Transcranial Magnetic Stimulation for Treatment-Resistant OCD

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What to Expect from this talk:
• What is TMS?
• TMS for Depression (in brief)
• Formulation & Neurobiology of OCD
• Proposed TMS Targets of Stimulation, TMS Protocol, & Mechanism of Action
• Efficacy from FDA Clearance Study
• TMS Health Solutions –Private Practice Data/Outcomes
• Selecting OCD Patients for TMS & Insurance Coverage
• Patient Testimonials & Q&A

What is TMS?
Transcranial Magnetic Stimulation
Based on Faraday Principle

- Rapidly fluxing magnetic field
- Induces electric current in underlying cortex
- Electric field → depolarization of neurons
- Allows focal manipulation of cortical activity
- Excitatory or inhibitory

rTMS: Figure 8 coil

Focused Magnetic Field
What does a course of TMS look like for patients?

- Administered in sessions lasting approximately 20-40 minutes, five times a week, over a period of 4-6 weeks
- No anesthesia or sedation is required and patients can resume their usual activities (including work) immediately
- Most responders show signs of response by the 2nd or 3rd week

TMS: Contraindications

- Non-removable metallic objects in or around the head
- Conductive, ferromagnetic or other magnetic sensitive metals that are implanted or are non-removable within 30 cm of treatment coil
- Implanted electrodes/ stimulators
- Deep Brain Stimulator
- Aneurysm clips or coils
- Cochlear implants
- Stents
- Bullet or other metal fragments
- Metallic tattoos

Contraindicated with metal clips or external hearing aids. Neuronetics Inc. Malvern, PA.
**TMS: Side Effects**

- Headache
- Scalp sensitivity
- Syncope
- Seizure
  - < 1%
  - No development of seizure disorders
  - No medical complications

**FDA Approved Target for Depression**

**Overall Summary of Effectiveness in Major Depression**

- 4 large, multisite, randomized controlled trials demonstrated clinically significant antidepressant effect of TMS (2 industry, 1 by NIH, 1 European augmentation study)
- Prospective, naturalistic RCT confirms these results in real-world practice settings
- Efficacy in private practice data
  - Remission rates from 15%-30% in the double-blind phase, and 30% or more in open-label
- Overall, 1 in 2 patients respond and 1 in 3 patients achieve remission
- TMS is generally associated with a high level of treatment adherence, >90% of patients completed acute treatment in both research setting and in clinical practice


**Current Approved Treatments for OCD**

- Exposure and response prevention first line for non-comorbid/mild OCD
- Medications:
  - Fluoxetine
  - Paroxetine
  - Sertraline
  - Fluvoxamine
  - Clomipramine

Above treatments result in ≥30% improvement for 40-60% of OCD patients

**Implicated Brain Targets**

- Cortico-Striato-Thalamic-Cortical (CSTC) loops
- Orbitofrontal Cortex (OFC)
- Anterior Cingulate Cortex (ACC)
- Ventromedial Prefrontal Cortex (VMPFC)
- Dorsomedial Prefrontal Cortex (DMPFC)
- Supplementary Motor Area (SMA)
- Ventral Striatum (VS)
- Thalamus
- Amygdala & Bed Nucleus of Stria Terminalis (BNST)

**ANTERIOR CINGULATE CORTEX (ACC)**

ACC acts as hub connecting three key networks (Salience, Reward, & Non-Reward) via CSTC loops

fMRI studies show pain, negative affect, and cognitive control all activate an overlapping region of the ACC, processing negative emotional and reinforcing information and then directing motivated behavior.

The estimator of "Expected Value of Control" (EVC)
- control signals can indicate "identity" & "intensity"
- control signal passed to "regulatory centers" (DLPFC & others)

ACC control signals are used to exert top-down control over downstream effector systems:
- problem solving & correction
- assessing salience of stimuli & emotion
- assessing motivational information
- role in conditioning, harm expectancy, extinction
DORSAL ACC ABERRANT CONTROL SIGNAL HYPOTHESIS

Mis-specified control signals - > persistent anxiety-producing sense of threat or unease generated by otherwise innocuous stimuli that cannot be extinguished.

Repetitive behaviors to reduce this distress signal are ineffective, but the individual persists with these maladaptive behaviors, unable to abandon them and switch to more useful strategies.

Ex. 1: Overestimating the threat of germs and exaggerating the importance of the act of cleaning lead to contamination obsessions and washing compulsions. Unable to quench the feeling of threat from the contaminant, the individual continues to perform the exaggerated cleansing rituals.

IN SUMMARY, OCD PATIENTS DEMONSTRATE:

- Impaired ability to inhibit intrusive thoughts, urges, feelings, and behaviors (motor control & response inhibition)
  - Decreased connectivity/inactivity in sensorimotor salience network
- Inappropriate automatic & subconscious threat responses or inappropriately sustained threat response
  - Mis-specification of control signal identity & intensity
  - Exaggerated amygdala or BST response to threat
- Decreased ability to effectively cancel behavior, cues, adopt, extinguish fear (salience & reward processing)
  - Dysregulation of medial & lateral OFC & mis-specification of control signal identity & intensity
  - Dysregulation of lateral OFC & its connection to amygdala & reward circuits
- Impaired evaluation of punishment over reward
  - Dysregulation of ACC, Reward network, & Non-Reward network

TMS for OCD

- Non-invasive, minimal side effects
- Standard depression protocols do not seem to consistently work in OCD
- Promising studies targeting SMA, DMPFC/ACC, and OFC
- Deeper TMS could allow greater variety of brain structures to be targeted
- Recent FDA Clearance for Brainsway H7 dTMS device in Aug 2018
**Supplementary Motor Area (SMA)**

https://neuroscientificallychallenged.com/glossary/supplementary-motor-area

**Dorsomedial Prefrontal Cortex (DMPFC) & Anterior Cingulate Cortex (ACC)**


*Only FDA cleared target for OCD.*

**Lateral Orbitofrontal Cortex (OFC)**

Ruffini et al., 2009; Nauczyciel et al., 2014
PROVOCATION OF OCD SYMPTOMS

- Effects of TMS may be more pronounced when the targeted circuit is active. (addiction, PTSD, smoking)
- Items that are stored in long-term memory become prone to change (stimulation) upon retrieval (following provocation).
- Personal provocations/hierarchy designed by treating clinician &/or therapist prior to Tx.
- OCD symptoms provoked for each subject using internal or external stimuli to induce the typical OCD sx and distress in that individual.
- Provocation/exposure done at beginning or just prior to treatment.
- Provocations should aim to achieve score of 4-7 on 10 point Visual analog scale (VAS) before proceeding with stimulation.

Carmi, 2017; Dinur-Klein, 2014; Isserles, 2013

MULTICENTER OCD STUDY

A Prospective Double Blind Randomized Controlled Study to Evaluate the Safety and Efficacy of H7 Deep Transcranial Magnetic Stimulation (dTMS) in Obsessive-Compulsive Subjects who Failed SSRIs

USA
- Mt. Sinai Medical Center
- Neuropharmacology Services
- University of California, Los Angeles
- University of California, San Diego
- University of Florida
- University of Chicago
- Advanced Mental Health Care
- Linder Center of Hope
- TMS Hope Center Long Island

CANADA
- Center for Addiction and Mental Health

ISRAEL
- Tel Hashomer Hospital

11 sites from North America and Europe

PI: Joseph Zohar MD, Abraham Zangen PhD

Led to FDA Clearance of Brainsway H7 device to treat OCD in Aug 2018

BrainsWay H7 Coil Targets the DMPFC and ACC
FDA Target for Depression

Standard depression protocols do not seem to work for OCD based on current evidence.

FDA Target for OCD

INCLUSION CRITERIA

- Outpatients, men and women 18-68 years of age
- Subjects with at least moderate OCD (Y-BOCS score of ≥ 20)
- Maintained on 50% of a therapeutic dosage for at least 3 months prior to study entry and for the duration of the trial
- and/or maintained on psychopharmacologic interventions in the maintenance stage (i.e., not during the assessment or skills acquisition or training stages)

DEMOGRAPHICS

- All patients met inclusion criteria
- 50% Male, 75% Caucasian
- Prior meds 98% (19% took 5 SSRI's), Prior CBT 69%
- Family hx OCD 55%
- Outpatients, men and women 22-68 years of age
- Subjects with at least moderate OCD (Y-BOCS score of ≥ 20)
- Maintained on SSRI’s at a therapeutic dosage for at least 2 months prior to study entry and for the duration of the trial
- and/or maintained on psychotherapeutic behavioral interventions in the maintenance stage (i.e., not during the assessment or skills acquisition or training stages)

Primary Objective: Change in Y-BOCS between the active and sham treatments groups at 6 wks

- Response Rate – reduction of at least 30% in YBOCS score from baseline
- Partial Response Rate – reduction of at least 20% in YBOCS score from baseline
- Remission Rate – defined as YBOCS score < 10

AVERAGE IMPROVEMENT IN YBOCS SCORES

Carmi et al. (2019)
RESPONSE RATES IN ACTIVE VS SHAM DEEP TMS

Full response (> 30%)

Partial response (> 20%)

MEAN CHANGE IN YBOCS FROM BASELINE
MEDICATION TRIALS VS DEEP TMS TRIAL

Data on SSRI medications based on meta-analysis (Soomro et al., 2008)

Dark = Treatment
Light = Sham

Carmi et al. (2019)

TMS HEALTH SOLUTIONS
Private Practice Outcomes

* Results to be shown during conference presentation

Carmi et al. (2019)
WHO IS RIGHT FOR TREATMENT AND IS TMS COVERED BY INSURANCE?

FDA Indicated for Major Depressive Disorder in adult patients who have failed to receive satisfactory improvement from a prior antidepressant medication at or above the minimal effective dose and duration in the current episode. Insurance currently covers treatment but can vary in requirements by plan.

Brainsway H7 tMS FDA cleared for OCD treatment but most insurance companies have not written their policies yet.

Patient Characteristics:
• In a recurrent or chronic episode
• Multiple medication attempts, yet still symptomatic
• Experiences frequent side effects from medication
• Obsessions/compulsions impede ability to use medications
• Inadequate response to exposure response prevention

SUMMARY & CONCLUSIONS:
• TMS is safe, non-invasive, & has been FDA approved for MDD for the last 10 years.
• 2018 - FDA clearance for OCD specifically for the Brainsway H7 system
• Multiple targets & protocols being explored: SMA, DFC, DRPFC/KCC, & low vs high freq
• Exposure/Provocation protocol is unique to OCD treatment and may enhance outcomes
• In treatment resistant OCD, TMS is a reasonable, low-risk, evidence-based option to prescribe
• Many clinicians already using TMS will likely be looking to provide this treatment, but may not have sufficient OCD experience to appropriately tailor treatment to individual patients. Having experienced OCD clinicians who also feel comfortable with TMS, or having TMS clinicians partner with experienced OCD clinicians, will be important in translating clinical trial results to actual real world results.

Questions?