

# Predictors of response to deep transcranial magnetic stimulation treatment in obsessive-compulsive disorder

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 16/11/2023	<b>Overall study status</b> Ongoing	<input checked="" type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 16/11/2023	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Repetitive transcranial magnetic stimulation (rTMS) is a method used for non-invasive brain stimulation. It's employed both for research purposes and as a treatment for various neurological and psychiatric disorders. Furthermore, it has been explored as a potential therapy for Obsessive-Compulsive Disorder (OCD). Traditionally, rTMS targets the prefrontal cortex, particularly the left, right, and bilateral dorsolateral prefrontal cortex, using a figure-of-eight coil.

In recent times, rTMS for OCD has focused on the dorsomedial prefrontal cortex, such as the anterior cingulate cortex, employing specialized coils like the H7 or double-cone coil to reach deeper into the cerebral hemispheres. Based on the findings of previous deep TMS (dTMS) studies in treating OCD, a recent analysis supports considering the H7-coil dTMS as the primary approach for individuals with treatment-resistant OCD, particularly those resistant to serotonin reuptake inhibitors (SRI-R).

However, the effectiveness of dTMS in reducing OCD symptoms varies significantly among patients. Approximately 50% of patients experience a significant decrease in OCD symptoms based on data from published dTMS studies. The presence of a considerable number of non-responders creates challenges, such as subjecting individuals to a treatment that doesn't benefit them, missing the opportunity for alternative treatments, and increasing healthcare costs.

To address these challenges, a research project aims to understand why some OCD patients do not respond to deep rTMS. The primary objective of the project is to investigate the effects of dTMS on the medial prefrontal cortex (mPFC) in OCD patients and identify the specific brain factors that might cause a lack of response to mPFC-dTMS.

In individuals with OCD, structural brain characteristics typically involve smaller volumes in certain mPFC regions, increased volume in the basal ganglia, and decreased volume in specific white matter regions. There are also functional changes in OCD, including altered communication between the ventromedial prefrontal cortex and the striatum, increased brain

wave activity when errors occur, and heightened amplitudes of slow-frequency EEG rhythms when the brain is at rest.

The project will test the hypothesis that the size and structure of certain brain regions before treatment can predict whether a patient will respond to dTMS. Additionally, the project will investigate changes in both gray matter and white matter in the brain after a six-week dTMS treatment to determine if the absence of these changes plays a role in non-responsiveness to dTMS.

The research will also examine pre-treatment levels of brain activity when errors are made, brain wave amplitudes at rest, functional brain activity when OCD symptoms are provoked, and communication within the mPFC as potential predictors of the response to dTMS treatment. The expectation is that changes in functional brain activity before and after treatment will be observed in individuals who respond positively to dTMS but not in non-responders.

Who can participate?

Adults aged 18-75 years with OCD.

What does the study involve?

The study includes a 6-week dTMS treatment with ongoing assessment of clinical status and repeated MRI and EEG examinations before and after dTMS treatment.

What are the possible benefits and risks of participating?

Benefits

Relief of OCD symptoms after dTMS treatment.

Risks

Adverse effects (AE) during dTMS treatment are usually very low, with headache being the most common AE. This AE should not lead to withdrawal and can be managed with non-prescription pain medication.

Where is the study run from?

National Institute of Mental Health (Czechia)

When is the study starting, and how long is it expected to run for?

May 2023 to February 2028

Who is funding the study?

National Institute of Mental Health (Czechia)

Who is the main contact?

Assoc. Prof. Monika Klířová M.D., Ph.D., [monika.klirova@nudz.cz](mailto:monika.klirova@nudz.cz)

## Contact information

**Type(s)**

Public, Scientific, Principal investigator

**Contact name**

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## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### ClinicalTrials.gov (NCT)

Nil known

### Protocol serial number

AZV-2024-1-0002 (RZPRO)

## Study information

### Scientific Title

Neural Predictors of Treatment Response to Deep Transcranial MAGnetic Stimulation (dTMS) of Medial Prefrontal Cortex in Obsessive-COMPulsive Disorder

### Acronym

MASCOD

### Study objectives

1. The volume of the striatum and medial frontal cortex (mPFC) prior to a course of a 6-week deep transcranial magnetic stimulation (dTMS) therapy will differentiate responders (>35 % drop in obsessive-compulsive disorder (OCD) symptoms) and non-responders.
2. The volume of the mPFC will increase following a course of dTMS therapy, especially in responders.
3. The structure of white matter (WM) in the sagittal stratum and cingulate bundle prior to treatment will differentiate responders and non-responders.
4. Functional connectivity (FC) of the striatum with (mPFC) and the orbitofrontal cortex (OFC) prior to treatment will differentiate dTMS non-responders from responders, and the FC will change following treatment in responders but not in non-responders.
5. Hyperactivation in different brain regions during symptom provocation prior to treatment will differentiate responders from non-responders, and activations in involved brain regions will decrease following treatment in responders but not in non-responders.
6. Amplitudes of delta and theta oscillations prior to treatment will differentiate dTMS responders and non-responders; amplitudes of delta and theta oscillations will decrease following treatment in responders but not in non-responders.

7. The amplitude of the error-related negativity (ERN) in the arrowed flanker task prior to treatment will differentiate dTMS responders and non-responders; ERN will decrease following a course of dTMS more in responders than in non-responders.

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

approved 18/05/2023, National Institute of Mental Health Ethics Committee (Topolova 748, Klecany, 25067, Czech Republic; +420 (0)283 088 312; ek@nudz.cz), ref: 102/23

### **Study design**

Randomized parallel-group double-blind placebo-controlled trial

### **Primary study design**

Interventional

### **Study type(s)**

Treatment

### **Health condition(s) or problem(s) studied**

Obsessive-compulsive disorder

### **Interventions**

Patients diagnosed with OCD will be included in the study.

Visit -1 (-20 - 0 days):

Anamnesis, including demographic data and medical history, checking the adequate maintenance treatment.

Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), Hamilton Depression Rating Scale (HAM-D), and Clinical Global Impression Scale (CGI).

Assessment of whether the subject can be included in the study, including determination of the motor threshold.

Informed consent.

Next, subjects will be randomly assigned to one of the groups (active n=60, sham n=15).

Visit MRI (-7 – 0 days).

Visit EEG (-7 – 0 days).

Visit 0 (-2 – 0 days): Y-BOCS, HAM-D, CGI, checking medications, if used.

dTMS:

Active stimulation: 20Hz mPFC-dTMS, 100% of motor threshold, 40 trains, 50 pulses per train, 18 minutes duration; 2000 pulses per session; 28 sessions in 6 weeks. Placebo: sham-dTMS applied to mPFC; 28 sessions in 6 weeks.

All mPFC-dTMS applications will be preceded by OCD symptoms provocation for five minutes before the start of the mPFC-rTMS/sham session (according to FDA protocol for rTMS in OCD).

Subjects will be on stable medication during the acute phase of the study (deep TMS treatment) if taken and on maintenance psychotherapy if attending.

Visit 1 (14 ± 2 days): Y-BOCS, HAM-D, CGI, and side effect TMS assessment, checking medications, if used.

Visit 2 (28 ± 2 days): Y-BOCS, HAM-D, CGI, and side effect TMS assessment, checking medications, if used.

Visit 3 (42±2 days): Y-BOCS, HAM-D, CGI, and side effect TMS assessment, checking medications, if used.

Visit MRI II (42 + 7 days).

Visit EEG II (42 + 7 days).

Follow-up visit 4W (70 ± 5 days): Y-BOCS, HAM-D, CGI, checking medications, if used.

Follow-up visit 12W (126 + 5 days): Y-BOCS, HAM-D, CGI, checking medications, if used.

## **Intervention Type**

Device

## **Phase**

Phase III

## **Drug/device/biological/vaccine name(s)**

MagPro R30 with a double-cone coil (Magventure) and deep TMS (DTMS) System with H7 coil (Brainsway). The first ten patients will be stimulated with MagPro R30 using a double-cone coil device, and the remaining 65 with a deep TMS system using an H7 coil.

## **Primary outcome(s)**

Neuronal predictors of therapeutic success of mPFC-dTMS in OCD patients using MRI by evaluating pre- and post-treatment dTMS-mPFC changes in grey matter (GM) in the anterior cingulate cortex (ACC), mPFC, OFC, and striatum, and WM in selected tracts and bundles using fMRI.

## **Key secondary outcome(s)**

Neuronal predictors of therapeutic success of mPFC-dTMS in OCD patients using EEG and MRI by evaluating pre- and post-treatment dTMS-mPFC changes in:

1. EEG resting state oscillations;
2. ERN during the Flanker task;
3. Resting-state FC of the ACC, striatum, and the prefrontal cortex (PFC)/OFC
4. Blood oxygenation level-dependent (BOLD) - functional MRI (fMRI) activations during the exposure to individual OCD symptoms-related visual stimuli.

## **Completion date**

28/02/2028

## **Eligibility**

**Key inclusion criteria**

1. Male and female outpatients aged 18-70 years;
2. Meeting DSM-V criteria for OCD;
3. Patients having completed at least one unsuccessful but adequate antidepressant treatment according to criteria for treatment-resistant OCD (treatment history is sufficient);
4. Being able to understand and sign the Informed Consent Form;
5. Being on a stable and adequate dose of antidepressants and/or antipsychotics (monotherapy or combination) for at least eight weeks before the commencement of dTMS, if used.
6. Y-BOCS score  $\geq 20$  corresponding to the Severity scale  $\geq$  three on Clinical Global Impression on the initial visit.

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

70 years

**Sex**

All

**Key exclusion criteria**

1. Psychiatric comorbidity on axis I and II according to DSM V six months before enrollment to the study except for depressive, anxiety, and obsessive-compulsive related disorders;
2. Personality disorder that makes participation in the trial difficult;
3. History of substance dependence in the last year except for nicotine;
4. Contraindications of rTMS/dTMS treatment;
5. Pregnancy or breast-feeding;
6. Patients with severe somatic disorders (cardiovascular disease, neoplasms, endocrinology disorders, etc.);
7. Patients treated with electroconvulsive therapy less than three months before enrollment or suffering from neurologic disorder (e.g., epilepsy, head trauma with loss of consciousness) and patients using any treatment that can strongly affect EEG;
8. Substantial suicidal risk as judged by the treating psychiatrist;
9. Sensory and motor impairment precluding the participation in computer tests.

**Date of first enrolment**

20/07/2023

**Date of final enrolment**

31/12/2027

# Locations

## Countries of recruitment

Czech Republic

## Study participating centre

National Institute of Mental Health

Topolova 748

Klecany

Czech Republic

250 67

# Sponsor information

## Organisation

3rd Medical Faculty, Charles University

# Funder(s)

## Funder type

Government

## Funder Name

National Institute of Mental Health, Czechia

# Results and Publications

## Individual participant data (IPD) sharing plan

After the article's publication, de-anonymized data will be made available for non-commercial academic projects. Data can be obtained by request to the corresponding author (Monika Klírová, monika.klirova@nudz.cz). The de-anonymized data files with a dictionary will be provided via a secure data transfer service.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes

