Neurostimulation in Adult Survivors of Childhood Acute Lymphoblastic Leukemia (ALL)

NOTE: When we say "you" in this consent, we mean "you or your child." When we talk about research, it can be called a clinical trial, research study or research protocol.

Key Information

To start we want to highlight the **risks and study requirements** that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more detail.

A. Why are you being asked to volunteer in this study?
You are being asked to volunteer for this research study because you are a survivor of childhood acute lymphoblastic leukemia (ALL). Because of your treatment you may have developed difficulties with thinking and learning.

B. What is the usual approach to this condition/cancer?
This is a new treatment that has not been used in clinical care. You may choose not to take part in the study.

C. Why is this study being done?
Survivors of childhood ALL can have problems with thinking and reasoning. These problems may cause difficulty in daily life. Transcranial Direct Current Stimulation (tDCS), a form of non-invasive brain stimulation, may be a helpful way to improve thinking and reasoning. Researchers at St. Jude Children's Research Hospital want to see if combining electrical stimulation with brain training games at home is an effective way to improve thinking and reasoning in survivors of childhood ALL.

D. What will happen if you decide to take part in this study?
Taking part in this study takes about 6 months. The first part of this study will take about 5 hours (2.5 hours brain testing, 1-hour magnetic resonance imaging (MRI), 1-hour training) at St. Jude or about 3 hours by computer or compatible electronic device (1.5-hour brain testing, 1.5-hour training). The St Jude visit will occur over 1 to 2 days. There is a part of the study that happens at home. The at-home part of this study will take 6 months to complete. You will be asked to complete 2 brain stimulation sessions every week (20 minutes each) and training (20 minutes) for 24 weeks. The last part of the study will take about 4 hours (2.5 hours testing, 1-hour MRI) and will occur at St. Jude or about 1.5 hours by computer or compatible electronic device (1.5-hour brain testing). This will occur over 1 to 2 days.

E. What are the research risks and benefits of taking part in this study?
There are very few risks associated with this study. The most common risk of using tDCS has been a mild tingling and itching during the stimulation. Rarely, a first-degree burn (similar to a mild sunburn) could occur at the site of the electrode placement. About 1% of people reported headache or trouble sleeping after the simulation. The benefits of tDCS are unknown at this time but it may improve your thinking and reasoning.

F. How many people will take part in this study?
About 104 survivors of childhood acute lymphoblastic leukemia will take part in this study.

G. What are your options?
a. Taking part in this research study is completely your choice.
b. If you decide to take part in this study, you can change your mind and stop at any time.
c. If you decide not to take part in this study, you may still receive care at St. Jude.

If you are still interested in taking part in the NEUROSTIM research study, more detail will be provided in the following pages.

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1. Why are you being asked to volunteer for this research study?

You are being asked to take part in this clinical trial, a type of research study, because you are a survivor of childhood acute lymphoblastic leukemia (ALL). Treatment for your cancer may or may not have caused long-term thinking and reasoning problems. The tDCS device is an investigational device that is not FDA approved. The way that the tDCS device is being used in this study is considered low risk. Take your time in deciding and feel free to discuss this research study with your family, friends and St. Jude staff. Before agreeing, it is important that you read this consent form that describes the study. After you understand the study and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

2. Who is sponsoring this study?

The study is being sponsored by St. Jude Children's Research Hospital.

3. What is the purpose of this study?

Survivors of childhood ALL can have thinking and reasoning problems such as thinking in a flexible way and keeping track of several things at the same time. These problems can cause difficulty in daily life. Transcranial Direct Current Stimulation (tDCS), a form of non-invasive brain stimulation, may be a way to improve thinking and reasoning. We will use tDCS to send a low electrical current to a specific area of your brain. The electrical current may make that area of the brain work better for a short period of time. During this time, you will play computer games meant to train your brain to work better. Researchers at St. Jude want to see if pairing the electrical stimulation with the brain games at home improves thinking and reasoning in long-term survivors of childhood ALL.

4. What will be done in this study?

All tests and procedures done in this study are for research purposes only.

The parts of this study are:

1. Testing of the brain
2. MRI (campus visit)
3. Home-based tDCS (brain stimulation)
4. Home-based cognitive training

Testing of the brain

You will complete some tests to help us determine if you can take part in this study. Most of these tests are part of the testing you already complete as a participant in the St. Jude Lifetime Cohort Study. Two additional tests may be included that are new to this study. These new tests will take roughly 15 minutes. All the tests will be given to you by a psychological examiner or completed on a secure website to evaluate how you process information. The tests will look at how you solve problems, how well you can remember information, how well you pay attention, and how quickly you understand information. These tests are standardized tests commonly used to evaluate brain functioning (i.e. memory, attention, and reasoning). The entire evaluation will take up to 2.5 hours to finish, including the new tests. This evaluation will be done at the beginning of the study and at the end of the study. If for whatever reason you decide to stop the study early, we will give you the option to still complete this testing and you will receive compensation. All of the tests in the study are being done for research. None of the tests are being done as part of your regular standard of care.

MRI (campus visit)

Magnetic resonance imaging (MRI) is a non-invasive way to take pictures of the body. For the MRI, you will lie on a narrow table for the exam. The person conducting the MRI will leave the room to conduct the test. You will be able to talk with the person conducting the MRI at any time by using an intercom. It is important that you remain still once the scan has started and breathe normally. To finish the test, you will be shown pictures of symbols while in the machine and asked to identify those that match by pressing a button. You will hear instructions over the intercom. As you are finishing these tasks, the MRI machine will be taking pictures of your brain to see how it

is working. The MRI exam will take about 1 hour to finish. You will do this evaluation at the beginning of the study and at the end of the study.

The MRI being obtained for this study is for research purposes only. It is not an MRI examination to detect and diagnose disease. The MRI will not replace for any MRI of the brain that your doctor may have recommended or prescribed for you. You should be sure to obtain any MRI examination that your doctor has prescribed at a facility as recommended and in the time frame prescribed by your doctor.

Home-based tDCS (brain stimulation)

You will be trained in person on how to use the mobile tDCS unit which will stimulate your brain. The portable unit consists of a battery pack, control unit and a headband with sponges. You will be randomly selected (like a flip of a coin) to receive either active brain stimulation or placebo (no active stimulation) for 20-minutes at least 2 times per week. You will complete the brain stimulation/placebo session 2 times per week for 6 months. The machines will require a unique code for each session. Study staff will video chat with you using an electronic device provided to you by the study team. The study team will observe you to confirm correct headstrap fit and sponge placement. If the headstrap is too big or too small, the session will be rescheduled and a new headstrap will be sent to you. For each session, two wet sponges will be attached to your head over clean, dry skin and be used to pass a weak electrical current from one sponge to the other. You will be given a code to enter into the tDCS unit to start the session. If you feel any pain or discomfort at any time, you can end the session. After about two weeks you will no longer have sessions with a staff member but instead will used a system called ElectraRx to answer questions about whether you are having any symptoms, receive a code to login, then proceed with the stimulation session on your own. Study staff are available for any questions or concerns.

Home-based Cognitive Training

After you start each tDCS session you complete, you will be asked to play brain games on the electronic device. You will use the electronic device to complete the games within 1 hour of every at-home tDCS session. The brain games were created by Lumosity and are intended to improve attention, brain speed, memory, and flexible thinking. The games will take 20 minutes to complete. There will be 5 games presented during each training session. You will complete a total of at least 48 training sessions.

Schedule for Campus Visit Participation

Part of Study	**Visit 1 (Initial Visit)**	**Home-based training sessions 1 through 48 (6 months total)**	**Visit 2 (approximately 6 months after Visit 1)**	**Receive Test Results**
Informed Consent	Approximately 30 minutes			no
Testing of the brain	Up to 2.5 hours		Up to 2.5 hours	Yes-Visit 1 No-Visit 2
MRI	Approximately 1 hour		Approximately 1 hour	no
tDCS training	Approximately 1 hour			
Home-based tDCS*		At least 2X per week (20 minutes per session) for 6 months		no
Home-based Cognitive training		At least 2X per week (20 minutes per session) for 6 months Complete within 1 hour of every tDCS session		no
Health symptoms form		Once per week for 6 months. Complete prior to tDCS session.		no
Compensation	$150.00	$100 e-gift card after completing midpoint assessment	$150.00	
* You will be randomly selected (like a flip of a coin) to receive either an active brain stimulation device or a placebo device for 20-minutes, two times per week				

Schedule for Remote Visit Participation

Part of Study	**Visit 1 (Initial Visit)**	**Home-based training sessions 1 through 48 (6 months total)**	**Visit 2 (approximately 6 months after Visit 1)**	**Receive Test Results**
Informed Consent	Approximately 30 minutes			no
Testing of the brain	Up to 2.5 hours		Up to 2.5 hours	no
MRI	Will not be done for remote visit		Will not be done for remote visit	no
tDCS training	Approximately 1 hour			
Home-based tDCS*		At least 2X per week (20 minutes per session) for 6 months		no
Home-based Cognitive training		At least 2X per week (20 minutes per session) for 6 months Complete within 1 hour of every tDCS session		no
Health symptoms form		Once per week for 6 months. Complete prior to tDCS session.		no
Compensation	$150.00	$100 e-gift card after completing midpoint assessment	$150.00	
* You will be randomly selected (like a flip of a coin) to receive either an active brain stimulation device or a placebo device for 20-minutes, two times per week				

5. What are the risks and benefits of taking part in this study?

a. Risks

tDCS: tDCS has been shown to be safe at the levels proposed in this study. You may notice some mild tingling or redness where the sponges are placed on your scalp. A rare side effect that could occur is a first-degree burn (similar to a mild sunburn). Making sure the sponges are moist and placed on clean, dry skin free of lotions, make-up etc. will greatly reduce the risk of any skin irritation. It is also possible that you may feel some fatigue after treatment or some itching under the site where the sponges are placed on your scalp. These effects are temporary and go away after stimulation. There is a slight risk of experiencing a flash of light; this is a harmless side effect and less likely to occur with correct placement of the sponges and headstrap. There is a small chance you will experience a headache or difficulty sleeping (about 1%). Recent studies have shown that the risk for side effects is no greater than placebo (no treatment).

Testing of the brain: Some participants may feel embarrassed or feel inadequate to answer questions related to memory, the ability to understand, etc. If you do not want to answer a question for any reason, please tell us, and we will skip the question. If you become upset, study staff will be available for you to discuss your feelings. You may choose to stop participating in the study at any time.

MRI: Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MRI scanner uses a very strong magnet that will attract some metals and affect some electronic devices. As metallic objects may be strongly attracted to the magnet, all patients will be screened for implanted metal prior to having an MRI. Female participants must have a pregnancy test before the MRI. If the test indicates a pregnancy, then you cannot continue in this study. You may feel anxious or uncomfortable in the MRI machine. You may exit the machine at any time.

Loss of privacy: Very rarely, personal information from your records could be given out by accident. This might make you upset, embarrass you, or affect your ability to get insurance. To stop this from happening, we:

- Store records apart from names or other personal information
- Only allow members of the study team to see the records
- Store electronic data only on computers protected with a password and encryption software
- Report study results on the whole group and never identify one single person in any reports

There may be other risks which are not known.

b. Benefits

You may benefit from the information researchers learn from evaluating your brain function. It may be possible to improve your brain function and your overall quality of life. In addition, the

information we learn from this study may help other cancer survivors. If you take part in the testing of the brain as part of your initial campus visit, you will receive your results as part of your St Jude LIFE test results. If you take part in the testing of the brain remotely (by computer and video conferencing) you will not receive these test results.

6. What are the risks to pregnancy, to an unborn child and to the ability to have children when taking part in this study?

The MRI portion of this study may involve risks to the participant/embryo or fetus if the participant becomes pregnant. Women who are pregnant or trying to become pregnant should not participate in the MRI. For all other study activities, there are no known risks to males regarding the ability to father children after taking part in this study and there are also no known risks to participant/embryo or fetus if the participant becomes pregnant.

7. Can you stop taking part in this study?

You may refuse to be in this research study or stop at any time. The decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital.

8. What are your other options?

The alternative to taking part in this study is not to take part.

9. How much will it cost you?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care not covered by your health insurer. This includes research-only costs. Research-only tests and procedures (such as optional biopsy, transcranial stimulation device, or blood samples for biomarker testing) will not be billed to you or your health care insurer.

10. Will you be paid for your time or expenses?

You will be paid for your time or expenses. You will receive $150 at the baseline visit (this typically includes both testing of the brain and the first tDCS training session) and $150 at 6-month follow-up, for a total of $300 for participation. This payment is not dependent upon your effort during the study or visits. Rather it is provided simply for your involvement in the study. You will also receive an electronic gift card for $50 at approximately the end of Week 6 of participation, a $100 electronic gift card at approximately the end of Week 12 (midpoint assessment) and a $50 electronic gift card at approximately the end of Week 18.

11. What if there is a problem?

If you have any questions about this study or if you are injured because of this study, contact Dr. Tara Brinkman at 901-595-5891 immediately. If you are injured from being in this research study, St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate. It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

12. How will new findings related to your participation in this study be shared with you?

The researcher will tell you of any new information learned during your study participation which might cause you to change your mind about continuing the study.

13. How will you find out the results of this study?

The researcher will give you information about the overall results of this study. Whether you will know your personal test results will be discussed in another part of this document. St. Jude researchers share information with people in studies in many ways including:

- Articles on www.stjude.org
- In newsletters
- In medical or scientific journals
- In the media
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by the U.S. Law. This website will not include information that can identify you. At most the Website will include a summary of the results. You can search this Website at any time.

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

14. What about privacy and confidentiality?

When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI (protected health information) may be used or given to someone outside the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude Internet website: www.stjude.org.

A decision to take part in this research means that you agree to let the research team use and share your PHI with other researchers for purposes of the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.

Federal agencies such as the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP), the National Institutes of Health (NIH), and St. Jude Children's Research Institutional Review Board (IRB), your insurance company and other health benefits plan (if charges are billed to these plans), as well as other regulatory agencies, committees, or persons involved in overseeing research studies may review your research and medical record.

As part of the study, Dr. Brinkman and her study team may share the results of the study and/or non-study information (brain evaluations, etc.), as well as parts of your medical record, to the groups named below. These groups may include people from:

1. The Office for Human Research Protections (OHRP).
2. St. Jude Children's Research Hospital Institutional Review Board (IRB), a committee that reviews the ethics and safety of research studies.
3. St. Jude Children's Research Hospital's clinical research monitors and auditors.
4. Information collected for the study will be sent to Dr. Kesler at the University of Texas MD Anderson Cancer Center, Department of Neuro-oncology for review. This data will be coded and only the investigators at St. Jude will have the code.

Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your Protected Health Information (PHI) private.

We will keep your medical records private to the degree allowed by law. The sponsor and/or St. Jude may give your health data, without identifiers, to others or use it for other research projects not listed in this form. The sponsor, St. Jude, Dr. Brinkman and their staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

We will not identify you personally in any text published about this study. Your personal information will not be in any text published about this study.

Only information needed for the study is recorded.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will also be kept for an unknown length of time.

Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

15. Permission to Use Your Data/Information: Authorization/HIPAA

If you sign this document, you give permission to the sponsor, Dr. Brinkman, and staff to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research may include information in a medical record, results of physical examinations, medical history, lab tests, or certain health information indicating or relating to a particular condition. The health information may be used by and/or disclosed (released) to all researchers and their staff at St. Jude Children's Research Hospital.

St. Jude Children's Research Hospital is required by law to protect your health information. By signing this document, you authorize St. Jude Children's Research Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

- You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to:

HIPAA Privacy Officer
St. Jude Children's Research Hospital
262 Danny Thomas Place, Mail Stop 280
Memphis, TN 38105

This Authorization does not have an expiration date.

16. Further Information and Contact Details for Questions about This Research Study

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or doctor, who will be able to provide you with up to date information about the drug(s)/procedure(s) involved. If you wish to read the research on which this study is based, please ask your study nurse or doctor.

If there is anything you do not understand, or have any other questions, please contact the researcher listed below.

IF AT ANY TIME DURING THE STUDY YOU EXPERIENCE ANY DISCOMFORT OR UNUSUAL SYMPTOMS, OR SIDE EFFECTS, PLEASE CONTACT ANY OF THE DOCTORS LISTED BELOW.

Dr. Tara Brinkman
St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN 38105
Tel: (901) 595-3300

If you require any medical or surgical treatments outside of St. Jude such as with your local doctor or another hospital during this study, your researcher and their team would need to be informed.

You can get more details about your rights as a research participant by calling the St. Jude Institutional Review Board at 901-595-4357 or the Research Participant Advocate at 901-595-4644 or 901-595-1139. The Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns, and questions. The Advocate can help you obtain information and can relay any input you may have concerning the research to the research study team. If you are outside of the Memphis area, please call toll-free 1-866-583-3472 (1-866-JUDE-IRB).

If you decide you would like to take part, then please read and sign the consent form. You will be given a copy of this information and the consent form to keep. A copy of the consent form will be filed in your patient notes, one will be filed with the study records and one may be sent to the Research Sponsor.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this information sheet and to consider this study.

St. Jude Children's Research Hospital
IRB NUMBER: 19-0053
IRB APPROVAL DATE: 03/01/2022

RESEARCH PARTICIPANT STATEMENT (Adult Participants 18 years and older):

I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this study.

_____ _____ _____AM/PM

Research Participant Signature Date Time (circle on)

RESEARCHER/DESIGNEE STATEMENT: I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

_____ _____ _____AM/PM

Research/Designee Signature Date Time
(circle on)

_____

Print Name