UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: Effects of non-invasive brain stimulation on cognitive function in patients with multiple sclerosis

This is a research study to see whether non-invasive brain stimulation might be helpful in improving cognitive abilities such as attention and memory in patients with multiple sclerosis (MS). Your study doctor, Riley Bove, M.D., from the UCSF Multiple Sclerosis Center, or a member of her laboratory, will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

Why is this study being done?

The purpose of this study is to determine if a form of brain stimulation, applied to the scalp, can help enhance mental processes such as attention and memory function. The brain stimulation procedures will be performed by using the Neuroelectrics Starstim device, which is an investigational device only and has not been approved by the U.S. Food and Drug Administration (FDA).

Funding for this study is provided by the National Multiple Sclerosis Society.

How many people will take part in this study?

About 60 participants will be enrolled in this study.

What will happen if I decide to take part in this research study?

Phase I (Baseline):

Prior to the brain stimulation procedure, you will be given assessments to measure your attention, memory, sensory and motor abilities. These assessments will be performed along with electroencephalography (EEG), a device that tracks and records brain activities from your scalp. Demographic information and clinical history will also be collected.

All of the following procedures of Phase I will be done at UCSF, taking approximately 2 hours:

Demographic and Clinical History: The research coordinator will ask questions about your personal demographics (age, sex, ancestry, etc.) and collect clinical characteristics (e.g. MS history and your weight and height).

Survey Questionnaires: You will complete online surveys through a secure web interface. These surveys may assess the following: mood, fatigue and pain.

Cognitive Tasks: A set of behavioral tests will be performed to measure your attention, memory, sensory and motor abilities.

EEG Cognitive Testing: The cognitive tasks will be performed along with EEG. Electrodes will be placed on your scalp with a water-soluble gel. You will be asked to complete tasks on a computer while we record brain waves with the EEG equipment.

MS Related Functional Tasks: You will take part in completing functional tasks including balance, walking ability, arm and hand function, vision and cognition.

Randomization: You will be "randomized" into one of the three study groups (i.e., two groups receiving brain stimulation (there are two different types of stimulation) or a control group). Randomization means that you are put into a group by chance. A computer program will place you in one of the three groups. Neither you nor your doctor can choose the group you will be in. The "double-blind" study design means that neither you nor the study personnel will know which group you have been placed in. You will have an equal chance of being placed in any of the groups. The group assignment will not be changed during the study.

- **If you are in stimulation group:** You will receive actual stimulation during phase II.
- **If you are in control group:** You will receive placebo stimulation during phase II. After you complete your participation, you will not switch to stimulation group.

Phase II (Intervention):

Within 1 week of Phase I, you will start Phase II of the study. You will receive brain stimulation, while you are performing tasks that measure attention, memory, sensory and motor abilities. The entire session should last one hour per day. All the procedures of phase II will be done at UCSF.

Brain Stimulation and Cognitive Testing: You will be asked to complete cognitive (attention and memory), motor and sensory tests while brain stimulation is applied. The brain stimulation is given by passing a weak electrical current (equivalent to what is used in hearing aids) through electrodes placed on your scalp. The electrical current passes between the stimulating electrodes causing momentary change in brain activity at the stimulation site. Procedures and equipment set-up will be performed by qualified research staff.
When the current is being applied, you might feel itching or a small shock similar to that caused by static electricity. These sensations are not painful but can be bothersome or irritating. You may also see small, brief flashes of light — called phosphenes — due to the stimulation of optical nerve or other visual brain regions. The brain stimulation will be applied for up to 30 minutes per day.

Phase III (follow-up): After the Phase II is complete, you will be given the same cognitive assessments and EEG testing as conducted during Phase I. No more than three follow-up sessions will occur, and no more than one year from the end of Phase II. An entire session should last no more than two hours. All the procedures of Phase III will be performed at UCSF.

How long will I be in the study?

The study includes 1 to 14 visits to UCSF. It may be a single visit to UCSF or 2 to 4 visits as pre- and post-intervention attentional assessments along with multiple visits for brain stimulation intervention.
There are three phases to the study, which, in total, will not exceed 14 experimental sessions over the course of one year. Time commitment will vary based on how many days there are in Phase II (intervention).

Phase I: no more than 1 sessions.
Session length not to exceed: 1.5 hours.

Phase II: up to 4 weeks, maximum of 10 sessions.
Maximum time per session: not to exceed 1 hours.
Total time not to exceed: 10 hours.

Phase III: no more than 3 sessions.
Session length not to exceed: 1.5 hours.
Total time not to exceed: 4.5 hours.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about ending the study early. The study doctor may stop you from taking part in this study at any time if she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

Cognitive Tasks: Depending on the nature of the cognitive tasks, mental fatigue or boredom are minor risks.

EEG: All of the EEG procedures have been used extensively in previous research. In some cases, EEG caps and gel can cause mild skin irritation/discomfort.

Brain Stimulation: The brain stimulation being used in this study is considered a very low-risk procedure. There is possibility for some discomfort during or following the stimulation; some of the more commonly reported effects include mild headache, tingling, itching, burning sensation, and skin redness in the area of stimulation. Some participants have reported the feeling of shock during the beginning of the stimulation sessions, described similar to a shock from static electricity. These effects may be more likely based on some individual characteristics such as skin type and hair.
You should know that brain stimulation might result in acute mood or temporary thought change. Other side effects such as dizziness, disorientation, sleepiness, or confusion may occur; if they do occur, these symptoms are typically temporary. Mood changes usually include a transient increase in the state of happiness or sadness. In addition, other mood symptoms such as irritation or a slight feeling of euphoria may occur. Please inform the study personnel if you experience any of the discomforts described.
The brain stimulation could induce lasting changes in memory, attention and other mental processes. This is a possible risk but none of the safety studies conducted have found negative side effects. For more information about potential risks and side effects, ask one of the researchers.

Are there benefits to taking part in the study?

There will be no direct benefit to you from participating in this study. If you are currently undergoing medical treatment, these procedures will not benefit or adversely affect you. At the end of the experiments, we will explain what we expect to learn from the study. We hope that this knowledge will be useful in the future treatment of cognitive impairment in MS patients. If

the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

What other choices do I have if I do not take part in this study?
You may choose not to participate in this study and you can receive clinical care as you normally would outside of this study. Please talk to your doctor about your choices before deciding if you will take part in this study.

Will information about me be kept private?
We will do our best to make sure that the personal information gathered for this study is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Are there any costs to me for taking part in this study?
No. The sponsor has agreed to pay for all items associated with this research study; you or your insurer will not be billed.

Will I be paid for taking part in this study?
In return for your time, effort and travel expenses, you will be compensated $20/hr for participating in the EEG, behavioral testing or brain stimulation testing. If compensated by check, a check will be mailed to you about 6-8 weeks after you complete your participation in the study (thus requiring us to obtain your social security number).

What happens if I am injured because I took part in this study?
It is important that you tell your study doctor, Riley Bove, MD, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call her at 415-502-7209.

Treatment and Compensation for Injury:
If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

What are my rights if I take part in this study?
Taking part in this study is your choice. You may choose either to participate or not to participate in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision is made, there will be no penalty to you, and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get medical care from our institution. We will tell you about new information or changes in the study that may affect your health or willingness to continue in the study. In the case of injury resulting from this study, you will not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?
You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctor, Dr. Bove, at riley.bove@ucsf.edu or 415-502-7209.
If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

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.

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you