Document Coversheet

Study Title: Theta Burst Stimulation for Alcohol Use Disorder

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	3/19/2025
NCT Number:	NCT06060496
IRB Number	86853
Coversheet created:	4/17/2025

PROTOCOL TYPE (VERSION 5)

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IRB Approval
3/19/2025
IRB # 86853
IRB6
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IMPORTANT NOTE:

If you accidentally select the wrong IRB type or "Protocol Process Type" while your Initial Review (IR) application is in draft form (unsubmitted), you may change your selections. Please contact the Office of Research Integrity (ORI) at 859-257-9428, IRBsubmission@uky.edu, or request a consult to resolve any questions regarding your selections *prior* to submitting your Initial Review application.

If your **submitted IR application has been returned to you for requested revisions or additional information,** to streamline the review process **do not make changes** to your selections here **unless instructed to do so by the ORI/IRB.**

Changes to this section cannot be made after initial approval has been issued (the option is not available for MR or CR).

For guidance, see:

- Which IRB?
- Which Protocol Process Type?
- "Getting Started"

Which IRB

- (●) Medical ( ) NonMedical

Protocol Process Type

- ( ) Exemption
- ( ) Expedited (Must be risk level 1)
- (●) Full

The revised Common Rule expanded exemption certification category 4 for certain secondary research with identifiable information or biospecimens. The regulations no longer require the information or biospecimens to be existing. For more information see the Exemption Categories Tool.

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CONTINUATION REVIEW/FINAL REVIEW

0 unresolved comment(s)

Based on your responses to the Continuation Review/Final Review questions, to be in accord with federal policy a final review report must be submitted to properly CLOSE OUT your protocol.

IF YOU WISH TO EXTEND YOUR IRB APPROVAL PERIOD, update your 'Anticipated Ending Date of Research Project' under the Project Information section and include any other supportive documentation for continuation of your study [NOTE: If you wish for your IRB approval to continue, but you do not request an extension and complete and submit your materials in a timely manner, IRB approval will expire at the end of the current approval period.].

To initiate your continuation review (CR)/annual administrative review (AAR), or properly close your study, complete this section and update/correct all other sections of your IRB application as applicable.

*****IMPORTANT*** Before leaving this page to update other sections of your application, be sure to SAVE this section first.**

If you have any questions, please contact the Office of Research Integrity at 859-257-9428 or email IRBsubmission@uky.edu

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1. Status of the Research

Check the statement(s) that best describe(s) the current status of your research:

- ☐ No subjects have enrolled to date.
- ☐ Recruitment and/or enrollment of new subjects or review of records/specimens continue.
- ☐ Study is closed to enrollment, but subjects still receive research-related interventions (e.g., treatment, blood draws).
- ☐ Study enrollment is permanently closed; subjects have completed all research-related interventions; and the study remains active only for long-term follow-up of subjects (see Tool Tip above for info on long-term follow-up of subjects).*
- ☐ Research has progressed to the point that it involves 1) Data analysis, including analysis of identifiable private information or identifiable biospecimens; and/or 2) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.*
- ☑ The remaining research activities are limited only to data analysis. There is access to records or specimens either directly or through codes or links to the data.*
- ☐ The remaining research activities are limited only to data analysis. There is no subject/record/specimen identifying codes or links to the data; the researcher or research team cannot readily ascertain the subject's identity.*
- ☐ All study activities are complete. IRB approval can be inactivated.

*Possibility that review will move from Full to Expedited.

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2. If subjects have been enrolled within the last year, and the IRB approved a consent/assent form for your study:

Please attach a complete, signed copy for the last two subjects enrolled with **each** consent/assent form/HIPAA form since the last annual review.
(Example: If 3 different approved consent forms were used since the last annual review, please provide the two most recent signed copies of each version for a total of six.)

Attachments

Attach Type	File Name
Entire Signed Consent Form	LAN-AIC-0008-Howard, Stephanie Signed ICF 5.3.2024.pdf
Entire Signed Consent Form	LAN-AIC-0007-Howard, Tyler ICF Signed 4.22.2024.pdf

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3. Informed Consent

If the study is **open to subject enrollment, please go to the Informed Consent section of the E-IRB Application and verify attachment(s) include:**

- One clean copy in PDF (without the IRB Approval stamp) of the currently approved consent/assent document(s), or,
- If requesting changes to the consent/assent document(s), submit one copy with the changes highlighted (and designate Document Type as "Highlighted"), and one clean copy in PDF (without the changes highlighted).

If the study is **open to subject enrollment and the IRB has waived the requirement to document informed consent, please go**

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to the Informed Consent section of the E-IRB Application and verify attachment(s) include:

- One clean copy in PDF of the currently approved document used for the informed consent process (e.g., cover letter, phone script), or,
- If requesting changes to the consent/assent document(s), submit one copy with the changes highlighted (and designate Document Type as "Highlighted"), and one clean copy in PDF (without the changes highlighted).

If the study is **closed to subject enrollment, please go to the Informed Consent section of the E-IRB Application and remove Informed Consent Documents designated to get an IRB approval stamp to avoid having them appear valid for enrollment.**

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4. Unanticipated Problems Involving Risk to Subjects or Others/Adverse Events Summary & Assessment

Did any **problems/adverse events** occur during the last 12 months?

○ Yes ◉ No

In the space below, provide a written summary of both unanticipated problems* and available information regarding adverse events since the last review (e.g., initial review or annual/continuing review). The amount of detail provided in such a summary will vary depending on the type of research being conducted; in many cases, such a summary could be a brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and investigator's brochure (if applicable). **The summary must include the PI's assessment whether the problems/adverse events warrant changes to the protocol, consent process, or risk/benefit ratio.**

Note: It is the IRB's expectation that all unanticipated problems involving risk to subjects or others or related deaths requiring prompt reporting are submitted in the appropriate time frame (See Policy [PDF]). Your response to this Annual/Continuing Review is considered assurance that all prompt reportable problems/adverse events have been submitted for IRB review.

*For multisite studies, the written summary should describe external events determined to be unanticipated problems involving risk to subjects or others.

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5. Subject Info To-Date

Our records for the previously approved IRB application indicate the **IRB approved estimate** of subjects to be enrolled (or records/specimens reviewed) is:

30

Enter the number of enrolled subjects (or records/specimens reviewed) that **have not been previously reported** to the IRB

4

Our records for the previously approved IRB application indicate the previous total # of subjects enrolled (or records/specimens reviewed) since activation of the study is:

4

The new total number of subjects enrolled (or records/specimens reviewed) since activation of the study:

8

Please review the Project Info section for the IRB approved estimate of subjects to be enrolled (or records/specimens reviewed). If this new total exceeds your approved estimate of subjects to be enrolled (or records/specimens reviewed), please update the number in the field for Number of Human Subjects in the Project Info section.

6. Data and Safety Monitoring Board (DSMB)/Plan (DSMP)

If your study is monitored by a DSMB or under a DSMP, attach all documentation (i.e. summary report; meeting minutes) representing Data and Safety Monitoring activities that have not been previously reported to the IRB.

Attachments

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7. Since the most recent IRB Initial/Continuation Review Approval:

Have there been any **participant complaints** regarding the research?

○ Yes ◉ No

If yes, in the field below, provide a summary describing the complaints.

Have any **subjects withdrawn** from the research voluntarily or by you as the PI for reasons related to safety, welfare, or problems related to the conduct of the research? If a participant does not meet the screening criteria for a study even if they signed a screening consent it is NOT considered a withdrawal.

○ Yes ◉ No

If yes, in the field below, provide a detailed explanation to the withdrawal(s) including if participants were lost to contact.

Has any **new and relevant literature** been published since the last IRB review, especially literature relating to risks associated with the research?

○ Yes ◉ No

If yes, attach a copy of the literature as well as a brief summary of the literature including, if pertinent, the impact of the findings on the protection of human subjects.

Attachments

Have there been any **interim findings?**

○ Yes ◉ No

If yes, attach a copy of **Interim Findings**.

Attachments

Have **subjects experienced any benefits?**

◉ Yes ○ No

If yes, in the field below, provide a description of benefits subjects have experienced.

Participants experienced a decrease in alcohol cravings.

Have there been any **inspections/audits/quality improvement reviews** of your research protocol resulting in the need for corrective action in order to protect the safety and welfare of subjects?

○ Yes ◉ No

If yes, please attach documentation evidencing the outcome(s) and any corrective action(s) taken as a result.

Attachments

Was an FDA 483 issued as a result of any inspections/audits?

○ Yes ◉ No

If yes, submit documentation using attachment button above.

8. Risk Level:

Our records for the previously approved IRB application show your research is:

Risk Level: 2

Has something during the course of your research changed the level of risk?

○ Yes ◉ No

If yes, go to the Risk Level section, mark the appropriate risk level, and in the field below, describe why the risk level has changed:

9. Funding/Support:

Our records for the **previously approved** IRB application indicate your research is being submitted to, supported by, or conducted in cooperation with the following external or internal agency(ies) or funding program(s):

- ☐ Grant application pending
- ☐ (HHS) Dept. of Health & Human Services
  - ☐ (NIH) National Institutes of Health
  - ☐ (CDC) Centers for Disease Control & Prevention
  - ☐ (HRSA) Health Resources and Services Administration
  - ☐ (SAMHSA) Substance Abuse and Mental Health Services Administration
- ☐ (DoJ) Department of Justice or Bureau of Prisons
- ☐ (DoE) Department of Energy
- ☐ (EPA) Environmental Protection Agency
- ☐ Federal Agencies Other Than Those Listed Here
- ☐ Industry (Other than Pharmaceutical Companies)
- ☐ Internal Grant Program w/ proposal
- ☐ Internal Grant Program w/o proposal
- ☐ National Science Foundation
- ☐ Other Institutions of Higher Education
- ☐ Pharmaceutical Company
- ☐ Private Foundation/Association
- ☐ U.S. Department of Education
- ☐ State

Other:

Internal

Please **update the Funding/Support section of your IRB application** if needed, including the following attachments if they contain changes not previously reported to the IRB:

- A current copy of your **protocol if you are conducting industry/pharmaceutical research;**
- A current **Investigator Brochure** (submit a copy with all changes underlined).
- A **new or revised grant application** for this project.

Did your project receive extramural funding?

○ Yes ◉ No

If yes, please review and correct if necessary, the OSPA Account # information under the **Funding/Support section** of your IRB application.

If the project is externally funded, has the sponsor offered any of the research team enrollment incentives or other personal benefit bonuses? (e.g., cash/check, travel reimbursements, gift checks, etc.)

○ Yes ◉ No ○ N/A

Note: It is University of Kentucky policy that personal benefit bonuses are not allowed. If these conditions change during the course of the study, please notify the IRB.

10. Project Information

Our records for the previously approved IRB application indicate your estimated project end date is:

12/31/2025

If you have a new estimated project end date, please go to the Project Info section and change the date in the field for Anticipated Ending Date of Research Project.

11. Study Personnel

Our records for the previously approved IRB application indicate the following individuals are study personnel on this project (if applicable):

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Last Name	First Name
No records to display.	

Please review the individuals listed above and update your records as needed in the Study Personnel section of the E-IRB application, being sure that each individual listed has completed or is up-to-date on the mandatory human research protection training [see the policy on Mandatory Human Subject Protection Training FAQs (required every three years)].

12. Progress of the Research

To meet federal requirements the IRB is relying on your RESEARCH DESCRIPTION as a protocol summary and their expectation is that it is up-to-date. If the currently approved protocol (or research description) in your E-IRB application is outdated, please make applicable changes, and describe in the field below any substantive changes and explain why they are essential. If none, insert "N/A" in the text field below. If you are closing your study, you may use the space below to summarize the final status of the research.

We are closing the study and need only data analyses. ICF is removed from attachments.

Note: No changes in the research procedures should have occurred without previous IRB review. Approval from the IRB must be obtained before implementing any changes.

Provide a brief **summary** of any **modifications that affect subject safety and/or welfare** approved by the IRB since the last initial or continuation review (If none, insert "N/A" in the text field below.):

N/A

Attach one copy of the most recent progress report sent to the FDA, if available. All PI-sponsored IND/IDE studies are required to submit a copy of the FDA progress report.

Attachments

13. Confidentiality/Security

Review your Research Description section and update the Confidentiality portion, if necessary, to describe measures for security of electronic and physical research records (e.g., informed consent document(s), HIPAA Authorization forms, sensitive or private data).

14. Subject Demographics

Our records for the previously approved IRB application indicate the following categories of subjects and controls are included in your research:

- ☐ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students
- ☐ UK Medical Center Residents or House Officers
- ☐ Impaired Consent Capacity Adults
- ☐ Pregnant Women/Neonates/Fetal Material
- ☐ Prisoners
- ☐ Non-English Speaking
- ☐ International Citizens
- ☐ Normal Volunteers
- ☐ Military Personnel and/or DoD Civilian Employees
- ☑ Patients
- ☐ Appalachian Population

Please review the Subject Demographics section of your IRB application for accuracy, and note the following:

If during the course of your research 1) any prisoners have been enrolled, OR 2) subjects have been enrolled that became involuntarily confined/detained in a penal institution that have not been previously reported to the IRB, go to Subject Demographic section in your E-IRB application and mark “prisoners” in the categories of subjects to be included in the study, if it is not already marked.

Note: If either 1 or 2 above apply, and you have received funding from the Department of Health and Human Services (HHS), a Certification Letter should have been submitted to the Office for Human Research Protections (OHRP); prisoners and individuals who have become involuntarily confined/detained in a penal institution cannot continue participation in the research until OHRP issues approval. If the Certification has not been submitted, contact the Office of Research Integrity.

Based on the **total # of subjects** who have enrolled, complete the subject demographic section below:

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native				
Asian				
Black or African American		1		
Latinx				
Native Hawaiian or Other Pacific Islander				
White	4	3		
American Arab/Middle Eastern/North African				
Indigenous People Around the World				
More than One Race				
Unknown or Not Reported				

If unknown, please explain why:

15. Research Sites

Our records for the previously approved IRB application indicate that you are conducting research at the following sites:

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☑ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital

- [ ] UK Hospital

Schools/Education Institutions Schools/Education Institutions

- [ ] Fayette Co. School Systems *
- [ ] Other State/Regional School Systems
- [ ] Institutions of Higher Education (other than UK)

Other Medical Facilities

- [ ] Bluegrass Regional Mental Health Retardation Board
- [ ] Cardinal Hill Hospital
- [ ] Eastern State Hospital
- [ ] Nursing Homes
- [ ] Shriner's Children's Hospital
- [ ] Other Hospitals and Med. Centers

- [ ] Correctional Facilities
- [ ] Home Health Agencies
- [ ] International Sites

Other:

If the above listed sites are not accurate, go to the Research Sites section of the E-IRB application to update the facilities at which research procedures have been or will be conducted.

If you are adding a new off-site facility, you may also need to update your E-IRB application Research Description, Research Sites, Informed Consent, and other affected sections as well as any documents which will list the off-site facility. Documents needing updating may include, but not limited to:

- Consent forms (attachment under Informed Consent section)
- Brochures (attachment under Additional Info section)
- Advertisements (attachment under Research Description section) ;
- Letter of support (attachment under Research Sites section)).

Please revise applicable sections and attachments as necessary.

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16. Disclosure of Significant Financial Interest

Disclosure of Significant Financial Interest:

Our records for the previously approved IRB application indicate that you, your investigators, and/or key personnel (KP) have a significant financial interest (SFI) related to your/their responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2):

○ Yes ◉ No

If you need to update your records, please go to the PI Contact Information section and/or Details for individuals listed in the Study Personnel section to change your response to the applicable question(s).

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17. Supplementals

To ensure the IRB has the most accurate information for your protocol you are expected to re-visit the E-IRB application sections and make corrections or updates as needed. At a minimum you are being asked to review the following sections for accuracy:

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STUDY DRUG INFORMATION—Please review for accuracy.
STUDY DEVICE INFORMATION—Please review for accuracy.
RESEARCH ATTRIBUTES—Please review for accuracy.
OTHER REVIEW COMMITTEES -- Please review for accuracy.

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PROJECT INFORMATION

0 unresolved comment(s)

Title of Project: (Use the exact title listed in the grant/contract application, if applicable).
If your research investigates any aspect of COVID-19, please include "COVID19" at the beginning of your Project Title and Short Title

Theta burst stimulation for alcohol use disorder IIII

Short Title Description
Please use a few key words to easily identify your study - this text will be displayed in the Dashboard listing for your study.

Theta burst stimulation for alcohol use disorder

Anticipated Ending Date of Research Project: 12/31/2025

Maximum number of human subjects (or records/specimens to be reviewed) 30

After approval, will the study be open to enrollment of new subjects or new data/specimen collection? ◉ Yes ○ No

Are you requesting that the UK IRB serve as the lead IRB for a multi-site study, **OR** that the UK IRB defer review to another IRB? [Click here for "IRB Reliance" help]

○ Yes ◉ No

If "Yes," before completing your IRB application, fill out the Reliance Request Form and submit it to irbreliance@uky.edu.

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PI CONTACT INFORMATION

0 unresolved comment(s)

Principal Investigator (PI) role for E-IRB access
The PI is the individual holding primary responsibility on the research project with the following permissions on the E-IRB application:

1. Read;
2. write/edit;
3. receive communications; and
4. submit to the IRB (IR, CR, MR, Other Review*).

If research is being submitted to or supported by an extramural funding agency such as NIH, a private foundation or a pharmaceutical/manufacturing company, the PI listed on the grant application or the drug protocol must be listed as PI here.

Please fill in any blank fields with the appropriate contact information (gray shaded fields are not editable). Required fields left blank will be highlighted in pink after you click "Save".

To change home and work addresses, go to myUK and update using the Employee Self Service (ESS) portal. If name has changed, the individual with the name change will need to submit a 'Name Change Form' to the Human Resources Benefits Office for entering into SAP. The new name will need to be associated with the individual's Link Blue ID in SAP before the change is reflected in E-IRB. Contact the HR Benefits Office for additional information.

The Principal Investigator's (PI) contact information is filled in automatically based on who logged in to create the application.

If you are not the Principal Investigator, do NOT add yourself as study personnel.
To change the PI contact information on an application in Researcher edit status:

- click "Change Principal Investigator";
- search for the PI's name using the search feature;
- click "Select" by the name of the Principal Investigator, then "Save Contact Information".

You will automatically be added as study personnel with editing permissions to continue editing the application.

Change Principal Investigator:

First Name:	Gopalkumar	Room# & Bldg:	Fountain Court
Last Name:	Rakesh	Speed Sort#:	40509
Middle Name			
Department:	Psychiatry - 7H800	Dept Code:	7H800
PI's Employee/Student ID#:	12461687	Rank:	
PI's Telephone #:	859-257-9402	Degree:	
PI's e-mail address:	Gopalkumar.Rakesh@uky.edu	PI's FAX Number:	
PI is R.N.	○ Yes ◉ No	HSP Trained:	Yes
		HSP Trained Date:	9/15/2022
		RCR Trained:	Yes

Do you, the PI/researcher, have a significant financial interest related to your responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2)?

○ Yes ◉ No

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RISK LEVEL

0 unresolved comment(s)

Indicate which of the categories listed below accurately describes this protocol

- ○ (Risk Level 1) Not greater than minimal risk
- ◉ (Risk Level 2) Greater than minimal risk, but presenting the prospect of direct benefit to individual subjects
- ○ (Risk Level 3) Greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
- ○ (Risk Level 4) Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of subjects.

*"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

Refer to UK's guidance document on assessing the research risk for additional information.

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SUBJECT DEMOGRAPHICS **0 unresolved comment(s)**

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc..) 21 to 60

Study Population:

Describe the characteristics of the subject population, including age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion.

Provide the following information:

- A description of the subject selection criteria and rationale for selection in terms of the scientific objectives and proposed study design;
- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group;
- Justification for the inclusion of vulnerable groups such as children, prisoners, adults with impaired consent capacity, or others who may be vulnerable to coercion or undue influence.

Please consider these resources:
NIH Diversity Policy
FDA Diversity Guidance

Inclusion criteria. Potential participants will be: 1) Patients seen at a clinic within the University of Kentucky Healthcare; 2) 21-60 years of age; 3) male or female gender 4) Able to read, understand and communicate in English; 5) willing to adhere to the general rules of the UK Healthcare; 6) Must fulfill DSM criteria for moderate alcohol use disorder.
Exclusion criteria. Positive pregnancy test for females, traumatic brain injury, history of seizure disorder, history of or current diagnosis of schizophrenia, intracranial metal shrapnel, previous adverse effect with TMS, sub-threshold consistency while performing behavioral tasks, failure to show baseline attentional bias to alcohol versus neutral cues.

Attachments

Indicate the targeted/planned enrollment of the following members of minority groups and their subpopulations. Possible demographic sources: Census Regional Analyst Edition, Kentucky Race/Ethnic Table, Kentucky Population Data.
(Please note: The IRB will expect this information to be reported at Continuation Review time for Pre-2019 FDA-regulated Expedited review and Full review applications):

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native:				
Asian:				
Black/African American:				
Latinx:				
Native Hawaiian/Pacific Islander:				
White:				
American Arab/Middle Eastern/North African:				
Indigenous People Around the World:				
More than One Race:				
Unknown or Not Reported:				

If unknown, please explain why:

Indicate the categories of subjects and controls to be included in the study. You may be required to complete additional forms depending on the subject categories which apply to your research. If the study does not involve direct intervention or direct interaction with subjects, (e.g., record-review research, outcomes registries), do not check populations which the research does not specifically target. For example: a large record review of a diverse population may incidentally include a prisoner or an international citizen, but you should not check those categories if the focus of the study has nothing to do with that status.

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Check All That Apply (at least one item must be selected)

- ☐ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students
- ☐ UK Medical Center Residents or House Officers
- ☐ Impaired Consent Capacity Adults
- ☐ Pregnant Women/Neonates/Fetal Material
- ☐ Prisoners
- ☐ Non-English Speaking (translated long or short form)
- ☐ International Citizens
- ☐ Normal Volunteers
- ☐ Military Personnel and/or DoD Civilian Employees
- ☑ Patients
- ☐ Appalachian Population

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook for more information on:

- Children/Emancipated Minors
- Students as Subjects
- Prisoners
- Impaired Consent Capacity Adults
- Economically or Educationally Disadvantaged Persons

Other Resources:

- UKMC Residents or House Officers [see requirement of GME]
- Non-English Speaking [see also the E-IRB Research Description section on this same topic]
- International Citizens [DoD SOP may apply]
- Military Personnel and/or DoD Civilian Employees

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Assessment of the potential recruitment of subjects with impaired consent capacity (or likelihood):

☐ Check this box if your study does NOT involve direct intervention or direct interaction with subjects (e.g., record-review research, secondary data analysis). If there is no direct intervention/interaction you will not need to answer the impaired consent capacity questions.

Does this study focus on adult subjects with any conditions that present a high *likelihood* of impaired consent capacity or *fluctuations* in consent capacity? (see examples below)

○ Yes ◉ No

If Yes and you are not filing for exemption certification, go to "Form T", complete the form, and attach it using the button below.

Examples of such conditions include:

- Traumatic brain injury or acquired brain injury
- Severe depressive disorders or Bipolar disorders
- Schizophrenia or other mental disorders that involve serious cognitive disturbances
- Stroke
- Developmental disabilities
- Degenerative dementias
- CNS cancers and other cancers with possible CNS involvement
- Late stage Parkinson's Disease
- Late stage persistent substance dependence
- Ischemic heart disease
- HIV/AIDS
- COPD
- Renal insufficiency
- Diabetes
- Autoimmune or inflammatory disorders
- Chronic non-malignant pain disorders
- Drug effects
- Other acute medical crises

Attachments

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INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

For creating your informed consent attachment(s), please download the most up-to-date version listed in "All Templates" under the APPLICATION LINKS menu on the left, and edit to match your research project.

Additional Resources:

- Informed Consent/Assent Website
- Waiver of Consent vs. Waiver of Signatures
- Sample Repository/Registry/Bank Consent Template

Consent/Assent Tips:

- If you have multiple consent documents, be sure to upload each individually (not all in a combined file).
- If another site is serving as the IRB for the project, attach the form as a “Reliance Consent Form” so the document will not receive a UK IRB approval stamp; the reviewing IRB will need to stamp the consent forms.
- Changes to consent documents (e.g., informed consent form, assent form, cover letter, etc...) should be reflected in a 'tracked changes' version and uploaded separately with the Document Type "Highlighted Changes".
- It is very important that only the documents you wish to have approved by the IRB are attached; DELETE OUTDATED FILES -- previously *approved* versions will still be available in Protocol History.
- Attachments that are assigned a Document Type to which an IRB approval stamp applies will be considered the version(s) to be used for enrolling subjects once IRB approval has been issued.
  Document Types that do NOT get an IRB approval stamp are:
  - "Highlighted Changes",
  - "Phone Script", and
  - "Reliance Consent Form",
  - "Sponsor's Sample Consent Form".

How to Get the Section Check Mark

1. You must:

   a) provide a response in the text box below describing how investigators will obtain consent/assent, and
   b) check the box for at least one of the consent items and/or check mark one of the waivers

2. If applicable attach each corresponding document(s) **as a read-only PDF**.
3. If you no longer need a consent document approved (e.g., closed to enrollment), or, the consent document submitted does not need a stamp for enrolling subjects (e.g., umbrella study, or sub-study), only select "Stamped Consent Doc(s) Not Needed".
4. After making your selection(s) be sure to scroll to the bottom of this section and SAVE your work!

Check All That Apply

- ☐ Informed Consent Form (and/or Parental Permission Form and/or translated short form)
- ☐ Assent Form
- ☐ Cover Letter (for survey/questionnaire research)
- ☐ Phone Script
- ☑ Informed Consent/HIPAA Combined Form
- ☐ Debriefing and/or Permission to Use Data Form
- ☐ Reliance Consent Form
- ☐ Sponsor's sample consent form for Dept. of Health and Human Services (DHHS)-approved protocol
- ☐ Stamped Consent Doc(s) Not Needed

Attachments

Informed Consent Process:

Using active voice, in the text box below, describe how investigators will obtain consent/assent. Include:

- the circumstances under which consent will be sought and obtained
- the timing of the consent process (including any waiting period between providing information and obtaining consent)

- who will seek consent
- how you will minimize the possibility of coercion or undue influence
- the method used for documenting consent
- if applicable, who is authorized to provide permission or consent on behalf of the subject
- if applicable, specific instruments or techniques to assess and confirm potential subjects' understanding of the information

Will electronic consent form/process be utilized on-site or remotely for this study?

○ Yes ◉ No

If yes, in addition to addressing the above bullet points, describe the e-consent method and platform, including any hyperlinks, videos, or enhancements used to convey information, if applicable. Attach a representation of the e-consent with signature fields. For guidance, see the ORI E-Consent web page.

Note: all individuals authorized to obtain informed consent should be designated as such in the E-IRB "Study Personnel" section of this application.

Special considerations may include:

- Obtaining consent/assent for special populations such as children, prisoners, or people with impaired decisional capacity
- *Research Involving Emancipated Individuals*
  If you plan to enroll some or all prospective subjects as emancipated, consult with UK legal counsel **prior to submitting this application to the IRB**. Include research legal counsel's recommendations in the "Additional Information" section as a separate document.
- *Research Involving Non-English Speaking Subjects*
  For information on inclusion of non-English speaking subjects, or subjects from a foreign culture, see IRB Application Instructions for Recruiting Non-English Speaking Participants or Participants from a Foreign Culture.
- *Research Repositories*
  If the purpose of this submission is to establish a research repository describe the informed consent process. For guidance regarding consent issues, process approaches, and sample language see the Sample Repository/Registry/Bank Consent Template.

Informed consent will be obtained after thorough discussion of the research project, what is required of the participant, the risks and benefits of participation in the study, and the procedures that are in place if/when challenges arise. This will be done by the PI, one of the co-investigators or research assistant during the first encounter with the subject, if they fulfill all eligibility criteria and are interested in study participation.
The research project is not connected to the SMART clinic (i.e., a person can be enrolled in the SMART clinic and their participation in the research project does not impact their standing in the SMART clinic and therefore the participation is truly voluntary in nature.
If you have questions about the study, you can contact the principal investigator for the study Gopalkumar Rakesh at 857-222-2276. If you have concerns or questions about your rights and/or welfare as a volunteer in this research, you can contact the staff in the Office of Research Integrity at The University of Kentucky at (859) 257-9428 or toll free at 1-866-400-9428. We will give you a signed copy of this consent form to take with you.

☐ Request for Waiver of Informed Consent Process

If you are requesting IRB approval to waive the requirement for the informed consent process, or to alter some or all of the elements of informed consent, complete, Section 1 and Section 2 below.

Note: The IRB does not approve waiver or alteration of the consent process for greater than minimal risk research, except for planned emergency/acute care research as provided under FDA regulations. Contact ORI for regulations that apply to single emergency use waiver or acute care research waiver (859-257-9428).

SECTION 1.

Check the appropriate item:

☐ I am requesting a waiver of the requirement for the informed consent process.

☐ I am requesting an alteration of the informed consent process.

If you checked the box for this item, describe which elements of consent will be altered and/or omitted, and justify the alteration.

SECTION 2.

Explain how each condition applies to your research.

a) The research involves no more than minimal risk to the subject.

b) The rights and welfare of subjects will not be adversely affected.

c) The research could not practicably be carried out without the requested waiver or alteration.

d) Whenever possible, the subjects or legally authorized representatives will be provided with additional pertin
after they have participated in the study.

e) If the research involves using or accessing identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

- Private information/specimens are “identifiable” if the investigator may ascertain the identity of the subject or if identifiers are associated with the information (e.g., medical records). This could be any of the 18 HIPAA identifiers including dates of service.
- If not using identifiable private information or identifiable biospecimens, insert N/A below.

☐ Request for Waiver of Signatures

If you are requesting IRB approval to waive the requirement for signatures on informed consent forms, **your research activities must fit into one of three regulatory options**:

1. The only record linking the participant and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality (e.g., a study that involves participants who use illegal drugs).
2. The research presents no more than minimal risk to the participant and involves no procedures for which written consent is normally required outside of the research context (e.g., a cover letter on a survey, or a phone script).
3. The participant (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk to the subject, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

Select the option below that best fits your study.

*If the IRB approves a waiver of signatures, participants must still be provided oral or written information about the study. To ensure you include required elements in your consent document, use the **Cover Letter Template** as a guide. There is an English and a Spanish version.*

○ **Option 1**

Describe how your study meets these criteria:

a) The only record linking the participant and the research would be the consent document:

b) The principal risk would be potential harm resulting from a breach of confidentiality (i.e., a study that involves subjects who use illegal drugs).

Under this option, each participant (or legally authorized representative) must be asked whether (s)he wants to sign a consent document; if the participant agrees to sign a consent document, only an IRB approved version should be used.

○ **Option 2**

Describe how your study meets these criteria:

a) The research presents no more than minimal risk to the participant:

b) Involves no procedures for which written consent is normally required outside of the research context (i.e. a cover letter on a survey, or a phone script):

○ **Option 3**

Describe how your study meets these criteria:

a) The subject (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm.

b) The research presents no more than minimal risk to the subject.

c) There is an appropriate alternative mechanism for documenting that informed consent was obtained.

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STUDY PERSONNEL **0 unresolved comment(s)**

Do you have study personnel who will be assisting with the research?
After selecting 'Yes' or 'No' you must click the 'Save Study Personnel Information' button.

(•) Yes ( ) No

Manage Study Personnel

Identify other study personnel assisting in research project:

- The individual listed as PI in the 'PI Contact Information' section should NOT be added to this section.
- If the research is required for a University of Kentucky academic program, the faculty advisor is also considered study personnel and should be listed below. ***Residents and students who are PI's are encouraged to designate the faculty advisor or at least one other individual as a contact with an editor role (DP).***
- Role: DP = Editor (individual can view, navigate, and edit the application for any review phase (IR, CR/FR, MR) or 'Other Review", and submit Other Reviews on behalf of the PI.)
- Role: SP = Reader (individual can view and navigate through the currently approved application only.)

To add an individual via the below feature:

- Search for personnel;
- Click "select" by the listing for the person you want to add;
- For each person, specify responsibility in the project, whether authorized to obtain informed consent, AND denote who should receive E-IRB notifications (contact status).

NOTE: Study personnel must complete human subject protection (HSP) and Responsible Conduct of Research (RCR) training before implementing any research procedures. For information about training requirements for study personnel, visit UK's HSP FAQ page, the RCR Getting Started page, or contact ORI at 859-257-9428. If you have documentation of current HSP training other than that acquired through UK CITI, you may submit it to ORI (HSPTrainingSupport@uky.edu) for credit.

Study personnel assisting in research project:

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI	Active
Alcorn	Joseph	Data Analysis/Processing	DP	Y	N	PhD	P	Y	03/13/2023	Y	N	03/21/2023	N	Y
Anderson	Danielle	Co-Investigator	SP	Y	N	MD	P	Y	05/31/2023	Y	N	05/31/2023	N	Y
Garth	Patricia	Study Coordinator	DP	Y	Y		P	Y	03/13/2023	Y	N	12/25/2023	N	Y
Himelhoch	Seth	Co-Investigator	DP	Y	N	MD MPH	P	Y	07/18/2022	N	N	03/21/2023	N	Y
Means	Natalya	Data Collection	DP	Y	Y		P	Y	10/15/2024	Y	N	10/21/2023	N	Y
Mosley	Donavyn	Project Assistance/Support	SP	Y	N		P	Y	05/31/2023	Y	N	06/05/2023	N	N
Rush	Craig	Co-Investigator	DP	Y	N	PhD	P	Y	08/16/2023	Y	N	03/21/2023	N	Y
Adams Jr.	Thomas	Faculty Advisor	SP	Y	N		P	Y	08/18/2022	Y	Y	05/31/2023	N	Y
Anand	Pavan	Data Analysis/Processing	SP	N	N		P	Y	10/18/2022		Y	05/31/2023	N	N
Bell	Robert	Recruitment	SP	N	N		P	Y	01/16/2025	Y	Y	05/31/2023	N	Y
Burris	Jessica	Recruitment	SP	Y	N		P	Y	06/03/2024	Y	Y	05/31/2023	N	Y
Christian	Amy	Recruitment	SP	Y	N		P	Y	04/09/2024	Y	Y	03/21/2023	N	Y
Cordero	Patrick	Data Analysis/Processing	SP	Y	N	MD	P	Y	11/02/2022		Y	03/21/2023	N	N
Elias	Madona	Data Analysis/Processing	DP	Y	N		S	Y	07/18/2022	Y	Y	10/21/2023	N	Y
Kahl	Joan	Recruitment	SP	Y	N		P	Y	11/14/2023	N	Y	03/21/2023	N	N
Khanal	Rebika	Recruitment	SP	Y	N		P	N	02/04/2022	N	Y	03/21/2023	N	Y
Thornton	Alice	Faculty Advisor	SP	N	N	MD	P	Y	04/06/2022	N	Y	03/21/2023	N	Y
Wesley	Michael	Faculty Advisor	SP	N	N	PhD	P	Y	11/07/2023	Y	Y	05/15/2023	N	Y

RESEARCH DESCRIPTION

0 unresolved comment(s)

You may attach a sponsor's protocol pages in the "Additional Information" section and refer to them where necessary in the Research Description. However, each prompt that applies to your study should contain at least a summary paragraph.

Pro Tips:

- **Save your work often to avoid losing data.**
- **Use one of the attachment buttons in this section or under the Additional Information section to include supplemental information with your application. During the document upload process, you will be able to provide a brief description of the attachment.**

Background

Include a brief review of existing literature in the area of your research. You should identify gaps in knowledge that should be addressed and explain how your research will address those gaps or contribute to existing knowledge in this area. For interventional research, search PubMed and ClinicalTrials.gov for duplicative ongoing and completed trials with same condition and intervention(s).

Alcohol use disorder (AUD) imposes significant financial burden on society globally and nationally. Alcohol use disorder is the leading risk factor for attributable burden of disease among people ages 25 to 49, the second-leading risk factor among ages 10 to 24, and the ninth-leading risk factor among all ages (1). Although pharmacotherapy and behavioral treatments have been approved for AUD, their effects sizes are modest (2). Noninvasive neuromodulation can offer an alternative treatment option for AUD (3). Transcranial magnetic stimulation (TMS) is a method of noninvasive neuromodulation that utilizes a magnetic field to focal electrical current in the brain (4). When these electrical currents are focused on specific brain regions, pertinent to the neurobiology of AUD it leads to modulation of behavior and plausibly decrease in alcohol craving and use (5).

Previous TMS studies have used heterogenous parameters, including frequencies ranging from 1 Hz to 20 Hz (3, 6-9). Regions targeted by these studies encompassed ventromedial prefrontal cortex, left dorsolateral prefrontal cortex (left dlPFC) and right dorsolateral prefrontal cortex (3). Two studies used a TMS paradigm with greater efficiency than other routine TMS paradigms, called continuous theta burst stimulation (6, 7). These studies delivered 3600 pulses of cTBS to the left frontal pole/ventromedial prefrontal cortex and showed significant reduction in alcohol cue reactivity and corroborative changes in both resting state and task based functional connectivity (6, 7). Of these two studies, one was notable in comparing active cTBS (3600 pulses per session, one session every day for ten days over two weeks) versus sham cTBS. This study showed that real cTBS led to a significantly greater reduction in brain reactivity to alcohol cues, specifically a reduction in MPFC-striatum and MPFC-insula connectivity 2 and 3 months after TBS treatment (6).

A deep TMS study that compared dTMS (15 sessions, five sessions every week for three weeks) to sham dTMS using an H7 coil (targeting medial prefrontal and anterior cingulate cortices) (9). This study showed decreased craving after treatment and percentage of heavy drinking days (9) in the active versus sham control group. Active dTMS was associated with decreased resting-state functional connectivity of the dorsal anterior cingulate cortex with the caudate nucleus and decreased connectivity of the medial prefrontal cortex to the subgenual anterior cingulate cortex (9).

No study has done multiple sessions of cTBS in a single day. In addition, no study has previously delivered cTBS to the left dlPFC, to modulate executive control. Previous studies delivered cTBS to the left frontal pole or ventromedial prefrontal cortex to modulate cue-reactivity.

References

1. Collaborators GBDRF. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396: 1223-1249. DOI: 10.1016/S0140-6736(20)30752-2.
2. Kranzler HR and Soyka M. Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. JAMA 2018; 320: 815-824. DOI: 10.1001/jama.2018.11406.
3. Philip NS, Sorensen DO, McCalley DM, et al. Non-invasive Brain Stimulation for Alcohol Use Disorders: State of the Art and Future Directions. Neurotherapeutics 2020; 17: 116-126. DOI: 10.1007/s13311-019-00780-x.
4. McClintock SM, Reti IM, Carpenter LL, et al. Consensus Recommendations for the Clinical Application of Repetitive Transcranial Magnetic Stimulation (rTMS) in the Treatment of Depression. J Clin Psychiatry 2018; 79. DOI: 10.4088/JCP.16cs10905.
5. Beynel L, Powers JP and Appelbaum LG. Effects of repetitive transcranial magnetic stimulation on resting-state connectivity: A systematic review. Neuroimage 2020; 211: 116596. 20200131. DOI: 10.1016/j.neuroimage.2020.116596.
6. Daniel M. McCalley NK, Julia P. Wolf, Ingrid E. Contreras, Sarah W. Book, Joshua P. Smith, and Colleen A. Hanlon. Medial Prefrontal Cortex Theta Burst Stimulation
Improves Treatment Outcomes in Alcohol Use
Disorder: A Double-Blind, Sham-Controlled
Neuroimaging Study. Biological Psychiatry: Global Open Science 2022; In press.
7. Hanlon CA, Dowdle LT, Correia B, et al. Left frontal pole theta burst stimulation decreases orbitofrontal and insula activity in cocaine users and alcohol users. Drug Alcohol Depend 2017; 178: 310-317. 20170530. DOI: 10.1016/j.drugalcdep.2017.03.039.
8. Kearney-Ramos TE, Dowdle LT, Lench DH, et al. Transdiagnostic Effects of Ventromedial Prefrontal Cortex Transcranial Magnetic Stimulation on Cue Reactivity. Biol Psychiatry Cogn Neurosci Neuroimaging 2018; 3: 599-609. 20180410. DOI: 10.1016/j.bpsc.2018.03.016.

9. Harel M, Perini I, Kampe R, et al. Repetitive Transcranial Magnetic Stimulation in Alcohol Dependence: A Rando
Blind, Sham-Controlled Proof-of-Concept Trial Targeting the Medial Prefrontal and Anterior Cingulate Cortices. Biol Psychiatry 2022;
91: 1061-1069. 20211206. DOI: 10.1016/j.biopsych.2021.11.020.

Objectives

List your research objectives. Please include a summary of intended research objectives in the box below.

To demonstrate whether two sessions of continuous TBS (cTBS) decreases attentional bias for alcohol cues, alcohol craving and changes resting state functional connectivity in people with alcohol use disorder (AUD) compared to two sessions of sham cTBS. We hypothesize 2 sessions of cTBS to the left dorsolateral prefrontal cortex (L. dlPFC) will significantly decrease attentional bias for alcohol cues, alcohol craving and change resting state functional connectivity in a population of people with AUD compared to sham cTBS.

Study Design

Describe and explain the study design (e.g., observational, secondary analysis, single/double blind, parallel, crossover, deception, etc.).

- *Clinical Research*: Indicate whether subjects will be randomized and whether subjects will receive any placebo.
- *Community-Based Participatory Research*: If you are conducting community-based participatory research (CBPR), describe strategies for involvement of community members in the design and implementation of the study, and dissemination of results from the study.
- *Qualitative research*: Indicate ranges where flexibility is needed, if a fixed interview transcript is not available, describe interview topics including the most sensitive potential questions.
- *Research Repositories*: If the purpose of this submission is to establish a Research Repository (bank, registry) and the material you plan to collect is already available from a commercial supplier, clinical lab, or established IRB approved research repository, provide scientific justification for establishing an additional repository collecting duplicate material. Describe the repository design and operating procedures. For relevant information to include, see the UK Research Biospecimen Bank Guidance or the UK Research Registry Guidance.

This will be a within participant single blinded trial. Recruitment for the study will be done by research assistant and/or principal investigator. All study participants will receive active cTBS first and sham cTBS stimulation one week later. Although participants will be blinded to the intervention, the PI (Gopalkumar Rakesh) and his research assistant will not be blind to the intervention and will deliver the sessions. We will recruit 30 subjects who will receive both active and sham cTBS.

On day one of the study, we will perform baseline assessments including breath alcohol level, alcohol attentional bias tasks using eye tracker, and collection of baseline demographics. All of these baseline assessments will take a total of three hours. We will also obtain resting and active motor threshold from the first dorsal interosseous (FDI) muscle. Following this subjects will be transported to Magnetic Resonance Imaging and Spectroscopy Center (MRISC), affiliated with University of Kentucky for collection of their baseline MRI brain scan that will last thirty minutes. A study team member will escort them to the MRISC and will be with them when the scan is obtained.

On day two of the study all study participants will receive active stimulation which is two sessions of continuous theta burst stimulation (cTBS) to the left dorsolateral prefrontal cortex. Both sessions will be separated by 50 minutes. Participants will perform the alcohol craving scale, AUDIT-C and attentional bias for alcohol cues before and after the two cTBS sessions. The same sequence of events will occur on day three of the study, but all participants will receive sham cTBS. We will acquire functional MRI (fMRI) scan on both study days 2 and 3, after the active cTBS sessions and sham cTBS session respectively. Study days 2 and 3 will be separated by a week.

Attachments

Subject Recruitment Methods & Advertising

Describe how the study team will identify and recruit subjects. Please consider the following items and provide additional information as needed so that the IRB can follow each step of the recruitment process.

- How will the study team identify potential participants?
- Who will first contact the potential subjects, and how?
- Will you use advertisements? If so, how will you distribute those?
- How and where will the research team meet with potential participants?
- If applicable, describe proposed outreach programs for recruiting women, minorities, or disparate populations.
- How you will minimize undue influence in recruitment?
- Attach copies of all recruiting and advertising materials (emails, verbal scripts, flyers, posts, messages, etc.).

For additional information on recruiting and advertising:

- IRB Application Instructions - Advertisements
- PI Guide to Identification and Recruitment of Human Subjects for Research

We will recruit 30 subjects from the various clinics within the University of Kentucky Medical Center including our clinics at Fountain Court. All providers in the clinics at Fountain Court will be provided multiple copies of the study flyer. Study members will interface with all providers in the clinic at Fountain Court on a daily basis. We will provide copies of the flyer to other clinics (Turfland, Team blue,

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Polk Dalton clinic) and referrals if any from these clinics will be scheduled for visit one if they fit our inclusion and e
are interested in the study.

Dr. Anderson will approach her patients who meet study criteria and ask about interest in participation. Dr. Anderson will serve as the medical screener for inclusion/exclusion appropriateness. Patients who are interested in participation will be referred to the study staff for more information.

Participants interested in the study can call the number provided on the flyer to express interest in the study. Once they express interest, participants will be scheduled for the first visit. Initial contact will be made with potential subjects by those having legitimate access to the subjects' identity and the subjects' information. No medical records will be accessed at any point (before, during or after the study).

Attachments

Attach Type	File Name
Advertising	Advertising Flyer MOD1 10.17.2023-STAMPED.pdf
Advertising	Love Gill Email.png
Advertising	CC-OD-24-5681.pdf

Research Procedures

Describe how the research will be conducted.

- What experience will study participants have?
- What will study participants be expected to do?
- How long will the study last?
- Outline the schedule and timing of study procedures.
- Provide visit-by-visit listing of all procedures that will take place.
- Identify all procedures that will be carried out with each group of participants.
- Describe deception and debrief procedures if deception is involved.

Differentiate between procedures that involve standard/routine clinical care and those that will be performed specifically for this research project. List medications that are explicitly forbidden or permitted during study participation.

On day one of the study, following informed consent, we will perform baseline assessments including breath alcohol level, alcohol craving questionnaire, alcohol attentional bias tasks using eye tracker, and collection of baseline demographics. All of these baseline assessments will take a total of three hours. We will evaluate for any contraindications for MRI using the MRI checklist (attached). We will also obtain resting and active motor threshold from the first dorsal interosseous (FDI) muscle. Following this subjects will be transported to Magnetic Resonance Imaging and Spectroscopy Center (MRISC), affiliated with University of Kentucky for collection of their baseline MRI brain scan that will last thirty minutes. A study team member will escort them to the MRISC and will be with them when the scan is obtained.

On the second day, subjects will receive two sessions of active cTBS. Sessions will be the same in dosing and will be delivered at an interval of fifty minutes. Each session will last five minutes regardless of it being cTBS or sham cTBS. Active cTBS sessions will be delivered 120% resting motor threshold (RMT) to the left dorsolateral prefrontal cortex using a figure 8 coil and MagVenture MagPro x100 device (MagVenture A/S, Denmark), with TMS coil position stabilized using BrainSight (Rogue Solutions, Montreal, Canada). Subjects will also perform a host of other tasks as shown in figure 1 before and after the two cTBS sessions. At the end of the cTBS sessions and tasks, post session MRI brain scan will be collected at MRISC.

On day three of the study, participants will receive two sessions of sham cTBS. The sham cTBS mimics the actual experimental one but does not deliver any electricity to the brain. The sham sessions will be separated by 50 minutes. Participants will perform a host of other tasks as shown in figure 1 before and after the two sham cTBS sessions. At the end of day three, we will have participants undergo an MRI brain scan at MRISC.

A medical doctor will be present or nearby during all stimulation sessions. No drug, pregnancy, etc. screening results will be obtained from a UK HealthCare laboratory.

Attentional Bias task
We will have participants perform an attentional bias task. They will view alcohol and neutral cues presented side by side for 2 seconds. We will measure attentional bias using a Tobii Pro Fusion 120 Hz eye tracker (Tobii Technology, Sweden) eye tracker. Eye tracking will record eye movements and fixation times for both cue types. Upon offset of the cues, a visual probe ('X') will appear on either the left or right side of the computer screen. The primary dependent variable will be mean fixation time (milliseconds) calculated by summing the total fixation time for each cue type and then dividing by the total number of critical trials (i.e., 40).

Alcohol craving scale
We will use the Penn alcohol craving scale that has five items and is rated on a scale of 1 to 6.

AUDIT-C
The Alcohol Use Disorders Identification Test (AUDIT-C) is an alcohol screen that can help identify patients who are hazardous drinkers or have active alcohol use disorders (including alcohol abuse or dependence).

Motor Threshold
Motor threshold (MT) is defined as the TMS pulse amplitude needed to elicit an EMG response of 50 μV peak-to-peak average amplitude in a target muscle. MT is the standard in the field for determining the intensity of TMS for everyone to reduce seizure risk. The MEP for the right first dorsal interosseus (FDI) will be measured with EMG. The scalp region producing the largest amplitude MEP will be identified. At that scalp location, we will determine the TMS intensity eliciting average MEP amplitude of 50 μV peak-to- peak in the first DI muscle using an amplitude titration procedure (at least 5/10 trials). Individual MT will be used to determine the intensity of theta burst stimulation for everyone, as recommended by safety guidelines.

cTBS application
A magnetic coil will be placed on the scalp and held in place with frameless stereotaxic equipment, using a sophisticated method of coil placement that will coregister scalp positions directly onto an average brain template. This Frameless Stereotaxic System Brainsight offers real-time three-dimensional display of cortical localization as the TMS coil is moved across the scalp. This will be used for coil positioning. This system uses a programmed robot arm to precisely position the TMS coil, and maintain its position, within 1 mm of the brain target chosen. Earplugs will be worn to protect hearing and low-volume white noise will be played through TMScompatible headphones to mask the sound of the coil clicks. The intensity of the stimulation will be 120% of resting motor threshold as reported in a previous studies. The participant will be seated comfortably with headphones and earplugs to protect the subject's hearing. We will collect heart rate data on the second and third days of study using a Fitbit that will be strapped to the

participant's wrist.

Attachments

Attach Type	File Name
ResearchProcedures	Purchase_Task.pdf
ResearchProcedures	AUDIT_C.pdf
ResearchProcedures	Penn_Alcohol_Craving_Scale_171.pdf
ResearchProcedures	Figure 1.png
ResearchProcedures	PreScrnF.pdf

Data Collection & Research Materials

In this section, please provide the following:

- Describe all sources or methods for obtaining research materials about or from living individuals (such as specimens, records, surveys, interviews, participant observation, etc.), and explain why this information is needed to conduct the study.
- For each source or method described, please list or attach all data to be collected (such as genetic information, interview scripts, survey tools, data collection forms for existing data, etc.).
- If you will conduct a record or chart review, list the beginning and end dates of the records you will view.

Motor Threshold
Eye tracking
AUDIT- C
FTND
MAST
DAST
History if any of traumatic brain injury or loss of consciousness.
Alcohol craving scale
TMS Side effects scale
Treatment acceptability questionnaire (TAQ)
Resting state functional magnetic resonance imaging (fMRI)
Heart rate data using Fitbit

Neuroimaging data will be acquired on a Siemens 3-Tesla (3T) PRISMA scanner at the Magnetic Resonance Imaging and Spectroscopy Center (MRISC), situated close to Markey Cancer Center. A high-resolution (1 cubic millimeter voxels) T1- weighted MP-RAGE structural image will be acquired for each subject. Functional images will be acquired using echo-planar imaging. Hyper-angulated volumes will be acquired with 37 ascending and interleaved slices at an angle 30-degrees to the anterior-posterior commissure to prevent OFC washout. Additional parameters will be similar to those used in other approved neuroimaging protocols in our lab (e.g., a repetition time (TR) of 2 seconds, echo time (TE) of 25 ms, a flip angle of 90 degrees, and functional voxels of size 3.4mm x 3.4mm x 4.0mm). Image preprocessing will be performed in Conn Toolbox.

Attachments

Attach Type	File Name
DataCollection	Demographics_TMSIRB86853.pdf
DataCollection	MAST.pdf
DataCollection	Fagerstrom_test.pdf
DataCollection	DAST-10-drug-abuse-screening-test.pdf
DataCollection	TMS Side effects.doc
DataCollection	Treatment acceptability questionnaire (TAQ).PNG

Resources

Describe the availability of the resources and adequacy of the facilities that you will use to perform the research. Such resources may include:

- Staffing and personnel, in terms of availability, number, expertise, and experience;
- Computer or other technological resources, mobile or otherwise, required or created during the conduct of the research;
- Psychological, social, or medical services, including equipment needed to protect subjects, medical monitoring, ancillary care, or counseling or social support services that may be required because of research participation;
- Resources for communication with subjects, such as language translation/interpretation services.

The TMS Suite is housed within the department of psychiatry (245 Fountain Court, Lexington, Kentucky 40509) at the University of Kentucky, Lexington. Currently it encompasses one experimental room covering about 600 sq feet on the second floor. We are in the process of purchasing a a MagPro X100 stimulator (MagVenture Inc, Atlanta,GA) with booster option and active cooling. The room will also also equipped with a laptop and a chair to provide TMS. The device is capable of producing rTMS over a wide range of parameters such as paired-pulse, theta burst stimulation, and both monophasic and biphasic waveforms. The machine weighs 35 kg and the cart encompassing the machine weighs 16 kg. Dimensions of the machine are 210 x 530 x 400 mm. We are also in the process of purchasing a frameless stereotaxic system (Brainsight Frameless, Rogue Research, Montreal, QC, Canada) for

coregistration of TMS coil position on the scalp with underlying cortical anatomy on the individual subject's three-di
rendered MRI scan.This permits navigation of the TMS coil to target cortical structures. Participants are administered TMS in a customized chair for stabilization of head and coil position. A coil holder especially designed for TMS ensures stable coil positioning. The Brainsight Neuronavigation system has three main components: (1) NDI Spectra infrared camera system, (2) stimulator, (3) chair with neck rest. The TMS coil is targeted to a user defined location selected on the individual 3-D Anatomical MRI with fMRI or PET data overlay with less than one millimeter error. The TMS coil is attached to a stimulator unit, which administers the TMS pulses to modulate brain function in a spatially and temporally precise fashion. The subject reclines in the chair and wears a headband equipped with a subject position tracker. The ceiling mounted infrared stereo camera detects the 3-D position of the subject tracker and also the coil position tracker, and continuously feeds this information into the control center software.

Eye Tracker. The Tobii Pro Fusion housed at 245 Fountain Court is an exceptionally flexible remote eye tracking system offering supreme tracking performance in a wide array of human behavior research studies. This small eye tracking research system offers unprecedented portability and freedom of head movement in combination with unparalleled tracking accuracy and robust participant tracking capability. It allows for both screen and real-world test scenarios. For screen based research, it can be used with a laptop, an external monitor or an all-in-one PC. It can be mounted below most screens. With the eye tracker flush mounted on a screen, researchers can achieve highly accurate results for stimuli presentation on screens. Using a desk stand, one can track larger screens. This gives researchers the freedom to present stimuli on a screen that best meets the specific needs of the study at hand. The eye tracking system captures data up to speeds of 250 Hz (available 60, 120, 250 Hz modes). It delivers unparalleled data accuracy within the whole tracking box and very robust participant tracking capability. Robust eye tracking capability ensures very low data loss in real life conditions. The system with automatic selection of bright or dark pupil eye tracking accommodates for large variations in experimental conditions and demographic populations. The system also comes fitted with Tobii Pro Lab. This is a versatile biometric software platform designed for extensive research into human behavior using eye tracking analysis. It also has added ability to be combined with other physiological data streams. From in-store shopper research to psychology experiments, Pro Lab makes it easy for anyone to start using various biometric tools in their research in order to further expand the scope and richness of their insights. Pro Lab works well with both screen-based and wearable eye trackers.

Magnetic Resonance Imaging and Spectroscopy Center (MRISC). The Magnetic Resonance Imaging and Spectroscopy Center (MRISC) is a service and consultation center supporting basic and clinical research at the University of Kentucky. The Center includes an advanced 3T Siemens PRISMA scanner with high performance gradients, echo-planar whole body imaging and hydrogen spectroscopic capabilities for both human and animal studies. For dedicated animal studies, a modern Bruker/Siemens 7T MR scanner has recently been installed. Recently renovated facilities for animal handling, preparation and care are available immediately adjacent to the 7T imager. There are also computing facilities, electronic and fabrication shops, and a multi-user laboratory available to support magnetic resonance and spectroscopy studies. Scientific and technical personnel are available to help in developing MR sequences and procedures as well as to help with image-processing analysis. The Center has multiple ongoing research trials https://www.research.uky.edu/magnetic-resonance-imaging-and-spectroscopy-center/human-research-projects. In 2017 the MRISC was awarded an NIH grant to upgrade its human MRI scanner from a Siemens TIM TRIO 3T to a Siemens MAGNETOM Prisma 3T. The Prisma 3T offers maximum performance under prolonged high-strain conditions and delivers improved resolution over the previous system by coils with the highest gradient strength currently available on the market. Of note, data collected with the Prisma 3T scanner are to a higher-quality standard and are therefore more attractive for inclusion into NIH-supported neuroimaging repositories, such as the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) and the Human Connectome Project (HCP). The Prisma 3T is equipped with a full complement of coils, updated image processing using Siemens Software 3D rendering, image fusion, perfusion, DTI fiber tracking, spectroscopy, volume rendering, shaded surface display, multiplanar reconstruction, and maximum intensity projection.

Ancillary Equipment in MRI Suite. 1) Applied Sciences Laboratories, Inc. Model 504LRO (long range optics) eye tracker complete with Real Eye software; 2) AVOTEC, Inc. Silent Vision SL-6011 LCD projection system used with Psychology Software Tools, Inc. visual presentation software, EPRIME; 3) MRA, Inc. 10 channel, fiber optic, patient response system with trigger interface and visual/auditory patient monitoring; 4) Current Designs, Inc. patient response fORP Interface Unit with 12 fiber optic cables and an MRI compatible, handheld, trackball mouse; 5) Medrad, Inc. SHS200 Power Injector; 6) InVivo Research, Inc. Precess MRI compatible patient monitor. with wireless digital SPO2, ETC02, heart rate and blood pressure recording; 7) Full suite of physiological monitoring equipment from S.A. INC for small animal imaging; and 8) Microcapstar Capnograph CO2 Analyzer and MRI-1ventilator from CWE instruments for small and medium sized animals.

Computing and Data Management. The following centralized computer and file server equipment is located in the MRISC and available (1) Server, Linux, 4U Rack mounted Dell PowerEdge 6850, 64bit - 4 Quad Core Xeon Tulsa, 16GB RAM, 1.5TB SAS RAID 5 array; (2) Two Disk Array, 3U Rack mounted Dell MD1000 Power Vault, 4.5TB SAS RAID 5 array; (3) Tape Backup, 2U Rack mounted Dell TL2000, 24 x 800GB/1.6TB cartridges; (4) Network Attached Storage (NAS), 1U Rack mounted NetGear, 2.0 TB SATA RAID 5 array; (5) Dell full size 4210 rack (42U slots total; 16U slots occupied including APC; 26U slots available). All computers and servers are protected with power supply backup and surge protecting UPSs. All MRI scans are sent to the NAS backup server immediately after the imaging session and burned to CD for permanent archiving. The MRI scanner host computer is connected to the Dell rack, containing equipment items 1-4, by 1 GB/sec fiber optic cable while the rest of the computers are
connected by Cat 5e cable on a 100 MB/sec network. Institution-wide upgrades to Cat 6a network cable are currently underway. Daily incremental tape backups are made from all data on all the servers, the NAS, and the MD1000 using Yosemite Backup software running on the Poweredge 6850. Full monthly tape backups are made and stored offsite. All computers and servers are behind the UK Medical Center firewall, have individual firewalls, are accessible only with valid usernames and passwords, and have automated operating system software updating.

Potential Risks & Benefits

Risks

- Describe any potential risks – including physical, psychological, social, legal, ability to re-identify subjects, or other risks. Assess the seriousness and likelihood of each risk.
- Which risks may affect a subject's willingness to participate in the study?
- Describe likely adverse effects of drugs, biologics, devices or procedures participants may encounter while in the study.
- *Qualitative research* - describe ethical issues that could arise while conducting research in the field and strategies you may use to handle those situations.
- Describe any steps to mitigate these risks.

Benefits

- Describe potential direct benefits to study participants – including diagnostic or therapeutic, physical, psychological or emotional, learning benefits. This cannot include incentives or payments.
- State if there are no direct benefits.
- Describe potential benefits to society and/or general knowledge to be gained.

Describe why potential benefits are reasonable in relation to potential risks. If applicable, justify why risks to vulnerable subjects are reasonable to potential benefits.

Risks with TMS
Seizure is a theoretical risk with TMS. In the Rossi et al. report it was stated that "The occurrence of seizures has been extremely rare, with most of the few new cases receiving rTMS protocols exceeding previous guidelines, often in patients under treatment with drugs which potentially lowered the seizure threshold." As Rossi et al. delineate, "rare" means that 16 cases (out of tens of thousands of rTMS sessions over the last two decades) of seizure related to rTMS have been reported. Eight occurred before safety parameters were established in 1997. Of the other eight reports, six occurred either when the safe rTMS parameters were exceeded or other safety guidelines ignored, and the actual occurrence of a seizure has been questioned in the other two (i.e., convulsive syncope or pseudoseizure may have occurred). In a workshop convened by the National Institute for Neurological Disorders and Stroke (NINDS) in 1996, researchers in the field agreed upon a set of rTMS consensus safety guidelines, including recommended stimulation parameters and contra-indications, and these consensus guidelines have been recently updated (Rossi et al., 2009). Widespread adherence to the 1996 guidelines has resulted in the virtual elimination of inadvertent seizures in rTMS studies (Rossi et al., 2009). Theta burst stimulation (TBS) that we will use in this study has been documented to be extremely safe. The risk of seizure with TBS is 0.1% (Rachid, 2017). There has been only one seizure instance reported with continuous TBS in a subject with no previous history of epilepsy but was sleep deprived after a long flight (Oberman and Pascual-Leone, 2009).

The most commonly reported side effect of rTMS is headache. This headache is typically of a muscle-tension type. It usually develops during or immediately after the stimulation and may last for minutes to hours following the end of the stimulation. It is typically limited to the day of stimulation, and usually responds promptly to single doses of over the counter pain medications. Neck pain or scalp pain may also occur. Both are usually managed easily with over-the-counter analgesics.

As noted in Rossi et al. (2009), Loo and colleagues reported mild and transient changes in auditory threshold in two depressed patients following a 2-4 week rTMS course of rTMS (16). Cases of tinnitus have been reported after rTMS treatments. In addition, recently in a study investigating the effects of rTMS on symptoms of depression, a patient experienced moderate to severe tinnitus after an rTMS session in which earplugs were not used. Rossi et al. recommended that hearing protection always should be worn during rTMS application, and that individuals with cochlear implants not receive rTMS. In the current study, earplugs will be worn by all subjects during rTMS procedures. Individuals with cochlear implants will be excluded from participation.

Risks to the unborn children of pregnant women receiving rTMS are unknown. Pregnant women will be excluded in this study. If sexually active, the subject must agree to use appropriate contraceptive measures for the duration of the study. Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with spermicide, or (4) an intrauterine device (IUD). Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. If the subject has any uncertainty about whether they could be pregnant, another urine pregnancy test will be performed before they can participate in this protocol.

Risks with MRI
MRI does not involve ionizing radiation and it has been approved FDA for routine clinical use. In addition to the risks of static and time-varying magnetic fields and Specific Absorption Rate (SAR), which are minimal in our FDA-approved 3T system, there are three main potential risks to take into account.

Potential presence of metal objects. A safety risk is posed by the attraction of ferromagnetic metal objects by the high strength magnetic fields. The presence of a metal foreign object implanted in the subject is determined by interviewing each potential subject and completing a detailed screening questionnaire. Participants and staff are instructed to remove all metal objects, including clothing with metal clasps before entering the magnet room. The magnetic properties of unknown material are tested outside the magnet room with a strong permanent magnet. Participants and staff are also instructed to enter the magnet room slowly and pause at the entrance to determine if any items on their person may be pulling toward the magnet.

Potential discomfort due to confinement. The second concern is the discomfort some participants encounter by the confinement within the bore of the MRI system. Some participants may feel uncomfortable or confined once positioned within the bore of the MRI system. This potential reaction is reduced by discussing the procedure prior to entry into the magnet room, by providing the subject with a mirror through which they can look out into the room, and by communicating with the subject over the intercom. During set-up and anatomical imaging, participants can choose to listen to music or the radio over their headphones. Nevertheless, if participants

continue to feel uncomfortable, the imaging procedure is terminated, and the subject is removed from the magnet participation.

Potential risk of hearing loss from the MRI. The third concern is the loud noise made by the gradients during imaging. These risks occur for all clinical MRI exams and are not increased by the proposed research. Participants are required to wear earplugs during scanning to reduce noise levels below FDA limits. The sound levels within our scanners and have determined that they are compliant with FDA guidelines.

Incidental findings in MRI. MRI data obtained are for scientific research purposes only, and the investigators will not be looking for any existing brain abnormalities. The researchers that will be analyzing the MRI recordings are not medical specialists and cannot provide any medical interpretation of this data. If a possible abnormality is incidentally observed in either the MRI data that a researcher believes might be of concern, a physician associated with Duke Hospital may be contacted to look at the data. If they conclude that additional testing is medically indicated, the participant will be informed of this so that he or she can consider pursuing any follow-up courses of action.

Other plausible risks include breach of confidentiality, development of suicidal thoughts and syncope (neurocardiogenic in nature). Vasodepressor (neurocardiogenic) syncope is a common reaction to anxiety and psycho-physical discomfort. It is a common experience that may occur more often than epileptic seizures during TMS testing and treatment. Suicidal thoughts have been observed to transiently develop only in subjects who have a previous history of major depressive disorder.

The study proper may benefit subjects in decreasing alcohol use. It will also help us learn how TMS affects cognitive functions, visual attention, craving and impulsivity in people with alcohol use disorder. There are no known long-term health risks to the use of rTMS per se when operated within consensus safety guidelines (Rossi 2009). In 2008, the FDA approved the use of high frequency rTMS in the treatment of depression. Also in 2008, an international consensus conference on safety guidelines for rTMS (1) systematically reviewed the thousands of healthy subjects and patients who have undergone rTMS in order to allow for a better assessment of relative risks. The relative infrequency of adverse events using rTMS was noted. They concluded that in the case of Class 3 studies (studies involving indirect benefit and low risk in normal subjects and patients that are expected to yield important data on brain physiology or safety, but have no immediate relevance to clinical problems), normal volunteers should be permitted to participate in rTMS research when it is likely to produce data that are of outstanding scientific or clinical value. They also concluded that this research can be performed in a non-medical setting (i.e., psychology labs, robotics labs, research institutions, etc. as opposed to a hospital or appropriately equipped outpatient clinic). The Rossi et al. consensus report went on to suggest safety guidelines based on the now rather extensive international experience with rTMS. These guidelines include the rTMS intensity and timing parameters considered safe, training, and planning for and managing emergencies. We will follow these guidelines, and have incorporated them into our screening and session procedures.

Participation in the study is completely voluntary, and there will be no pressure or time constraints regarding the decision to participate. If subjects experience headaches, they can withdraw without any ramifications pertaining to their respective clinic. There are no benefits to the participants except for the compensation, as well as the good will of helping the progress of scientific research. The information learned from this study may aid our understanding of the role of the TMS in modulating cognition and brain function in patients with alcohol use disorder.

References pertinent to this section
Rossi S, Hallett M, Rossini PM, Pascual-Leone A, Safety of TMSCG. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol. 2009;120(12):2008-39.

Rachid F. Safety and Efficacy of Theta-Burst Stimulation in the Treatment of Psychiatric Disorders: A Review of the Literature. J Nerv Ment Dis. 2017;205(11):823-39.

Oberman LM, Pascual-Leone A. Report of seizure induced by continuous theta burst stimulation. Brain Stimul. 2009;2(4):246-7.

Available Alternative Opportunities/Treatments

Describe alternative treatments or opportunities that might be available to those who choose not to participate in the study, and which offer the subject equal or greater advantages. If applicable, this should include a discussion of the current standard of care treatment(s).

We will not offer any alternative treatment options.

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Records, Privacy, and Confidentiality

Specify where the data and/or specimens will be stored and how the researcher will ensure the privacy and confidentiality of both. Specify who will have access to the data/specimens and why they need access.

Describe how data will be managed after the study is complete:

- If data/specimens will be maintained, specify whether identifiers will be removed from the maintained information/material.
- If identifiers will not be removed, provide justification for retaining them and describe how you will protect confidentiality.
- If the data/specimens will be destroyed, verify that this will not violate retention policies and will adhere to applicable facility

requirements.

If this study will use de-identified data from another source, describe what measures will be taken to ensure that subject identifiers are not given to the investigator.

If applicable, describe procedures for sharing data/specimens with collaborators not affiliated with UK.

For additional considerations:
Return of Research Results or Incidental Research Findings
HIPAA policies
FERPA policies
Procedures for Transfer agreements
Information regarding multi-site studies
NIH Genomic Data Sharing (GDS) Policy
Digital Data

Personal information of participants (Subjects' age, comorbid medical or psychiatric illnesses, history of substance use, history of traumatic brain injury/loss of consciousness, previous adverse effects with TMS, medication history, urine drug screens, breathalyzer test results) will be stored in an excel sheet on a protected laptop at P208, 2nd floor, UK Department of Psychiatry at 245 Fountain Court (In a locked office and behind a protected firewall). Any data sharing will be restricted to the coded data. Data will be kept for a minimum of 7 years, and electronically destroyed by UK Policy A13-050 and UK Policy A05-055. Urine samples will be collected prior to every TMS session to perform drug screening.

UK IRB policies state that IRB-related research records must be retained for a minimum of 6 years after study closure. Check this item to confirm that you will retain all IRB-related records for a minimum of 6 years after study closure.

Payment

Describe the incentives (monetary or other) being offered to subjects for their participation. If monetary compensation is offered, indicate the amount and describe the terms and schedule of payment. Please review this guidance for more information on payments to subjects, including restrictions and expectations.

Participants will be paid $50 for day 1, $100 for day 2 and $100 for day 3.
Participants will be paid a total of $250, by check mailed within two weeks after the study days.

Costs to Subjects

Include a list of services and/or tests that will not be paid for by the sponsor and/or the study (e.g., MRI, HIV). Keep in mind that a subject will not know what is "standard" – and thus not covered by the sponsor/study – unless you tell them.

There will be no cost to subjects

Data and Safety Monitoring

The IRB requires review and approval of data and safety monitoring plans for greater than minimal risk research or NIH-funded/FDA-regulated clinical investigations.

- If you are conducting greater than minimal risk research, or your clinical investigation is NIH-funded, describe your Data and Safety Monitoring Plan (DSMP). Click here for additional guidance on developing a Data and Safety Monitoring Plan.
- If this is a non-sponsored investigator-initiated protocol considered greater than minimal risk research, and if you are planning on using a Data and Safety Monitoring Board (DSMB) as part of your DSMP, click here for additional guidance for information to include with your IRB application.

We will monitor the safety of participants, i.e., potential adverse events resulting from participation; and have procedures to safeguard against adverse events. We will actively screen and exclude any potential participants with a history of seizure disorder. We will also monitor every study session with a physician on site for every stimulation session. In case a seizure were to occur, having a physician on site in the room with the participant will help us in managing the event. All staff will also be trained in how to provide first aid in the event of a seizure ie lay the participant on their side and move any objects that can cause harm out of their vicinity.

We will also monitor for side effects after every stimulation session including headaches and neck pain. We will actively exclude participants with metal implants or piercings so that no adverse events occur during the MRI scan.

We will assure data accuracy and protocol compliance, including quality-control procedures in place to assure data accuracy and completeness. Appropriate procedures range, for example, from regular data verification and protocol compliance checks performed by a data manager and a principal investigator, to a formal external data audit process by an external agent.

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Future Use and Sharing of Material (e.g., Data/Specimens/Information)

If the material collected for this study will be used by members of the research team or shared with other researchers for future studies, please address the following:

- list the biological specimens and/or information that will be kept
- briefly describe the types, categories and/or purposes of the future research
- describe any risks of the additional use
- describe privacy/confidentiality protections that will be put into place
- describe the period of time specimens/information may be used
- describe procedures for sharing specimens/information with secondary researchers
- describe the process for, and limitations to, withdrawal of specimens/data

WILL YOUR INFORMATION (OR SPECIMEN SAMPLES) BE USED FOR FUTURE RESEARCH?

All identifiable information (e.g., your name, medical record number, or date of birth) will be removed from the information or samples collected in this study. This means that no link or code to your identity will be kept. After all identifiers have been removed, the information or samples may be used for future research or shared with other researchers without your additional informed consent, Once you give your permission to have your de-identified information or samples stored, they will be available indefinitely and cannot be removed due to the inability to identify them.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information.
The following sections of the form describe how researchers may use your health information.
The Researchers may use and share your health information with:
• The University of Kentucky's Institutional Review Board/Office of Research Integrity;
• Law enforcement agencies when required by law;
• University of Kentucky representatives;
• UK Hospital
• Food and Drug Administration

The researchers agree to only share your health information with the people listed in this document. Should your health information be released to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information may still be regulated by applicable federal and state laws.
You may not be allowed to participate in the research study if you do not sign this form. If you decide not to sign this form, it will not affect your:
• Current or future healthcare at the University of Kentucky;
• Current or future payments to the University of Kentucky;
• Ability to enroll in any health plans (if applicable); or
• Eligibility for benefits (if applicable).

Are you recruiting or expect to enroll **Non-English Speaking Subjects or Subjects from a Foreign Culture**? (does not include short form use for incidentally encountered non-English subjects)

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

Recruitment and Consent:

Describe how information about the study will be communicated to potential subjects appropriate for their culture, and if necessary, how new information about the research may be relayed to subjects during the study.
When recruiting Non-English-speaking subjects, provide a consent document in the subject's primary language. After saving this section, attach both the English and translated consent documents in the "Informed Consent" section.

Cultural and Language Consultants:

The PI is required to identify someone who is willing to serve as the cultural consultant to the IRB.

- This person should be familiar with the culture of the subject population and/or be able to verify that translated documents are the equivalent of the English version of documents submitted.
- The consultant should not be involved with the study or have any interest in its IRB approval.
- Please include the name, address, telephone number, and email of the person who agrees to be the cultural consultant for your study.
- ORI staff will facilitate the review process with your consultant. Please do not ask them to review your protocol separately.

For more details, see the IRB Application Instructions on Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture.

Local Requirements:

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If you will conduct research at an international location, identify and describe:

- relevant local regulations
- data privacy regulations
- applicable laws
- ethics review requirements for human subject protection

Please provide links or sources where possible. If the project has been or will be reviewed by a local ethics review board, attach a copy in the “Additional Information/Materials” section. You may also consult the current edition of the International Compilation of Human Research Standards

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Does your study involve **HIV/AIDS research and/or screening for other reportable diseases (e.g., Hepatitis (**
○ Yes ◉ No

HIV/AIDS Research

If you have questions about what constitutes a reportable disease and/or condition in the state of Kentucky, see ORI's summary sheet: "Reporting Requirements for Diseases and Conditions in Kentucky" [PDF].

HIV/AIDS Research: There are additional IRB requirements for designing and implementing the research and for obtaining informed consent. Describe additional safeguards to minimize risk to subjects in the space provided below.

For additional information, visit the online IRB Survival Handbook to download a copy of the "Medical IRB's requirements for Protection of Human Subjects in Research Involving HIV Testing" [D65.0000] [PDF], and visit the Office for Human Research Protections web site for statements on AIDS research, or contact the Office of Research Integrity at 859-257-9428.

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

1) involves testing a Nonsignificant Risk (NSR) Device, or
2) is being conducted under an investigator-held Investigational New Drug (IND) or Investigational Device Exemption (IDE)?
○ Yes ◉ No

PI-Sponsored FDA-Regulated Research

If the answer above is yes, then the investigator assumes the regulatory responsibilities of both the investigator and sponsor. The Office of Research Integrity provides a summary list of sponsor IND regulatory requirements for drug trials [PDF], IDE regulatory requirements for SR device trials [PDF], and abbreviated regulatory requirements for NSR device trials [PDF]. For detailed descriptions see FDA Responsibilities for Device Study Sponsors or FDA Responsibilities for IND Drug Study Sponsor-Investigators.

- Describe the experience/knowledge/training (if any) of the investigator serving as a sponsor (e.g., previously held an IND/IDE); and
- Indicate if any sponsor obligations have been transferred to a commercial sponsor, contract research organization (CRO), contract monitor, or other entity (provide details or attach FDA 1571).

IRB policy requires mandatory training for investigators who are also FDA-regulated sponsors (see Sponsor-Investigator FAQs). A sponsor-investigator must complete the applicable Office of Research Integrity web based training, (drug or device) before final IRB approval is granted.

Has the sponsor-investigator completed the mandatory PI-sponsor training prior to this submission?
○ Yes ○ No
If the sponsor-investigator has completed equivalent sponsor-investigator training, submit documentation of the content for the IRB's consideration.
Attachments

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HIPAA

0 unresolved comment(s)

Is HIPAA applicable? ◉ Yes ○ No

(Visit ORI's Health Insurance Portability and Accountability Act (HIPAA) web page to determine if your research falls under the HIPAA Privacy Regulation.)

I have attached a HIPAA Waiver of Authorization. ○ Yes ◉ No

Attachments

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STUDY DRUG INFORMATION

0 unresolved comment(s)

The term drug may include:

- FDA approved drugs,
- unapproved use of approved drugs,
- investigational drugs or biologics,
- other compounds or products intended to affect structure or function of the body, and/or
- complementary and alternative medicine products such as dietary supplements, substances generally recognized as safe (GRAS) when used to diagnose, cure mitigate, treat or prevent disease, or clinical studies of e-cigarettes examining a potential therapeutic purpose.

Does this protocol involve a drug including an FDA approved drug; unapproved use of an FDA approved drug; and/or an investigational drug?

○ Yes ◉ No

If yes, complete the questions below. Additional study drug guidance.

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

Note: Inpatient studies are required by Hospital Policy to utilize Investigational Drug Service (IDS) pharmacies (Oncology or Non-Oncology). Use of IDS is highly recommended, but optional for outpatient studies. Outpatient studies not using IDS services are subject to periodic inspection by the IDS for compliance with drug accountability good clinical practices.

Indicate where study drug(s) will be housed and managed:

☐ Investigational Drug Service (IDS) UK Hospital

Other Location:

Is the study being conducted under a valid Investigational New Drug (IND) application?

○ Yes ○ No

If Yes, list IND #(s) and complete the following:

IND Submitted/Held by:

Sponsor: ☐	Held By:	
Investigator: ☐	Held By:	
Other: ☐	Held By:	

☐ Checkmark if the study is being conducted under FDA's Expanded Access Program (e.g., Treatment IND) or if this is an Individual Patient Expanded Access IND (FDA Form 3926).

FDA's Expanded Access Program Information for Individual Patient Expanded Access INDs, and attach the following:

- FDA Form 3926;
- FDA expanded access approval or correspondence;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Expanded Access SOP.

Complete and attach the required Study Drug Form picking "Study Drug Form" for the document type. Any

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applicable drug documentation (e.g., Investigator Brochure; approved labeling; publication; FDA co
etc.) should be attached using "Other Drug Documentation" for the document type.

Attachments

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STUDY DEVICE INFORMATION

0 unresolved comment(s)

A DEVICE may be a:

- component, part, accessory;
- assay, reagent, or in-vitro diagnostic device;
- software, digital health, or mobile medical app;
- other instrument if intended to affect the structure or function of the body, diagnose, cure, mitigate, treat or prevent disease; or
- a homemade device developed by an investigator or other non-commercial entity and not approved for marketing by FDA.

For additional information, helpful resources, and definitions, see ORI's Use of Any Device Being Tested in Research web page.

Does this protocol involve testing (collecting safety or efficacy data) of a medical device including an FDA approved device, unapproved use of an approved device, humanitarian use device, and/or an investigational device?

◉ Yes ○ No

[Note: If a marketed device(s) is only being used to elicit or measure a physiologic response or clinical outcome, AND, NO data will be collected on or about the device itself, you may answer "no" above, save and exit this section, (Examples: a chemo drug study uses an MRI to measure tumor growth but does NOT assess how effective the MRI is at making the measurement; an exercise study uses a heart monitor to measure athletic performance but no safety or efficacy information will be collected about the device itself, nor will the data collected be used for comparative purposes against any other similar device).]

If you answered yes above, please complete the following questions.

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

MagProX100 with Magoption Magnetic Stimulator

Is the study being conducted under a valid Investigational Device Exemption (IDE), Humanitarian Device Exemption (HDE) or Compassionate Use?

○ Yes ◉ No

If Yes, complete the following:
IDE or HDE #(s)

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Check if this is a Treatment IDE or Compassionate Use under the Food and Drug Administration (FDA) Expanded Access program.

For Individual or Small Group Expanded Access, see FDA's Early Expanded Access Program Information, and attach the following:

- FDA expanded access approval or sponsor's authorization;
- An independent assessment from an uninvolved physician, if available;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Medical Device SOP.

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Does the intended use of any research device being tested (not clinically observed) in this study meet the regul
Significant Risk (SR) device?

- ○ Yes. Device(s) being tested in this study presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
- ◉ No. All devices being tested in this study do not present a potential for serious risk to the health, safety, or welfare of subjects/participants.

Complete and attach the required Study Device Form, picking the "Study Device Form" for the document type. Any applicable device documentation (e.g., Manufacturer information; patient information packet; approved labeling; FDA correspondence, etc.) should be attached using "Other Device Documentation" for the document type.

Attachments

Attach Type	File Name
Other Device Documentation	StudyDevice_266761.pdf
Study Device Form	86853_StudyDevice_881865.pdf

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RESEARCH SITES

0 unresolved comment(s)

To complete this section, ensure the responses are accurate then click "SAVE".

A) Check all the applicable sites listed below at which the research will be conducted. If none apply, you do not need to check any boxes.

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☑ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital
- ☐ UK Hospital

Schools/Education Institutions

- ☐ Fayette Co. School Systems *
- ☐ Other State/Regional School Systems
- ☐ Institutions of Higher Education (other than UK)

***Fayette Co. School systems, as well as other non-UK sites, have additional requirements that must be addressed. See ORI's IRB Application Instructions - Off-site Research web page for details.**

Other Medical Facilities

- ☐ Bluegrass Regional Mental Health Retardation Board
- ☐ Cardinal Hill Hospital
- ☐ Eastern State Hospital
- ☐ Norton Healthcare
- ☐ Nursing Homes
- ☐ Shriner's Children's Hospital
- ☐ Veterans Affairs Medical Center
- ☐ Other Hospitals and Med. Centers

- ☐ Correctional Facilities
- ☐ Home Health Agencies
- ☐ International Sites

Research activities conducted at performance sites that are not owned or operated by the University of Kentucky (UK) or at sites that do not fall under the UK IRB's authority, are subject to special procedures for coordination of research review. Additional information is required (see IRB Application Instructions - Off-Site Research web page), including:

- A letter of support and local context is required from non-UK sites. See *Letters of Support and Local Context* on the IRB Application Instructions - Off-Site Research web page for more information.
- Supportive documentation, including letters of support, can be attached below.
- NOTE: If the non-UK sites or non-UK personnel are engaged in the research, there are additional federal and university requirements which need to be completed for their participation. For instance, the other site(s) may need to complete their own IRB review, or a cooperative review arrangement may need to be established with non-UK sites.

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- Questions about the participation of non-UK sites/personnel should be discussed with the ORI staff a
  9428.

List all other non-UK owned/operated locations where the research will be conducted:

Describe the role of any non-UK site(s) or non-UK personnel who will be participating in your research.

Please describe the plan for the management of reporting unanticipated problems, noncompliance, and submission of protocol modifications and interim results from the non-UK sites:

Attachments

B) If your research involves collaboration with any sites and/or personnel outside the University of Kentucky, then it is considered multisite research and IRB reliance issues will need to be addressed. This may include national multi-center trials as well local studies involving sites/personnel external to UK. If you would like to request that the University of Kentucky IRB (UK IRB) serve as the lead IRB for your study, or if you would like the UK IRB to defer review to another IRB, please contact the IRBReliance@uky.edu.

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RESEARCH ATTRIBUTES

0 unresolved comment(s)

Instructions: For various reasons, it is necessary to determine whether your research activities meet the definition of clinical research and/or a clinical trial. Your responses to the next series of questions will make that determination. For more details on the definitions, go to ORI's clinical research vs. clinical trial web page or visit NIH's decision tree for the NIH Clinical Trial definition.

My research activities include one or more of the following:

Patient-oriented research regarding mechanisms of human disease, therapeutic interventions, clinical studies, or development of new technologies
◉ Yes ○ No

Material of human origin (such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects
○ Yes ◉ No

Epidemiologic or Behavioral Studies
○ Yes ◉ No

Outcomes Research or Health Services Research
○ Yes ◉ No

Does your research study involve one or more human subjects prospectively assigned into one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes?
◉ Yes ○ No

Indicate the items below that apply to your research. Depending on the items applicable to your research, you may be required to complete additional forms or meet additional requirements. Contact the ORI (859-257-9428) if you have questions about additional requirements.

☐ Not applicable

Check All That Apply

☐ Academic Degree/Required Research
☑ Alcohol/Drug/Substance Abuse Research
☐ Biological Specimen Bank Creation (for sharing)
☐ Cancer Research
☐ CCTS-Center for Clinical & Translational Science
☐ Certificate of Confidentiality
☐ Collection of Biological Specimens for banking and use
☐ Community-Based Participatory Research
☐ Deception
☐ Educational/Student Records (e.g., GPA, test scores)
☐ Emergency Use (Single Patient)
☐ Gene Transfer
☐ Genetic Research
☐ NIH Genomic Data Sharing (GDS) (databases such as GWAS, dbGaP, GenBank)
☐ Treatment with Human Cells, Tissues, and Cellular and Tissue Based Products
☐ Individual Expanded Access or Compassionate Use
☐ International Research
☐ Planned Emergency Research Involving Exception from

For additional requirements and information:

- Cancer Research (MCC PRMC)
- Certificate of Confidentiality (look up "Confidentiality/Privacy...")
- CCTS (Center for Clinical and Translational Science)
- Clinical Research (look up "What is the definition of....)
- Clinical Trial
- Collection of Biological Specimens for Banking (look up "Specimen/Tissue Collection...")
- Collection of Biological Specimens (look up "Specimen/Tissue Collection...")
- Community-Based Participatory Research (look up "Community-Engaged...")
- Data & Safety Monitoring Board (DSMB)

  *For Medical IRB: Service Request Form for CCTS DSMB

- Data & Safety Monitoring Plan
- Deception*

  *For deception research, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"

- Emergency Use (Single Patient) [attach Emergency Use Checklist] (PDF)
- Genetic Research (look up "Specimen/Tissue

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Informed Consent

- ☐ Recombinant DNA
- ☐ Registry or data repository creation
- ☐ Stem Cell Research
- ☐ Suicide Ideation or Behavior Research
- ☐ Survey Research
- ☐ Transplants
- ☐ Use, storage and disposal of radioactive material and radiation producing devices
- ☐ Vaccine Trials

Collection...")

- Gene Transfer
- HIV/AIDS Research (look up "Reportable Diseases/Conditions")
- Screening for Reportable Diseases [E2.0000] (PDF)
- International Research (look up "International & Non-English Speaking")
- NIH Genomic Data Sharing (GDS) Policy (PDF)
- Planned Emergency Research Involving Waiver of Informed Consent*

*For Planned Emergency Research Involving Waiver of Informed Consent, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"

- Use, storage and disposal of radioactive material and radiation producing devices

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FUNDING/SUPPORT

0 unresolved comment(s)

If the research is being submitted to, supported by, or conducted in cooperation with an external or internal agency or funding program, indicate below all the categories that apply.

☐ Not applicable

Check All That Apply

- ☐ Grant application pending
- ☐ (HHS) Dept. of Health & Human Services
  - ☐ (NIH) National Institutes of Health
  - ☐ (CDC) Centers for Disease Control & Prevention
  - ☐ (HRSA) Health Resources and Services Administration
  - ☐ (SAMHSA) Substance Abuse and Mental Health Services Administration
- ☐ (DoJ) Department of Justice or Bureau of Prisons
- ☐ (DoE) Department of Energy
- ☐ (EPA) Environmental Protection Agency
- ☐ Federal Agencies Other Than Those Listed Here
- ☐ Industry (Other than Pharmaceutical Companies)
- ☐ Internal Grant Program w/ proposal
- ☐ Internal Grant Program w/o proposal
- ☐ National Science Foundation
- ☐ Other Institutions of Higher Education
- ☐ Pharmaceutical Company
- ☐ Private Foundation/Association
- ☐ U.S. Department of Education
- ☐ State

Click applicable listing(s) for additional requirements and information:

- (HHS) Dept. of Health & Human Services
- (NIH) National Institutes of Health
- (CDC) Centers for Disease Control & Prevention
- (HRSA) Health Resources & Services Administration
- (SAMHSA) Substance Abuse & Mental Health Services Administration
- Industry (Other than Pharmaceutical Companies) [IRB Fee Info]
- National Science Foundation
- (DoEd) U.S. Department of Education
- (DoJ) Department of Justice or Bureau of Prisons
- (DoE) Department of Energy Summary and Department of Energy Identifiable Information Compliance Checklist
- (EPA) Environmental Protection Agency

Other:

Internal

Specify the funding source and/or cooperating organization(s) (e.g., National Cancer Institute, Ford Foundation, Eli Lilly & Company, South Western Oncology Group, Bureau of Prisons, etc.):

Cancer Center Support Grant

Add Related Grants

If applicable, please search for and select the OSPA Account number or Electronic Internal Approval Form (eIAF) # (notif #) associated with this IRB application using the "Add Related Grants" button.
If required by your funding agency, upload your grant using the "Grant/Contract Attachments" button.

Add Related Grants

Grant/Contract Attachments

The research involves use of Department of Defense (DoD) funding, military personnel, DoD facilities, or other DoD resources. (See DoD SOP and DoD Summary for details)

○ Yes ◉ No

Using the “attachments” button (below), attach applicable materials addressing the specific processes described in the DoD SOP.

DOD SOP Attachments

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Additional Certification: (If your project is federally funded, your funding agency may request an Assurance/ Certification/Declaration of Exemption form.) Check the following if needed:

☐ Protection of Human Subjects Assurance/Certification/Declaration of Exemption (Formerly Optional Form – 310)

Assurance/Certification Attachments

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OTHER REVIEW COMMITTEES

0 unresolved comment(s)

If you check any of the below committees, additional materials may be required with your application submission.

Does your research fall under the purview of any of the other review committees listed below? [*If yes, check all that apply and attach applicable materials using the attachment button at the bottom of your screen.*]

○ Yes ◉ No

☐ Institutional Biosafety Committee
☐ Radiation Safety Committee
☐ Radioactive Drug Research Committee
☐ Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)
☐ Graduate Medical Education Committee (GME)
☐ Office of Medical Education (OME)

Additional Information

- Institutional Biosafety Committee (IBC) - Attach required IBC materials
- Radiation Safety Committee (RSC) - For applicability, see instructions and attach form
- Radioactive Drug Research Committee (RDRC)
- Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)** - Attach MCC PRMC materials, if any, per instructions.
- Office of Medical Education (OME)
- Graduate Medical Education Committee (GME)

Attachments

**** If your study involves cancer research, be sure to select "Cancer Research" in the "Research Attributes" section.** ORI will send your research protocol to the Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC). The MCC PRMC is responsible for determining whether the study meets the National Cancer Institute (NCI) definition of a clinical trial and for issuing documentation to you (the investigator) which confirms either that PRMC approval has been obtained or that PRMC review is not required. Your IRB application will be processed and reviewed independently from the PRMC review.

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ADDITIONAL INFORMATION/MATERIALS

0 unresolved comment(s)

Do you want specific information inserted into your approval letter? ○ Yes ◉ No

Approval Letter Details:

If you wish to have specific language included in your approval letter (e.g., serial #, internal tracking identifier, etc…), type that language in the box below exactly as it should appear in the letter. The text you enter will automatically appear at the top of all approval letters, identical to how you typed it, until you update it. Don't include instructions or questions to ORI staff as those will appear in your approval letter. **If these details need to be changed for any reason, you are responsible for updating the content of this field.**

Additional Materials:

If you have other materials you would like to include for the IRB's consideration, check all that apply and attach the corresponding documents using the Attachments button below.

- ☐ Detailed protocol
- ☐ Dept. of Health & Human Services (DHHS) approved protocol (such as NIH sponsored Cooperative Group Clinical Trial)
- ☐ Other Documents

Protocol/Other Attachments

NOTE: Instructions for Dept. of Health & Human Services (DHHS)-approved protocol]

If you have password protected documents, that feature should be disabled prior to uploading to ensure access for IRB review.

To view the materials currently attached to your application, click “All Attachments” on the left menu bar.

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SIGNATURES (ASSURANCES)

0 unresolved comment(s)

Introduction

All IRB applications require additional assurances by a Department Chairperson or equivalent (DA), and when applicable, a Faculty Advisor or equivalent (FA). This signifies the acceptance of certain responsibilities and that the science is meritorious and deserving of conduct in humans. The person assigned as DA *should not* also be listed in the Study Personnel section, and the individual assigned as FA *should* be listed in the Study Personnel section.

For a list of responsibilities reflected by signing the Assurance Statement, refer to "What does the Department Chairperson's Assurance Statement on the IRB application mean?"

For a detailed illustration of how to complete this section, please review the short online video tutorial "Signatures (Assurance) Section - How to Complete." Otherwise, follow the steps below.

Required Signatures:

Individuals chosen as signees may remove the application from their Inbox without signing the Assurance Statement by clicking "Return to PI" with a comment about why it is being returned (e.g., specific edits are deemed necessary).

The PI, and personnel chosen as a contact, will receive an email notification that edits are needed, and can find the draft application in both the "Draft" folder and the "Signatures Status" folder located in the menu in the left margin of the default Inbox page. The researcher does not have a 'reply' option to the signee's comments and must make the requested edits directly in the application, or communicate outside the E-IRB system as to why not. Once the response is finalized, the researcher must re-visit the "Assurances Required" section to click the "Return to Signee" button for their re-consideration; the signee will receive an email notification at that time.

Hover your mouse cursor here for additional instructions.

First Name	Last Name	Role	Department	Signee Return Comment	Date Signed	
Gopalkumar	Rakesh	Principal Investigator	Psychiatry		04/06/2023 09:55 AM	View/Sign
Elizabeth	Arnold	Department Authorization	Psychiatry		10/24/2023 08:11 AM	View/Sign

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects and I agree:

1. To comply with all IRB policies, decisions, conditions, and requirements;
2. To accept responsibility for the scientific and ethical conduct of this research study;
3. To obtain prior approval from the Institutional Review Board before amending or altering the research protocol or implementing changes in the approved consent/assent form;
4. To report to the IRB in accord with IRB/IBC policy, any adverse event(s) and/or unanticipated problem(s) involving risks to subjects;
5. To complete, on request by the IRB for Full and Expedited studies, the Continuation/Final Review Forms;
6. To notify the Office of Sponsored Projects Administration (OSPA) and/or the IRB (when applicable) of the development of any financial interest not already disclosed;
7. Each individual listed as study personnel in this application has received the mandatory human research protections education (e.g., CITI);
8. Each individual listed as study personnel in this application possesses the necessary experience for conducting research activities in the role described for this research study.
9. To recognize and accept additional regulatory responsibilities if serving as both a sponsor and investigator for FDA regulated research.

☑ Furthermore, by checking this box, I also attest that:

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- I have appropriate facilities and resources for conducting the study;
- I am aware of and take full responsibility for the accuracy of all materials submitted to the IRB for review;
- If applying for an exemption, I also certify that the only involvement of human subjects in this research study will be in the categories specified in the Protocol Type: Exemption Categories section.
- If applying for an Abbreviated Application (AA) to rely on an external IRB, I understand that certain items above (1, 3, 4, 7-8) may not apply, or may be altered due to external institutional/IRB policies. I document my agreement with the Principal Investigator Reliance Assurance Statement by digitally signing this application.

*You will be able to "sign" your assurance after you have sent your application for signatures (use Submission section). Once all Assurance Statement signatures have been acquired, return to this section to submit your application to ORI.

Department Authorization

☑ This is to certify that I have reviewed this research protocol and that I attest to the scientific validity and importance of this study; to the qualifications of the investigator(s) to conduct the project and their time available for the project; that facilities, equipment, and personnel are adequate to conduct the research; and that continued guidance will be provided as appropriate. When the principal investigator assumes a sponsor function, the investigator has been notified of the additional regulatory requirements of the sponsor and by signing the principal investigator Assurance Statement, confirms he/she can comply with them.

*If the Principal Investigator is also the Chairperson of the department, the Vice Chairperson or equivalent should complete the "Department Authorization".

**IF APPLICABLE FOR RELIANCE: I attest that the principal investigator has been notified of the regulatory requirements of both the Reviewing and Relying IRBs, according to the information provided in the E-IRB application. The attached Reliance Assurance Statement, signed by the principal investigator, confirms that he/she can comply with both sets of IRB requirements.

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SUBMISSION INFORMATION

0 unresolved comment(s)

***** If this Continuation Review entails a change in the scope of your activities to include COVID-19 related research, please insert "COVID19" at the start of your Project and Short Titles.*****

Each Section/Subsection in the menu on the left must have a checkmark beside it (except this Submission section) indicating the Section/Subsection has been completed. Otherwise your submission for IRB review and approval cannot be sent to the Office of Research Integrity/IRB.

If applicable, remember to update the Approval Letter Details text box under the Additional Information section

If your materials require review at a convened IRB meeting which you will be asked to attend, it will be scheduled on the next available agenda and you will receive a message to notify you of the date.

If you are making a change to an attachment, you need to delete the attachment, upload a highlighted version that contains the changes (use Document Type of "Highlighted Changes"), and a version that contains the changes without any highlights (use the appropriate Document Type for the item(s)). Do **not** delete approved attachments that are still in use.

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects, and I attest to:

1. Having reviewed all the investigational data from this study, including a compilation of all internal and external unanticipated problems.
2. Having reviewed, if applicable, information from the sponsor including updated investigator brochures and data and safety monitoring board reports.

I also attest that I have reviewed pertinent materials concerning the research and concluded:

- The human subject risk/benefit relationship is unaffected, mitigated, or eliminated by closure of the study and all pertinent materials for closure of the research are being submitted to the IRB for consideration.

☑ By checking this box, I am providing assurances for the applicable items listed above.

Your protocol has been submitted.

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Download all

	Document Type	File Loaded	Document Description	File Size	Modified By	Mod Date
	StudyClosure	StudyClosure.pdf		0.079	ovmo223	3/19/2025 4:05:09 PM
	CR_EntireConsent	LAN-AIC-0007-Howard, Tyler ICF Signed 4.22.2024.pdf	ICF Signed Participant 7	0.423	ngmean2	3/19/2025 11:06:36 AM
	CR_EntireConsent	LAN-AIC-0008-Howard, Stephanie Signed ICF 5.3.2024.pdf	ICF Signed Participant 8	4.184	ngmean2	3/19/2025 10:58:17 AM
	Advertising	CC-OD-24-5681.pdf	Certificate of confidentiality	0.087	gra252	2/28/2024 4:42:49 PM
	DataCollection	DAST-10-drug-abuse-screening-test.pdf	DAST	0.177	gra252	10/23/2023 9:29:26 AM
	DataCollection	Fagerstrom_test.pdf	FTND	0.254	gra252	10/23/2023 9:29:11 AM
	DataCollection	MAST.pdf	MAST	0.012	gra252	10/23/2023 9:29:00 AM
	DataCollection	Demographics_TMSIRB86853.pdf	Demographics and clinical details collected from the participant	0.039	gra252	10/23/2023 9:26:05 AM
	ResearchProcedures	Purchase_Task.pdf	Alcohol Purchase Task	0.110	gra252	10/23/2023 9:17:20 AM
	Advertising	Love Gill Email.png	Email from Love Gill_MCC protocol review	0.067	gra252	10/23/2023 9:11:13 AM
	Advertising	Advertising Flyer MOD1 10.17.2023-STAMPED.pdf	Study Flyer	0.281	gra252	10/21/2023 3:15:56 PM
	StudyDevice	86853_StudyDevice_881865.pdf		2.700	gra252	5/15/2023 6:55:14 AM
	ResearchProcedures	PreScrnF.pdf	MRI checklist for all participants	0.459	gra252	5/9/2023 3:41:35 PM
	ResearchProcedures	Figure 1.png	Design and tasks_Figure 1	0.035	gra252	4/5/2023 1:22:52 PM
	DataCollection	Treatment acceptability questionnaire (TAQ).PNG	TAQ	0.067	gra252	4/5/2023 11:33:29 AM
	DataCollection	TMS Side effects.doc	TMS Side effects Scale	0.048	gra252	4/5/2023 11:33:11 AM
	ResearchProcedures	Penn_Alcohol_Craving_Scale_171.pdf	Alcohol Craving Scale	0.032	gra252	4/5/2023 11:24:54 AM
	ResearchProcedures	AUDIT_C.pdf	AUDIT	0.168	gra252	4/5/2023 11:24:38 AM
	OtherDeviceDocumentation	StudyDevice_266761.pdf	TMS device description	0.262	gra252	3/28/2023 12:13:05 PM

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Protocol Changes

Protocol Number: 86853

Click link to sort Changed Date
HIPAA HIPAADeIdentificationCertForm changed by ngmean2 on 3/19/2025 1:17:49 PM
~~N~~
Informed Consent ElectronicConsent changed by ngmean2 on 3/19/2025 1:16:42 PM
N
Research Attributes ClinicalResearch changed by ngmean2 on 3/19/2025 1:20:58 PM
~~Y~~
Research Attributes ClinicalTrial changed by ngmean2 on 3/19/2025 1:23:17 PM
Y
Research Attributes ClinicalTrial changed by ngmean2 on 3/19/2025 1:23:17 PM
Y
Research Attributes ClinicalTrial changed by ngmean2 on 3/19/2025 1:20:58 PM
~~Y~~
Research Attributes ClinicalTrial changed by ngmean2 on 3/19/2025 1:20:58 PM
~~Y~~
Research Attributes EpidemiologicBehavioralStudies changed by ngmean2 on 3/19/2025 1:20:58 PM
N
Research Attributes MaterialOfHumanOrigin changed by ngmean2 on 3/19/2025 1:20:58 PM
N
Research Attributes OutcomesHealthServicesResearch changed by ngmean2 on 3/19/2025 1:20:58 PM
N
Research Attributes PatientOrientedResearch changed by ngmean2 on 3/19/2025 1:20:58 PM
Y
Research Sites MultisiteLeadInvestigator changed by ngmean2 on 3/19/2025 1:18:00 PM
~~N~~

Study Personnel Changes:

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No comments

Statistical analysis plan

We will calculate the mean and standard deviation values for PACS scores and alcohol cue attentional bias values for two time points (baseline and following the second session). This will be done across both cTBS and sham cTBS sessions. We will compare changes in these outcome measures across cTBS and sham cTBS sessions using t-tests.

Consent to Participate in a Research Study

KEY INFORMATION FOR Theta Burst Stimulation for Alcohol Use Disorder

We are asking you to choose whether or not to volunteer for a research study about the effects of non-invasive, non-significant risk transcranial magnetic stimulation on how your brain makes decisions and focusses attention. We are asking you because you fulfill eligibility criteria for the study. You are also being asked to participate because you have expressed interest in participating in this study, and because you passed the medical screen. If you volunteer to take part in this study, you will be one of about 30 people to do so at the University of Kentucky. This page is to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

The purpose of this study is to learn more about how multiple sessions of non-invasive, non-significant risk transcranial magnetic stimulation influences the brain's decision-making process and visual attention in people with alcohol use disorder. By doing this study, we hope to learn how the brain chooses short term versus long term rewards, in addition to learning how your eyes focus attention when seeing images related to alcohol versus neutral images. Your participation in this research will last three days. This is a research project, not a treatment program. The transcranial stimulation we use is called transcranial magnetic stimulation (TMS). In this study, TMS will be used in a manner which is an investigational procedure, aimed at temporarily changing the way that a part of your brain works. TMS has been approved by the Food and Drug Administration (FDA) as a treatment for depression, but in this study TMS is being used to investigate if changes in the activities of certain areas of the brain affect memory. You will also be asked to undergo brain MRI scans before and after the TMS session. The study will last three days.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

This research study may have direct benefit to you for alcohol use. The study will inform us about how transcranial magnetic stimulation affects cognitive functions in alcohol use.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

This study requires you to come to 245 Fountain Court for three days and to Magnetic Resonance Imaging and Spectroscopy Center (MRISC) for 3 days. If this will be an issue, you may not want to volunteer for this study. For a complete description of risks from the study, refer to the Detailed Consent. If you experience headaches from the TMS procedure, you can withdraw from the study without ramifications regarding your clinical care.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study contact Gopalkumar Rakesh MD, Assistant Professor, Department of Psychiatry at 859-382-7611 during regular business hours. If outside regular business hours, please contact the Psychiatry department On Call Group at (859) 226-7063 and explain to the physician that you are a study participant.

If you have any concerns or questions about your rights as a volunteer in this research, contact staff in the University of Kentucky (UK) Office of Research Integrity (ORI) between the business hours of 8am and 5pm EST, Monday-Friday at 859-257-9428 or toll free at 1-866-400-9428.

DETAILED CONSENT:

ARE THERE REASONS WHY YOU WOULD NOT QUALIFY FOR THIS STUDY?

You should not participate if you have a history of epilepsy or seizures, current or past history of schizophrenia, metal implants or shrapnel in your head, or history of previous adverse events with TMS. If you are a female, you should not participate if you are pregnant or plan on becoming pregnant during your participation in this experiment. You must be using an effective form of birth control (e.g. birth control pills, surgically sterilized, IUD, cervical cap with a spermicide, or abstinence), and you must be willing to take a pregnancy test before being accepted into the research study.

WHERE WILL THE STUDY TAKE PLACE AND WHAT IS THE TOTAL AMOUNT OF TIME INVOLVED?

The research procedures will be conducted at the TMS Research Suite, Department of Psychiatry, 245 Fountain Court, Lexington, Kentucky 40509 and at the MRI Scanning Center (MRISC), located at 740 Rose Street, Lexington, 40536You will need to come in three times during the study. Each of these visits will take three to four hours. The total amount of time you will be asked to volunteer for this study is 10-12 hours over the three days.

WHAT WILL YOU BE ASKED TO DO?

If you agree to take part in this study, in your first visit, you will be asked to sign and date this consent form prior to any procedures. You will then be asked to provide a sample for urine drug screen and undergo an alcohol breathalyzer test. You will also undergo psychological screening, including questionnaires to rule out major mental health conditions. We will also administer scales to assess craving for alcohol. You will also perform cognitive tasks to measure your visual attention bias towards alcohol. If you are a woman of childbearing potential, you will also undergo a urine test to make sure you are not pregnant. Then we will ask you to get a brain MRI scan on day one. This will be done at MRISC and we will transport you to the MRISC. Prior to your brain MRI session, we will administer an MRI safety checklist. MRI uses magnetic fields to measure brain structure and brain activity. It involves lying down on a padded platform that is loaded into the circular center of the MRI machine. During a scanning session, you will be asked to remain still as images of your brain are acquired. You will be instructed to remove all jewelry and other metal-containing objects. Because the magnetic field will affect any metallic object, you should not participate if you have any type of metallic implant in your body, including pacemakers, aneurysm clips, shrapnel, metal fragments, orthopedic pins, screws, or plates, IUD's, or piercings that you cannot remove.

You will receive two sessions of actual TMS each on day two and sham TMS on day three. Sham TMS will mimic the actual TMS but not deliver any stimulation. This helps us compare the effects of actual TMS. Each TMS session will last three minutes, regardless of actual or sham TMS. The TMS paradigm we will use is called continuous theta burst stimulation (cTBS) which is a short, and efficient TMS stimulation. Days two and three will be separated by at least one week. Sessions will be separated by 50 minutes and during this time, you will perform a visual attention task and a scale to measure your craving for alcohol. We will also measure your heart rate on days two and three, using a Fitbit watch strapped on your wrist. On days two and three we will also assess craving for alcohol. At the end of days two and three, we will obtain MRI brain scans.

Study Task	Study Day 1	Study Day 2	Study Day 3
Attentional Bias for alcohol	X	X	X
Alcohol purchase task	X	X	X
MRI brain scan at MRISC	X	X	X
Motor threshold	X		
Continuous Theta Burst Stimulation (TBS)		X	
Sham cTBS			X
Behavioral Scales to measure craving for alcohol	X	X	X
Fitbit to measure heart rate		X	X

The TMS equipment consists of an electric stimulator and a wire coil. Turning the stimulator on and off produces brief electrical currents in the coil, and these currents create a short-lived magnetic field around that coil (also called a 'magnetic pulse'). The wire coil is coated in plastic in order insulate the stimulator current, it is shaped like an '8', and it is a little larger than a letter-size piece of paper. When the coil is held close to the head, and it generates a

magnetic pulse, the pulse can induce very small electric currents in the part of the brain that is closest to the coil. These currents are similar to the currents that the neurons in the brain produce when communicating with each other. By inducing these currents with the TMS coil, we can temporarily change the way that brain region functions, either making the region work harder or less hard.

Before applying TMS, the study doctors will need to determine what strength of stimulation to use for you by establishing your personal "motor threshold" – a measure of the excitability of the area of the human brain called the motor cortex. To establish this threshold, the study doctor or a member of the study staff will first place the stimulator over the part of your brain that controls the motor activity in your right hand. You will hear a clicking sound and feel a tapping sensation at your scalp. The stimulator will be adjusted to give just enough energy so that the motor region of the brain sends signals to your hand muscles, to make your hand twitch. The smallest amount of energy required to make your hand twitch is called the "motor threshold." Everyone has a different motor threshold. This procedure will take about 20 minutes and will be done only on day one of the study. Then we will administer cognitive tests to assess how your brain makes decisions and chooses hypothetical rewards. You will also perform a visual attention test to assess how your eyes focus attention when seeing images related to alcohol versus neutral images.

During the TMS session, you will be seated comfortably in a chair, facing a computer screen placed about 5 feet away. Earplugs will be worn to protect your hearing. Your head will be held steady by a frame with a chin rest and the TMS coil holder frame, and study staff will ensure your comfort during the entire procedure. The study staff will administer the magnetic stimulation. You will be required to sit still while you receive the stimulation. To block out the clicking noise of the TMS procedure, we will provide you with earplugs. After each TMS session, you will then be administered the cognitive tests, and craving scale again. The motor threshold will take place only on day one. On day one and all other days, you will perform the urine drug screens, alcohol breathalyzer test, receive the stimulation and perform cognitive tests, the visual test, and scales before and after stimulation.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider. The most serious known risk of TMS is the production of a seizure. TMS procedures are associated with a very low risk of seizures. Out of tens of thousands of people given various forms of TMS to date, 16 people have been reported to have had a seizure. TMS can produce a seizure when a series of pulses is given at high power and when repeated series of pulses are given extremely close together. This study will use only levels of TMS that are within safety guidelines. Levels of TMS that fall within the safety guidelines have not been associated with seizure in appropriately screened individuals. No seizures have occurred in normal volunteers with the dosage of TMS used in this study. To minimize this risk, we will medically screen you for any of the known characteristics that could lead to seizure. For example, if you have epilepsy you cannot participate in this study. You will be visually monitored during the TMS for any signs of seizure or muscle twitching. In spite of these precautions, there is a chance that you will experience a seizure. Should this occur, our study doctor will be called and will assess if you need to be taken to the Emergency Department at UK Medical Center.

If you have a seizure, you may require hospital admission and follow-up neurological evaluation. Having had a seizure may make it difficult for you to obtain medical insurance, future employment, and to drive. It is not known whether having had one seizure will make a person more prone to have future seizures. Should you have a seizure caused by TMS in this protocol, we will provide you with a letter documenting that the seizure was experimentally induced.

The most common side effect of TMS is a "muscle-tension" type headache. We expect that about three out of ten people may experience a headache with the types of TMS used in this study. We will make every effort to reduce any discomfort by adjusting the position of the TMS coil on your head, altering the stimulation output of the coil, or taking breaks as required. If a headache occurs, it usually starts during or immediately after the TMS and lasts from minutes to hours after TMS. The headache usually goes away with standard over-the-counter pain medications. Neck pain may also occur. You may also experience some discomfort on your head where the coil is held. This is due to contraction of scalp muscles. Temporary numbness of the face has also been reported in rare instances that may last for several weeks after treatment.

The click noises produced by the TMS procedure are loud enough to be damaging to your ears. You will therefore be required to wear earplugs, provided by the experimenter. Additional side effects considered to be rare in TMS

are dizziness, memory impairment, trouble concentrating, and acute mood changes. If these occur, these effects do not last long (minutes to hours, but not day) and will resolve without need for treatment. There may be other risks that are currently unknown. The long-term effects of TMS are not known. There is also a risk of potential loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

While in the MRI scanner you may become too hot or too cold, in which case you may ask for an adjustment of room temperature or a blanket. Some people may become nervous or feel claustrophobic while in the scanner. If this happens, you may ask to be withdrawn and will be removed from the scanner immediately. A small number of people experience a sense of dizziness or vertigo while in the scanner due to the magnetic field. If this occurs and disturbs you, you may ask to be withdrawn and you will be removed immediately.

The Fitbit can cause an allergic reaction causing your skin to become red at its point of contact with your wrist. We will remove the Fitbit if you develop itching or skin redness after it is strapped on your wrist.

There is always a chance that any research procedure can harm you. The research procedures in this study are no different. In addition to risks described in this consent, you may experience a previously unknown risk or side effect. If you experience any adverse events (a bad effect) after leaving the study, please contact Gopalkumar Rakesh MD, Assistant Professor, Department of Psychiatry at 859-382-7611 during regular business hours. If outside regular business hours, please contact the Psychiatry department On Call Group at (859) 226-7063 and explain to the physician that you are a study participant. For women of child-bearing potential: The risks of exposure to magnetic fields during pregnancy are unknown. Women of childbearing capacity will be asked to take a pregnancy test before exposure to MRI. You will be excluded from the study if the test indicates that you may be pregnant.

Risk	Ranking (rare/occasional/often)
Seizures	Rare
Hearing issues	Rare
Headache	Occasional
Dizziness/vertigo in scanner	Rare
Neck pain	Occasional

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

You may benefit from taking part in this study in helping you from drinking alcohol. The study will inform us about how transcranial magnetic stimulation affects cognitive functions, visual attention, and craving in people with alcohol use disorder.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you do not want to be in the study, there are no other choices except not to take part in the study.

WHAT WILL IT COST YOU TO PARTICIPATE?

The University of Kentucky will not bill your insurance company, Medicare, or Medicaid for the study as it is done strictly for research. You will not incur any costs, should you decide to participate in this study.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

Every effort will be made to maintain the confidentiality of your study records. We will make every effort to prevent anyone who is not on the research staff from knowing that you gave us information, or what that information is. When we write about or share the results from the study, we will write about the combined information. We will keep your name and other identifying information private.. Your identity will remain confidential, unless you give prior written approval or unless it is required by law. Your name, address and social security number will be listed on the receipt for payment that you receive, as required by the Internal Revenue Service (IRS); but no information about your participation in this research project will be released. The study will also be registered on www.clinicaltrials.gov and collective data on number of patients recruited into this trial will be reported on the website. To ensure the study is conducted properly, officials of University of Kentucky may look at or copy pertinent portions of records that identify you. We are required to enter the urine drug screen results from the study day into your medical record, these results may be visible to providers who may review your medical record for your treatment.

You should know that in some cases we may have to show your information to other people because of special circumstances. For example, the law may require us to share your information with:

- a court or agencies, if you have a reportable disease/condition.
- Authorities, if you report information about a child being abused; or if you pose a danger to yourself or someone else.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

You can choose to leave the study at any time. You will not be treated differently if you decide to stop taking part in the study. If you decide to withdraw from the study early, you will not receive any of the completion allowance described below. The data collected until that point of withdrawal from the study will remain in the study database and may not be removed. The study investigators can discontinue your participation for the following reasons: (1) if you verbally or physically assault another volunteer, patient or staff member at 245 Fountain Court; (2) if your behavior is disruptive to the other volunteers, patients, research staff or medical staff at 245 Fountain Court; (3) failure to comply with the alcohol, and drug use restrictions; (4) failure to comply with the pregnancy restrictions; (5) failure to complete a scheduled experimental sessions; (6) failure to perform the behavioral tasks to the best of your ability. If you are discharged from the study for any of these reasons, you will not receive the completion allowance described below. The medical doctor on this project can terminate your participation if he/she does not feel that it is medically safe for you to continue. If you experience intractable headaches with TMS, you can withdraw from the study with no ramifications to your clinic appointments. If your participation is terminated for medical reasons, you will receive the completion allowance for each of the sessions you completed.

ARE YOU PARTICIPATING, OR CAN YOU PARTICIPATE, IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may take part in this study if you are currently involved in another research study. It is important to let the investigator/your doctor know if you are in another research study. You should discuss this with the investigator/your doctor before you agree to participate in another research study while you are in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or get sick because of something that is done in this study, you should immediately call Gopalkumar Rakesh MD, Assistant Professor, Department of Psychiatry at 859-382-7611. After business hours, please call the Psychiatry department On Call Group at (859) 226-7063 and explain to the physician that you are a study participant. The physician will determine what type of treatment, if any, is best for you at that time.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

Medical costs related to your care and treatment because of study-related harm will be your responsibility. You do not give up your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You can receive up to a total of $250 for taking part in this study. You will be paid $50 for day one of the study, $100 for days two and three of the study. If you choose to withdraw from the study after day one or two, you will still receive $50 or $100 respectively and an additional prorated amount depending on number of hours you spent in the study.

With a few exceptions, study payments are considered taxable income reportable to the Internal Review Service (IRS). A form 1099 will be sent to you if your total payments for research participation are $600 or more in a calendar year.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

We will tell you if we learn new information that could change your mind about staying in the study. We may ask you to sign a new consent form if the information is provided to you after you have joined the study.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?

The investigators on this project will share with you any significant new findings that may develop during the course of your participation. At that time, you will be allowed to decide if you wish to continue in the study. If you choose not to continue, you will receive the completion allowance for each of the visits you attended.

WILL WE CONTACT YOU WITH INFORMATION ABOUT PARTICIPATING IN FUTURE STUDIES?

The research staff would like to contact you in the future with information about participating in additional studies. If so, it will be limited to two times per year.

Do you give your permission to be contacted in the future regarding your willingness to participate in future research studies?

☐ **Yes** ☐ **No** **Initials**_____

WHAT ELSE DO YOU NEED TO KNOW?

Before you decide whether to accept this invitation to take part in this research study, please ask any questions now. Later, if you have questions about the study, you can contact the investigators directly at the phone numbers listed above. If you have concerns or questions about your rights and/or welfare as a volunteer in this research, you can contact the staff in the Office of Research Integrity at The University of Kentucky at (859) 257-9428 or toll free at 1-866-400-9428. We will give you a signed copy of this consent form to take with you.

A description of the clinical trial will be available on ClinicalTrials.gov as required by 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.

WILL YOUR INFORMATION (OR SPECIMEN SAMPLES) BE USED FOR FUTURE RESEARCH?

All identifiable information (e.g., your name, medical record number, or date of birth) will be removed from the information or samples collected in this study. This means that no link or code to your identity will be kept. After all identifiers have been removed, the information or samples may be used for future research or shared with other researchers without your additional informed consent, Once you give your permission to have your de-identified information or samples stored, they will be available indefinitely and cannot be removed due to the inability to identify them.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. The following sections of the form describe how researchers may use your health information.

Your health information that may be accessed, used and/or released includes:

- Medical record number (MRN) and urine drug screen results on days 2 and 3 of the study.

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity;
- Law enforcement agencies when required by law;
- University of Kentucky representatives;
- UK HealthCare and their representatives
- UK Health system (EPIC, the electronic medical records) and health systems outside of UK for which you have a patient relationship;

You may not be allowed to participate in the research study if you do not sign this form. If you decide not to sign this form, it will not affect your:

- Current or future healthcare at the University of Kentucky;
- Current or future payments to the University of Kentucky;
- Ability to enroll in any health plans (if applicable); or
- Eligibility for benefits (if applicable).

After signing the form, you can change your mind and NOT let the researcher(s) collect or release your health information (revoke the Authorization). If you revoke the authorization:

- Send a written letter to: Gopalkumar Rakesh MD, Assistant Professor, Department of Psychiatry to inform him of your decision.
- Researchers may use and release your health information **already** collected for this research study.
- Your protected health information may still be used and released should you have a bad reaction (adverse event).

You will not be allowed to review the information collected for this research study until after the study is completed. When the study is over, you may have the right to access the information.

The use and sharing of your information has no time limit.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the business hours of 8am and 5pm EST, Monday-Friday at (859) 323-1184.

INFORMED CONSENT SIGNATURES

This consent includes the following:

- **Key Information Page**
- **Detailed Consent**

You will receive a copy of this consent form after it has been signed.

_____ **Signature of research subject**	_____ **Date**
_____ **Printed name of research subject**	
_____ Printed name of [authorized] person obtaining informed consent and HIPAA authorization	_____ Date