Study Title:
Brain State-dependent Stimulation to Improve Movement (BrainSTIM)

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Informed Consent Form

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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: Multi-session investigations of state-dependent brain network manipulation

Company or agency sponsoring the study: This study is financially sponsored by the University of Michigan School of Kinesiology and National Institutes of Health (NIH).

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

Michael Vesia, Ph.D., Assistant Professor of Movement Science, School of Kinesiology, Brain Behavior Laboratory, University of Michigan

Study Coordinator:

Ashley Rettmann, CCRP, Brain Behavior Laboratory – Lab Manager, School of Kinesiology, 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.

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 adverse effects due to non-invasive brain stimulation (NIBS), or breach of confidentiality, but these risks are very rare and the researchers have taken steps to minimize these risks as much as possible. More detailed information will be provided later in this document.

This study may not offer any benefit to you now but may benefit others in the future by revealing information that may be used to create new or improve existing treatment options to benefit individuals

suffering from neuromotor impairments (such as might occur from stroke, brain injury, or neurodegenerative disease). More information will be provided later in this document.

We expect the amount of time you will participate in the study will be up to 9 visits with at least 24 hours between each visit.

You can decide not to be in this study. This study is voluntary and there are no alternatives to participation.

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:

Noninvasive Brain Stimulation (NIBS) is rapidly developing as a powerful, noninvasive brain stimulation technique that uses magnetic fields to induce electrical activity in specific brain areas to help better understand brain function. It is an especially promising tool in the treatment of many neurological and movement disorders such as stroke and Parkinson's disease. However, we have a limited understanding of how NIBS affects a person's brain and their control of grasping behaviors. For that reason, this study's purpose is to better understand how NIBS alters brain function, and how it can be used to improve a person's ability to make hand movements necessary for daily life activities such as eating, dressing, tool-use and writing.

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?

Healthy, right-handed, English-speaking adults between the ages of 18 and 50 years with no history of neurological disorder can take part in this study.

If you agree to take part in the study, Dr. Vesia or his associates will determine if you have any condition that will prevent you from being in the study. Screening should take no more than 5 minutes.

You should **not** participate in this study if you:

- are left-handed
- are younger than 18 or older than 50 years old
- are pregnant, suspect you might be pregnant or are attempting to become pregnant
- have a pacemaker, intracardiac lines or any other medically implanted device or medicine pump
- have cochlear hearing implants
- are taking GABAergic, NDMA-receptor antagonist, or other drug known to influence neural receptors that facilitate neuroplasticity
- have non removable body piercings or have foreign objects in body
- have metal anywhere in the head that could increase your risk of serious injury (not including braces, dental fillings, etc.):

  - deep brain or vagus nerve stimulator
  - aneurysm clips or coils
  - stents in neck or brain
  - implanted stimulators
  - electrodes to monitor brain activity
  - metallic implants in eyes or ears
  - shrapnel or bullet fragments in or near the head
  - facial tattoos with metallic or magnetic-sensitive ink
  - other metal devices or objects implanted in or near the head,
- have any of the below conditions that would put you at increased risk of having a seizure:
  - a personal or family history of seizure/epilepsy
  - taking prescription drugs that lower the threshold for seizures
  - recent history of excessive alcohol consumption
  - history of alcohol addiction/dependence
  - recent history of recreational drug use
  - history of drug addiction/dependence
- have been diagnosed with any of the following:
  - a stroke, brain hemorrhage, brain tumor, encephalitis, multiple sclerosis,
  - Parkinson's disease or Alzheimer's disease
  - depression in the past 6 months
  - attention deficit disorder, schizophrenia, manic depressive (bipolar) disorder,
  - normal pressure hydrocephalus or increased intra-cranial pressure
  - diabetes requiring insulin treatment
  - any serious heart disorder or liver disease

Currently there are no known risks associated with TMS to a developing baby, but women who are pregnant, suspect they are pregnant or are attempting to become pregnant should not participate in this study. Participants will be asked to confirm whether or not they are pregnant prior to participating in the study; a self-administered urine pregnancy test will be provided to those who want one.
However, if you are uncertain about the possibility of being pregnant, you should not participate in this study.

In addition, subjects will be excluded from the MRI component of this study if they have any relevant history of open-heart surgery, artificial heart valve, brain aneurysm surgery, braces or extensive dental work, cataract surgery or lens implant, or artificial limb or joint. Subjects will also be excluded if have any history of foreign metallic object in the body such as bullets, BB's, pellets, shrapnel, or metalwork fragments. Subjects will be excluded if they are claustrophobic, have uncontrollable shaking, or cannot lie still for one hour.

You also should inform a member of the study team if you have had trouble sleeping (i.e. <6 hours of sleep), are experiencing jetlag, or consumed alcohol the night before an experimental session.

3.2 How many people are expected to take part in this study?
65 healthy, right-handed adults between the ages of 18-50 years old are expected to take part in this study

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

If you decide to take part in this study, you will participate in up to 9 separate sessions. You will know how many sessions you will be asked to take part in before signing this document. The first session is a screening session to confirm eligibility. All remaining sessions will be scheduled after successful completion of the screening session and will be at least 24 hours apart. Each session will be separated into several separate blocks of activity to allow you time to rest in between. All sessions will take place at either the Brain Behavior Laboratory TMS lab located in the Kinesiology Building (830 N University Ave, Ann Arbor, MI 48109) or the functional MRI Laboratory located in the Bonisteel Interdisciplinary Research Building (2360 Bonisteel Blvd, Ann Arbor, MI 48109).

This study involves both measuring brain activity and stimulating parts of the brain using a form of non-invasive brain stimulation (NIBS) called repetitive transcranial magnetic stimulation (rTMS). This process is considered noninvasive because it does not involve placing anything under your skin or inside your body. This study also involves functional magnetic resonance imaging (fMRI), which is a process where we can "take pictures" of your brain. Participants in this study will be randomly assigned to one of three study groups.

You will be asked questions that confirm your eligibility for fMRI and rTMS prior to completing any tasks, including whether or not you believe you might be pregnant. A self-administered urine pregnancy test will be provided free of charge to participants who want one.

<u>Transcranial magnetic stimulation (TMS)</u>

TMS involves sending magnetic fields into a person's brain to stimulate nerve cells. Using TMS to stimulate the brain and measure brain activity is not currently FDA-approved for healthy people and is considered experimental. For this study, TMS will be used to repetitively stimulate the brain, referred to as repetitive TMS (rTMS).

Before testing, we will place electrodes on the skin of your hands. These electrodes will record muscle activity from your hands.

A device called a coil will rest on your head (*see* **Figure 1**). We will send an electric current through the coil to create a magnetic field. The magnetic field will pass through your skin and skull and into your brain. You will not feel the magnetic field, and it will not hurt or damage your body. During this part of the experiment, you will hear a click, and it may feel like someone has lightly tapped your head. We will determine the intensity of stimulation needed for you; this is because everyone's brain is different.

Figure 1

You will be seated in a chair with your arms placed in molded hand rests during the experiment. We will place one coil over the part of your brain called the motor cortex. We will place a second coil over a different part of your brain involved in planning voluntary hand movements. During the TMS procedure, you will experience slight twitching and muscle contractions in your arm and hand. During stimulation, we will measure your hand muscle activity through the electrodes. We will use TMS to study the

excitability of the two parts of your brain and how different regions of your brain send commands to your left- and right-hand muscles.

Neurophysiological & Behavioral Measures

We will collect measures of your hand muscle activity before, immediately after, 30 minutes after, and one hour after the TMS stimulation. We'll take some of the measurements while your hand is at rest and others while you make reach-to-grasp movements toward an object in front of you. You will be given 5-15-minute breaks throughout the collection to avoid fatigue.

Magnetic Resonance Imaging

Functional MRI involves lying on a table which then moves into a hollow machine. The actual MRI examination of your body will take less than 1 hour, and you will be asked to remain as still as possible during the entire period. You will hear knocking noises and will be able to talk with the operator or researcher through an intercom at various points during the scanning session. You will also be able to trigger an audible alarm at any time.

We are also asking permission to store your fMRI image data obtained during the scanning session in a database for future research studies related to brain structure and function.

For some research studies, such as the one you are being asked to join, it is important that you do not learn the results of certain tests. 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.

Besides the information about the main study, the following information is specific to unspecified future use of identifiable data and/or biospecimens. We would also like your permission to keep the data we collect (fMRI scans, neurophysiological and behavioral measures), so that we may study it in future research. The future research may be similar to this study or may be completely different. These data will be de-identified, meaning that your identifiable private information or identifiable biospecimens will be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent

You can take part in the main study even if you decide not to let us use your data for future research.

If you give us your permission, we will use your data (fMRI scans, neurophysiological and behavioral measures) for future research. Even if you give us permission now to keep some of your data, you can change your mind later and ask us to destroy it. Keep in mind, however, that once we have analyzed your data we may not be able to take the information out of our research.

We may share your de-identified data with other researchers, so that they can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your de-identified data with other researchers, we will not be able to get it back. Future use of your data will be conducted in compliance with applicable regulatory requirements.

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

You will not find out the results of future research on your de-identified data. Allowing us to do future research on your data will not benefit you directly.

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.

As a subject participating in this research study, you have certain responsibilities that may apply to this study, such as ensuring that you arrive at all of your scheduled appointments and report any adverse reactions you may have during the study.

4.2 How much of my time will be needed to take part in this study?
You will take part in up to 9 sessions total with each session scheduled at least 24 hours apart. The visit schedule is as follows:

Session 1: Screening + behavioral & neurophysiological measures (approx.2 hours)
Session 2: fMRI (approximately 1 hour)
Session 3: TMS (approximately 30 min)
Session 4: TMS (approximately 30 min)
Session 5: TMS (approximately 30 min)
Session 6: TMS + behavioral & neurophysiological measures (approximately 3 hours)
Session 7: TMS + fMRI (approximately 1 hour)
Session 8*: fMRI (approximately 1 hour)
Session 9*: behavioral & neurophysiological measures (approximately 1 hour)
*Option to complete visits 8 and 9 on the same day

4.3 When will my participation in the study be over?
Participation in this study will be over at the end of your final session.

4.4 What will happen with my information and/or biospecimens used in this study?
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?
TMS – Potential Risks

1) Local scalp pain near stimulation site (common, not serious): Activation of muscles and nerves near the site of stimulation can cause substantial pain and discomfort, depending on the intensity and frequency of stimulation.
2) Headache or neck pain (common, not serious): Headache and neck pain, typically lasting up to a few hours on the day of stimulation, are the most frequent side effects of TMS. If you have a history of migraines, there is a chance you could experience one after TMS.

3) Sound exposure (rare, serious): When producing a magnetic pulse train, the stimulating coil produces a series of brief clicks. No evidence of hearing loss has been found in humans exposed to TMS, despite extensive exposure to repeated stimulations over several years.
4) Risk of Seizure Induction (rare, serious): The major safety concern about TMS is the possibility of eliciting a seizure, although TMS has rarely been associated with the induction of seizure, even in patients with epilepsy. Thus, seizure risk, while not zero, is so low as to be difficult to estimate. Even with rTMS therapy for depression, patients are routinely treated on psychotropic medications, and the risk of seizure induction is estimated at 1/30,000 treatments.
5) Light headedness and/or Syncope (rare, not serious): In the setting of altered sensory stimulation, subjects occasionally experience brief loss of consciousness, usually attributable to vasovagal syncope.
6) Magnetic or induced stimulation (very rare, serious): there is some risk of these currents interacting with metals or implanted devices in a potential subject.
7) For women of child-bearing potential: It is unknown if TMS can pose a risk to fetuses.

Steps taken to reduce risk:

1) Local scalp pain near stimulation site (common, not serious): The coil will be moved slightly or the stimulation magnitude will be turned down.
2) Headache or neck pain (common, not serious): These side effects are usually managed well with standard analgesics (e.g., single doses of aspirin, acetaminophen, or ibuprofen). If you have a headache after stimulation that persists the following day, please contact us using the information at the end of this form.
3) Sound exposure (rare, serious): Earplugs will be used in this study in all subjects as a precautionary measure.
4) Risk of Seizure Induction (rare, serious): For all studies, the parameters used will fall within the safety parameters established at the International Workshop on the Safety of Repetitive Transcranial Magnetic Stimulation from 2009, as well as the safety guidelines for TMS protocols that are not repetitive in nature (e.g., single- and paired- pulse studies). In the event that a seizure occurs, you will receive counseling about the low likelihood of a recurrent seizure. Mindful of the potential consequences of a report of a seizure in a medical record for a subject's insurability, driving, etc., our medical documentation will include full details about the provoked nature of the seizure in an experimental protocol.

   In addition the following steps will be taken:

   - Subject Screening: You will have been screened multiple times before signing this form, to ensure you are not at increasing risk of having a seizure or other adverse reaction.
   - Training of all individuals who administer TMS: All personnel involved in TMS sessions will be familiar with the safety guidelines and with the seizure protocol.
   - Seizure protocol: A seizure protocol will be posted in a visible location in the room where TMS will be delivered.

5) Light headedness and/or Syncope: You are encouraged to be well-hydrated in advance of the sessions. During breaks and upon completion of the protocol, we will ask that you rise slowly from the chair and we will monitor you for any signs of fading consciousness.
6) Magnetic or induced stimulation: Although the risk of adverse events due to magnetic fields or induced electrical currents acting on tissue at the parameters proposed in this

experiment is virtually non-existent, there is some risk due to these currents interacting with metals or implanted devices in a potential subject. Therefore, rigorous screening procedures will occur to minimize this risk to acceptable levels.

7) For women of child-bearing potential: Participants are asked during their screening whether they are pregnant or are trying to become pregnant, and are not enrolled in the study if they are. Sexually-active women of child-bearing potential will be asked to use a reliable birth control method for the duration of this study.

fMRI – Potential Risks

1) A minor risk of discomfort or anxiety from being in the confined space of the MRI scanner.
2) Fast imaging sequences, such as those employed in this study, have the potential to induce peripheral nerve stimulation (PNS). PNS can be described as a light touching sensation on the skin surface and may cause mild discomfort, but is not harmful.
3) Risks of hearing damage due to loud noises produced by the scanner.
4) Risk that the magnetic resonance image will reveal a minor or significant lesion in the brain (e. g. a tumor), previously unknown to the subject, and requiring additional follow-up.
5) Risk of injury from objects accelerated by the strong magnetic field of the magnet, striking the subject; or metallic substances on the skin or foreign bodies implanted deliberately or accidentally in the subject that acquire kinetic or thermal energy from the magnetic or radiofrequency emissions of the MRI, causing tissue injury.
6) Sometimes, subjects report a temporary, slight dizziness or light-headedness when they come out of the scanner.
7) Potential risk for pregnant women: According to the NIMH Council Workgroup on MRI research and Practices (September, 2005), "there is no known risk of MR brain scanning of a pregnant woman to the developing fetus for scanning at 4T or less, and no known mechanism of potential risks under normal operating procedures." Nevertheless, subjects should be warned about potential risks not yet discovered.

Steps taken to reduce risk:

1) The risk of discomfort and anxiety will be minimized by custom pads and pillows to make you as comfortable as possible. You will be able to communicate with the machine operator via an intercom and may trigger an audible alarm at any time. If you were to experience an anxiety reaction, the study would be halted, and you would receive immediate counseling from staff, with option to meet with the P.I. You will be given the P.I.'s contact information at the end of this form and, if there is any doubt that your anxiety has been relieved, we will follow up with you via phone in the days following the session.
2) The MRI machine is operated within FDA guidelines, so the potential for inducing PNS is low.
3) All subjects are required to wear foam earplugs to reduce the risk of hearing damage.
4) In the event of anomalous finding on MRI, the PI would contact you and advise you to speak to your healthcare provider about obtaining a clinical MRI scan. Many such abnormalities are not clinically significant, but you may need or want to investigate them further. Such a finding might

require additional studies, and maybe even treatment, which would not be paid for by the investigators, the sponsor, or the University of Michigan. However, you should also know that your scan images will not be routinely examined by a specialist trained to make medical diagnoses. Any abnormalities that you may currently have may not be noticed in the images obtained in this experiment. If you have any current health concerns, you should consult your doctor.

5) The MRI suite is kept clear of all objects that could be picked up by the magnetic field. MRI personnel are trained in safety procedures, which include training on what materials cannot be brought into the scanner room. Before the scan you will be asked to fill out a safety form to assess your suitability to enter the MR environment. The MR technologist will review this form with you, and you will be asked multiple times to ensure there are no metallic objects on your person. Lockers are available for you to store your personal items during the scan.
6) To minimize risks from nausea, you will be carefully eased out of the scanner, and the MR technologist will guide you from the scanner bed. They will make sure you rise slowly and ensure you have adequate balance before standing.
7) Pregnancy, or the intention to become pregnant, are contraindications to receiving a research MRI scan. If you are pregnant or are trying to become pregnant, you cannot participate in this study. You will be given urine pregnancy tests prior to any MRI procedure. Additionally, . Sexually-active women of child-bearing potential will be asked to use a reliable birth control method for the duration of this study.

If you feel any discomfort, nausea or light headedness please inform a member of the study team. During all study tests, you will be allowed breaks to minimize the risk of fatigue and may leave the study if you want to. You will be asked about your experience upon completion of each study visit.

As with any research study, there may be additional risks that are unknown or unexpected. If you have any questions or are unsure about anything, please do not hesitate to ask Dr. Vesia or his associates.

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.

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 doctor.

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.

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?
This is not a treatment study; therefore, there are no other options available if you do not participate. This study is voluntary, and you may stop at any time, though.

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?
There is no harm or potential risk of withdrawing from the study early. This study is completely voluntary. If you withdraw during TMS stimulation, the researcher may recommend waiting for up to 30 minutes prior to you leaving for observance.

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?
There are no costs or billing for this study.

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 one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes

you injury, you will have to arrange for treatment on your own, as the study will not provide medical treatment or provide any compensation to you. You or your insurance provider will be billed for all costs of treatment for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

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?

You will be paid upon the completion or withdrawal from the study in the following manner:

- Screening session: $10/hour (estimated total length: 2 hours; $20)
- Remaining sessions: $20/hour (estimated total length: 10 hours, $200)

You will also be paid an extra $50 for completing all study sessions, for a total of $270. If you withdraw from the study before completing it, you will be paid based on the amount of time you took part in the study, following the above rates.

8.3 Who could profit or financially benefit from the study results?

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

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?

Multiple steps are taken to ensure the confidentiality of sensitive information. This study is voluntary—you do not have to answer questions that make you feel uncomfortable. The confidentiality of all information gathered directly from you or obtained from your medical records is assured by assigning records a coded research number and identifying all computer and paper files only by this code. A single tracking file will link the codes with subject identifiers, such as name and age. In addition, consent forms and payment forms will be kept in a separate, locked room, apart from research data. All files will be kept in locked file drawers in locked rooms, to which only authorized research personnel have access. Electronic records will be kept on secure servers, and records with identifying information will be kept separate from records used to collect research data. Only staff members who have a need to know personal identifying information will have access to this information. All research staff are trained in research ethics and HIPAA regulations pertaining to protected health information.

Screening forms for subjects who do not qualify for the study will be destroyed, except for anonymous information that cannot be linked to the subjects (such as age, gender and education). After the completion of data analysis, the record linking subjects to the research codes will be destroyed, thereby anonymizing the data. Only with your permission will we retain identifying information (i.e. if you would like to participate in future research).

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 SPONSOR 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.

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

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 information 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.

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.
- 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
- 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 accounting department may need your name, address, Social Security number, payment amount, and related information for tax reporting purposes.

- 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 leave before the study is finished?
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 left the study 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, it is protected by privacy policies. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected.

9.4 When does my permission to use my information 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:	Michael Vesia, Ph.D.
Mailing Address:	SKB 4140 830 N University Ave. Ann Arbor MI 48109-2214
Telephone:	734-764-5237
Email:	mvesia@umich.edu
Study Coordinator:	Ashley Rettmann, CCRP

Mailing Address: SKB 4100 WS 4_4
830 N University Ave.
Ann Arbor, MI 48190
Telephone: 734-763-2790
Email: arettman@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 3214
Ann 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 will receive electronic 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.)*
- "Pregnancy Screening for B2Lab Research Studies"

12. SIGNATURES

Sig-A

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 [NAME OF STUDY TEAM MEMBER OBTAINING CONSENT] _____. 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.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Sig-D

Consent/Assent to Collect for Unspecified Future Research

This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether or not to allow future use of my specimens. 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.

_____ Yes, I agree to let the study team keep my specimens for future research.

_____ No, I do not agree to let the study team keep my specimens for future research.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Sig-G

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 (mm/dd/yy): _____