Explosive Synchronization of Brain Network Activity in Chronic Pain

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UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: Explosive Synchronization of Brain Network Activity in Chronic Pain

Company or agency sponsoring the study:
National Center for Complimentary & Integrative Health (NCCIH), U.S. National Institute of Health, Department of Health and Human Services

Names, degrees, and affiliations of the principal investigator and study coordinator (if applicable):

Principal Investigators:
Alexandre F. DaSilva, DDS, DMedSc, Department of Biologic and Materials Sciences, School of Dentistry, University of Michigan
Richard E. Harris, PhD, Department of Anesthesiology, University of Michigan
UnCheol Lee, PhD, Department of Anesthesiology, University of Michigan

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find child care, or make other plans. In your decision to participate in this study, consider all of these matters carefully.

This research is studying the action of an approved device in small numbers of people to learn about its safety and its effect on your body at certain brain areas as a treatment for Fibromyalgia. This study will determine if certain brain patterns are related to action of non-invasive brain stimulation techniques. Your health-related information will be collected for this research study.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include discomfort during or temporarily after some of the testing procedures, new symptoms from use of the high-definition transcranial direct current stimulation (HD-tDCS) such as head or neck pain, or no improvement in your current Fibromyalgia (FM). More detailed information will be provided later in this document.

IRBMED informed consent template—11-12-2018
Instructions revised 11-12-2018
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This study may offer some benefit to you now or others in the future by helping researchers better understand FM and chronic pain conditions, which could lead to better treatment options for patients in the future. It is also possible that some participants may see an improvement in their symptoms following HD-tDCS treatment. More information will be provided later in this document.

We expect the amount of time you will participate in the study will be:

- AIM 1 - Healthy Control (HC) and Fibromyalgia (FM) Participants: 1 week (with a 2-week screening window and a 2-week run-in)
- AIM 3 - Fibromyalgia Participants (FM): Up to 6 weeks

You can decide not to be in this study. Alternatives to joining this study include not participating in the study. Your regular doctor will be able give you information about standard treatments for Fibromyalgia.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The information gathered in this study will help researchers learn more about brain network activity in Fibromyalgia. Researchers in this study hope to identify brain regions that may be important for treating FM in the future. Individuals with FM are thought to have brain characteristics that are different from pain-free individuals. Past research has found that patients with FM are more likely to have brain networks that respond with rapid, widespread responses to small changes. This abnormal hypersensitivity is called explosive synchronization (ES). In this study, researchers will evaluate the impact of ES and its treatment with non-invasive brain stimulation in FM.

In the past, researchers have used non-invasive brain stimulation to reduce chronic pain in some FM patients by changing their brain activity. Those participating in Aim 3 will help researchers will learn how brain activity may be affected by high definition transcranial direct current stimulation (HD-tDCS), and whether or this treatment has an impact on Fibromyalgia symptoms.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Fibromyalgia Participants:

- Right-handed females and males age 19 – 75 who satisfy the study's FM criteria
- Willing to limit the introduction of any new medications or treatments for control of FM symptoms during the study.
- Able to travel to the study site to receive HD-tDCS treatments 5 times weekly for 2 weeks (Aim 3 only)

Healthy Control Participants:

- Right-handed females and males age 19 – 75 who do not have Fibromyalgia or any other chronic medical illness or psychiatric disorder

You may NOT take part in this study if you:

- Have an autoimmune and/or inflammatory disease that causes pain
- Have a history of head injury with substantial loss of consciousness
- Have a history of peripheral neuropathy of known cause that interferes with activities of daily living
- Routinely (i.e., daily) use opioid analgesics, marijuana, or have a history of substance abuse
- Use stimulant medications, such as those used to treat ADD/ADHD or the fatigue associated with sleep apnea or shift work
- Are participating in other therapeutic trials
- Are unwilling to refrain from over the counter (OTC) pain medications (NSAIDs, etc.) on the day of EEG
- Are unwilling to refrain from opioid analgesics 48 hours prior to EEG
- Are currently pregnant or nursing
- Have severe psychiatric illness
- Are ineligible for EEG, and/or HD-tDCS
- Have a history of vascular surgery in lower limbs or current lower limb vascular dysfunction
- Subjects with Worker's Compensation, Workman's Compensation, civil litigation or disability claims pertinent to the participant's FM; current involvement in out-of-court settlements for claims pertinent to the participant's FM; or currently receiving monetary compensation as a result of any of the above.

Additional eligibility criteria apply. We will review your eligibility to participate at the time of your initial visit.

3.2 How many people are expected to take part in this study?

For Aim 1, 35 healthy controls (25 female, 10 male) and 35 participants with Fibromyalgia (25 female, 10 male) are expected to participate. For Aim 3, we plan to enroll 50 female participants with Fibromyalgia.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

AIM 1: Participation in this portion of the study will consist of a Screening Visit, 14 day run-in observation period, Behavioral Session with EEG, and an EEG/MRI session. Please see below for more details.

Screening/Visit 0

The Screening/Eligibility visit will be an in-person visit at Domino's Farms in Ann Arbor to find out if you are interested in joining the study. If so, we will give you more information and obtain your informed consent. We will review and confirm whether you qualify for the study, ask you to provide your contact information, and complete an eligibility questionnaire. If you are eligible, the following will occur:

- Complete questions about your demographics, pain symptoms, medical history, medications, functioning, and overall health.
- Measure your height/weight.
- PainTrek mobile initial pain entry.
- Collect a urine sample for a pregnancy test (females of childbearing potential only).
- We will demonstrate the devices used in this study, including the EEG machine and calf cuff, that will be used throughout the study to measure your pain. This will give you an opportunity

to undergo practice tests, become familiarized with the study devices, and ask any questions you may have about them.

Run-In Observation Period

Following the Screening Visit, for 14 days prior to your Behavioral Session/Visit 1, study staff will either phone, text, or email you daily to collect pain ratings and ask if you have made any medication changes. On days 7 and 14 of this period, we will ask some additional questions related to your Fibromyalgia and functioning.

Behavioral Session with EEG/Visit 1

This visit will occur between 15-30 days after your Screening/Week 0 Visit and will be scheduled at Domino's Farms in Ann Arbor. This visit involves:

- Surveys - Completion of questionnaires related to your pain, functioning, overall health, and other symptoms, and completion of PainTrek mobile app survey.
- Pregnancy Test - Collect a urine sample for a pregnancy test (females of childbearing potential only).
- Quantitative Sensory Testing (QST) – For this assessment we will attach an inflatable cuff (similar to a blood pressure cuff) to your lower leg just below the knee. We will then inflate the cuff to determine the range of pressure pain you find tolerable. We'll start with a low intensity of pressure and then increase it, according to your rating of pain intensity. We will then conduct another test using the cuff device, but this time the cuff pressures will be applied in a random (i.e., by chance) order. The amounts of cuff pressure will be the same as in the first test, but in a random order.
- Electroencephalogram (EEG) with Quantitative Sensory Testing QST and Cognitive Assessment - An EEG machine records your brain's electrical activity, using electrodes that rest on your scalp. We'll attach the electrodes to your head with a special cap and some gel. The EEG takes about 30-45 minutes to set up, and then you'll rest for 16 minutes while the EEG machine records your brain's electrical activity. Next, while you are still connected to the EEG machine, cuff pressure will be continuously applied to your calf for 8 minutes, and ratings of pain intensity and unpleasantness will be collected from you during regular intervals. At the end of this we will have you rest again for a further 14 minutes while we record your brain's electrical activity. After that, you will complete a visual task, during which you will view a video display of a visual stimulus consisting of a flashing checker board and a fixed plus sign for approximately 6 minutes. These two stimuli will alternate every 20 seconds during the task. Finally, you will complete a 13-minute cognitive task that will evaluate reaction time and memory during EEG recording.
- Computerized Neuropsychological Assessment – For this assessment, you will complete a set of tests on an electronic tablet that will take approximately 30 minutes to complete. If necessary, we can arrange for this portion to be completed at a separate visit, up to 3 days later.

Simultaneous Electroencephalography and Functional Magnetic Resonance Imaging (EEG/fMRI)/Visit 2

This session will occur either on the same day as, or within 3 days of, your Behavioral Session with EEG/Visit 1, and will take place at the Functional MRI Laboratory located on the North Campus of the University of Michigan. Here you will undergo a brain scan. We will use functional Magnetic Resonance Imaging (fMRI) to monitor areas of the brain that are involved in thinking and processing pain. The scanner stimulates the brain to send out signals that we will record and analyze. The fMRI procedure

involves lying on a table that slides into a hollow machine. You will lie in the scanner with a coil around your head. This coil keeps your head still so the magnet can obtain clear images of your head and the blood flow in your brain.

Additionally, during the fMRI, we will record your brain's electrical activity with the EEG machine. Before entering the fMRI scanner, the EEG cap will again be placed on your head, which takes 30-45 minutes. If this session occurs the same day as your Visit 1, you may already be wearing the cap, in which case less setup time may be required.

During the scan first part of the fMRI scan, you will be wearing the EEG cap while we take images of your brain function, some while you are resting and some while applying 8 minutes of continuous cuff pressure to the lower leg and assessing your pain.

About halfway through the scan, you will exit the fMRI scanner so that the EEG cap can be removed from your head. After this is complete, you'll re-enter the MRI scanner for a few additional scans while you are not wearing the EEG cap. This will include an additional 11-minute cuff pressure test on the calf, similar to the tests conducted during Visit 1.

During this session, you'll spend up to 90 minutes in the scanner. Additional time may also be required to setup the EEG cap prior the fMRI. The full session may take up to 2-3 hours.

AIM 3: Only female Fibromyalgia participants will be enrolled in this portion of the study. Participation will consist of a Screening Visit (as described above) followed by a 14 day run-in observation period (as described above).

After that, within 30 days of the Screening Visit, you will participate in the "Behavioral Session with EEG," as described above (*with the exception of the Cognitive Assessment and Computerized Neuropsychological Assessment, both of which will only be conducted in Aim 1.)*

Next, participants will undergo 5 HD-tDCS treatments over the course of one week. After the first 5 treatments, participants will undergo an "EEG Visit". That will be followed by an additional week of 5 HD-tDCS treatments, then a second "EEG Visit" will occur. During these EEG sessions, we will conduct two, six (6) minute EEG assessments, one with eyes open, and one with eyes closed.

For some research studies, such as the one you are being asked to join, it is important that you do not know some details of the study treatment. Whether you intend it or not, sometimes learning this information may make you change your actions and behaviors in ways that could impact the outcome of the study. This is called blinding. In this study, participants will be blinded as to when they are receiving active or sham treatment.

During Aim 3 of this study you will participate in a total of 10 sessions of HD-tDCS treatments (5 active and 5 sham). These sessions will at the M-CARP Clinical Research Unit, Headache & Orofacial Pain Effort (H.O.P.E.) laboratory, Center for Human Growth and Development in the North Ingalls Building in Ann Arbor, Michigan.

- For active stimulation treatments, four electrodes will be placed over the scalp. A cloth cap with a chinstrap will then be placed on the head to hold the electrodes in place. A small amount of conductive gel will be injected into the electrode casings. During active treatments, current stimulation will be applied for 20 minutes.
- For sham treatments, setup will be similar, but the current will be applied only for 30 seconds, though the session will still last 20 minutes.

- You will be blinded as to when you are receiving active or sham treatment; however, all participants who complete Aim 3 will receive 5 active and 5 sham treatments over the course of the study. "Blinded" means that you will not be told which treatment type you are receiving during your participation – only select members of the study team will know this information

PainTrek – **AIM 1 & AIM 3**: Those with an iPhone or Android smartphone may also participate in survey questions using PainTrek, which is a mobile application that a study team member will teach you how to install on your smartphone. Health Information such as the location and intensity of your pain symptoms, the impact of pain on your daily activities, your medication use, and other health management details may be collected by this app. The app may also collect: Contact Details,
Personal Demographics, Product Feedback, and Transaction History.

The University of Michigan owns PainTrek. All data collected through the app is housed on HIPAA compliant servers at the University of Michigan.

Participants in both Aims 1 and 3 will complete a PainTrek survey at their initial visit, during the 14-day Run-In period, and at every subsequent study visit.

In addition, participants in Aim 3 will be asked to complete additional PainTrek survey entries on your smartphone from home (or other location of choosing) during the study, on weekdays only, between the start of the Run-In (Day -14) until one week after treatment concludes.

If you do not have a compatible smartphone, you may still be able to participate in this study. Any charges accrued due to data usage or messaging rates will be the responsibility of the participant and will not be paid by the study.

4.2 How much of my time will be needed to take part in this study?

AIM 1 - Those who participate in Aim 1 will participate in three in-person visits over the course of up to 33 days, which includes a 14 day run-in observation period leading up to Visit 1.

- **Screening (Visit 0)** – about 2 hours
- **Run-in Observation** – a few minutes per day over 14 days
- **Behavioral Session with EEG (Visit 1)** – half-day visit (up to 4.5 hours)
- **Computerized Neuropsychological Assessment** – 30 mins; may be conducted during Behavioral Session or up to 3 days later
- **EEG/MRI (Visit 2)** – about 2-3 hours; may be conducted on the day of the Behavioral Visit or up to 3 days later
- **PainTrek Surveys** – a few minutes per day on your smartphone

AIM 3 – Participation in Aim 3 will be more extensive than Aim 1 and includes 15 in-person visits over a 96-day period:

- **Screening (Visit 1)** – about 2 hours
- **Run-in Observation** – a few minutes per day over 14 days
- **Behavioral Session with EEG (Visit 2)** – half day visit (up to 4.5 hours); must occur at least 15 days after the Screening Visit but no more than 30 days later.
- **Treatment Week 1 (Visits 3-7 [Days 3-11]) -** Five stimulation treatments (1 hour per session) which must occur in the same week.
- **EEG (Visit 8 [occurs between Days 14-18]):** About 2-3 hours

- **Treatment Week 2 (Visits 9-13 [Days 19-27]) -** Five stimulation treatments (1 hour per session) which must occur in the same week.
- **EEG (Visit 14 [occurs between Days 28-32]) -** About 2-3 hours
- **Follow-Up (Visit 15 [Day 60-66]) -** 1 hour; occurs four weeks after your final EEG scan (may be completed remotely)
- **PainTrek Surveys –** a few minutes per day on your smartphone

4.3 When will my participation in the study be over?
Your participation in the study is over at the conclusion of the final visit. For Aim 1 participants, the final visit will be the EEG/MRI (Visit 2) (for some participants, the 30-minute Computerized Neurological Assessment may be the final visit, as it may occur up to 3 days after the Behavioral Visit).

For Aim 3 participants, the final visits will be the second EEG (Visit 14), followed by completion of surveys four weeks later at Follow-Up/Visit 15.

The entire study will last about 5 years.

4.4 What will happen with my information and/or biospecimens used in this study?
Your biospecimens and collected information may be shared with the study sponsor, which is the National Center for Complimentary & Integrative Health (NCCIH).

With appropriate permissions, your biospecimens and collected information may also be shared with other researchers, here, around the world, and with companies.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks are:
Questionnaires: There is a possibility of discomfort associated with being asked personal questions about health history, symptoms, or emotional feelings.

Quantitative Sensitivity Testing:

- Cuff Testing: The pressure testing on the lower leg using the inflated cuff may cause discomfort or pain during or temporarily after the testing is conducted. Risks of cuff pain include mild transient bruising associated with inflation of the cuff which is estimated to occur is less than 5% of cases.
- Visual Stimulation Assessment: The possible discomfort of the visual stimulation task may be headache or nausea while or after performing this task.

Cognitive Assessment: There is a possibility of emotional discomfort associated with completing challenging tasks of cognitive functioning. Therefore, administrators will assess individuals' discomfort with testing accordingly.

HD-tDCS Treatments: tDCS is considered a safe technique that poses a non-significant risk to participants (as classified by the FDA). The most common known side effects are itching, tingling, headache, burning sensation, and discomfort. On rare occasions, the treatment has led to skin burns. No serious adverse events (SAEs) thought to be caused by tDCS have been reported in more than 10,000 participants in published studies from 1998 through 2014.

fMRI: (Aim 1 only) Participants may experience discomfort from lying still in the scanner for an extended period of time. There may be discomfort from noise produced by the MRI machine. Individuals will be provided with foam earplugs. The primary risks known to occur from MRI are due to the magnet's ability to pull metal objects toward it. This pull can cause metal objects in the body (e.g. surgical clips or staples) to move and cause bleeding or disruption of surrounding tissue. Metal objects carried or worn by a person (e.g. jewelry, hair clips, tools) can be pulled toward the magnet and, if free to fly through the air, could strike an individual. The MRI can cause pacemakers or stimulators implanted in the body to malfunction.

There is also a risk that metallic objects in or on the body may be heated by the radio frequency waves, possibly causing burns. Individuals will be screened for implanted metal objects and will be asked to remove all other metal objects. Also, claustrophobia may be problematic, and individuals will be screened for this problem. Women of childbearing potential are advised to use an appropriate and effective method of birth control during their participation in this study given the unknown risk of the magnet to the fetus. Women of childbearing potential will be screened for pregnancy before they enter the scanner.

Finally, there exists a potential to cause peripheral nerve stimulation (PNS). PNS is a light touching sensation on the skin surface, lasting only a few seconds. It may cause mild discomfort, but it is not harmful.

The type of imaging used in this study is for research purposes only. It is not meant to diagnose illnesses, find tumors, or pick up any other problems in your brain. The scanning procedures used for this study will not be read by a specialist trained to make medical diagnoses from the scan. That is, even if there is a defect in your body, it is likely that it would not be discovered by the people who inspect the images. Therefore, it is likely that any defect that you may currently have will not be revealed by the images obtained in this experiment. However, there is still a chance that this MRI could show a problem that is already in your brain, such as a cyst or tumor. Such a finding might require more studies, and maybe even medical treatment, neither of which would be paid for by the investigators, the sponsor, or the University of Michigan.

Electroencephalogram (EEG) - EEG is a non-invasive method to assess brain electrical activity. EEG involves wearing a cap with electrodes that contain gel that are in contact with the scalp. During testing participants may experience scalp pain, scalp burning, or scalp itching/tingling. These sensations are typically mild and resolve after testing.

PainTrek Smartphone Application - Participation in the PainTrek Smartphone Application could result in some anxiety, distress, embarrassment, and inconvenience from increased alerts from your cell phone.

The researchers will try to minimize these risks by:
Questionnaires: You may decline to answer any questions that may be uncomfortable.

Quantitative Sensitivity Testing:

- Cuff Testing: Researchers will be educated in how to perform these tests safely. You may stop the tests at any time if the testing becomes too uncomfortable. A simple button press can rapidly deflate the cuff, ensuring participant safety. You will be able to notify us of any distress and end the cuff testing during the Behavioral Visit and/or fMRI scan at any time.

- Visual Stimulation Assessment: If you experience discomfort while viewing the flashing checker board or fixed plus sign, you may stop the test at any time. Participants with a history of photo-induced migraines or seizures will not participate in the visual portion of the study.

Cognitive Assessment: Participants may elect to discontinue this assessment at any time.

HD-tDCS Treatments: Researchers will be educated and trained in how to administer these treatments safely. You may stop the treatments at any time if you experience discomfort.

fMRI (Aim 1): To ensure safety during the fMRI scan, all participants will be asked to bring or wear clothing that is free of metal, and to remove jewelry and any other metal objects from their body**. Please advise the study team if you have any implanted devices such as a pacemaker, surgical implant, intrauterine device, etc.** We will also assess whether metallic objects that may be implanted (e.g., surgical clips or staples) are hazardous or acceptable.

We will provide pads and blankets to make sure you are as comfortable as possible while lying in the scanner. Additionally, you will wear foam earplugs and have padding placed around your head to reduce the loud noises made by the scanner.

If you experience discomfort during the fMRI procedure, the researchers can stop the scan at any time that you request. You will be able to talk to the technician throughout the scan, and will be able to let them know immediately if you want to stop the procedure and exit the scanner.

The MRI machine is operated within FDA guidelines so the potential for inducing PNS is low.

Women of childbearing potential will be asked to take a urine pregnancy before undergoing the fMRI scan. If you do not wish to take the pregnancy test, you may be excluded from any further aspects of the study.

EEG - All staff performing EEG will be trained in the proper technique. You may ask to stop the procedure at any time.

PainTrek Smartphone Application - To reduce risks, participants will be encouraged to use the app for this study in private, being mindful that people could attempt to look at their screen, such as if one were to use an ATM in public.

Additionally, there may be a risk of loss to confidentiality or privacy. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may not receive any personal benefits from being in this study. However, others may benefit from the knowledge gained from this study. However, it is possible that some participants who undergo the HD-tDCS treatments may see an improvement in their Fibromyalgia symptoms.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?
Taking part in this study is voluntary. You have the right to choose not to take part in the study. Ask your regular doctors about other treatment options if you decide not to take part in the study.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information”.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
No, there is no known risk if you decide to leave the study early.

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researcher's telephone number listed in Section 10.1.

If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact Kathy Scott (734-998-7022). If taking part in the study makes you sick or causes you injury, you or your insurance provider will be billed for all costs of treatment as the study does not provide compensation for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?

AIM 1: You may receive up to $294 for participation in Aim 1 of the study. You will receive compensation for each study contact in which you participate, as described below:

- Screening (Visit 0): $25
- Run-In Observation (14 days): $1 per day
- Behavioral Session with EEG, and Cognitive and Neuropsychological Assessments (Visit 1): $105
- EEG/fMRI (Visit 2): $150

AIM 3: You may receive up to $464 for participation in Aim 3 of the study. You will receive compensation for each study contact in which you participate, as described below:

- Screening (Visit 1): $25
- Run-In Observation (14 days): $1 per day
- Behavioral Session with EEG (Visit 2): $75
- HD-tDCS/Sham Treatments (up to 10 per participant): $15 per treatment
- EEG Visits (Visits 8 and 14): $75
- Follow-Up (Visit 15): $50

8.3 Who could profit or financially benefit from the study results?
The University of Michigan is an owner and PI Dr. Alex DaSilva is an inventor of a tool being used in this research (PainTrek). This means the University of Michigan and Dr. DaSilva could financially benefit from this study.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. You will be identified in the research records only by a code name or number. Information that identifies you personally will not be released without your written permission. However, the study sponsor or federal agencies with appropriate regulatory oversight [e.g., Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), Office of Civil Rights (OCR), etc.] may review your research records.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the NIH/NICCIH which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child, adult, or elder abuse or neglect. We may also disclose your information to the appropriate authorities if we suspect or learn about cases of child or elder abuse or neglect, or that you may harm yourself or others.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

When the results of this research are published or discussed in conferences, no information will be included that would reveal your identity. All data will be kept in your study file until after 7 years or until the study findings are published, whichever is longer. They will then be destroyed.

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.

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan finance department will need your name and address for tax reporting purposes. In a calendar year if: 1) your payments total greater than $400 for this study or 2) if you receive payments of greater than $400 for being in more than one study, the University of Michigan finance department will also require your Social Security Number for tax reporting purposes. If you do not wish to provide your Social Security Number, you may continue to participate in research studies, but you will not be able to receive payment for the remainder of the calendar year.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities. (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator:
Alexandre Dasilva, DDs, DMedSc
Mailing Address: Department of Biologic and Materials Sciences
University of Michigan School of Dentistry
1011 North University Ave.
Ann Arbor, Michigan 48109
Telephone: 734-763-5280

Study Coordinator: Jacqueline Dobson
Mailing Address: H.O.P.E. Lab
300 North Ingalls (room 1012)
Ann Arbor, MI 48109
Telephone: 734-763-8469
Email: jdobs@umich.edu

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies, include the appropriate calling codes.)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:
This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

I would like to participate in (check all that apply):

☐ **Aim 1** [Healthy Control and Fibromyalgia Participants]

☐ **Aim 3** [Female Fibromyalgia Participants only]

Print Legal Name: _____

Signature: _____

Date of Signature: _____

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name:_____

Title: _____

Signature: _____

Date of Signature: _____