MONASH University

EXPLANATORY STATEMENT

Project ID: 42604
Project title: A pilot study for network modelling informed personalized brain stimulation for alcohol use disorder

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You are invited to take part in this study. Please read this Explanatory Statement in full before deciding whether to participate in this research. If you would like further information regarding any aspect of this project, you are encouraged to contact the researchers via the phone numbers or email addresses listed above.

What does the research involve?

We are developing a method for using brain imaging techniques to personalise treatments for Alcohol Use Disorder (AUD). Specifically, our first aim is to validate a personalisation technique that uses an fMRI-based Alcohol craving task to capture a person's unique brain activation patterns. This will be used to determine if we can utilise this information to determine which type of biological intervention is best suited to address your unique biology. Our second aim is to use this personalisation technique in a pilot study of a non-invasive brain stimulation intervention, selecting the target of 'repetitive transcranial magnetic stimulation' (rTMS) based on a person's unique brain activations captured by our personalisation technique. We will evaluate this approach and the effectiveness of the personalised intervention by observing a suite of neurobiological, metabolomic, and behavioural measures. Specifically, we will ask you to complete the following activities:

(1) Online questionnaires which ask you to report some general demographic and health-related history, and reflect on your behaviour and experiences regarding alcohol and related behaviours (~20 minutes to complete).
(2) If you are eligible, we will contact you to confirm your eligibility with a standardised interview protocol, which we will organise to take place over the phone or Zoom at a time that is convenient to you (45-60 minutes to complete).
(3) If we confirm your eligibility, we will invite you to complete a battery of cognitive tasks (2-2.5 hours) and attend 2 x face-to-face experimental session at Monash University, BrainPark. The cognitive tasks will be completed either during the face-to-face session or online at home*. The face-to-face session will take 6-7 hours (plus additional time for the cognitive battery if completed during the session) and ***will require abstaining from alcohol for at least 36 hours before the session*** (confirmed with a blood alcohol concentration readings with a breathalyser). ***Please also come to the session fasted (no food from the midnight prior).***

In the session:

a. We will take biological samples, including body composition (height, weight, waist, and hip measures), measuring blood pressure and heart rate, collect a hair sample, and collect a small amount of blood from a fingerpick test and by putting a needle into a vein in your arm. We will follow the standard method used to obtain blood for tests, performed by a professional trained in phlebotomy.
b. You will experience 2 x brain scans in a Magnetic Resonance Imaging (MRI) scanner while you engage with an fMRI-based Alcohol craving task

c. You will experience 2 x non-invasive brain stimulation rounds designed to temporarily influence the connectivity of a particular brain region involved in alcohol craving.
d. You will complete cognitive tasks (if they are to be completed during the session rather than online at home)
e. We request you use a phone application (EARS) for an Ecological Momentary Assessment and Observational study (EMA-O) that will prompt you to complete short survey questions a few times a day (one-minute surveys; for 90 days) and collect observational data. Specifically geographical location, motion level and activity types (e.g. stationary/ walking/ etc), and keyboard strokes will be collected.

We may also subsequently invite you to other related studies, for which we will provide more details and ask you to provide written consent separately. This study will only increase our knowledge of our ability to change the neural activation patterns based on personalise information and is not expected to provide any direct benefits to participants. However, the knowledge we will generate has potential to inform the development of new and more effective treatments for AUD.

*If the cognitive tasks cannot be completed during the in-person session (due to time constraints) or online at home (due to internet access or personal reasons), you may be invited back for an additional in-person session to complete the cognitive tasks

Source of funding

This study is funded by the Wellcome Leap Untangling Addiction Program.

Consenting to participate in the project and withdrawing from the research

Before you begin you will be asked to sign a consent form to indicate that you understand what is required from you for the study and that you wish to proceed. Your participation in this study is voluntary and you can withdraw from further participation at any stage before completion of the study, without any implication. You will be asked to separately provide consent to engage in the screening process, the cognitive tasks, and the experimental session. If you want to withdraw your data, you can request this at any time by contacting the Chief Investigator. Please note that we are required to retain critical safety data to ensure correct safety reporting for this study.

Possible benefits and risks to participants

By taking part in this study, you will be helping us to find out more about the between brain activation patterns and successful biological interventions for AUD using non-invasive brain stimulation. Success with this study may help us to develop more effective personalised treatment approaches for AUD. However, there are some potential risks to consider:

Brain imaging.
Magnetic resonance imaging (MRI) is a non-invasive brain imaging procedure routinely used in human clinical and research contexts. *There is currently no evidence that prolonged exposure causes any adverse health effects.* Nonetheless, the scanning environment can elicit feelings of anxiety in some people, particularly if people feel claustrophobic in the enclosed space of the scanner. The MRI scanner will make loud hammering noises during some of the scan, we will therefore provide you with headphones or earplugs to lessen the noise. In some individuals, transient nausea or mild discomfort (e.g., a minor headache) can occur during or after an MRI. Headaches after MRI can be treated with over-the-counter pain medication and usually subside within 30 minutes. When in the scanner, you will be given a buzzer that can be used to alert staff to any discomfort or emergency. You should press the buzzer if you feel uncomfortable or if you want to withdraw participation. You are free to withdraw participation at any time.

Non-invasive brain stimulation

The main concern when using rTMS is its potential to induce a seizure. This risk is very low, particularly in those who do not have a previous history of seizures (this has been estimated as being considerably lower than the seizure risk with commonly prescribed medications, such as the anti-smoking medication Zyban). We will also minimise this risk by following established safety guidelines and excluding participants with an elevated risk of seizure. Very few seizures (less than 15 worldwide) have occurred since these guidelines were introduced over a decade ago. Monash Biomedical Imaging has an established protocol for dealing with seizure-related emergencies in the unlikely event that seizure does occur.

As rTMS can be noisy, it can occasionally cause ringing in the ears or short-term hearing loss. We will minimise this risk by providing you with earplugs. rTMS can produce a tension type of headache through the stimulation of local scalp muscle contraction (~ 5% of subjects with high frequency stimulation in treatment studies). The incidence of this is dependent on the site of stimulation and especially the frequency. It is recommended that people who suffer from migraines or frequent severe headaches do not participate in TMS studies. Some participants feel faint or dizzy following TMS, usually those who also feel faint following other medical procedures (e.g., giving blood). It is recommended that you do not participate if you have a history of fainting or dizziness. If the stimulation feels uncomfortable, please notify the researcher so they can make alterations to minimise these sensations. Headaches after stimulation can be treated with over-the-counter pain medication and usually subside within 30 minutes. If you have any concerns about TMS, please let us know. You are free to withdraw at any time.

You will be requested to provide an emergency contact for safety purposes, as is standard practice for studies involving TMS. This contact would only be used in the unlikely event of an event during stimulation.

EMA-O

The smartphone-based assessment platform collects sensitive personal data, including geographical location, motion levels and types, and keystrokes. It is important to note that the keyboard logger does not record information entered into secure fields, such as passwords or credit card numbers. Each participant's data is linked only to an anonymized participant ID, ensuring that personal information remains confidential. Data stored in the cloud will be encrypted and access will be restricted to Ksana Health personnel and a limited number of research staff directly involved in the study. The only risk involves the potential loss or theft of data or a breach of confidentiality. You may opt out of any specific aspect of mobile data collection at any time.

Blood draws

The risks of having blood drawn from your arm include some pain when the needle goes in and a small risk of bruising and/or infection at that site. Some people get lightheaded, nauseous, or faint. You are less likely to have these problems if you drink at least 2 glasses of water before the blood draw.

Research involving diagnostic testing or possible incidental findings

While the MRI scans acquired are not for clinical purposes, a radiologist will inspect them for the presence of any incidental findings. In some cases (~2%), a previously unknown brain abnormality can be uncovered. You will be required to nominate a General Practitioner or another physician of your choice to who these incidental and/or adverse findings can be reported. If incidental findings are identified, they will be sent to your nominated GP, and you will be informed, and you may choose to follow up with your GP.

Payment

You will be reimbursed for the study with digital gift cards that will be emailed to you. The gift cards can exchange for goods or services in retail stores but will exclude the ability to purchase alcohol. Reimbursements will be given as compensation for the time commitment associated with participation in each activity for the study:

(1) For each experimental session, we will provide you with $150 in gift cards.
(2) For the series of cognitive tasks, we will provide $30 in gift cards.
(3) For the EMA-O study, we will provide you with $2 per day (in gift cards) for completing the EMA one-minute surveys each day (up to $180 in gift cards over the 90-day period), and up to a $100 bonus in gift cards scaled to the overall percentage of surveys completed.

Confidentiality

Any information obtained in connection with this study that can identify you will remain confidential. It will only be disclosed with your permission, except as required by law. In any publication and/or presentation of this study, information will be provided in such a way that you cannot be identified, except with your permission. Publicly presented data will only include numerical data and statistical analyses. It will not include any information which may identify you.

Storage of data

In accordance with Monash University regulations, if you decide to take part in this study, you will be assigned an alphanumeric ID number and all hard copy and electronic files containing data from you will be labelled with this number, rather than your name or other information, which could directly identify you. A document detailing which number corresponds with you, and any other details that could identify you, will be kept on a password-protected computer hard drive accessible at the at the Monash Biomedical Imaging Centre only to researchers directly involved in this study. This document will be deleted at the conclusion of this study to protect your confidentiality. We will keep your data for 5 years and then destroy it by shredding (for hard copy files) or deletion (for electronic files).

The data collected using the EARS tool will be securely uploaded from your phone to a secure cloud service using encrypted communication protocols. Each participant's data will be linked only to an anonymized participant ID, ensuring your personal information remains confidential. The data stored in the cloud will be encrypted, and access will be restricted to Ksana Health personnel and a limited number of research staff directly involved in the study. You may opt out of any specific aspect of mobile data collection at any time.

If recruited via TrialFacts, the screening data you provide for recruitment purposes will be securely uploaded from your device to a secure cloud service using encrypted communication protocols. The data stored in the cloud will be encrypted, and access will be restricted to Recruitment personnel and a limited number of research staff directly involved in the study. Trialfacts will delete your information from its records upon your request.

Your hair and blood samples will be sent for analysis to the Integrative Pharmacology and Systems Neuroscience Group and the Monash Proteomics & Metabolomics Platform. To protect your privacy, only your ID number will be associated with the sample, and the sample will be destroyed after analysis.

Use of data for other purposes

In accordance with data sharing guidelines, de-identified data may be made available for use by the other researchers. This data will be held on secure public repositories and may be a requirement of some journals prior to publication. Any shared data will not include your identifying details.

Results

A summary of the results will be available after 01/06/2025. Please contact the Chief Investigator if you would like to receive a copy once the results are finalised.

Complaints

Should you have any concerns or complaints about the conduct of the project, you are welcome to contact the Executive Officer, Monash University Human Research Ethics Committee (MUHREC):

Executive Officer Monash University Human Research Ethics Committee (MUHREC) Office of Research Ethics and Integrity Room 116, Administration Building B (3D) 26 Sports Walk, Clayton Campus Monash University VIC 3800 Tel: +61 3 9905 2052 Email: muhrec@monash.edu	