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AS MODIFIED
Dec 26, 2023

Laureate Institute for Brain Research, Inc., Tulsa, OK, United States

RESEARCH SUBJECT INFORMATION AND CONSENT FORM	
TITLE:	*Modulating repetitive negative thinking related brain networks in young adults with depression*

This consent form contains important information to help you decide whether to participate in a research study.

The study staff will explain this study to you. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this consent form to think about and discuss with family or friends.

- **Being in a study is voluntary – <u>your choice</u>.**
- **If you join this study, you can still <u>stop at any time</u>.**
- **<u>No</u> one can <u>promise</u> that a study will help you.**
- **Do not join this study unless all of your <u>questions</u> are <u>answered</u>.**

After reading and discussing the information in this consent form you should know:

- Why this research study is being done;
- What will happen during the study;
- Any possible benefits to you;
- The possible risks to you;
- Other options you could choose instead of being in this study;
- How your personal health information will be treated during the study and after the study is over;
- Whether being in this study could involve any cost to you; and
- What to do if you have problems or questions about this study.

Please read this consent form carefully.

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RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Modulating repetitive negative thinking related brain networks in young adults with depression

PROTOCOL NO.: 2023-002
WCG IRB Protocol #20231559

SPONSOR: Laureate Institute for Brain Research

INVESTIGATOR: Aki Tsuchiyagaito, Ph.D.
6655 South Yale Avenue
Tulsa, Oklahoma 74136-3326
United States

STUDY-RELATED PHONE NUMBER(S): Aki Tsuchiyagaito, Ph.D.
918-502-5112 (office)
918-200-6475 (cell)

Study Coordinator
918-703-1889 (cell)

Study Psychiatrist
Salvador Guinjoan, M.D., Ph.D.
918-502-5119 (office)
918-370-3598 (cell)

Laureate Psychiatric Clinic and Hospital
918-502-5155
918-481-4000 (24 hours)

Taking part in this research is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have any questions, concerns, or complaints or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we

believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

What should I know about this research?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

How long will I be in this research?

We expect you to be in the study for about 4-5 weeks across two in-person visits and one or two remote visits.

Why is this research being done?

This study aims to explore how investigational real-time fMRI neurofeedback (rtfMRI-nf) can influence brain activity and decrease repetitive negative thinking during different tasks, such as self-referential tasks. We hope the findings will enhance our understanding of how to use rtfMRI-nf to improve treatment outcomes for individuals with depression.

What happens to me if I agree to take part in this research?

If you decide to take part in this research study, the general procedures include a psychiatric evaluation, questionnaires, urine tests, emotional thought processing tasks, and magnetic resonance imaging (MRI) scans.

Could being in this research hurt me?

The most important risks or discomforts that you may expect from taking part in this research include feeling uncomfortable from the questions asked or tasks in the MRI scanner, discomfort and claustrophobia/anxiety during the MRI scans.

Will being in this research benefit me?

As we are delivering only a single session of rtfMRI-nf and it is still unproven as a treatment for depression, it is not expected that you will personally benefit from this research. However, your participation may help us better understand how the brain circuitry is involved in repetitive negative thinking.

What other choices do I have besides taking part in this research?

Your alternative is simply not to participate in the study. This study is for research purposes only as the effects of rtfMRI-nf are still unproven and we are not providing a full course of treatment. Common treatments for depression and anxiety include talking therapy (for example cognitive behavioral therapy or behavioral activation therapy) and

medications (for example selective serotonin reuptake inhibitors or bupropion). Please speak to your primary care provider if you are interested in treatment.

DETAILED RESEARCH CONSENT

Taking part in this research is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have any questions, concerns, or complaints or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

This consent form describes a research study. Research studies involve only individuals who choose to participate. Please take your time to make your decision about participating in the study.

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

Why Have You Been Asked to Participate in this Study?

You have been asked to take part in this study because you are an English-speaking individual, aged 18-35, with major depression and a high tendency for repetitive negative thinking.

Why is this Study Being Done?

The study will use functional Magnetic Resonance Imaging (fMRI) of the brain. An MRI uses a magnetic field to produce an image. This study aims to better understand how investigational real-time fMRI neurofeedback (rtfMRI-nf) can modulate brain activity during various tasks, including self-referential tasks, and potentially reduce repetitive negative thinking and depression. By using an MRI scanner, we will monitor your brain activity while you receive either real or sham feedback (rtfMRI-nf or sham-nf). Our goal is to determine whether rtfMRI-nf can effectively change brain activity and help us improve treatment outcomes for young adults with depression. We hope this research will contribute to our understanding of the brain systems affected in neurological and psychiatric illnesses and the underlying mechanisms of repetitive negative thinking and regulation strategies.

What Devices are Involved in this Study?

This study involves a magnetic resonance imaging (MRI) scanner, which uses a magnetic field and radio frequency pulses to produce images of the brain. The MRI scanner will not be used for purposes outside of its intended application. A physiological recording system will also be used to monitor bodily responses such as heart rate and breathing.

How Many Subjects Will Take Part in this Study?

Approximately 110 participants will take part in this study at the Laureate Institute for Brain Research (LIBR). Participants will be divided in two arms of active and sham neurofeedback (50% each). You have an equal chance of being in either arm.

What is Involved in this Study?

If you take part in this study, you may complete the following tests and procedures:

Real-time fMRI neurofeedback (rtfMRI-nf) session (Visit1): You will have one rtfMRI-nf session, during which you may receive either real feedback or sham (fake) feedback. You will not be informed of the type of feedback you receive, and the research staff will also be unaware. In case of an emergency, the investigators can find out which group you were assigned to.

Screening procedures: The screening interview will involve multiple questionnaires. You have the right to refuse to answer any questions you don't want to. The screening results will only be used for this research and will not be part of your medical record. You will also complete a brief medical history questionnaire and screening form. If undesirable medical findings emerge during the interview, screening, or MRI scanning, they will remain confidential and be discussed with you by a study researcher.

Questionnaires & Worksheets: You will be asked to complete surveys remotely or on-site with a member of the study staff before and after the MRI session. Additionally, you will be asked to complete worksheets on-site with assistance from a study researcher. These questionnaires and surveys will assess your mental state, including rumination (deep thought about something), repetitive thinking, worry, emotion regulation, cognition, sleep, depression symptoms, anxiety symptoms, and affect. You have the right to leave this study at any time for any reason.

rtfMRI-nf procedures: You will receive a 60-minute session of real or sham neurofeedback. In real neurofeedback (rtfMRI-nf), you will receive a feedback signal from your brain. In sham neurofeedback (sham-nf), you will receive an artificially generated fake feedback signal, not associated with your brain activity. During the

rtfMRI-nf or sham-nf session, you will lie quietly in the MRI scanner. You may also be asked to provide ratings of how you feel while in the scanner.

MRI procedures: Before MRI scanning, you will learn how to complete the cognitive task that will be presented to you in the scanner, and will practice those tasks with a research staff. You will then be placed in the MRI scanner to receive the rtfMRI-nf or sham-nf and perform the task. The MRI scanner rapidly takes pictures of the brain. The MRI scanner is a metal tube surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the tube. You will be asked to lie still during scanning. Earplugs will be provided to lessen the loud "knocking" sounds that the scanner makes while it is imaging your brain.
First, you will receive a series of short scans that allow us to know where your head is inside the tube. You will then receive a scan lasting 5 to 15-minutes that gives us more detailed pictures of your brain. Finally, you will undergo a series of scans lasting about 60 minutes, during which you will lie at rest, receive rtfMRI-nf or sham-nf and perform the tasks. During all of these scans, it will be very important to remain still. Your time in the scanner will be about 1.0~1.5 hours.

If you are female, a urine pregnancy test will be obtained. An over-the-counter urine pregnancy test will be completed just prior to any MRI scanning. You will not be allowed to participate in the study if the pregnancy test reads positive.

Follow-up procedures (Visit2): One week after the rtfMRI-nf or sham-nf session, you will return to the LIBR to complete interviews and questionnaires, and perform a self-regulation fMRI task without feedback. This follow-up visit aims to evaluate the transferred effect of the session. The MRI procedures during this visit will be similar to those during the first visit and will last about 30mins.

How Long will You be in the Study?

We expect that you will take part in this research study for 4~5 weeks.
The table below is an estimate of the amount of time it will take to complete all visits.

Visit Schedule	Screening Day 0 (remote)	Visit 1 Day 0~7 rtfMRI-nf or sham-nf	Visit 2 Day 7~14 1 week follow-up	Follow-up Day 28~35 1 month follow-up (remote)
Pre-scan assessments	x	x	x	x
Physiological measurement		x	x	
MRI		x	x	
Assessments during MRI		x	x	

Post-scan assessments		x	x	
MRI time		1~1.5 hours	0.5 hours	
Total time	1.5 hours	2.5~3 hours	1.5 hours	15mins

Participation in the study will require up to 2 visits. The first visit will include self-report surveys, a 60-minute scan including some assessments, and post-scan assessments. The second visit will include self-report surveys, a 30-minute scan including some assessments, and post-scan assessments. The first and second visits will last between 1.5 and 3.0 hours. The time in the scanner will not exceed 2.0 hours for each visit.

There may be circumstances under which your participation in the study may be stopped by the investigator without your consent. Functional MRI is dependent upon measuring very small changes in blood flow in the brain. Therefore, there may be times in which the information collected will be unusable due either to a scanner malfunction or from you moving your head too much. Under these circumstances your participation may be stopped without your consent.

You may stop participating in this study at any time. You may also refuse to be contacted again in the future about participating in studies again.

What are the Risks of the Study?

The study may involve the risks described in this section.

It is possible that your medical and psychiatric histories or cognitive screening tests might reveal unanticipated medical or psychiatric findings. You have the right to refuse to answer any question that you do not wish to answer and to withdraw from participating in the study at any time.

This study is being done solely for research and not to provide medical or psychiatric care.

If medical or psychiatric problems arise or are found during the screening process, we may not be able to provide treatment for these conditions. It is important that you understand that treatment will not be offered in this study.

If unanticipated findings occur, we will provide you with all results of screening tests and will assist you in communicating these results to your primary physician, so long as you provide written consent for us to do so.

The risks of the study procedures are listed and discussed below.

1. ***Questionnaires and Worksheets***: The questionnaires and worksheets about your health, mood, and behavior are not physically harmful but may be stressful to complete and may be sensitive and emotionally distressing. You may experience temporary discomfort, including anxiety and sadness, when discussing a personal event and hearing or seeing the description of the event. We ask only that you try your best. Members of the research staff are trained to help you if you have an unusually strong reaction to these events. You can also stop the procedure at any time. Also, if you show a strong reaction, such as extreme sadness, to any part of the study, researchers will stop the procedure and help you relax before leaving the LIBR.

2. ***MRI scanning***: People are at risk for injury from the MRI magnet if they have any of the following metal implants or fragments:

    - pacemakers or other implanted electronic devices
    - brain stimulators
    - dental implants
    - aneurysm clips (metal clips on the wall of a large artery)
    - metallic prostheses (including metal pins and rods, heart valves, and cochlear implants)
    - permanent eyeliner
    - implanted delivery pump
    - shrapnel fragments

You will be asked to complete and sign an MRI screening form for each MRI scan. You will be screened for implants or metal fragments before the study, and if you have any of them, you will not receive an MRI scan and cannot be in the study. Tell the study doctor if you are uncertain whether you have any metal objects in your body. In addition, all magnetic objects (for example, watches, coins, jewelry, and credit cards) must be removed before entering the MRI scanner room.

Welders and metal workers are also at risk for injury because they may be unaware of small metal fragments in the eye.

Because of potential unknown risk to an unborn baby, women who are pregnant are excluded from having an MRI and cannot be in the study.

There are no known long-term risks or consequences of MRI scans. However, you may become uncomfortable because you will be lying in a small space. Some people are bothered by the loud thumping noises made by the scanner. You will wear earplugs to reduce the noise and increase your comfort during scanning. LIBR study staff will

closely and continuously monitor you throughout the scanning procedure. You will be removed from the scanner immediately if you request to be removed.

3. **Unknown Risks: Since this is an investigational instrument for depression, the rtfMRI-nf procedure may involve risks that are currently unforeseeable.**

Are There Benefits to Taking Part in the Study?

There is no known medical benefit to you for being in this study. Your participation might help us understand how the brain circuitry involved in repetitive negative thinking is different in healthy controls and depressive populations.

What are the Costs of Participating in the Study?

Neither you nor your health insurance will be charged for any of the study tests, procedures, or activities. If you need to be hospitalized, voluntarily or involuntarily, Laureate Institute for Brain Research does not intend to provide payment for this, and you or your insurance provider will be billed for these costs.

Will You be Paid for Participating in this Study?

For the study activities and procedures (excluding the MRI scans), you will be paid $10 per half hour. While you are in the MRI scanner, you will be paid $25 per half hour. Your time in the MRI scanner will not exceed 1.5 hours per session. When you completed both visits, you will be paid $50 as an incentive.

	Approximate Time in Hours	Estimated Compensation	Incentive Earned
Screening			
Consent	0.5	$10	
Assessments	1.0	$20	
Total for Screening	2.5	$30	
Visit 1			
Assessments (pre MRI)	0.75	$15	
Practice (outside of MRI)	0.5	$10	
MRI scan	1.0	$50	
Assessments (post MRI)	0.25	$5	
Total for Visit 1	2.5	$80	
Visit 2			
Assessments (pre MRI)	0.75	$15	

MRI scan	0.5	$25	
Assessments (post MRI)	0.25	$5	
Total for Visit 2	1.5	$45	
Follow-up			
Assessments	0.25	$5	$15
Total for Follow-up	0.25	$20	
Total for completing the study		$175	

If you do not complete the entire study, your payment will be prorated according to the table above. Your payment can be adjusted according to extra time you are needed to spend on this project based on the standard institutional rates. You will be paid through a ClinCard (similar to a debit card) that may be used 48 hours after the visit. The compensation for each visit will be provided within 48 hours after completion of those visits. We will need to obtain certain information from you in order to process the ClinCard. This information will be your name, address, and social security number. This information will only be used for processing your payment and will only be seen by the investigators and the accounting department that processes the payment to you. If you receive $600 or more in subject payments in one year you will receive a 1099 form to file with the IRS. This is to comply with IRS guidelines.

Your specimens (even if identifiers are removed) may be used for commercial profit. You will not share in this commercial profit.

What Other Options are There?

Your alternative is simply not to participate in the study. This study is for research purposes only as the effects of rtfMRI-nf are still unproven and we are not providing a full course of treatment. Common treatments for depression and anxiety include talking therapy (for example cognitive behavioral therapy or behavioral activation therapy) and medications (for example selective serotonin reuptake inhibitors or bupropion). Please speak to your primary care provider if you are interested in treatment.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits

We will do everything we can to keep others from learning about your participation in this study. To further help us protect your privacy, we will obtain a Certificate of Confidentiality from the United States Department of Health and Human Services (DHHS). With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify you in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except to prevent serious harm to you or others, and as explained below.

You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, or your involvement in this study.

If an insurer or employer learns about your participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy. Disclosure will be necessary, however, upon request of DHHS for the purpose of audit or evaluation, and is limited only to DHHS employees involved in the review.

You should understand that we will in all cases, take the necessary action, including reporting to authorities, to prevent serious harm to yourself, children, or others. An example of a reportable incident would be child abuse or neglect.

What happens to the information collected for this research?
The purpose of this study is research and not clinical treatment or care; thus, results of your individual participation will not be shared with you. We may use, maintain and share the information we collect about you during the research for data analysis and it may be used in future research studies. If we share your information with other researchers it will be de-identified, which means that it will not contain your name or other information that can directly identify you. This research may be similar to this study or completely different. We will not ask for your additional informed consent for these studies. The results of this study may be published in an article or presentation, but we will keep your name and other identifying information confidential.

Who may use and give out information about you?
Investigators at the Laureate Institute for Brain Research frequently collaborate with researchers at other nonprofit research institutions or commercial organizations. The data collected as part of this study, including interviews and medical information, research test results, and blood samples may be shared with these collaborators. Identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research

studies without additional informed consent from the subject. Any data shared will not include your name or other personally identifiable information. Your permission to use your personal and medical information for this research study will not expire.

Who might get this information?
The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- WCG Institutional Review Board (WCG IRB)

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

What if I decide not to give permission to use and give out my health information?
You will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
At any time after signing this Authorization, you can change your mind and revoke it. To revoke this Authorization, you will send a written letter to:

Aki Tsuchiyagaito, PhD
Laureate Institute for Brain Research
6655 South Yale Avenue
Tulsa, Oklahoma 74136

- If you revoke this Authorization, researchers may only use and disclose the Personally Identifiable Information (PII) already contributed to this research study.
- If you change your mind and revoke the Authorization, you will not be allowed to continue to participate in the study.

Is my health information protected after it has been given to others?
Although we will always try to protect your personal information, there is a risk that your information will be given to others without your permission.

Does my authorization expire?
Unless revoked, your authorization will not expire.

If you have any questions or concerns about your privacy rights, you should contact the LIBR Privacy Officer at 918-502-5155 or via email at privacy@laureateinstitute.org.

What If You Are Injured While Participating in This Study?
In case you get hurt or sick resulting from this study, emergency medical treatment is available. In the event of emergency, you should call 911. Be sure to tell the emergency staff and other healthcare providers of your participation in this study. Contact the investigator of this study, Aki Tsuchiyagaito, PhD as soon as possible using the contact information at the beginning of this consent. You can call the Investigator if you have questions or concerns. Your health insurance provider may be billed to cover the cost of the medical or emergency services provided. No funds have been set aside by the Laureate Institute for Brain Research to compensate you in the event you are hurt or get sick.

Who Will Provide Funding?
Funding for this research study will be provided by the National Institutes of Health.

What Are Your Rights as A Participant?
Taking part in this study is voluntary. You may choose not to participate. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. If you agree to participate and then decide against it, you can withdraw for any reason and leave the study at any time. You may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any of the following reasons:

- if it is in your best interest;
- you do not consent to continue in the study after being told of changes in the research that may affect you;
- or for any other reason.

What If There Are New Findings?
We will provide you with any significant new findings developed during the course of the research that may affect your health, welfare or willingness to continue your

participation in this study. You may be asked to sign a revised consent form if this occurs.

Whom Should You Call If You have Questions or Problems?
If you have questions, concerns, or complaints about the study or have a research-related injury, contact the investigator, Aki Tsuchiyagaito, PhD, Laureate Institute for Brain Research at 918-502-5112, 918-200-6475 (cell), 918-481-4000 (24 hours) or for emergencies call 911.

If you have questions about your rights as a research subject or if you have questions, concerns, or complaints about the research, you may contact:

WCG Institutional Review Board (WCG IRB)
Telephone: 855-818-2289
E-mail: researchquestions@wcgirb.com

WCG IRB is a group of people who perform independent review of research.

WCG IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WCG IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

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.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Your contact person for this study is: Aki Tsuchiyagaito, PhD.

She can be reached during business hours by: (918) 502-5112 or (918) 200-6475 (cell).

If you agree to be in this study, you will be given a signed and dated copy of this consent form.

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Consent and Signature

I have read the information in this consent form. I have been given an opportunity to ask questions. All my questions about the study and my participation in it have been answered.

I agree to participate in this study.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent form for the purposes described.

PRINTED NAME OF SUBJECT

Consent Signature

SUBJECT SIGNATURE Date

I confirm that the research study was thoroughly explained to the subject. I reviewed the consent form with the subject and answered the subject's questions.

Printed Name of Person Conducting the Informed Consent Discussion

Position

Signature of Person Conducting the Informed Consent Discussion

Date