Impact of Repetitive Transcranial Magnetic Stimulation (TMS) on Spike Frequency and Brain Connectivity in Children With Benign Epilepsy With Centrotemporal Spike (BECTS)

Informed Consent Form

NCT04325282

March 14, 2023

Please check all that are applicable:

☐ I am an adult participant in this study.

Print your name here:

_____

☐ I am the parent or guardian granting permission for a child in this study (the use of "you" refers to "your child" or "your ward.")

Print child's name here:

_____

Are you participating in any other research studies? _____ Yes _____No

PURPOSE OF RESEARCH

You or your child are invited to participate in a research study of brain excitation in benign epilepsy with centrotemporal spikes (BECTS, otherwise known as Rolandic Epilepsy) and its relationship with cognition and learning. We hope to learn about how differences in brain excitation, brain plasticity and brain connectivity relate to difficulty with language, attention and learning in this condition. We will be assessing the brain with electroencephalogram (EEG) as well as transcranial magnetic stimulation (TMS), in which a magnetic pulse is administered to the scalp and the response of brain waves and muscle twitches is measured.

You or your child were selected as a possible participant in this study because of a current or past diagnosis of BECTS.

Alternatively, you are being selected as a possible healthy comparison subject because you do not have BECTS or other neurologic problems.

If you decide to terminate your participation in this study, you should notify Dr. Fiona Baumer at 650-721-8496.

This research study is looking for 50-65 children with BECTS, 20 adolescents or adults with a history of BECTS that is now resolved, and 30-50 healthy control participants in the United States.

VOLUNTARY PARTICIPATION

You or your child's participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your child's or your/his/her medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you or your child is entitled.

DURATION OF STUDY INVOLVEMENT

This research study is expected to take approximately 2-3 days. This is a multi-part study. The first session involves cognitive testing and will take between 90-120 minutes. The second session involves transcranial magnetic stimulation (TMS) with electroencephalogram (EEG) and is expected to take 2-4 hours. The third session involves just EEG and is expected to take 2-3 hours. You will be asked to participate in the cognitive testing as well one or both of the other sessions.

PROCEDURES

If you or your child choose to participate, Dr. Fiona Baumer and her research study staff will request that you participate in three types of sessions. During the first session, you or your child will undergo cognitive testing. This testing will include answering questions, solving problems and puzzles, completing tasks on the computer, and learning some fine motor tasks. The purpose of this testing is to evaluate language, attention and learning abilities. In addition, we will review you or your child's medical history with you and perform a brief neurologic exam. This session will take 2-3 hours.

During the second session, which will be scheduled within several days to weeks of the first session, you or your child will undergo transcranial magnetic stimulation (TMS).

TMS involves applying a magnetic pulse to the scalp that stimulates the brain underneath. This allows us to measure the balance between excitation and inhibition in

the brain as well as measure synaptic plasticity, which is how quickly brain cells adapt to stimulation. It also allows us to evaluate how different regions of the brain are connected.

- At the beginning of this session, we will place a special cap on the head that measures brain wave response to TMS (called an electroencephalogram or EEG cap) and a special sticker on the hand that measures the muscle response to the TMS (called an electromyogram or EMG lead). Placing the cap and lead may take up to an hour. We will measure the brain waves for 10-15 minutes before we begin the TMS.
- We will use special markers on the EEG cap and TMS wand to digitally align you or your child's head with a map of the brain on our computer. This will help us know where to apply the magnetic pulse. This will take less than 5 minutes.
- We will then apply the magnetic pulse to the scalp using a special wand and we will measure the responses on the EEG and EMG. During the first part of the study, the pulses will be applied until we identify the motor cortex (the part of the brain that controls movement of the hand). The pulses are very brief (<1 second). This may take 10-30 minutes. We will then apply the pulses to the motor cortex in three ways: 1) a single pulse; 2) paired pulses with two pulses separated by several milliseconds; and 3) repetitive pulses with multiple pulses given back-to-back over the course of seconds to minutes. TMS will allow us to measure brain excitation, inhibition, and plasticity. The TMS session will take approximately 1-2 hours. You may be asked to perform some basic tasks, like naming objects or playing simple computer games, during the TMS.
- We will also have session of sham TMS on a separate day in which we use a coil that does not actually stimulate the brain to be a control.
- Since TMS sessions can be lengthy, we will have the option of breaking them up into shorter sessions over several days to make it easier on you or your child.
- For children taking seizure medications, we will obtain a blood sample at the time of TMS to measure the blood level of the medication.

During the third session, which will also be scheduled within several days to weeks of the cognitive testing, you will undergo an EEG. EEG allows us to record brain waves to see how they respond to certain activities and to measure how different brain regions are connected.

- At the beginning of this session, we will place a special EEG cap on the head that measures brain waves. Placing the cap may take 15 minutes to 1 hour.
- We will use special markers on the EEG cap to digitally align you or your child's head with a map of the brain on our computer. This will help us know where the different EEG electrodes are positioned relative to your brain. This will take less than 5 minutes.

- We will then record brain waves. We will do this both when you are resting and when you are performing some basic tasks, like naming objects or playing simple computer games. This will take 1-2 hours.

PARTICIPANT RESPONSIBILITIES

As a participant, you or your child's responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Keep your or your child's study appointments. If it is necessary to miss an appointment, please contact the Protocol Director or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you or your child may have.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue participation at any time. Your decision will not affect your or your child's ability to receive medical care for your/his/her disease and you/he/she will not lose any benefits to which you/he/she would otherwise be entitled.

If you decide to withdraw your consent to participate in this study, you should notify Dr. Fiona Baumer at 650-721-8496. If you choose to withdraw, there are no anticipated consequences of your withdrawal. Please contact Dr. Fiona Baumer as above to alert her to your decision.

The Protocol Director may also withdraw you or your child from the study without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your child's participation could be harmful to him/her.
- The study is cancelled.
- Other administrative reasons.

- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions.

One potential risk is breach of confidentiality related to the collection of sensitive medical information or test scores. Several precautionary steps are taken to ensure the protection of confidential information and all personnel are carefully trained to keep information private. All testing and medical information gathered is identified by a subject number and is kept in a safe locked file cabinet or a secure electronic data base. Audio or video recordings of testing sessions may also be stored in this manner. Paper copies of test records and forms may be retained alongside digital copies. Digital copies of all data will be stored indefinitely. A single encrypted file linking subject numbers to identifiable information is only accessible to the trained research staff and Dr. Baumer.

TMS has been used for various conditions since 1985 and it is generally considered to be safe. There are no associated scalp needles, surgery or even haircuts associated with the study. TMS is delivered by a wand held next to the head.

Common side effects include:
- Scalp discomfort
- Headaches during or after treatment in about 20-40%
- Neck or backaches from sitting still in a chair for the TMS sessions
- Boredom during sessions (you may be able to watch videos)
- Inconvenience and expense of having to come to sessions

Uncommon, but potentially serious, side effects include:
- Scalp burn. The coil has built-in cooling and cuts off if too hot, but a burn is possible.
- Hearing problems. The coil makes loud clicks. You will need to wear earplugs to protect your hearing.
- Mood or thinking changes. These are not expected but could happen
- TMS-induced seizures. This is rare with the type of stimulation used, but sometimes TMS provokes a seizure or seizures during stimulation in patients with epilepsy.
- Other unknown long-term effects of TMS due to changing brain excitability

Effects from TMS usually wear off over time, so any side effects are unlikely to be permanent, but this cannot be guaranteed.

EEG has been used for nearly 100 years. It is safe and completely non-invasive. Rarely, people find the EEG cap uncomfortable or have mild skin irritation with the adhesive used. These effects stop once the EEG is removed. Other potential side effects include boredom during the session and inconvenience and expense of coming to sessions.

POTENTIAL BENEFITS

There are no direct benefits to you or your child for participating in this study. However, the knowledge we gain may lead to a better understanding of the causes of cognitive problems in BECTS that eventually lead to better treatment options.

We cannot and do not guarantee or promise that you or your child will receive any benefits from this study.

ALTERNATIVES

This study is investigational and optional. The alternative is not to participate. Participants and their parents should discuss the important potential risks and benefits of the alternatives with a physician.

PARTICIPANT'S RIGHTS

You or your child should not feel obligated to agree to participate. You and your child's questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director.

You and/or your child will be told of any important new information that is learned during the course of this research study, which might affect your child's condition or your willingness to continue participation in this study.

CONFIDENTIALITY

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your or your child's identity and/or personal health information will not be disclosed except as authorized by you or as required by law**.**

However, there is always some risk that even de-identified information might be re-identified.

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

CERTIFICATE OF CONFIDENTIALITY

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 specimens 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 specimens 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

Authorization To Use Your Health Information For Research Purposes

Because information about you or your child and your/his/her health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you and your child about how your health information will be used or disclosed in the study. You or your child's information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my child's health information be utilized in the study?

The purpose of the research study is to test whether excessive brain excitability contributes to cognitive and learning problems in children with

BECTS. Brain excitability will be measured with TMS and cognitive function will be measured with a series of tests. By learning more about the causes of cognitive and learning problems in BECTS, we may be able to better design future treatments. You or your child's health information will be used to confirm the diagnosis of BECTS (or in the case of healthy subjects, to confirm that there is no neurologic disease). Furthermore, the information will be used to assess if the level of brain excitation measured by TMS correlates with cognitive scores. Data will be made anonymous and you or your child's personal health information will not be disclosed.

Do I have to sign this authorization form?
You do not have to sign this authorization form. But if you do not, you or your child will not be able to participate in this research study. Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?
If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your or your child's health information (and to discontinue any other participation in the study) at any time. After any revocation, your or your child's health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using the information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of you or your child's health information in this study, you must write to: Fiona Baumer, MD at 750 Welch Rd suite 317, Palo Alto, CA 94304.

What Personal Information Will Be Obtained, Used or Disclosed?
Your or your child's health information related to this study may be used or disclosed in connection with this research study, including, but not limited to, you or your child's name, date of birth, contact information, gender, medical history including details regarding birth, development, medication, and epilepsy history, physical exam findings, and test results such as EEG results, imaging results, MRI, and blood tests.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your or your child's health information in connection with this research study:

- The Protocol Director, Dr. Fiona Baumer
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary
- Research Staff

Who May Receive or Use the Information?

The parties listed in the preceding paragraph may disclose your or your child's health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- Food and Drug Administration
- The National Institutes of Health (NIH)
- Doris Duke

Your or your child's information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?

Your authorization for the use and/or disclosure of your child's health information will end on February 28, 2030 or when the research project ends, whichever is earlier.

_____ _____

Signature of Adult Participant Date

_____
Print Name of Adult Participant

_____ _____
Signature of Legally Authorized Representative (LAR) Date
(e.g., parent, guardian or conservator)

_____
Print Name of LAR

_____
LAR's Authority to Act for Participant
(e.g., parent, guardian or conservator)

FINANCIAL CONSIDERATIONS

Payment

You or your child will receive an Amazon gift card of $25 for each of the sessions.

Costs

There is no cost to you for participating in this study, other than basic expenses like transportation and the personal time it will take to come to the study visits.

Sponsor

Lucile Packard Children's Hospital and Stanford Hospital are providing the equipment and office space necessary to conduct this study. The National Institutes of Health and Doris Duke are providing financial support and/or material for this study.

Consultative or Financial Relationships

Dr. Fiona Baumer and Dr. Robert Fisher do not have any consultative or financial relationships to disclose.

COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you or your child might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you or your child in obtaining appropriate medical treatment. In the event that you or your child has an injury or illness that is directly caused by your/his/her participation in this study, reimbursement for all related costs of care first will be sought from your insurer, managed care plan, or other benefits program. **You will be responsible for any associated co-payments or deductibles as required by your insurance.**

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director will assist you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

You do not waive any liability rights for personal injury by signing this form.

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its risks and benefits, or alternative courses of treatment, you

should ask the Protocol Director, Dr. Fiona Baumer at 650-721-8496. You should also contact her at any time if you feel you have been hurt by being a part of this study.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

Appointment Contact: If you need to change your appointment, please contact Dr. Fiona Baumer at 650-721-8496.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant, you or your child has the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you about future studies that may be of interest to you?
____ Yes ____ No

You give consent for [your/your child's] audio recordings to be used to re-listen back to sessions, check scoring, and make notes about the session.
___Yes ___No

You give consent for [your/your child's] video recordings to be used to re-watch back to sessions, check scoring, and make notes about the session.
___Yes ___No

Signing your name means you agree to have your child participate in this study and that you will receive a copy of this signed and dated consent form.

_____ _____
Signature of Adult Participant Date

_____
Print Name of Adult Participant

_____ _____
Signature of Legally Authorized Representative (LAR) Date
(e.g., parent, guardian or conservator)

_____
Print Name of LAR

_____
LAR's Authority to Act for Participant
(e.g., parent, guardian or conservator)

_____ _____
(If available) Signature of Other Parent or Guardian Date

_____
Print Name of Other Parent or Guardian

_____
Authority to Act for Participant

The IRB panel determined that this study falls under 21 CFR 50.53 and therefore two parent signatures are required.
The permission of the other parent was not obtained because:
[] This parent is deceased
[] This parent is unknown
[] This parent is incompetent
[] This parent is not reasonably available*
[] One parent has legal responsibility for the care and custody of the child
*Not reasonably available
Means the other parent is not contactable by phone, mail, email or fax or the other parent's whereabouts are unknown. Does not mean the other parent is at work, at home, lives in another city, state or country, but is contactable by phone, mail, email or fax. Examples of not reasonably available:
The other parent is on active military duty and is not contactable by phone, mail, email or fax.
The other parent is incarcerated and is not contactable by phone, mail, email or fax. The whereabouts of the other parent are unknown

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent

The following witness line is to be signed only if the consent is provided as a summary form and accompanied by a short form foreign language consent.

_____
Signature of Witness

_____ _____
Print name of Witness Date
(e.g., staff, translator/interpreter, family member)

- Translated short form must be signed and dated by both the participant (or their LAR) AND the witness.
- The English consent form ("summary form"):

Must be signed by the witness AND the Person Obtaining Consent (POC).
The non-English speaking participant/LAR does not sign the English consent.
The non-English speaking participant/LAR should not sign the HIPAA participant line
if the participant or the LAR is non-English speaking, the Person Obtaining Consent (POC) must ensure that 1) the LAR's Description of Authority is completed and 2) that any questions or options presented by the consent form are documented and initialed by the POC on the Summary Form, per the participant's wishes, as they are understood during the consent process