

Transcranial Magnetic Stimulation (TMS) Brainsway H7 Coil for Obsessive Compulsive Disorder

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FDA Approval of H7 Coil for Treatment of OCD

The Brainsway dTMS device is intended for the treatment of OCD *in conjunction with SSRI medications* approved for treatment of OCD *and/or psychotherapeutic behavioral interventions.*

Disclosures

- ▶ Greenbrook TMS - Salary and Equity
- ▶ Neuronetics - Paid Consultant, Research
- ▶ Brainsway - Research

The information presented here is the opinion of the author and does not represent Greenbrook TMS or any other entity.

Obsessive Compulsive Disorder

A. Presence of obsessions, compulsions, or both:

Obsessions as defined by (1) and (2):

1. **Recurrent and persistent thoughts, urges, or images** that are experienced, at some time during the disturbance, as intrusive and unwanted and that in most individuals cause marked anxiety or distress
2. The person attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion)

Compulsions as defined by (1) and (2):

1. **Repetitive behaviors or mental acts** that the person feels driven to perform in response to an obsession, or according to rules that must be applied rigidly
2. The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts either are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive

OCD Features

- B. The O/C are time consuming (for example, take more than 1 hour a day) or cause clinically significant distress or impairment in functioning.
- C. The O/C symptoms are not due to the direct physiological effects of a substance or a GMC
- D. The content of the obsessions or compulsions is not restricted to the symptoms of another mental disorder

OCD Qualifiers

- ▶ *Good or fair insight*: Recognizes that OCD beliefs are definitely or probably not true, or that they may or may not be true
- ▶ *Poor insight*: Thinks OCD beliefs are probably true
- ▶ *Absent insight/delusional beliefs*: Completely convinced OCD beliefs are true
- ▶ *Tic-related OCD*: The individual has a lifetime history of a chronic tic disorder

Type of Obsessions

Type of Obsession	Examples
Contamination	Bodily fluids, disease, germs, dirt, chemicals, environmental contaminants
Religious Obsessions	Blasphemy or offending God, high concern about morality and what is right and wrong.
Superstitious ideas	Lucky numbers, colors, words
Perfectionism	Evenness and exactness, “needing” to know or remember, fear of forgetting or losing something
Harm	Fear of hurting others through carelessness, fear of being responsible for something terrible happening
Losing Control	Fear of acting on an impulse to harm self or others, fear or unpleasant mental images, fear of saying offending things to others
Unwanted Sexual Thoughts	Forbidden or “perverse” sexual thoughts, images, or impulses; obsessive thoughts about homosexuality; obsessions involving children or incest; obsessions about aggressive sexual behavior

Types of Compulsions

Type of Compulsion	Examples
Checking	Making sure that you did not (or will not) harm yourself or others, or that you did not make a mistake, or that nothing “terrible” happened
Repeating	Repeating things in multiples or a certain number of times, certain body movements, rereading or rewriting
Washing / Cleaning	Washing hands excessively, excessive showering or bathing, cleaning outside the norm
Mental compulsions	Cancelling out bad thoughts with good ones, counting while walking or performing some task, prayer to prevent something terrible from happening
Hoarding	Collecting items due to compulsions
Ordering and Arranging	Putting things in “proper” order or until it “feels right”

Demographics of OCD

- ▶ 75% of cases develop before age 30 (onset in men earlier than women)
 - ▶ Sudden onset and later life may be neurologically association (infarct, seizure)
- ▶ 31% of cases between ages 10 and 15
 - ▶ PANDAS - Group A Strep infection
- ▶ 28% Obsessional predominate, 20% compulsion predominate, 50% both (Foa 1995)
- ▶ Overall heritability for OCD estimated to be 48%.”
- ▶ OCD affects 2.5% of the population (Regier 1988)
- ▶ 55% have a constant or progressive course and only 11% have fluctuating course with periods of remission (Black 1974)

Prevalence of Subtypes

% of OCD Cases Reporting each Symptom

Checking	79.3
Hoarding	62.3
Ordering	57.0
Moral	43.0
Sexual/religious	30.2
Contamination	25.7
Harming	24.2
Illness	14.3
Other	19.0

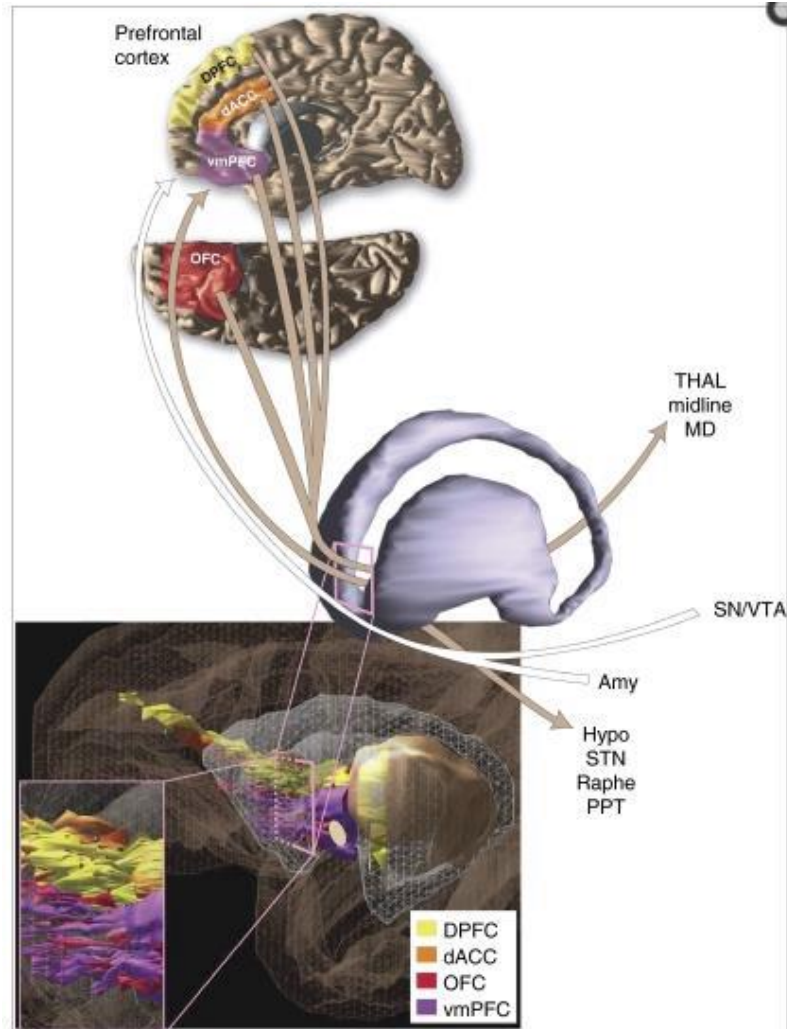
OCD Comorbidities

- ▶ 76% have lifetime history of another anxiety disorder
- ▶ 63% have lifetime history of mood disorder (MDD 41%)
- ▶ 23-32% have comorbid obsessive compulsive personality disorder
- ▶ 29% have lifetime history of tic disorder
- ▶ 12% Schizophrenia

Treatments for OCD

- ▶ Current Approved Treatments for OCD
 - ▶ Fluoxetine
 - ▶ Paroxetine
 - ▶ Sertraline
 - ▶ Fluvoxamine
 - ▶ Clomipramine (NOT SUPERIOR TO SSRI's)
- ▶ Above treatments result in 30% improvement for 40-60% of OCD patients
- ▶ Therapy
 - ▶ Exposure/Response Prevention
 - ▶ CBT much less effective
 - ▶ Other therapies ineffective

OCD has Well-Defined Neurologic Basis



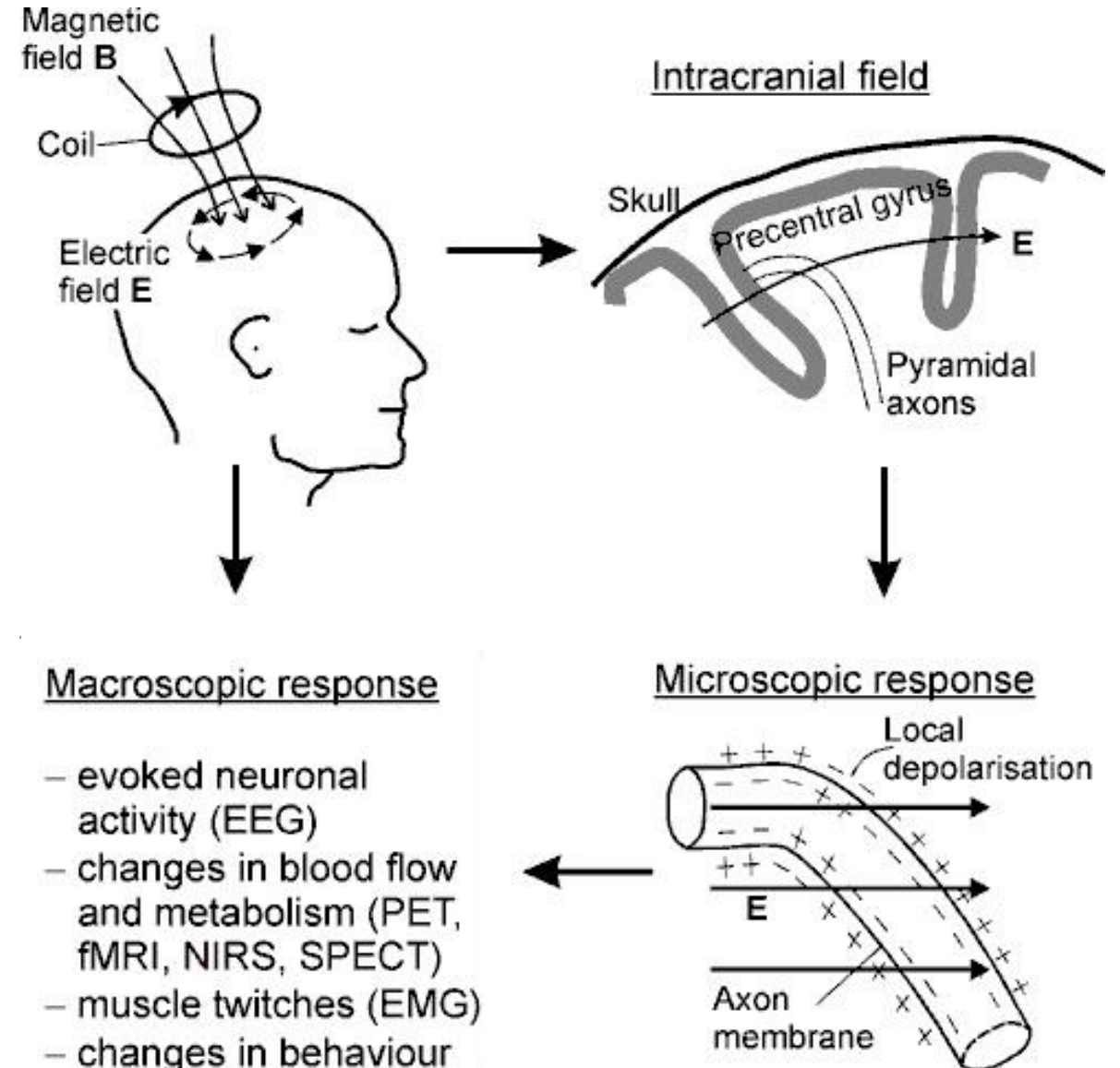
Cortical - Striatal - Thalamic - Cortical

Poor thalamic gating may increase Anterior Cingulate Cortex (ACC) activity

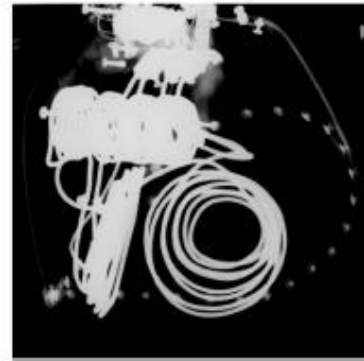
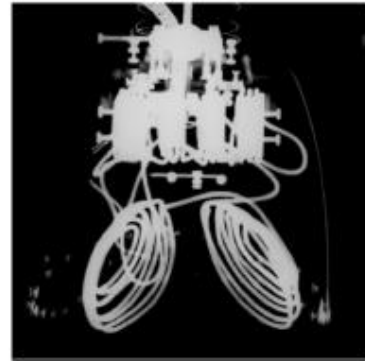
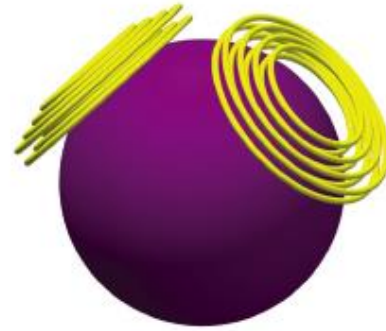
Medial pre-frontal stimulation decreases ACC activity

Basic Principles of TMS

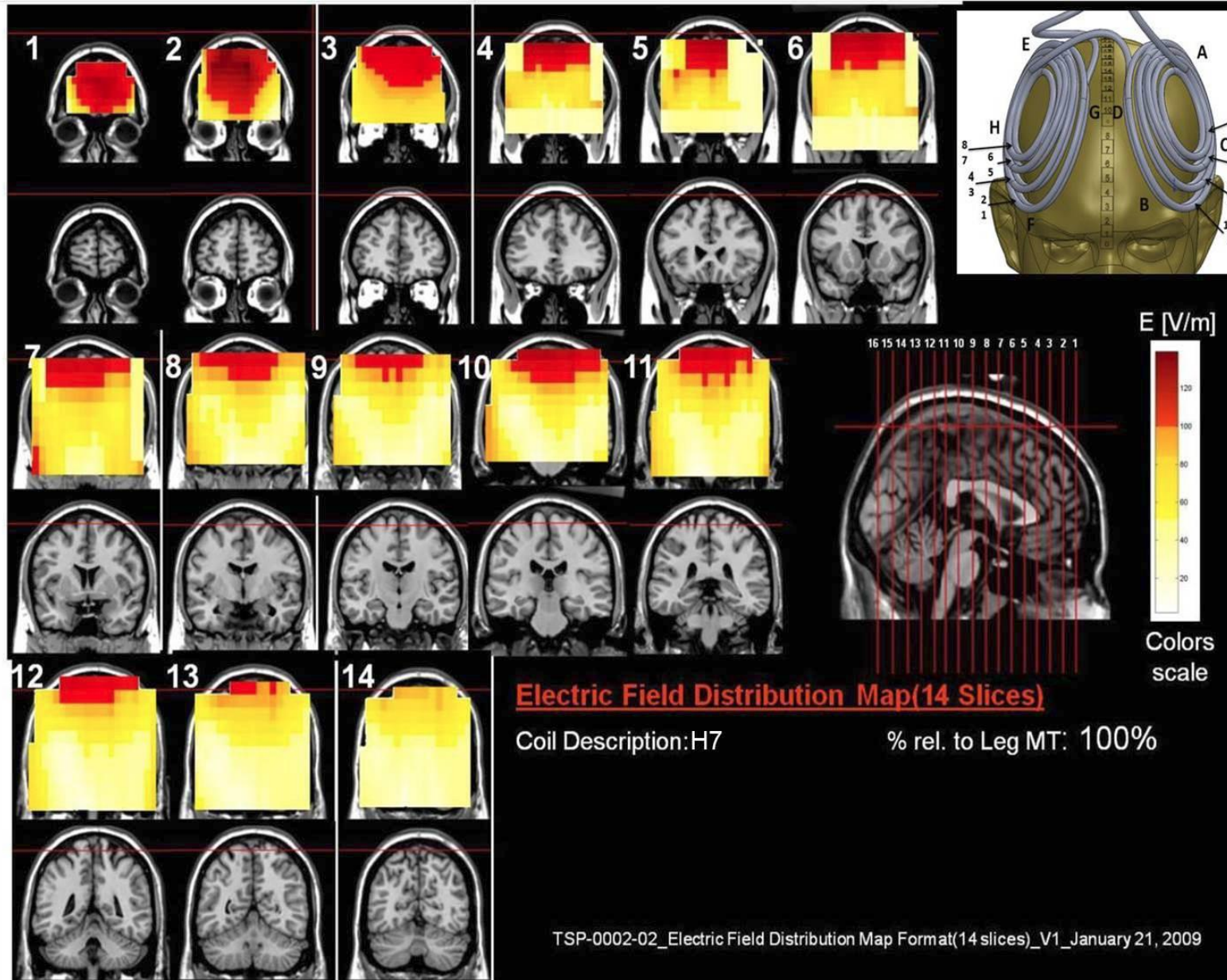
- Michael Faraday (1831) - Rapidly changing electrical currents induce rapidly changing magnetic fields
- Electric field (E-field) applied over neuronal tissue has been used for many decades of research to induce **neuronal depolarization and action potentials**
- The more the neuron and current are aligned, the greater the activation



The H7 Coil



H7 Magnetic Field Generation

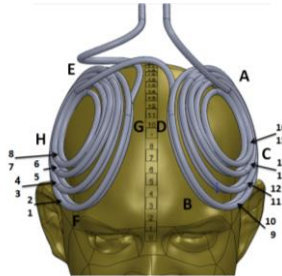
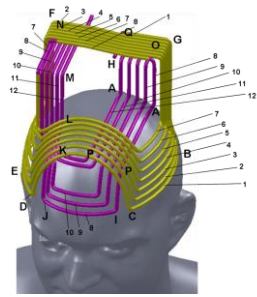
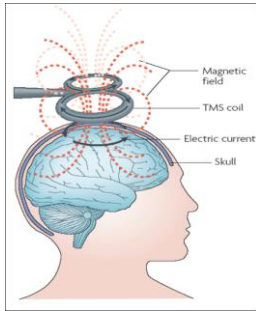


Key Technical Differences

Figure 8

H1

H7



**0.7 cm
Subdural**

**1.8 cm
Subdural
✓ 2.5x
Deeper**

**3 cm
Subdural
✓ 4x Deeper**

**3 cm³
Volume**

**18 cm³
Volume
✓ Millions of
More
Neurons**

**70 cm³
Volume
✓ Millions of
More
Neurons**

Deep TMS for OCD was FDA-Cleared based on a Multicenter Double-Blind RCT (AJP 2019)

Study Title

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

Principal Investigators

Joseph Zohar, MD
Abraham Zangen, PhD

Study Sites

11 sites from North America and Europe

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

Israel

- Tel Hashomer Hospital

Canada

- Center for Addiction and Mental Health

94 Patients Met the Inclusion-Exclusion Criteria, and Double Blinding Was Effective



Demographics



- ▶ 58% Male
- ▶ 75% Caucasian
- ▶ 83% over 12 years of education
- ▶ Mean Age of onset 13(6.5)
- ▶ Mean age first sought help 23(10)
- ▶ Prior meds 98% (19% took 5 SSRI's)
- ▶ Prior CBT 69%
- ▶ Family hx OCD 55%

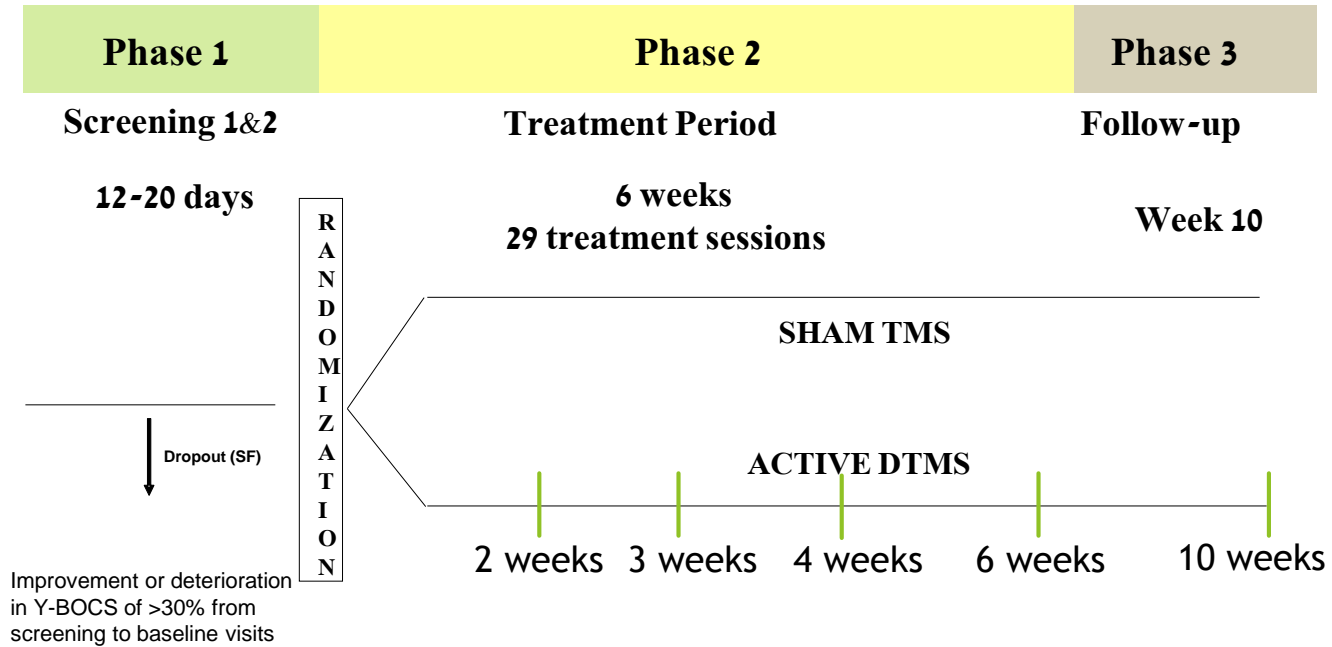
Participant Blinding

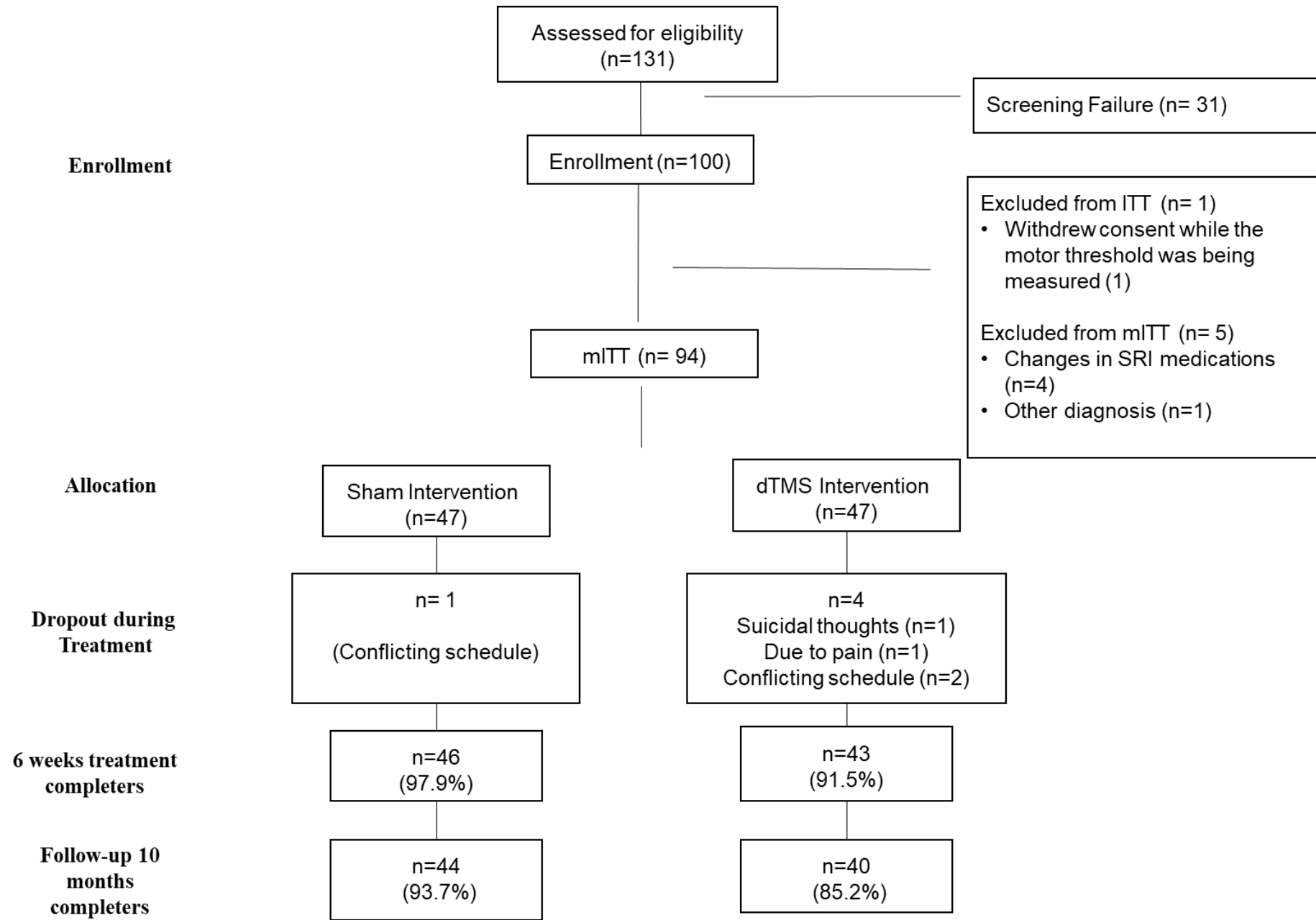
- At the end of the first session participants were asked which treatment they received
- A logistic model was used to assess if the response to the forced question is predictive to the treatment received. The p-value of the type III for the forced question was 0.1043.

Inclusion Criteria

- ▶ Outpatients
- ▶ Men and women 22-68 years of age
- ▶ Diagnosed as suffering from OCD according to DSM-IV-TR
- ▶ Subjects with at least moderate OCD (Y-BOCS score of ≥ 20)
- ▶ Subjects are maintained on SSRI medications approved for treatment of OCD at a therapeutic dosage for at least 2 months prior to study entry and for the duration of the trial and/or undergoing psychotherapeutic behavioral interventions (in the maintenance stage (i.e. not during the assessment or skills acquisition or training stages)).

STUDY FLOW CHART





BrainsWay H7 was shown to be safe, generally well-tolerated, with no serious adverse events (AE)

Overall Adverse Events Reports

- Active dTMS group: 35 subjects (73%)
- Sham group: 35 subjects (69%)
- No significant difference (chi-square p-value: 0.6393)
- Most frequent AE was headache (37.5% of patients receiving dTMS; 35.3% of patients receiving sham)
- No device-related serious adverse event

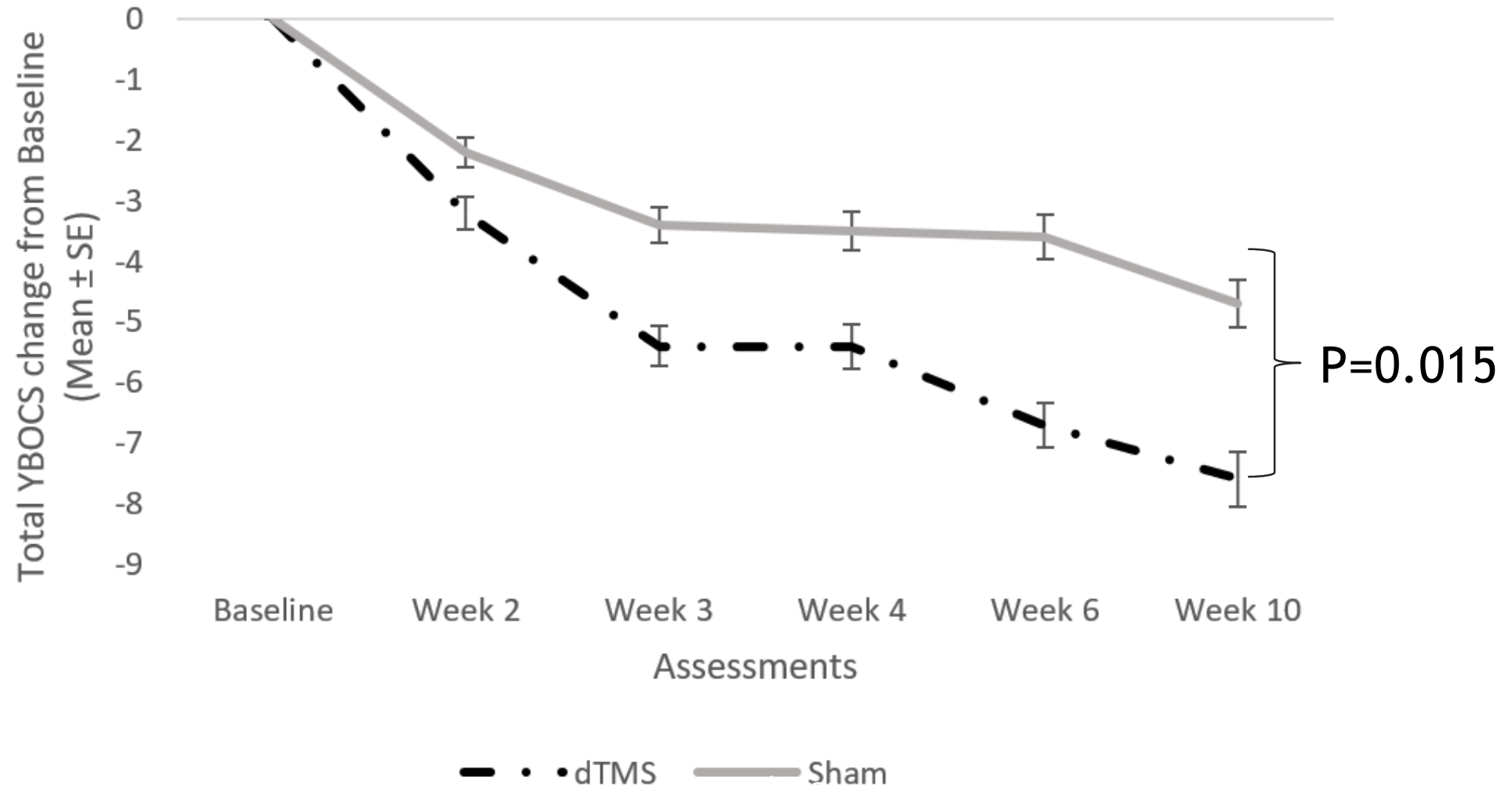
Common Side Effects

- Head aches and scalp discomfort
- Resolved after the treatment
- Only one drop out due to pain

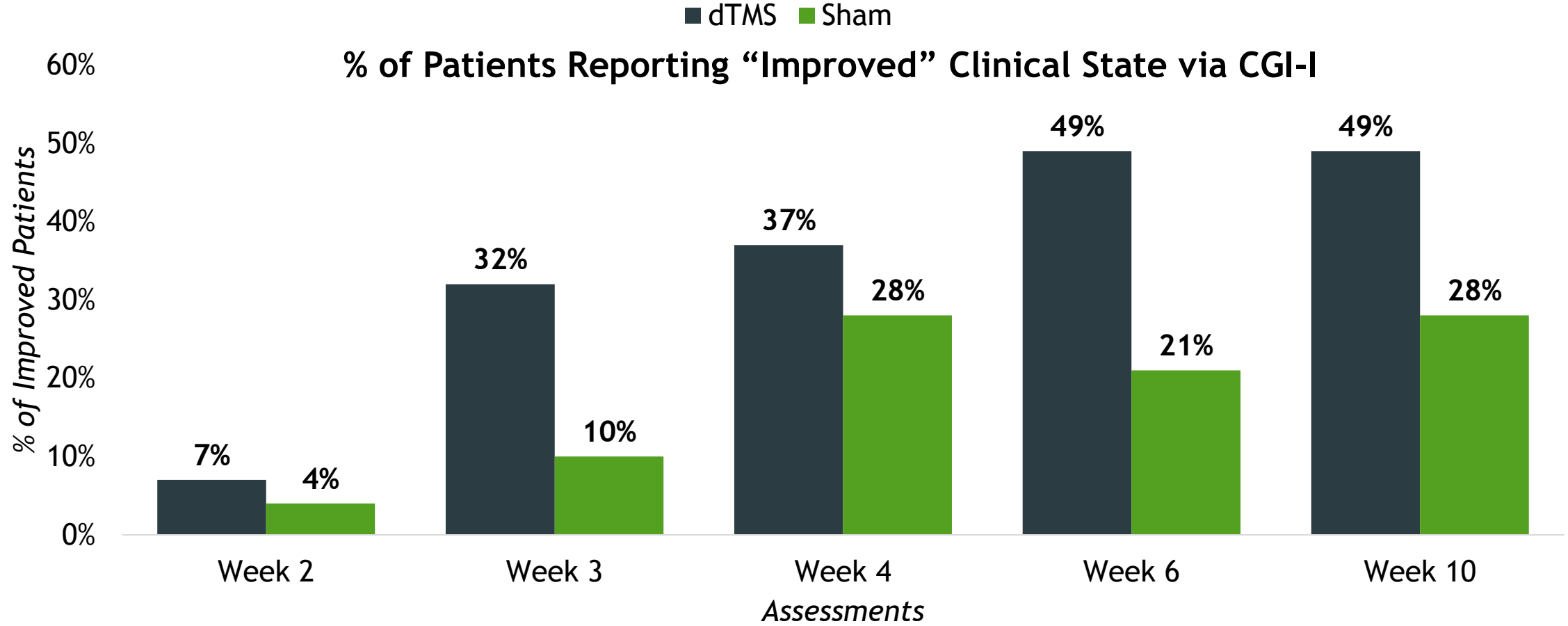
Low Drop-Out Rate

- By week 6: 10 drop outs (6 active and 4 sham)
- By week 10: additional 4 drop outs (1 active and 3 sham)

Substantial Improvement Was Seen in Y-BOCS Scores

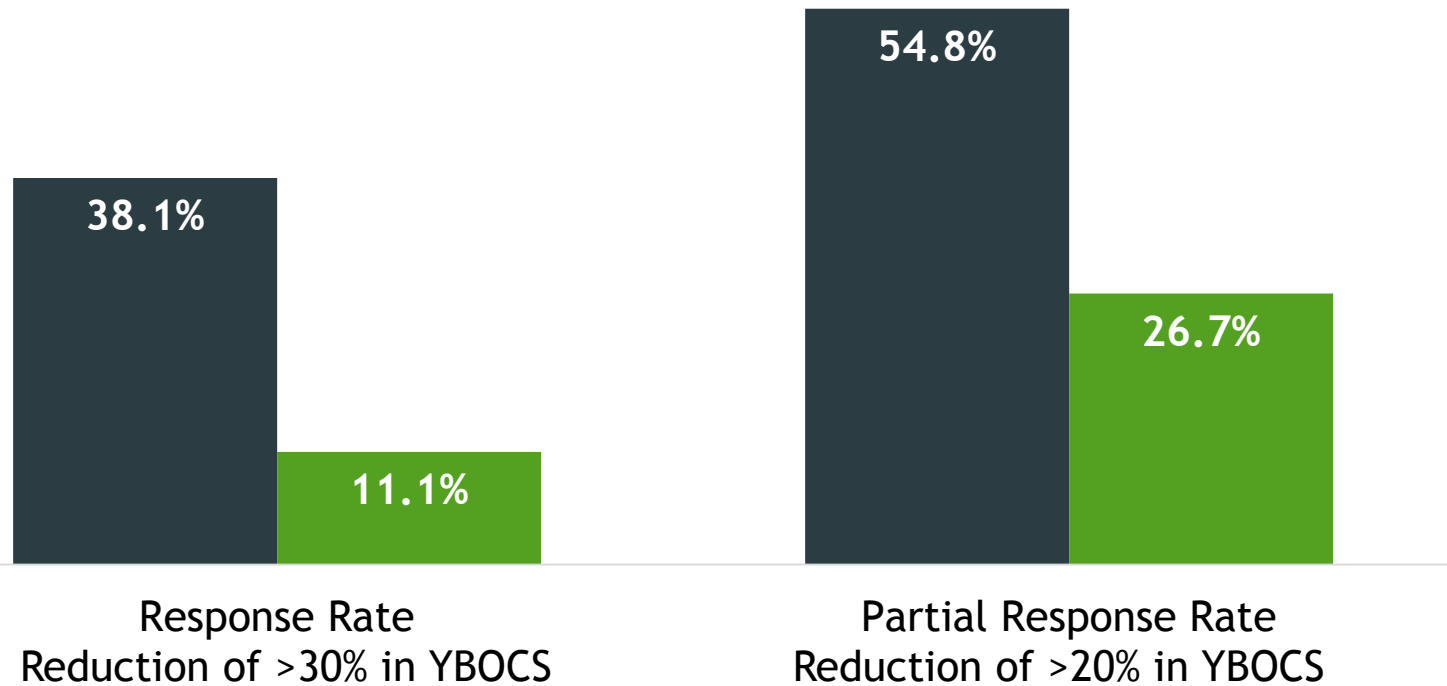


Significant Improvement Was Also Seen in CGI-I Scores, Which Was Sustained Through Week 10



Response & Partial Response Rates at 6 Weeks

■ dTMS ■ Sham



Response was achieved among patients who did not experience relief from SSRIs or psychotherapy

Number Need to Treat (NNT) for Response after 6 weeks of treatment is 3.7

OCD Symptoms Must Be Provoked

- Provocation consists of an internal or external stimuli which will provoke or induce typical OCD symptoms and distress in that subject
 - *Internal provocations are questions related to thoughts, images or impulses that usually trigger the compulsive behavior*
 - *External provocations typically use photos, auxiliary tools, or asking the patient to complete part of a task*
- The subject will be exposed to it for a period of up to 5 minutes
- The goal of the provocation is to induce a moderate-to-major distress (VAS score of 4-7) immediately before initiating dTMS

Visual Analog Scale

How much does the script/photo cause you distress right now?



Provocations Are Designed in an 7-Step Process



The Provocation is Important

7

Review With Operators

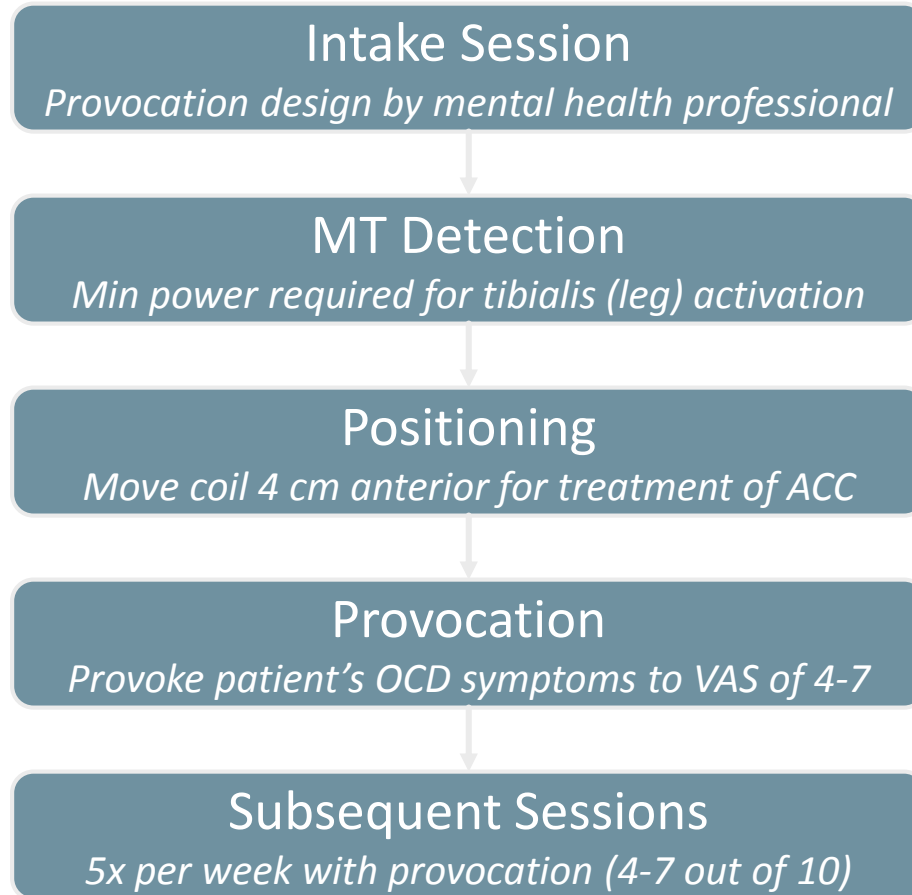
- VERY IMPORTANT! Discuss and review the provocations with the operators so they are clear on the manifestations of the obsession or compulsion
- Example:
 - *Operator provokes about a dirty floor and believes the provocation's reasoning is the patient's will to be clean. However, the patient only gets distressed if the floor is dirty from orange or red clay, not sand or soil and the provocation is less effective*

Leg Motor Threshold

- ▶ Shoes and socks off
- ▶ Legs stretch out, bend at the knee, toes passively pointed to ceiling
- ▶ Coil 8cm AP at midline. 50% MO. Increase by 5% until impulse
- ▶ Move coil front back and up-down to maximal impulse. NOTE: UP-DOWN is new!
- ▶ Decrease intensity for minimal impulse (digital muscle activity in 3 or 6 trials)
- ▶ Localize further (if location is < 3 or > 15 then the location is wrong)
- ▶ Can perform active MT by raising leg and foot off ground, but must stimulate at 115% of this value
- ▶ Treatment location is 4cm anterior to the LMT (Leg Motor Threshold)



Provocations Must Occur *After* Measuring the Patient's Motor Threshold and Positioning the Coil for Treatment



Treatment Parameters

- ▶ dMPFC & ACC (4cm anterior to leg MT)
- ▶ **Power:** 100% of resting foot MT
- ▶ **Frequency:** 20 Hz
- ▶ **Duration:** 2 sec
- ▶ **# Pulses:** 40 pulses
- ▶ **Inter-Train Interval:** 20 sec
- ▶ **# Trains:** 50 trains
- ▶ **Total # of Pulses:** 2000 stimuli per session
- ▶ **# Sessions:** 29 treatment sessions
- ▶ **Treatment Time:** 18.3 minutes
- ▶ The number of treatment sessions consists of 5 daily sessions for 5 weeks, and 4 daily session in the 6th week.

Managing Intolerance

1. Apply a trial train of 0.5 sec, 20 Hz, at a power output of 100% of the MT.
2. Apply a trial train of 1 sec, 20 Hz, at a power output of 100% of the MT.
3. Apply a trial train of 2 sec, 20 Hz, at a power output of 100% of the MT.

Decreasing MT percent stimulation below 100 is NOT recommended

Brainsway H7 Device



Summary

- ▶ OCD is a common disorder with limited treatment options
- ▶ OCD has its etiology in neural network dysfunction
- ▶ Transcranial Magnetic Stimulation with the H7 coil offers a novel mechanism to alter neural network dysfunction in OCD and alleviate symptoms

Questions?