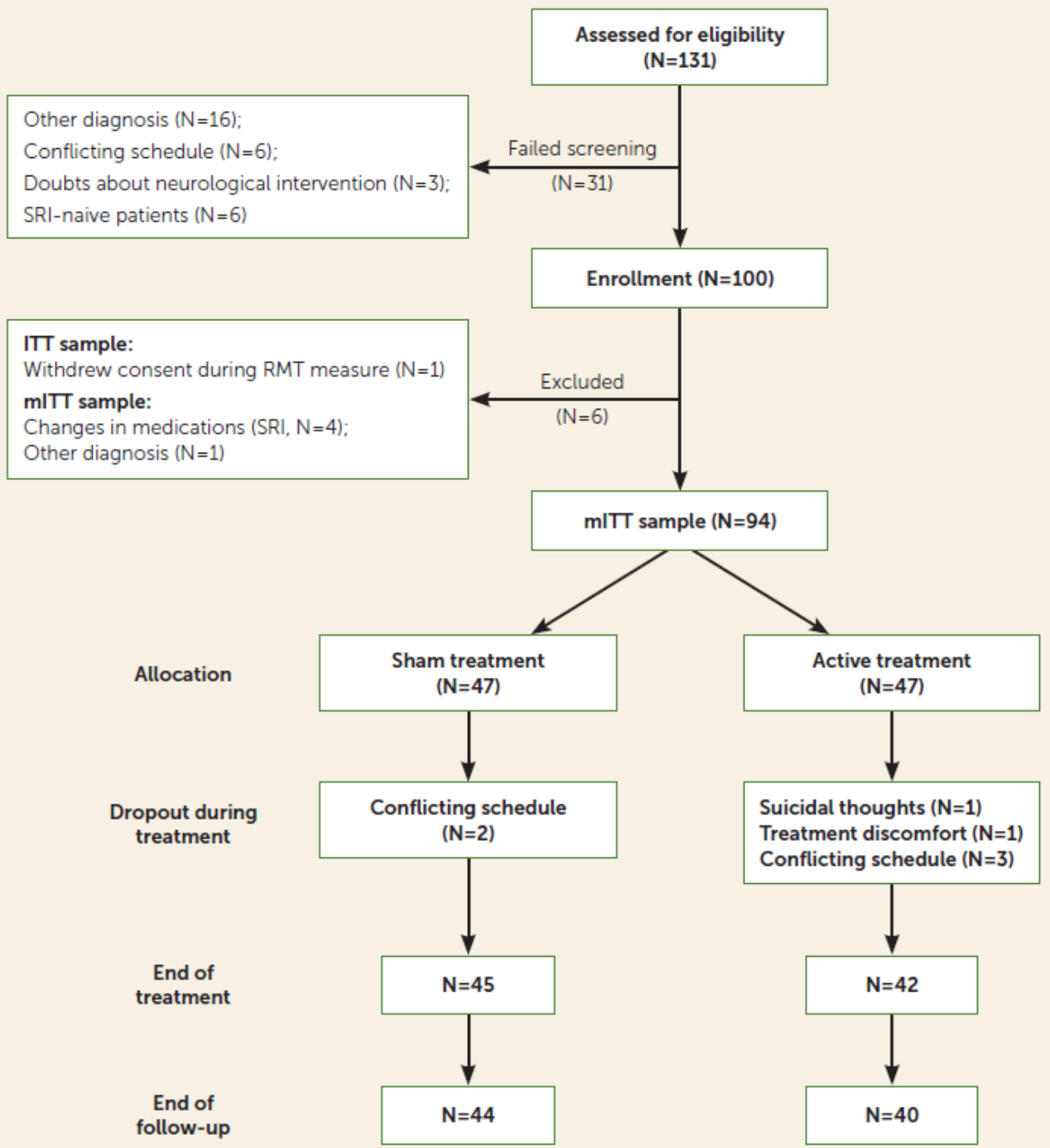
Ventromedial
Prefrontal
Cortex

- Ventral Orbitofrontal Cortex
- Ventral Part of Medial Frontal Gyrus
- Ventral Anterior Cingulate Cortex
- Amygdala



Efficacy and Safety of Deep Transcranial Magnetic Stimulation for Obsessive-Compulsive Disorder: A Prospective Multicenter Randomized Double-Blind Placebo-Controlled Trial

Lior Carmi, Ph.D., Aron Tendler, M.D., Alexander Bystritsky, M.D., Eric Hollander, M.D., Daniel M. Blumberger, M.D., Jeff Daskalakis, M.D., Herbert Ward, M.D., Kyle Lapidus, M.D., Wayne Goodman, M.D., Leah Casuto, M.D., David Feifel, M.D., Noam Barnea-Ygael, Ph.D., Yiftach Roth, Ph.D., Abraham Zangen, Ph.D., Joseph Zohar, M.D.



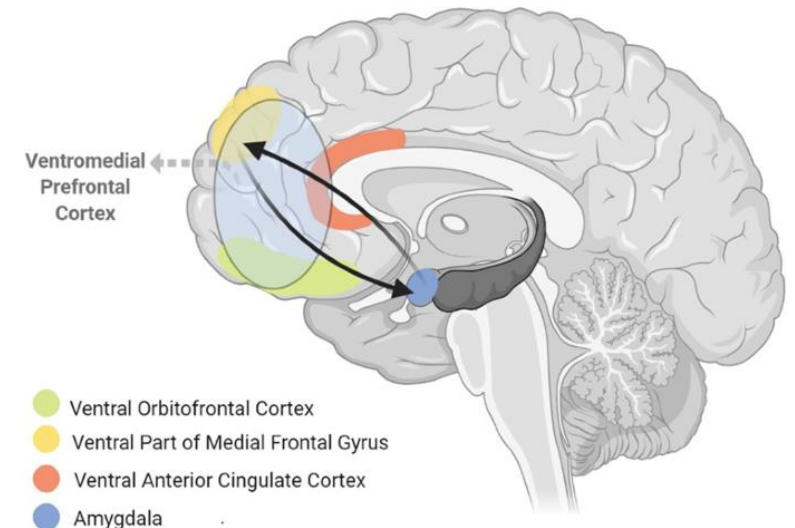
- Multisite
- 2014-17
- 6 weeks
- Moderate severity OCD (YBOCS ≥ 20)
- Failed serotonin reuptake inhibitor or cognitive behavioral therapy
- On an 'antidepressant' for 2 months or be getting cognitive behavioral therapy

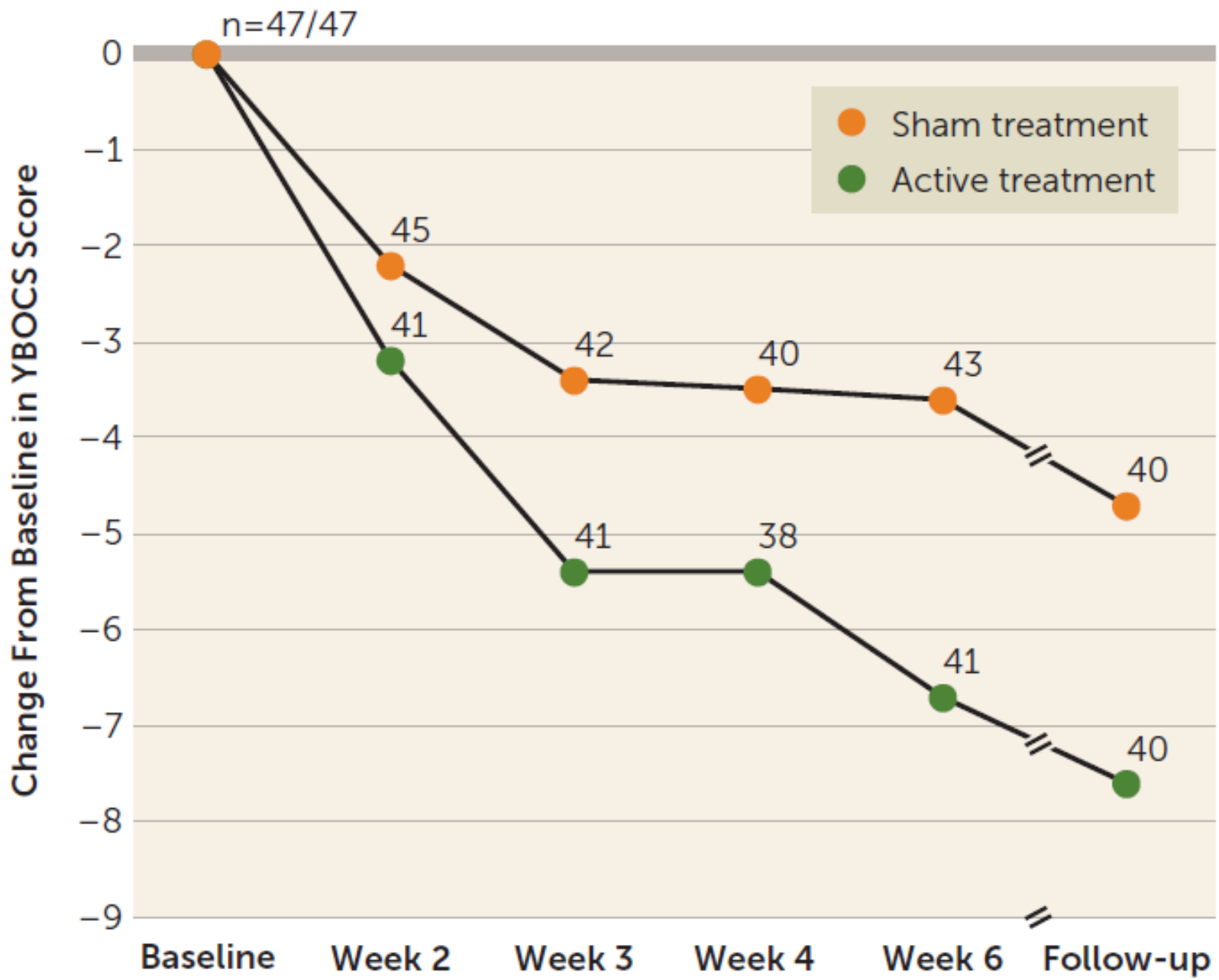
Personalized symptom provocation

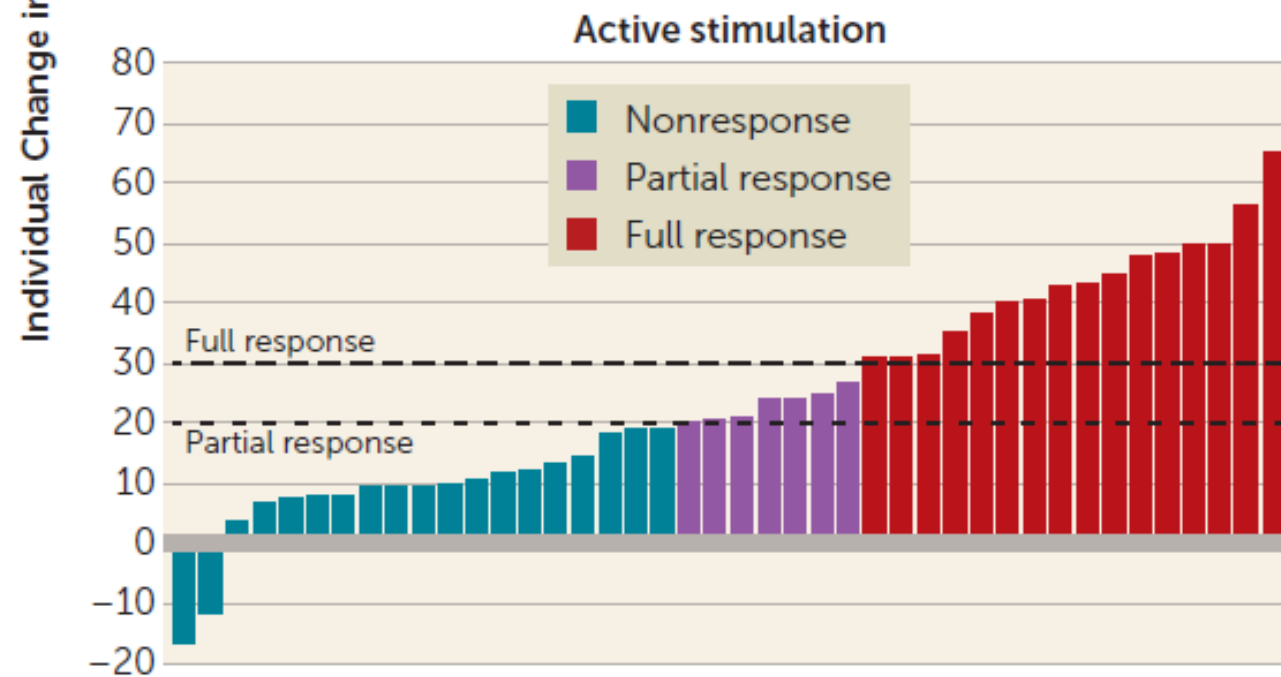
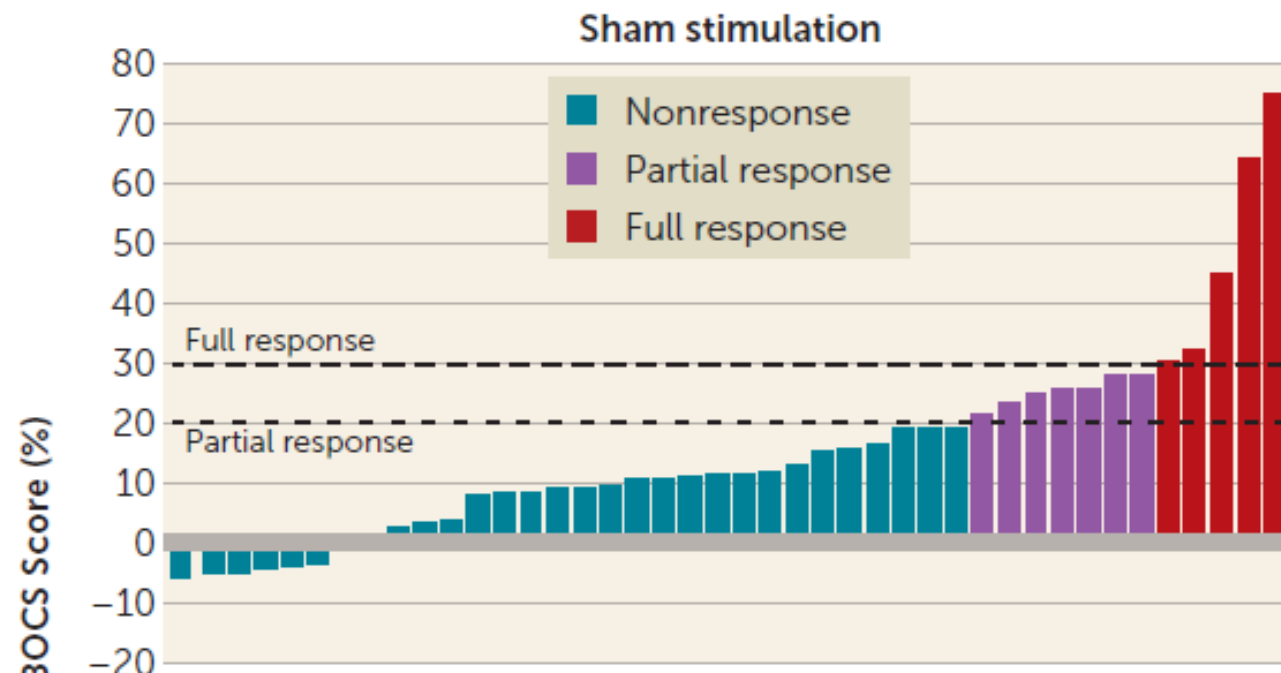
- 3-5 minute provocation “to activate the relevant neuronal circuit”
- Subjective distress 4-7/10

Transcranial magnetic stimulation

- 'Deep' TMS
- Foot motor threshold
- Targeting the medial prefrontal cortex
- 20Hz at 100% rMT
- 2s trains, 20 second intertrain interval (18min 20s)
- 2000 pulses/treatment









Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

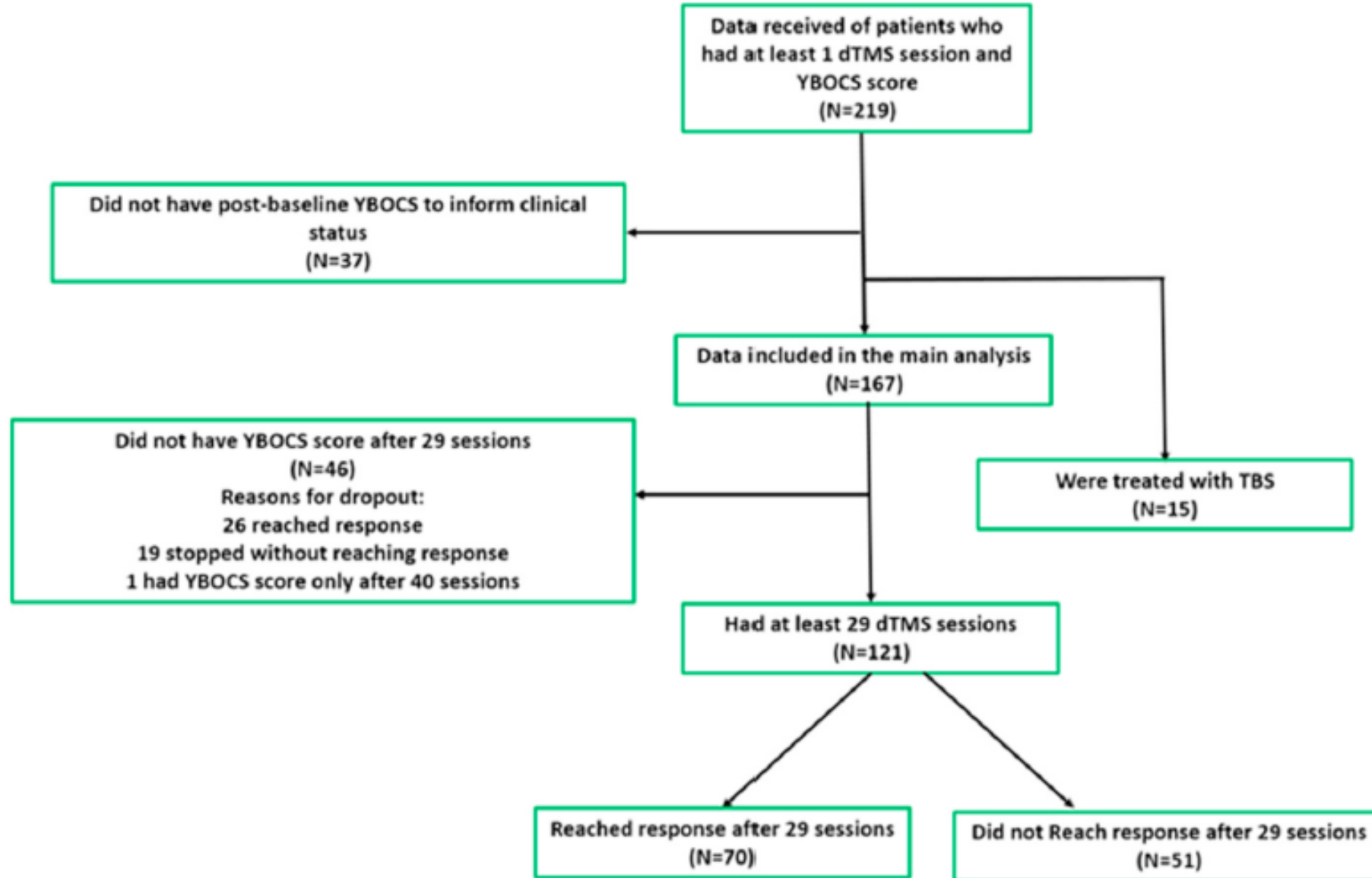
Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires



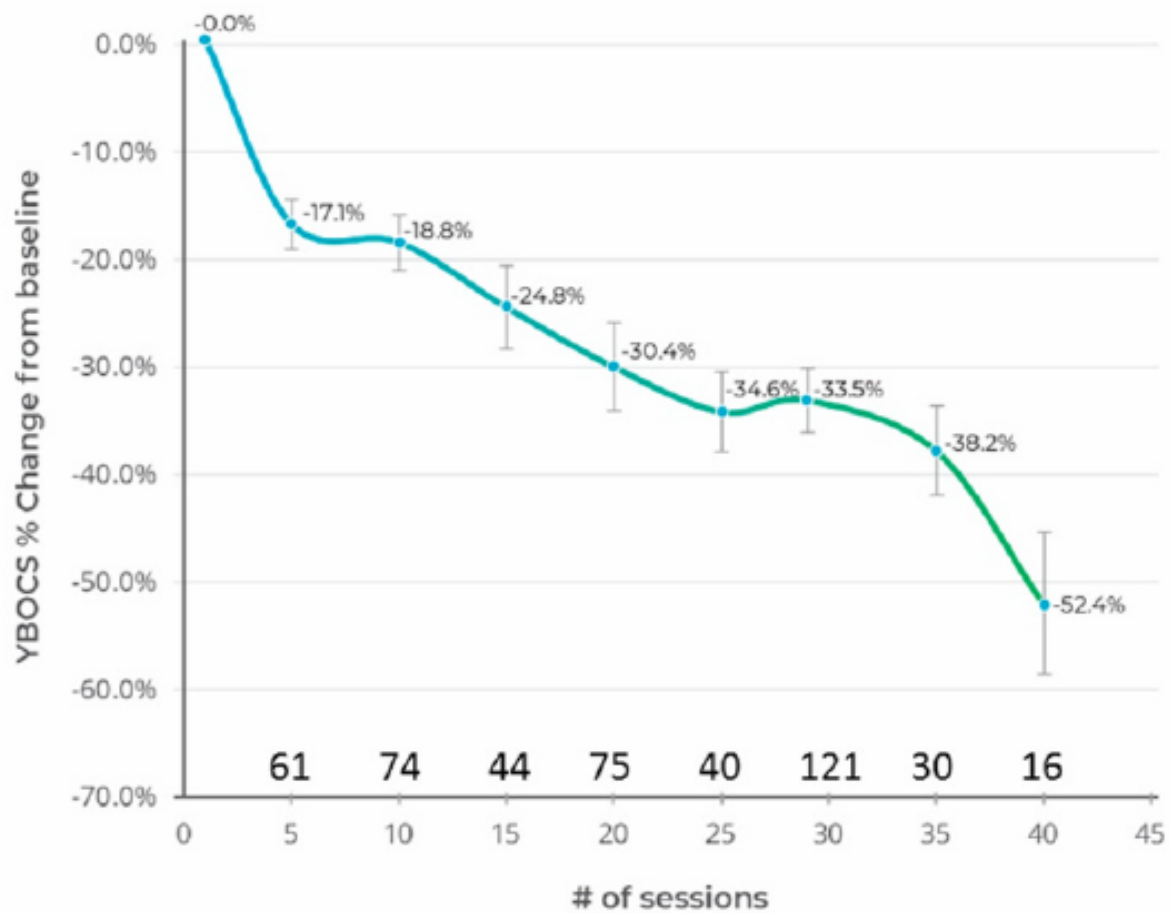
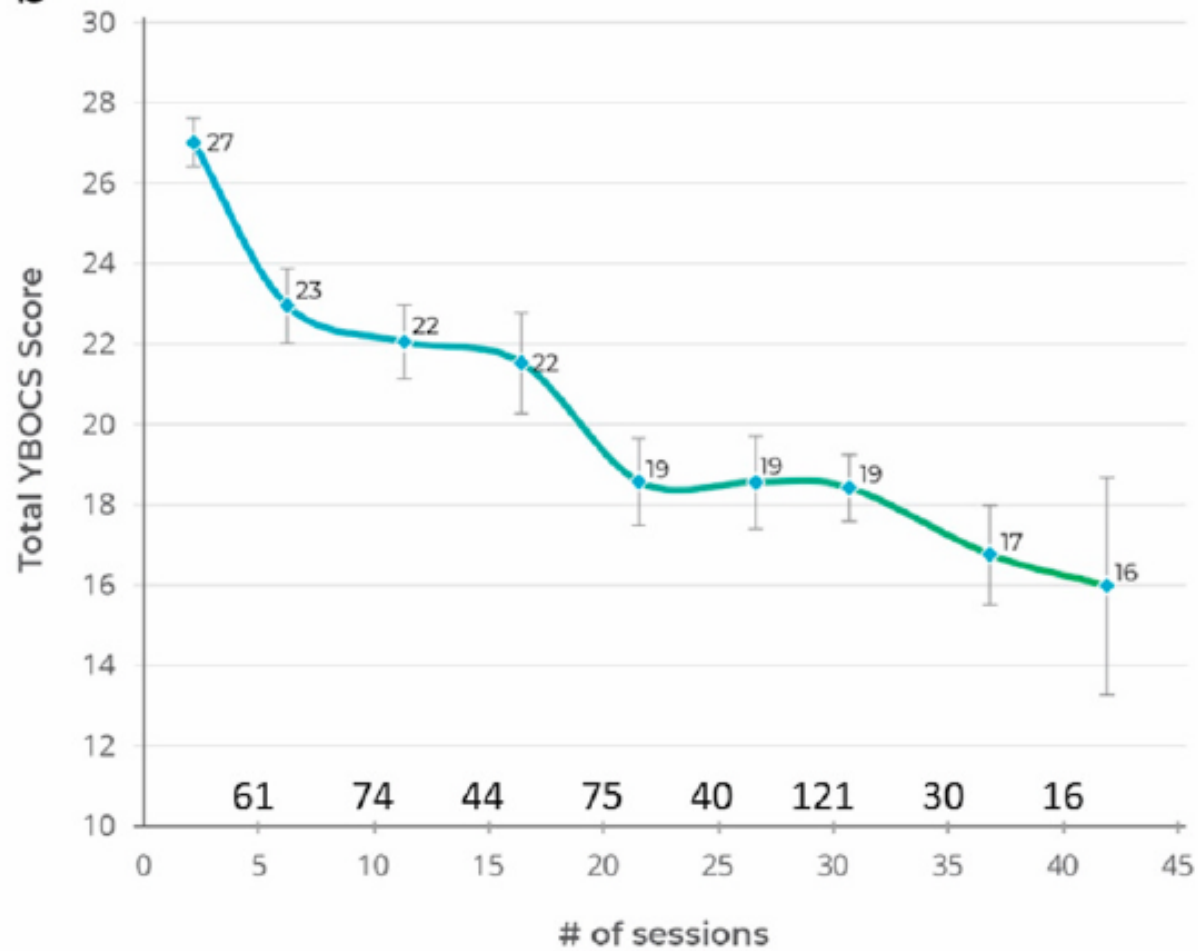
Real-world efficacy of deep TMS for obsessive-compulsive disorder: Post-marketing data collected from twenty-two clinical sites

Yiftach Roth^{a,b,*}, Aron Tendler^{a,b,c}, Mehmet Kemal Arikan^d, Ryan Vidrine^e, David Kent^f, Owen Muir^g, Carlene MacMillan^h, Leah Casutoⁱ, Geoffrey Grammer^j, William Sauve^j, Kellie Tolin^k, Steven Harvey^l, Misty Borst^m, Robert Rifkin^l, Manish Shethⁿ, Brandon Cornejo^o, Raul Rodriguez^p, Saad Shakir^q, Taylor Porter^r, Deborah Kim^s, Brent Peterson^t, Julia Swofford^u, Brendan Roe^u, Rebecca Sinclair^g, Tal Harmelech^b, Abraham Zangen^a

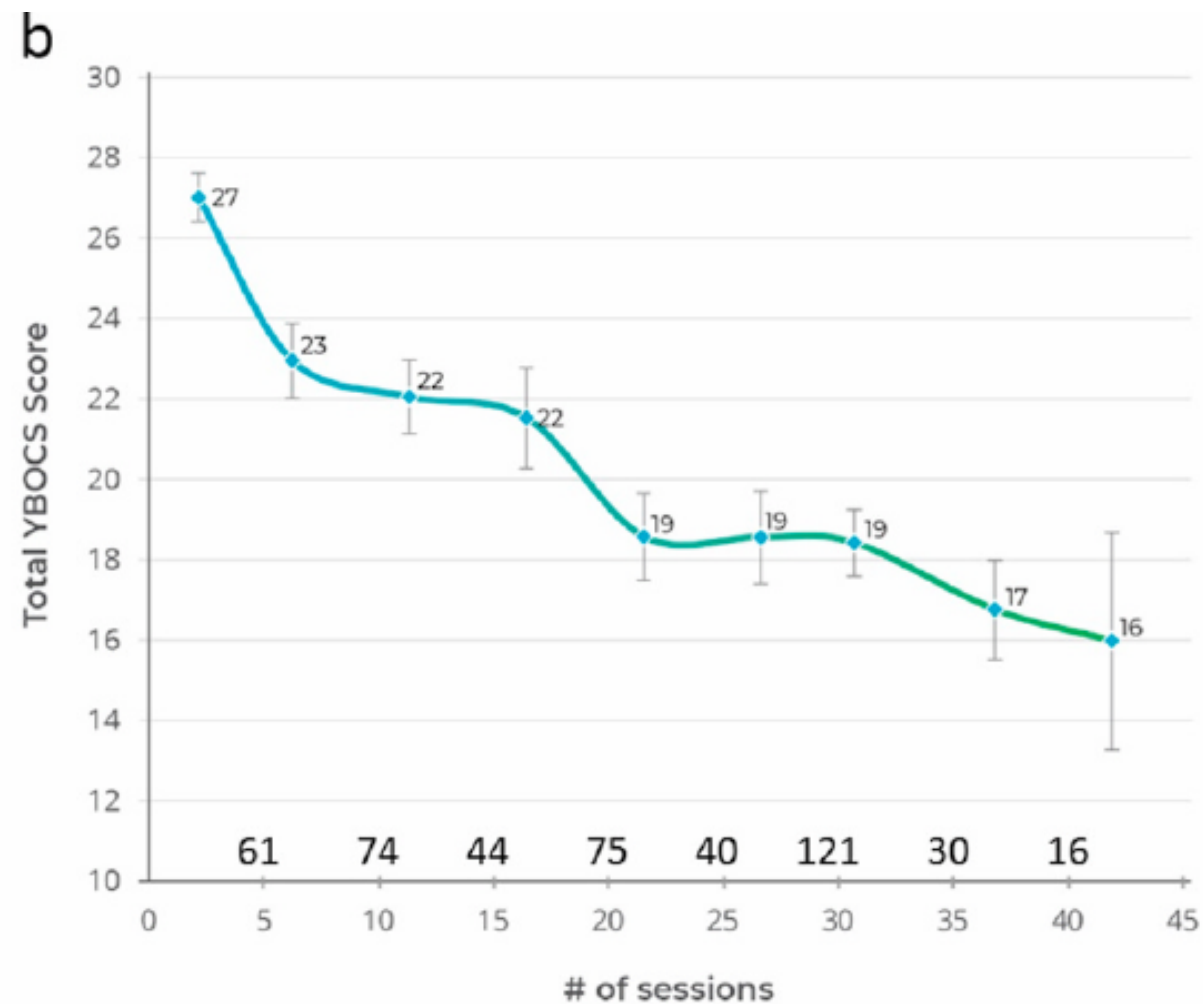
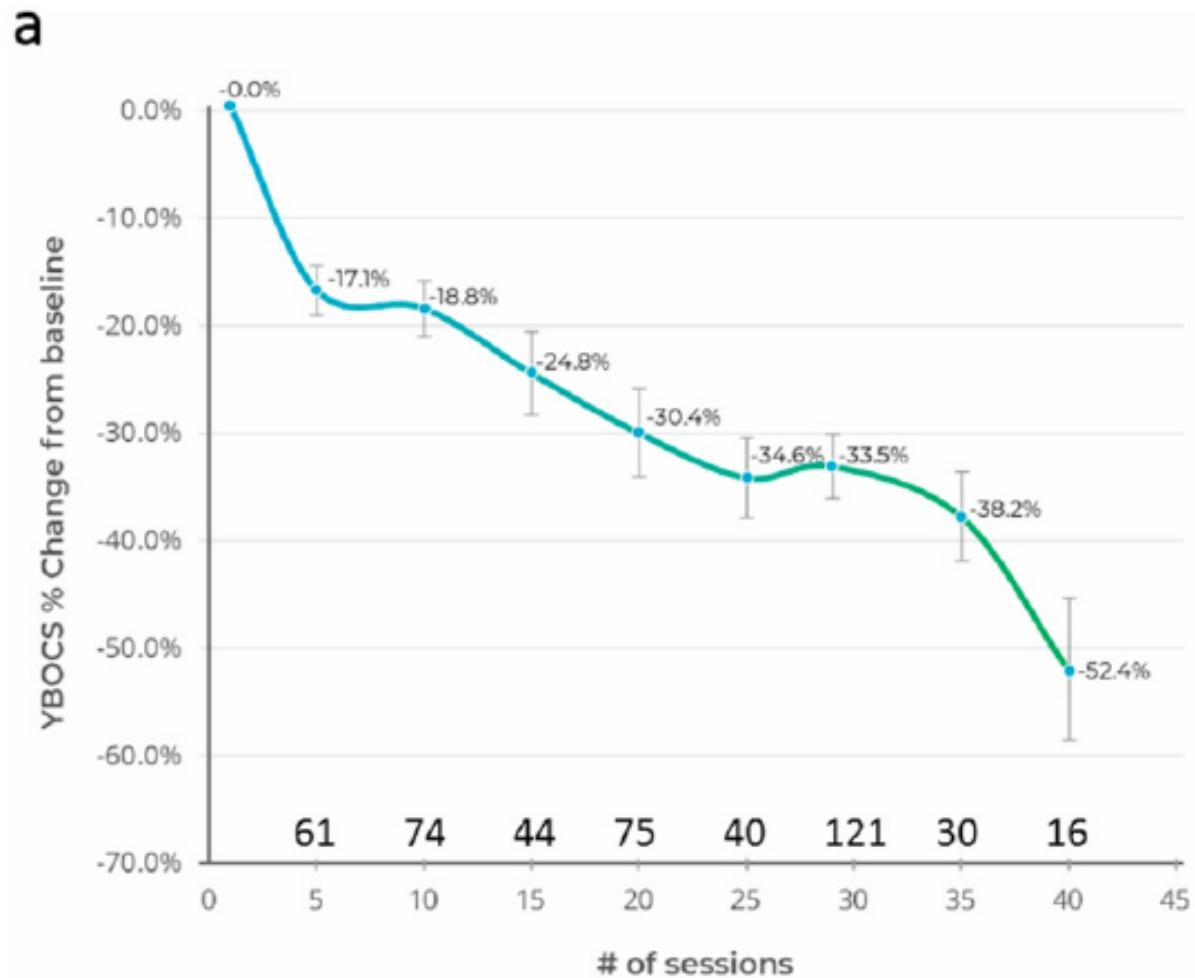


Interventions

- H7 coil – medial PFC
- Heterogeneous
 - 20Hz
 - Intermittent theta burst stimulation
- Symptom provocation
- Up to 29 treatments

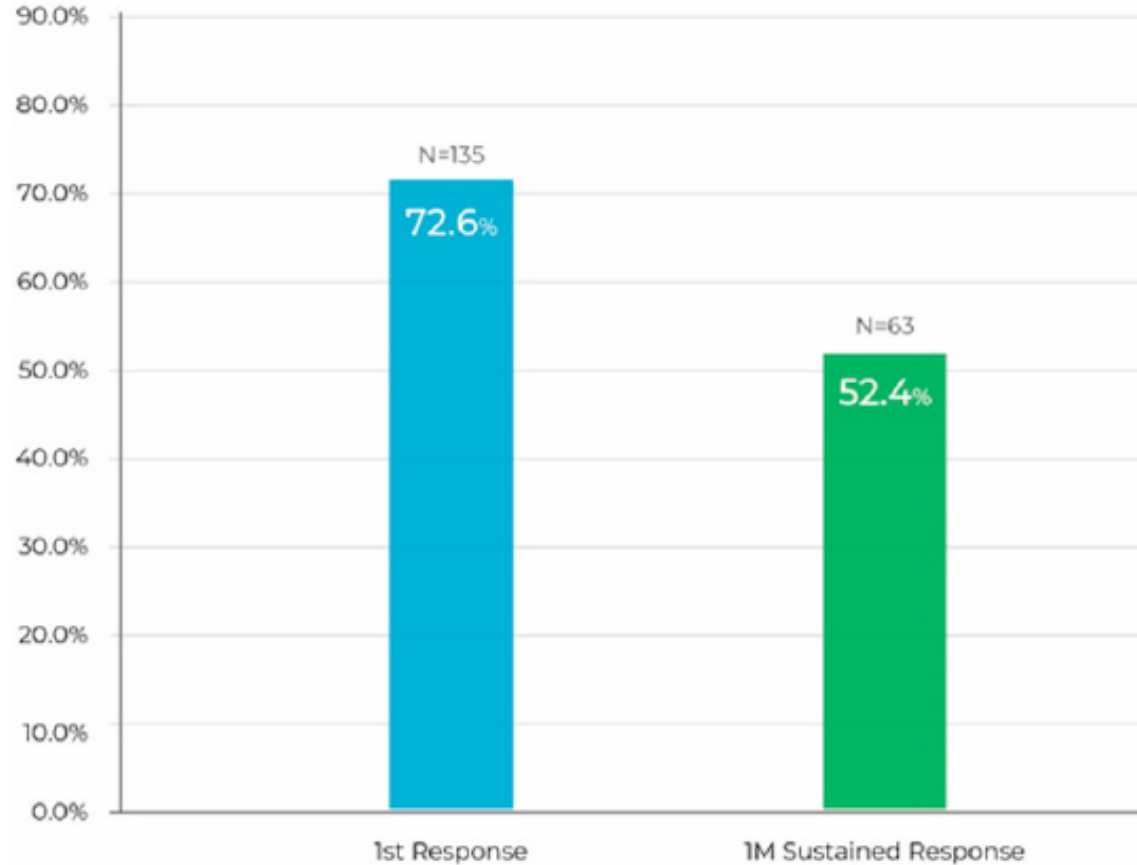
a**b**

Real World Results



Real World Results

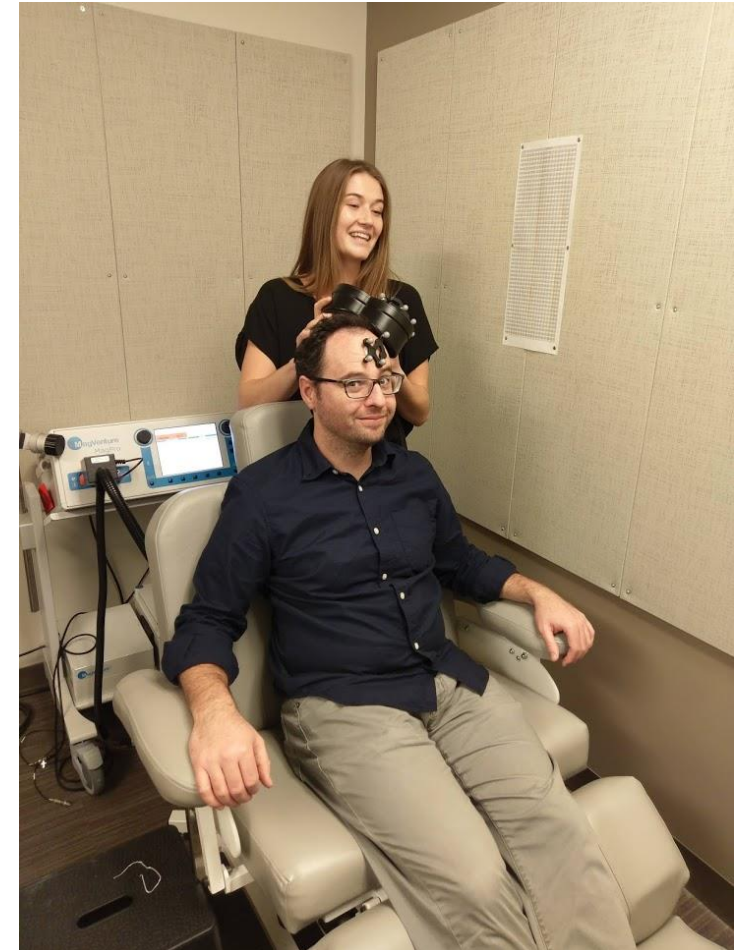
- 'Response' defined as 30% improvement on the YBOCS



What are we doing in the McGirr?

Repetitive Transcranial Magnetic Stimulation (rTMS) and Theta-Burst Stimulation (TBS)

- Most established evidence base for non-invasive neurostimulation treatment.
- Protocols of patterned pulses drive **synaptic plasticity** at cortical targets.
- Leverage reciprocal connections with cortical and subcortical regions.



Leveraging pharmacological adjuncts targeting the NMDA receptor to enhance the *physiological effect* of iTBS.



Are you living with Obsessive Compulsive Disorder (OCD)?

The University of Calgary is currently recruiting volunteers who have been diagnosed with Obsessive Compulsive Disorder for a treatment study evaluating the effect of pairing rTMS with a medication. rTMS is a non-invasive (does not enter the body) technique that is **FDA approved as a treatment for OCD.**

Who can participate?

- People with a diagnosis of Obsessive Compulsive Disorder
- People 18 - 65 years of age
- People with no major unstable medical problems

What does this study involve?

- This study involves a screen visit and 4 weeks of rTMS sessions (20 sessions).
- You will continue with current medication/therapy.
- Participants will be compensated for each assessment visit completed.

To learn more please contact our study team:

Phone: (403) 210 6504

E-mail: jaeden.cole1@ucalgary.ca



This study has been reviewed by the University of Calgary Conjoint Health Research Ethics Board.
REB#: REB21-0265
Department of Psychiatry
Mathison Centre for Mental Health Research & Education
3280 Hospital Dr. NW. Calgary, AB, T2N 4Z6

June 2021
Version 2.0