INFORMED CONSENT FORM FOR PARTICIPATION IN RESEARCH PROTOCOLS

Study Title: **Randomized trial, parallel-group to compare effect of low-intensity transcranial magnetic stimulation (Li-TMS) on sleep disorders, inflammation levels, and brain-derived neurotrophic factor in patients with depression.**

NCT ID not yet assigned. 05/12/2024.

Registration number: R-2024-785-075.

Rationale and objective of the study:

Major depressive disorder (abbreviated as MDD) is a condition that affects a person's mood, with its main characteristics being a constant feeling of sadness, and an inability to derive pleasure from activities that once brought joy (going out with friends, reading a book, playing sports, eating, etc.). This can lead to difficulty falling asleep, impairing the quality of life for those affected and having significant consequences for their personal, social, and work relationships. Currently, there are many treatment options to improve symptoms; however, only 30 to 40 out of every 100 people show improvement—that is, less than half of all those receiving medication and/or psychological therapy—leading to relapses, worsening, or persistence of depressive symptoms. New treatments have now been developed to complement medication and/or psychological therapy in improving symptoms. "Transcranial Magnetic Stimulation" is a non-invasive therapy that involves generating a low-intensity magnetic field (similar to the energy produced by a magnet when brought near metal), which is applied at specific points on the head at a certain distance. This stimulates brain cells, reducing symptoms such as sadness, despair, and guilt, and improving sleep at the start of treatment, with few or almost no side effects; the most common is a headache, which usually goes away without medication a few minutes after the device is removed. It is expected that with the application of transcranial magnetic stimulation, you will experience a decrease of at least 9 points on the Hamilton Depression Scale, as well as a reduction of 15 minutes in the time it takes to fall asleep when you go to bed and that your sleep will be continuous, a reduction in feelings of fatigue during the day, and a reduction in blood inflammation levels as evidence of improved depression compared to your initial tests, along with an increase in the brain-protective substance known as BDNF. However, you may not experience any of the aforementioned improvements; the results obtained may help in recommending this therapy for other patients with the same condition.

Possible risks and side effects:

Psychological tests will be used, which do not pose any significant risk, either immediate or long-term. Risks associated with blood sampling. Among the possible complications associated with blood sampling, it is worth noting the occurrence of a bruise, which is defined as a change in skin color to a violet or purple hue, typically less than 2 cm in size, about the size of a bean, that appears in approximately 2 out of every 10 people who require a blood sample via puncture and usually resolves on its own within the following 2 weeks. Other possible complications or discomforts include pain at the time of the puncture, which may last 5 to 10 minutes after the procedure.

Risks associated with "Transcranial Magnetic Stimulation" treatment: local discomfort or a sensation of heat in the area of the scalp where the magnetic stimulation is applied, as well as mild to moderate headaches; headaches have been reported in 10 out of every 100 patients undergoing Transcranial Magnetic Stimulation; they usually resolve on their own within 30 minutes to 2 hours after the Transcranial Magnetic Stimulation device is removed, It is important for you to know that headaches can be caused by other factors, such as stress or lack of sleep, as well as the consumption of certain foods and substances. If you experience a headache at any time other than during transcranial magnetic stimulation, it is important that you notify the research team and describe the circumstances that led to its onset or whether it occurred without the use of the stimulator, so that our team can determine what caused it or whether it was related to the transcranial magnetic stimulation device. Other possible complications include nausea or vomiting (reported in 5 out of every 100 patients). With the type of treatment, you will receive, no seizures have been reported; however, it has been observed that in

patients with arteriovenous malformations, those taking medications such as olanzapine, risperidone, and other antipsychotics, as well as those with intracranial tumors, the risk of seizures with the use of transcranial magnetic stimulation is 2 per 100,000 sessions, so our team will be on alert. In the event of a seizure, you will receive immediate medical attention; the therapy will be suspended, and you will be taken to the Emergency Department where you will receive appropriate treatment and undergo evaluation to identify the cause.

Should any symptoms arise, the unit has all the necessary medical and technical resources to provide care.

If, during the course of the study, you notice that your depression-related symptoms worsen, or if you experience suicidal thoughts, you should follow these steps: 1) If you are currently undergoing "Transcranial Magnetic Stimulation," you must immediately notify the research team, who will notify, a physician assigned to the Psychiatry Department at UMAE 1, who will manage the exacerbations. If symptoms warrant it, you will be taken (always accompanied by a researcher) to the Emergency Department at UMAE 1 to receive the most appropriate treatment; 2) If symptoms worsen while you are outside the Research Unit, you must notify by phone or email, and inform a family member; you must go immediately to the UMAE 1 Emergency Department—if possible, always accompanied by someone—to receive the most appropriate care; If you are unable to go to the UMAE T1 Emergency Department, you will receive emotional support and guidance there. Although this situation is not related to the use of transcranial magnetic stimulation, it is considered an emergency within the course of Major Depressive Disorder and should therefore be treated as such.

Potential benefits you may receive by participating in the study:

A 20-session course of transcranial magnetic stimulation. Potential reduction in the severity of depressive symptoms, as well as potential improvement in symptoms associated with insomnia, such as easier falling asleep and longer sleep duration. Information on blood levels of inflammation markers and neurotrophic factors, which will provide an overall picture of health status and response to treatment for depressive symptoms.

Information on test results and treatment options:

There are alternatives to treatment for depressive disorder, such as antidepressant medication and psychotherapy. Should new options emerge that are safer and more effective than expected with this type of treatment, you will be provided with the necessary information so that you can decide whether or not to continue with Transcranial Magnetic Stimulation. You will also be informed if new evidence regarding Transcranial Magnetic Stimulation therapy indicates any other adverse effects or if another treatment is recommended. During this procedure, you will not discontinue your current treatment.

Participation or withdrawal

Participation is voluntary, involves no cost to the participant, and does not provide any financial compensation. As a participant, you may withdraw from the study at any time and for any reason you deem appropriate, without this affecting your regular psychiatric treatment or your care for any other reason within the Mexican Social Security Institute. In the event that the researcher observes the expected effect earlier than anticipated, or if another research team conducting a similar project notifies you, you will be informed so that you may receive the intervention if you are in the group not receiving Transcranial Magnetic Stimulation.

Privacy and confidentiality:

The participant's name or personal identifying information will not appear in any part of the study, presentations, or publications that may result from it; their personal information will be kept strictly confidential, respecting their privacy at all times through the assignment of a reference number.

Conflict of interest

The researchers have no conflicts of interest.

In the case of biological material collection (blood sample) (Storage period: 15 months)

- I do not consent to the collection of the sample.
- I consent to the collection of the sample for this study only.
- I consent to the collection of the sample for this study and future studies.

If you have any questions or need further clarification regarding the study, please contact:

If you have any questions or need clarification regarding your rights as a participant, please contact: IMSS CNIC Research Ethics Committee: 330 Cuauhtémoc Avenue, 4th Floor, Block "B" of the Congress Center, Colonia Doctores. Mexico City, CP 06720. Phone (55) 56 27 69 00 ext. 21230, Email: comiteeticainv.imss@gmail.com

If, during your participation in the study, you experience or notice any discomfort, pain, irritation, skin changes, or other events resulting from taking or receiving the treatment, please contact: Pharmacovigilance Department, by phone at (55) 56276900, ext. 21222,

Name and signature of the person obtaining consent

Name and signature of the subject

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