An open-label trial of sequential bifrontal low frequency repetitive transcranial magnetic stimulation (r-TMS) in the treatment of primary insomnia.

NCT:02196025

Informed consent

8/21/2019

UF IRB-01 Approved UF

UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position:_____

Please read this form which describes the study in some detail. A member of the research team will describe this study to you and answer all of your questions. Your participation is entirely voluntary. If you choose to participate you can change your mind at any time and withdraw from the study. You will not be penalized in any way or lose any benefits to which you would otherwise be entitled if you choose not to participate in this study or to withdraw. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 2739600.

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study?

An open label trial of sequential bifrontal low frequency repetitive transcranial magnetic stimulation (r-TMS) in the treatment of primary insomnia.

3. Who do you call if you have questions about this research study?

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Principal Investigator: Richard Holbert, M.D. 352-265-4357

4. Who is paying for this research study?

The sponsor of this study is the University of Florida.

5. Why is this research study being done?

The purpose of this research study is to evaluate the effectiveness and safety of a possible new treatment for insomnia called repetitive Transcranial magnetic stimulation (r- TMS).TMS is a non-invasive treatment that uses magnetic stimulation to modulate brain activity in a superficial part of brain called the cerebral cortex. This area has shown to be more active in patients with insomnia. TMS has been shown to be effective in alleviating depressive symptoms, however, it is not yet known if it can be used as a non-medication treatment for insomnia.

You are being asked to be in this research study because you have insomnia and are interested in this non-medication treatment.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

6. What will be done as part of your normal clinical care (even if you did not participate in this research study)?

Normal clinical care for insomnia includes evaluation and treatment with one or more of the techniques that include medications, cognitive behavior therapy for insomnia or a combination of the two. To meet entry criteria for this study, you must have insomnia. Transcranial magnetic stimulation treatment for insomnia is experimental and not an approved treatment modality for insomnia.

7. What will be done only because you are in this research study?

If you decide to participate, you will be asked to read, sign, and date this informed consent before any study-related procedures are performed. In order to find out if you meet the requirements to participate in the study, you will be evaluated by study doctors and members of the research staff. During this time you will be asked a series of questions by interview about your symptoms. The evaluation will also involve collecting basic information (such as age, sex, and race) and psychiatric, medical, and family history. You will also have a general physical exam that will include measuring vital signs (heart rate and blood pressure).

If you continue to meet eligibility requirements and choose to participate, you will also be required to wear an actigraph (a wrist watch that tracks your sleep-wake activity). You will be asked to wear it 24 hours a day during the 3 weeks of

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treatment. The actigraph is waterproof and you can shower with it on. We will also ask you to fill in daily sleep logs throughout the study. If you are a female of child bearing potential you will receive a urine pregnancy test on Day 1 to make sure that you are not pregnant. It is important that you use a highly reliable birth control method throughout the study period. Acceptable forms include hormonal contraceptives, barrier methods, and abstinence.

We will also ask you not to make any changes to your current medications if possible during your participation in the study. Should a medical situation arise and you need to start or stop a medication please let the study doctor know right away.

As a study participant, you will be asked to return to the clinic every weekday for 3 weeks to receive treatment with r-TMS for about 80 (40 minutes on each side of the head) minutes each day. With NeuroStar TMS Therapy, the “stimulator” provides electrical energy to a “treatment coil” that delivers a magnetic field in short bursts or “pulses”. When the coil is placed against the scalp on the left front region of the head, the pulsed magnetic field is focused into a region of the brain that is thought to be involved in causing depression. Some patients have described the sensation as a slight tapping on the head. Below is a picture of the NeroStar System.

You will also be asked to answer some questions by interview and fill in questionnaires about your symptoms on days 1, 7, 14 and 21. This will take —an additional 30 minutes.

The following questionnaires/measures will be completed:

Insomnia severity Rating Index: It is a 7-item self-report questionnaire assessing the nature, severity, and impact of insomnia.

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PIRS: Pittsburgh Insomnia Rating Scale: It is a 66-item self-report questionnaire used to rate severity of insomnia.
PSQI: Pittsburgh Sleep Quality Index: It is a 10-item scale evaluating various domains of subjectively reported sleep.
ESS: Epworth Sleepiness Scale: It is an 8-item self-report questionnaire used to determine the level of daytime sleepiness.
MADRS: Montgomery Asberg Depression Rating Scale: it is a 10-item questionnaire used by clinicians to rate the severity of depression.
Clinical Global Impressions-Severity: The CGI-S is a 7-point rating by a clinician of how severe your symptoms appear. Severity ratings range from 0 (no illness) to 6 (extremely severe).
Mini-Mental State Examination (MMSE) -assesses potential impairment in thinking.
Sleep diary: Sleep diaries are used both in research and clinical practice in the treatment of insomnia. You will be asked to complete the sleep diary daily during the 3 week treatment period, reporting bedtime, wake up time, awakenings and various other daytime activities.
Actigraphy: You will be asked to wear an actigraph for the 21 days of TMS treatment. An actigraph is a wrist device that is worn like a watch. It records physical activity, light exposure and provides objective information about the rest-activity/sleep cycle.

Schedule of Events	Day 1	Day 2-6	Day 7	Day 8-13	Day 14	Day 15-20	Day 21
Informed Consent	X						
Physical Exam	X						
Psychiatric interview	X						
Vital Signs	X*						
Insomnia severity Rating Index	X*		X		X		X
Pittsburgh Sleep Quality Index	X*		X		X		X
MADRS	X*		X		X		X
CGI	X*		X		X		X
MMSE	X*		X		X		X
Sleep diary	X*	X	X	X	X	X	X
Actigraphy	X*	X	X	X	X	X	X
TMS treatment	X*	X	X	X	X	X	X
Adverse Events and Concomitant Medications	X*	x	x	x	x	x	x

*You will complete these activities only if you are determined to be eligible on the basis of the preliminary exams and psychiatric interview. If you have any questions now or at any time during the study, please contact one of the research team members listed in question 3 of this form.

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8. How long will you be in this research study?

If you agree to take part in this study, your involvement will last approximately 3 weeks.

9. How many people are expected to take part in this research study?

We expect to enroll 35 subjects in the study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

10. What are the possible discomforts and risks from taking part in this research study?

In clinical trials involving 10,000 active treatments with the NeuroStar TMS Therapy System, less than 5% of patients studied discontinued treatment due to side effects. The most common reported side effect associated with TMS treatment was pain or discomfort at or near the treatment location. This can be experienced as scalp irritation or headache. Not all patients experienced this side effect and, when present, it was generally mild to moderate in intensity and tended to decrease after the first weeks of treatment. You may choose to take an over the counter pain reliever recommended by your physician such as acetaminophen (Tylenol) or ibuprofen (Motrin) before a treatment to decrease these sensations. If you feel a lot of discomfort, adjustments can be made to make treatments more tolerable.

There is a rare chance of seizure. In clinical trials using the NeuroStar Therapy System, which included over 10,000 TMS treatments, no seizures were reported. The current device labeling warns that the expected and observed frequency and of occurrence of seizure is approximately 1 in 30,000 treatments (0.003%) and 1 in 1000 patients (0.1%).

In the event that you have a seizure, the study staff will immediately stop the treatment session. You will be observed for a period of time after the seizure to make sure you are feeling well, and someone will be asked to drive you home that day.

Because the NeuroStar Therapy TMS System emits a loud noise, and there is a small risk of temporary hearing loss, you will wear protective ear plugs during treatment.

The effect on pregnancy and the unborn fetus are unknown and pregnant women are excluded from the study. Women of child bearing potential should use a

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medically acceptable birth control method during the trial. Acceptable methods are described earlier under section 7, above.

Other possible risks to you may include mild discomfort resulting from answering the questionnaires and checklists and discussing potentially difficult topics. However, most people welcome the opportunity to discuss their experiences with a trained clinician.

Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 17-21 in this form discuss what information about you will be collected, used, protected, and shared.

This study may include risks that are unknown at this time.

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform one of the research team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the research team members listed in question 3 in this form.

11a. What are the potential benefits to you for taking part in this research study?

The possible benefit you may experience from this study is a decrease in your insomnia. However, there is no guarantee that you will benefit from being in this research.

11b. How could others possibly benefit from this study?

The results of this research may improve the treatment of insomnia in the future.

11c. How could the researchers benefit from this study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator listed in question 3 of this form may benefit if the results of this study are presented at scientific meetings or in scientific journals.

12. What other choices do you have if you do not want to be in this study?

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Although you may meet criteria for participating in this research study, it does not mean that it is the only option you have. People with insomnia may show improvement with a particular combination of medications and cognitive behavior therapy for insomnia. Cognitive behavioral therapy for insomnia aims to improve sleep habits and behaviors. The cognitive part teaches you to recognize and change beliefs that affect your ability to sleep. For instance, this may include learning how to control or eliminate negative thoughts and worries that keep you awake. The behavioral part of helps you develop good sleep habits and avoid behaviors that keep you from sleeping well.
There is also the possibility that new medications may be developed in the future that may be effective for your case.

When considering more novel approaches, you will need to carefully weigh the pros and cons, the potential benefits and the potential risks. Just remember that there are always other options. Please discuss these options with one of the research team members listed in question 3 of this form.

13a. Can you withdraw from this study?

You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled.

If you decide to withdraw your consent to participate in this study for any reason, please contact one of the research team members listed in question 3 of this form. They will tell you how to stop your participation safely.

If you have any questions regarding your rights as a research subject, please call the Institutional Review Board (IRB) office at (352) 273-9600.

13b. If you withdraw, can information about you still be used and/or collected?

If you withdraw from the study, information that has been collected to that point may be used in the analysis of data.

13c. Can the Principal Investigator withdraw you from this study?

You may be withdrawn from the study without your consent for the following reasons:

- You do not qualify to be in the study because you do not meet the study requirements. Ask the Principal Investigator if you would like more information about this.
- You need a medical treatment not allowed in this study.
- The investigator decides that continuing in the study would be harmful to you.
- Study treatments have a bad effect on you.

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- You become pregnant, and the study treatment could be harmful to the baby.
- The study is cancelled by the Food and Drug Administration (FDA), and/or other administrative reasons.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

14. If you choose to take part in this research study, will it cost you anything?

Study Services

The Sponsor will provide all items and services required for your participation in this study. There will be no cost to you. If you receive a bill related to this study, please contact the Principal Investigator in question 3 of this consent form.

Items/Services Not Paid for by the Sponsor

Any other medical services provided to you that are not directly related to the study will be billed to you or your insurance company. You will be responsible for paying any deductible, co-insurance, and/or co-payments for these services, and any noncovered or out-of-network services.

Some insurance companies may not cover costs associated with studies. Please contact your insurance company for additional information.

15. Will you be paid for taking part in this study?

You will be paid $10 per visit for taking part in this research study, for a total of $150 if you complete all fifteen treatments. You will only be reimbursed for the visits you complete. You will receive payment at the end of each week. If you are paid for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment. You are responsible for paying income taxes on any payments provided by the study. If the payments total $600 or more, the University must report the amount you receive to the Internal Revenue Service (IRS).

16. What if you are injured because of the study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

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You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact one of the research team members listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this study.

17. How will your health information be collected, used and shared?

If you agree to participate in this study, the Principal Investigator will create, collect, and use private information about you and your health. This information is called protected health information or PHI. In order to do this, the Principal Investigator needs your authorization The following section describes what PHI will be collected, used and shared, how it will be collected, used, and shared, who will collect, use or share it, who will have access to it, how it will be secured, and what your rights are to revoke this authorization.

Your protected health information may be collected, used, and shared with others to determine if you can participate in the study, and then as part of your participation in the study. This information can be gathered from you or your past, current or future health records, from procedures such as physical examinations, x-rays, blood or urine tests or from other procedures or tests. This information will be created by receiving study treatments or participating in study procedures, or from your study visits and telephone calls. More specifically, the following information may be collected, used, and shared with others:

- Complete medical and psychiatric history to determine eligibility criteria
- Physical exam
- Questionnaires about symptoms of insomnia and other medical and psychiatric disorders
- Information related to your current and past treatments for insomnia and other psychiatric illnesses if applicable.

This information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices.

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Some of the information collected could be included in a "limited data set" to be used for other research purposes. If so, the limited data set will only include information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, social security number, photographs, or other codes that link you to the information in the limited data set. If limited data sets are created and used, agreements between the parties creating and receiving the limited data set are required in order to protect your identity and confidentiality and privacy.

18. For what study-related purposes will your protected health information be collected, used, and shared with others?

Your PHI may be collected, used, and shared with others to make sure you can participate in the research, through your participation in the research, and to evaluate the results of the research study. More specifically, your PHI may be collected, used, and shared with others for the following study-related purpose(s):

 to determine the effectiveness of the study device in treating insomnia

Once this information is collected, it becomes part of the research record for this study.

19. Who will be allowed to collect, use, and share your protected health information?

Only certain people have the legal right to collect, use and share your research records, and they will protect the privacy and security of these records to the extent the law allows.

These people include:

- the study Principal Investigator (listed in question 3 of this form) and research staff associated with this project.
- other professionals at the University of Florida or Shands Hospital that provide study-related treatment or procedures.
- the University of Florida Institutional Review Board (IRB; an IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research).

20. Once collected or used, who may your protected health information be shared with?

Your PHI may be shared with:

- the study sponsor (listed in Question 4 of this form).

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- United States and foreign governmental agencies who are responsible for overseeing research, such as the Food and Drug Administration.

Otherwise, your research records will not be released without your permission unless required by law or a court order. It is possible that once this information is shared with authorized persons, it could be shared by the persons or agencies who receive it and it would no longer be protected by the federal medical privacy law.

21. If you agree to take part in this research study, how long will your protected health information be used and shared with others?

Your PHI will be used and shared with others as described above throughout your participation in the study. Once you complete the study, your protected health information will be anonymized (that is, all identifying links between you and your information will be removed), used, shared with others and maintained in a secure database indefinitely.

You are not required to sign this consent and authorization or allow researchers to collect, use and share your PHI. Your refusal to sign will not affect your treatment, payment, enrollment, or eligibility for any benefits outside this research study. However, you cannot participate in this research unless you allow the collection, use and sharing of your protected health information by signing this consent and authorization.

You have the right to review and copy your protected health information. However, we can make this available only after the study is finished.

You can revoke your authorization at any time before, during, or after your participation in this study. If you revoke it, no new information will be collected about you. However, information that was already collected may still be used and shared with others if the researchers have relied on it to complete the research. You can revoke your authorization by giving a written request with your signature on it to the Principal Investigator.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and | Date

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Authorization

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described in sections 17-21 above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing	Date