brighton and sussex medical school

PARTICIPANT INFORMATION SHEET

Study title: Transcutaneous Vagal Nerve Stimulation in misophonia: an intervention exploring underlying neurophysiological mechanisms

We would like to invite you to take part in a research study. Please take time to read the following information carefully and discuss it with others if you wish. Before you decide whether to take part, it is important for you to understand why the project is being done and what it will involve. Please email Dr Louisa Rinaldi (l.rinaldi@sussex.ac.uk) or Dr Giulia Poerio (g.l.poerio@sussex.ac.uk) if there is anything that is unclear, or if you would like more information. Take time to decide whether you wish to take part.

1. What is the purpose of the study?

Misophonia is a sound sensitivity disorder in which certain sounds (referred to as "triggers") generate unusually strong negative reactions. Trigger stimuli are often sounds generated by the human body (e.g. voices, chewing, and breathing), causing strong feelings of anxiety, anger, and disgust. Misophonia can have a profound negative impact on daily life across social, educational, and work contexts, making understanding, and treating misophonia important. In this study, we are testing a new potential treatment for misophonia called transcutaneous Vagal Nerve Stimulation (tVNS). tVNS is a safe and non-invasive method of stimulating the vagus nerve with a small hand-held device. The device sends gentle electrical pulses to regions of the ear for short periods (e.g. 30 minutes) over the course of several weeks. Because tVNS has been shown to improve symptoms in disorders such as migraine, tinnitus, epilepsy and depression, we are interested in exploring whether it might also help people with misophonia. We are also interested in understanding whether tVNS might change how people react to misophonic triggers. To explore this we will measure participants' brain and bodily responses to trigger sounds/sights before and after tVNS. As part of the study we will also be interested in different placement positions of tVNS in the ear, you will be randomly allocated to a group. If you end up in a group with less effective tVNS you will be given the opportunity to try the other location at the end of the study.

2. Why have I been invited to participate?

You have been invited to participate because you meet criteria for moderate to severe misophonia and have expressed interest in taking part in research studies on misophonia.

3. Do I have to take part?

No. It is up to you to decide whether you wish to join the study. We will describe the study in this information sheet and if you agree to take part, you'll need to complete a consent form. Even if you do decide to take part, you are still free to withdraw at any time and without giving a reason. If you would like your responses to be removed from the dataset, then please email the post-doctoral researcher Dr Rinaldi (L.Rinaldi@sussex.ac.uk). You are able to do this for up to two weeks after participating in the study.

4. What will happen to me if I take part?

First, we will check that it is safe for you to have an MRI brain scan and receive tVNS and that you meet the criteria to be included in this study. If you meet the criteria, then you will be contacted by a member of the research team who will schedule your first study visit.

Who can take part? Please note that you must fulfil the following criteria if you want to take part in this study: you must be:

- 18-40 years old

- Right-handed
- Native-English speaker
- Have moderate to severe misophonia
- Have no history of brain injury
- Have normal or corrected-to-normal vision
- Have normal hearing (except for hyperacusis, tinnitus, or misophonia)
- Have a smartphone (so you can download the tVNS application)

You cannot participate in the study if you:
- Do not fulfil the above criteria
- Are or could be pregnant
- Have active implants (e.g., cochlear or other metallic implant, implanted vagal nerve stimulator, cardiac pacemaker)
- Have a cerebral shunt (e.g., for the treatment of hydrocephalus)
- Have wounds or skin diseases at or near the ear
- Have a history or family history of heart problems (e.g., cardiac arrhythmias)
- Have a history of seizures
- Are receiving active treatment for misophonia or are planning to for the duration of the study
- Have any other contra-indications to an MRI scan

There is a risk factor involved if you:
- Have depression, there is a risk of temporary worsening of symptoms

☐ Please TICK to confirm you meet the criteria for this study. If you are unsure or have questions about your eligibility then please contact a member of the research team.

If you confirm that you meet the criteria for this study, then a member of the research team will contact you to arrange your first site visit. We'll then ask you to complete some online questionnaires at least 1-3 days before your first site visit. The questionnaires will ask you about your misophonia symptoms, general mental and physical health, and any potential hearing problems (such as tinnitus or hyperacusis). The questionnaire will take around 30 minutes.

Site Visit 1 (between 3 hours total – with breaks):
- During your first site visit we will begin at the MRI building and ensure that you understand what is involved in the study and ask you to complete a consent form
- The scanning process. Before going in the scanner you will be asked to read and sign the MRI safety document and the researcher will explain the scanning task to you. After this, a radiographer will go through the safety questionnaire with you and then ask you to remove all metal from your body. The radiographer may ask you to remove your make-up and it is possible that you will be asked to change into MRI compatible clothing (i.e, no metal), which you can bring with you or come wearing on the day. Then the radiographer will position you in the brain scanner. This will involve lying on your back on a narrow bed that will be moved into the MRI machine. The technician will provide padding for your head to make you more comfortable. You will be able to communicate with the technician during the MRI using a microphone and speaker in the MRI machine.
- The scanning session will take around 1 hour total – some of this will simply require you to lie in the scanner (~15 minutes). You'll then be asked to watch video clips (including misophonic triggers), imagine misophonic triggers and other sounds, and view striped patterns. You'll also be asked several questions about these tasks such as how difficult they were and how they made you feel. This part of the scanning session will last around 40 minutes.
- We'll then take a short walk over to the Brain and Body Unit in the Psychology building. Here you'll be given a break and will first be asked to answer some questionnaires before completing a short audiology session where we'll ask you some questions about which sounds you can hear.
- After another break you will then complete a sound task on a computer lasting 30 minutes. This is a computer task where you will have to respond to different sounds (including misophonic sounds) whilst we monitor your heart rate and skin conductance (i.e., how sweaty your fingers

get). Your bodily responses will be measured with sensors attached to fingers on your non-dominant hand and placed on your chest and hip. You will not have to disrobe, but will need to move clothing in order to place the sensors. You are welcome to bring a chaperone for this part, but they will be asked to wait outside for the rest of the study. These sensors will not be uncomfortable or cause you any harm but will simply measure several aspects of your bodily responses (such as your heart rate and your sweat response).

- Showing you how to use your tVNS device. Once you've had a break a researcher will show you how to use the tVNS machine and the associated smartphone app which will track your stimulation and send you reminders. You will set your stimulation parameters so that they are at a comfortable level for you, guided by the researcher. This will take around 30 minutes and we will also give you additional information about how to administer the tVNS to take home with you as well as some safety information about the use of the device. Administering tVNS at home (20 hours stimulation over 4 weeks)

Administering tVNS at home (20 hours stimulation over 4 weeks)

- The tVNS administration will involve you turning on the tVNS device and attaching the earpiece electrode to the correct location on your left ear. Once fitted correctly you will need to wear the earpiece for 30-minutes. You'll need to do this twice a day for at least 5 days per week for the next 4 weeks.
- At the end of every week, we will send you a questionnaire to monitor any potential side effects of the tVNS and check in on your progress. However, you are free to contact the researcher at any point during the study if you have questions about the device or are experiencing any adverse effects. You can also stop the stimulation at any time.
- At the end of the 4 weeks, we will send you a final online questionnaire which will ask about your misophonia symptoms, general mental and physical health, and any potential hearing problems (such as tinnitus or hyperacusis). We will also ask you some more general questions about how you found the tVNS treatment (e.g., how easy was it to use).

Site Visit 2 (between 2-3 hours total – with breaks):

- During your second site visit at the Brain and Body Research Unit you will return your tVNS device and take the MRI session, the audiology session and the computer-task session for the second time
- All the procedures will be exactly the same as your first study visit

Online Questionnaire (4 weeks after visit 2):

- After 4 weeks we'll send you a final questionnaire to complete at home
- We will fully debrief you about the study
- We'll also pay you after you've completed this questionnaire.

In total the study should take no more than 30 hours of your time for which you will be compensated £100. We are also able to compensate travel costs for site visits for those travelling from outside a 10-mile radius of the University of Sussex (up to £30 per person).

5. What are the possible benefits of taking part?

A possible benefit is that the study may help improve your misophonia symptoms, but this cannot be guaranteed. However, even if there is no direct benefit to you, your participation will help improve our knowledge about misophonia and potential treatments. We hope that in the future information gained from this study will benefit other people with misophonia.

6. Are there any possible disadvantages or risks of taking part?

Risks of tVNS. The device being used to deliver tVNS is a CE certified medical device that has undergone appropriate and rigorous checking to ensure its safe use. It is classified as a class IIa non-invasive, putting it into the same category as medical devices such as hearing aids and catheters and is similar to TENS machines (Transcutaneous Electrical Nerve Stimulation) that are commercially available to treat pain. There has been lots of research on the safety profile and effects of tVNS. The most common side effect (experienced by up to 18% of people) is skin irritation or discomfort at the site

of stimulation (the ear). This is often mild and resolves quickly. Other reported, but extremely rare, side effects (occurring in less than 1% of people) include nasopharyngitis (cold like symptoms), headache, dizziness, and nausea). As stated above if you have depression there is also a risk of a temporary worsening of symptoms. We will ask you to monitor any side effects during stimulation through a weekly questionnaire and will contact you at regular intervals to check that you are not experiencing adverse effects. We also ask you to contact us if you are experiencing any adverse effects which we will further investigate and may ask you to pause or stop the stimulation. You are also free to stop the stimulation at any time if you become concerned. Since the device being used is an electrical one, there are also several potential hazards (e.g., if the device malfunctions or overheats). We will provide you will a safety booklet as part of the study which informs you how to use it correctly and other things to ensure safety (e.g., not using the device when sleeping, keeping the device out of reach of children when not in use).

Risks of MRI Scan. MRI scanning has been used for over 20 years in medicine, and every year approximately 10 million people are scanned worldwide. There are no known side effects, and MRI causes no pain or damage. Taking part in this study will involve being in the MRI scanner for a long period of time (approximately 1 hour) which is a small space and can generate loud noises. Throughout the study you will be able to take short breaks at the end of each session; and the videos you will be watching have audio which will limit the amount of noise you hear from the scanner. Please note that the images that will be acquired are not for diagnostic purposes and the examination should not be considered an alternative to a proper medical consultation. Occasionally, something may be found in the images and an expert opinion sought. If there are any unexpected findings that need further tests, your GP will be contacted in the first instance. The GP will then contact you if further tests are required. If you have any concerns about this, please contact a member of staff.

Exposure to misophonic stimuli and potentially aversive patterns. During each of the site visits we will show you videos and ask you to listen to sound clips that include misophonic sounds (e.g., people eating) and negative sounds (e.g., a car alarm) as well as showing you striped patterns that may be uncomfortable to view. If you feel that viewing/listening to these sounds/patterns would cause you significant lasting distress beyond what you would experience in your everyday life then we would advise you not to participate. If you find yourself becoming too distressed at any point during the study where you are exposed to these sounds/patterns and would like them to stop you can tell the researcher who will stop them immediately. If you are concerned about your own emotional wellbeing or mental health, then here are some immediate sources of support to consider:

- Samaritans - 116 123 (lines are open 24hrs)
- SANEline - 0300 304 7000 (lines are open from 6pm-11pm)
- Shout crisis text line - text SHOUT to 85258 (open 24/7).

If you were to experience distress, then you may also consider speaking to your local healthcare provider.

7. What about confidentiality?

All the information about your participation in this study and all information collected during the course of the research will be kept strictly confidential, with the exception of rare circumstances in which the brain images reveal something that looks unusual. In these situations, we will consult an expert radiologist and may inform your GP. This means we might share your name, and details (e.g., Brain Images) with a radiologist and your GP. You, and your data, will be assigned a unique identifier that will be used to name the files. Outputs arising from the research (e.g., scientific publications) will not contain any personal data that would permit identification. Your name and contact details will be stored separately from your data in a password protected file on the University servers (OneDrive). Hard copies of your personal data will be stored in a locked filing cabinet in a locked office at the University and kept for up to five years and after this time will be destroyed. All data will be stored securely.

8. What will happen if I don't want to carry on with the study?

You are free to withdraw from the study at any time during the study and up to two weeks after finishing the study. You do not need to give a reason. You can withdraw by informing the researcher either in person or via email, indicating whether you would like your data to be removed too. You will be reimbursed for any time you have dedicated to the study up to the point of withdrawal.

9. **What should I do if I want to take part?**

   If you would like to take part, then please contact a member of the research team who will be in contact to arrange your study visit and re-check your eligibility. You will then be sent some online questionnaires (for which you will be asked to complete an initial consent form). We will ask again for your consent at the first onsite visit at the University of Sussex where you will be asked to sign a hard copy of the consent form.

10. **What will happen to the results of the research study?**
    The results of the study may be presented at research conferences or public meetings and used as pilot data for grant applications (to fund further research in this area). The findings will be written up and published in a scientific journal. If you wish, a summary of the findings can be sent to you when published. You can indicate this on the consent form with your preferred contact details to do so.

11. **Who is organising and funding the research?**
    This research is being funded by a grant from the Misophonia Research Fund (MRF) awarded by the REAM foundation.

12. **Who has approved this study?**
    The research has been approved by the Brighton and Sussex Medical School Research Governance and Ethics Committee (RGEC). The ethical review application number of this study is: ER/GLP28/4.

13. **What if there is a problem?**
    If you have any concerns about any aspect of this study or complaints about the way you have been treated during the study or possible harm you might suffer, you should ask to speak with the researchers who will do their best to answer your questions. The researchers' contact details are provided at the end of this sheet.

    If you experience any adverse events (a bad effect) during the tVNS stimulation period, please contact the research associate and stop administering stimulation. We will discuss whether you should continue with the study depending on your experiences.

    If you have any concerns about any aspect of this study or complaints about the way you have been treated during the study or possible harm you might suffer, you are able to contact the University of Sussex Research Governance Office (rgoffice@sussex.ac.uk). They are an independent complaints process who can help with any ethical concerns.

14. **Contact for further information?**
    If you have any queries about this project or your participation in it, please contact either of the principal researchers Dr Louisa Rinaldi: L.Rinaldi@sussex.ac.uk or Dr Giulia Poerio: g.l.poerio@sussex.ac.uk.

15. **Insurance**
    The Universities of Brighton and Sussex have insurance in place to cover their legal liabilities in respect of this study.

Thank you for taking the time to read this information sheet