Participant Information Sheet

Study title: High-definition transcranial grey noise stimulation (HD-tGNS) as an intervention for generalized anxiety disorder: A proof of concept study

Locality: Department of Surgical Sciences, University of Otago, New Zealand.

Ethics committee ref.: 2022 FULL 13910

Lead investigator(s): Prof. Dirk De Ridder
Dr. Divya Adhia
Prof. Paul Glue
Cindy van Sleeuwen

Contact phone number: 03 470 9337

You are invited to take part in a study evaluating the safety and the effect of new brain stimulation waveforms on generalized anxiety disorder (GAD). Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you would like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide, you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 10 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

VOLUNTARY PARTICIPATION AND WITHDRAWAL FROM THIS STUDY

- Your participation in this study is voluntary.
- You may withdraw from this project at any time and without any disadvantage to you of any kind. Besides, the study staff may decide to withdraw you from the study if there are any side effects from the intervention or if they have any other concerns.

WHAT IS THE PURPOSE OF THE STUDY?

The purpose of this study is to evaluate and explore the effect of a grey noise brain stimulation design in adults diagnosed with GAD. The brain stimulation design will be compared to a non brain stimulation design, during which no current will be applied to the

scalp. This study will involve stimulating activity of the brain regions that have been demonstrated to be altered in people with GAD. The results obtained from this study may help us to develop new treatments for alleviating anxiety symptomatology in individuals diagnosed with GAD.

WHO ARE WE SEEKING TO PARTICIPATE IN THE PROJECT?

We are seeking approximately 24 adults diagnosed with GAD, aged between 18-60 years old, with no history of any cognitive problems or neurological disorders.

You are not eligible to participate if you have the following condition(s):

- History of neurological disorders
- History of epilepsy or seizures
- Alcohol or substance abuse (i.e., consuming more than 3 drinks on any day or more than 7 drinks per week for women, and more than 4 drinks on any day or more than 14 drinks per week for men).
- Previous treatment with neuromodulation (e.g. Transcranial magnetic stimulation, electroconvulsive therapy, Neurofeedback, etc.)
- Dyslipidaemia
- Cognitive impairments: A total score of 24 or below on Mini-Mental State Examination
- History of uncontrolled/untreated hypertension
- Presence of any pacemaker or defibrillator
- Presence of any electronic implants or metal implant in the body (particularly head and neck)
- Recent or current pregnancy

You will be screened for the above-mentioned conditions by a researcher, either by phone or by email, to determine your eligibility to participate in this study.

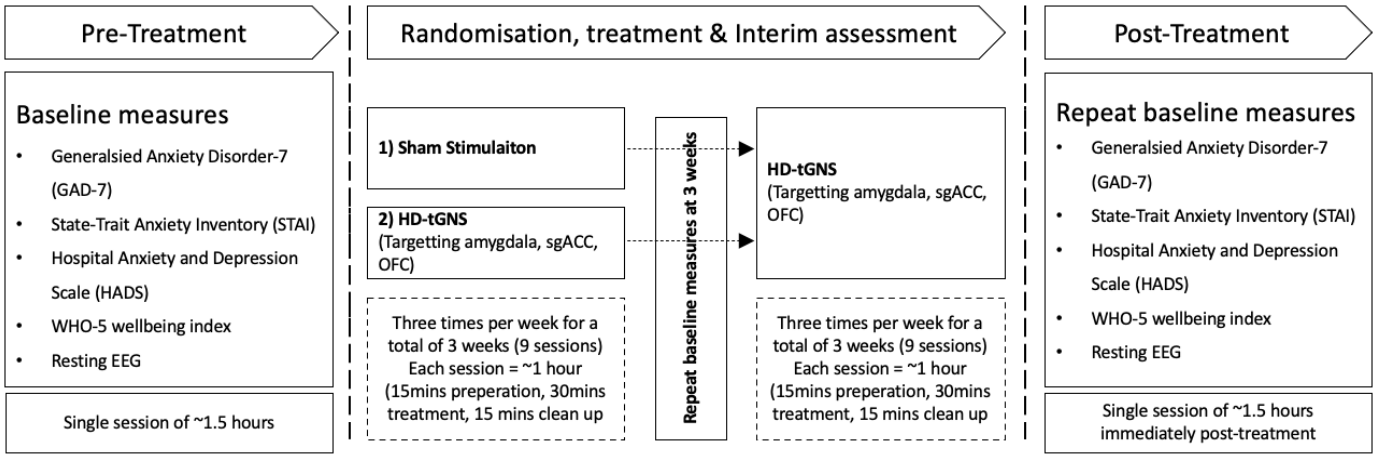
You will also be asked to provide contact details of your GP or other current provider. We will tell your GP or other current provider that you have agreed to take part in this study, and to inform them of any unusual findings that are recorded during assessments.

You must have a support person who will be willing to assist you to attend all your appointments, to-and-from the hospital to your resident. The primary role of the support person is to help you with transportation after the study session. You can have multiple support persons to assist you throughout the study period and you are not required to withdraw should the support persons opt out. Another support person can be arranged in this case.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

As shown in Picture 1 over-leaf, you will be required to attend **3 sessions per week for 6 consecutive weeks, and 3 assessment sessions**, at Dunedin hospital (201 Great King Street, 6th Floor, Room 626).

Each intervention session will be of approximately 1 hour duration and would involve external brain stimulation. Each assessment session (before the start of the intervention, and mid- and post-intervention) will involve the recording of brain activity using an electrode cap and the completion of questionnaires.
Your total time commitment will be approximately 22.5 hours.



Picture 1. Study phases and time-duration for each phase

Before-intervention tests: The following tests will be conducted after obtaining written informed consent.

- **Questionnaires:** You will be asked to complete questionnaires about yourself (age, gender, education, ethnicity, and well-being), and the nature and severity of your anxiety symptomatology.

- **Brain wave testing:** You will be asked to wear a cap with electrodes attached to it (see Picture 2). According to the Tikanga Māori and Pacific culture, the head is considered very tapu (sacred), *"he tapu te upoko"*. The researcher will obtain permission from you before touching your head, and also respect other cultural aspects (e.g., not sitting directly on pillows/tables; not passing food over anybody's head, etc). You will rest in a comfortable chair with your eyes closed for 10 minutes and your brain activity will be recorded.

Picture 2. Brain wave testing and brain stimulation device and the intervention position

Intervention phase:

- After baseline assessments, you will receive one of the interventions (i.e., the brain stimulation waveforms or no brain stimulation) for 30 minutes.

- You and the researchers conducting the assessments will not know if you are receiving brain stimulation or not, i.e., you will be blinded to the intervention you receive. This blinding

will help us to find out whether any changes in anxiety symptomatology are due to the brain stimulation.

Mid- and after-intervention tests: Following the intervention protocol, the same tests that were done before the intervention sessions will be repeated.

WHAT I CAN AND CANNOT DO DURING THE STUDY PHASES?

Before testing sessions: We request that you ***don't do*** the following:

- Drink alcohol for 24 hours before the session
- Smoke for 4 hours before the session
- Consuming caffeinated drinks for one hour before the session
- Apply any hair products (oil, gel) before the session

After intervention sessions: Side effects from stimulation, if any, should disappear soon after stimulation. But for safety reasons, you will not to be able to drive for at least 2 hours after the intervention sessions. Your support person will take you back to your home. In case your support person cannot take you back home, the research team will be able to arrange and pay for the taxi (Driving Miss Daisy) to drop you home.

You will be provided with some refreshments (e.g., crackers, tea, or juice) after each session.

If you are non-compliant with the above restrictions, your session will be rescheduled to another date. However, repeated (> 2 times) non-compliance might result in withdrawal and discontinuation from further participation in the study.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

- Other studies have demonstrated that this type of brain stimulation is a safe procedure. The most common side-effects reported include:
  - Headache
  - Fatigue
  - Nausea
  - Insomnia
  - Mild tingling sensation, transient redness or itching under the stimulation electrodes.
- Most side effects are mild and disappear soon after stimulation, and the intervention is expected to be well tolerated. In the unlikely case where any adverse effect is severe, medical staff will be available to provide advise/management, and referrals will be made as deemed appropriate.
- Other severe but rare risks include the onset of seizures and it cannot be predicted when these could occur. In the unlikely event that this occurs, the intervention will be stopped immediately. We have tested the similar stimulation design in healthy people (n=80) and other clinical populations (n=20 people with major depressive disorder, n=9 people with early Alzheimer's disease, n=40 people with chronic low back pain), and it was safe, with **no** reported case of seizures. All the stimulation dosage and parameters are according to the guidelines and hence the research team is reasonably confident that the risk of the adverse events is very low.

- You will be closely monitored for your responses during all the testing procedures, and sufficient rest will be provided between each test. Any side effects will be formally recorded and addressed if medical attention is required.

WHO PAYS FOR THE STUDY?

This study is internally funded.

There will be no costs to you for participating in the study. You will receive a total of $150 vouchers as a reimbursement for your time, travel, and parking expenses. We will give you $50 vouchers in the first, third, and sixth weeks of intervention.

WHAT IF SOMETHING GOES WRONG?

If you were injured in this study, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

During this study the research staff will record information about you and your study participation. This includes the results of various measures (e.g., anxiety symptomatology, function, brain activity) by way of questionnaires, and assessments. If needed, information from your hospital records and your GP may also be collected. You cannot take part in this study if you do not consent to the collection of this information.

Identifiable Information:

Identifiable information is any data that could identify you (e.g., your name, date of birth, or address). Only researchers involved in the research program will have access to your identifiable information. Identifiable information will be destroyed at the end of the project.

De-identified (Coded) Information:

To make sure your personal information is kept confidential, information that identifies you will not be included in any report generated by the researcher. Instead, you will be identified by a code. The researcher will keep a list linking your code with your name, so that you can be identified by your coded data if needed.

The results of the study may be published in an international scientific journal or presented, but not in a form that would reasonably be expected to identify you. Only a summary of the data will be mentioned in the research publication. The data included in the publication will in no way be linked to any specific person, and your identity will not be recorded with the data. You are welcome to request a copy of the study results. These will be available in approximately August 2023.

Future Research Using Your Information:

If you agree, your coded information may be used for future research related to the brain stimulation intervention or brain activity. If you agree, your coded information may also be used for other medical and/or scientific research that is unrelated to the current study.

This future research may be conducted overseas. You will not be told when future research is undertaken using your information. Your information may be shared widely with other researchers. Your information may also be added to information from other studies, to form much larger sets of data. You will not get reports or other information about any research that is done using your information.

Your information may be used indefinitely for future research unless you withdraw your consent. However, it may be extremely difficult or impossible to access your information or withdraw consent for its use once your information has been shared for future research.

Security and Storage of Your Information:

Your identifiable information is held at the University of Otago during the study. After the study it is transferred to a secure archiving site and stored for 10 years, then destroyed. Your coded information will be entered into electronic case report forms. Coded study information will be kept in secure, cloud-based storage indefinitely. All storage will comply with local and/or international data security guidelines.

Risks:

Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee that you cannot be identified. The risk of people accessing and misusing your information (e.g., making it harder for you to get or keep a job or health insurance) is currently very small, but may increase in future as people find new ways of tracing information.

Rights to Access Your Information:

You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected.

Please ask if you would like to access the results of your brain wave tests during the study.

You may access other study-specific information before the study is over, but this could result in you being withdrawn from the study to protect the study's scientific integrity.

If you have any questions about the collection and use of information about you, you should ask the researcher.

Rights to Withdraw Your Information:

You may withdraw your consent for the collection and use of your information at any time, by informing your Study Doctor.

If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you.

If you agree, information collected up until your withdrawal from the study will continue to be used and included in the study. You may ask for it to be deleted when you withdraw, unless you withdraw after the study analyses have been undertaken.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns, or complaints about the study at any stage, you can contact:

Name: Dr. Divya Adhia **Position**: Research Fellow **Department:** Department of Surgical Sciences, University of Otago, Dunedin.	**Phone number:** 03 470 9337 **Email**: divya.adhia@otago.ac.nz
Name: Professor Dirk De Ridder **Position**: Chair, Neurosurgery **Department:** Department of Surgical Sciences, University of Otago, Dunedin.	**Phone number:** 03 470 9337 **Email**: dirk.deridder@otago.ac.nz
Name: Cindy van Sleeuwen **Position**: Research Assistant, Neurosurgery **Department:** Department of Surgical Sciences, University of Otago, Dunedin.	**Phone number:** 021 029 546 64 **Email**: c.van.sleeuwe@student.vu.nl

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678).
Email: advocacy@advocacy.org.nz
Website: https://www.advocacy.org.nz/

To ensure ongoing cultural safety, the Southern District Health Board encourage those who identify as Māori, and who are participating in health research or clinical trials, to seek cultural support and advice from their own Kaumātua or Kuia in the first instance, or please contact:

Wendi Raumati & Eleanor Russell Kaiāwhina Te Ara Hauora - Māori Health Unit Dunedin Hospital Phone: (03) 474 0999 ext 58649	Andrea Jerry Kaiāwhina Te Huinga Tahi Māori Health Cultural Support Southland Hospital Phone: (03) 218 1949 ext 48509

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS
Email: hdecs@health.govt.nz

This project has been reviewed and approved by the Health and Disability Ethics Committee (Ref: 2023 FULL 13910).

Consent Form

By signing this form, you indicate your consent to the following:

I have read, or have had read to me, and I understand the Participant Information Sheet.		
I have had enough time to think about whether or not to participate in this study.		
I have had a chance to use a legal representative, whanau/ family support, or a friend to help me ask questions and understand the study.		
I am happy with the answers I have been given regarding the study, and I have a copy of this consent form and information sheet.		
I understand that taking part in this study is voluntary (my choice) and that I may pull out from the study at any time without this affecting my medical care.		
I consent to the research staff collecting and processing my information, including information about my health.		
I understand the risks associated with the testing and intervention procedures, which are explained in the Participant Information Sheet.		
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.		
I know that I will be given vouchers (*a value of $200*) to cover travel expenses associated with study participation.		
I understand the compensation provisions in case of injury during the study.		
I know whom to contact if I have any questions about the study in general.		
I understand my responsibilities as a study participant.		
I agree with my GP or other current provider being informed of my participation in this study.		
I agree for the researchers to contact my GP or other current provider if needed to determine my eligibility for participation in the study, and to be notified if any incidental findings is recorded.		
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethics Committee, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.		
I understand that the data collected from me in this study may be used for other future medical and/or scientific research that is <u>unrelated</u> to the current study.	Yes ☐	No ☐
If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐
I wish to receive a summary of the results of the study.	Yes ☐	No ☐

Declaration by participant:

I hereby consent to take part in this study.

Participant's name:

Signature: Date:

Support person:

Please specify a contact person (a friend or a relative), in case of an emergency during the study participation. The contact details will be deleted from the file following completion of the study phases.

Name of a friend or relative:

Contact number:

Declaration by a member of the research team:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date:
