Principal Investigator – Dr Nicola Baker (Clague-Baker)
Research Assistant: Karen Leslie
Contact: Nicola Clague-Baker
Tel: 07912950671
Email: Nicola.Baker@liverpool.ac.uk or
Karen Leslie: karen.leslie@liverpool.ac.uk

Study title: A Phase II feasibility trial of transcutaneous auricular vagus nerve stimulation for people with Myalgic Encephalomyelitis

INFORMATION LEAFLET

You are invited to take part in a research study. Before you decide whether or not to take part, we would like to explain why the study is being done and what it will involve. Please read the following information and ask us if anything is not clear, or if you would like more information, using one of the contact options listed above.

What is the purpose of this study?

The aim of this study is to conduct a pilot study to identify the acceptability, sample sizes, rates of recruitment and retention for a definitive study that will investigate the effect of transcutaneous auricular vagus nerve stimulation (taVNS) for People with Myalgic Encephalomyelitis (ME). People with ME are using taVNS but there are no studies that investigate the effect of this approach for people with ME.

Why have I been invited?

You have been invited because you have ME and have not tried taVNS before.

What will happen if I decide to take part?

Please read this information sheet that we have emailed to you. If you are interested in taking part please contact the Principal Investigator, Nicola Clague-Baker: nicola.baker@liverpool.ac.uk. We will then contact you to arrange a time to have a chat about the study and see if you fit the requirements of the study. If after this chat you would still like to be involved and you fit the criteria we will then arrange a date for the first day of the study.

On the day of the assessment (arranged to fit into your schedule and at your home), you will be asked to fill out the consent form and three questionnaires (which can be completed in your own time if it is too much on the day of the assessment). Your medical history and medications will also need to be recorded but you can send that through separately if it is too much to do it all in one session. You will then have a heart rate variability monitor fitted on your chest (see picture 1) and a mask fitted on your face attached to a portable metabolic chamber (see picture 2). These two devices monitor your heart and breathing during the following activities: lying for 5 mins and standing for up to 10 mins (depending on what you can cope with), up to 5 mins bathroom activities, going downstairs, up to 5 mins kitchen activities, going upstairs and up to 5 mins cognitive activities. You can rest as long as you need between each of these activities. Your blood pressure (BP) (see picture 3 - BP monitor), heart rate (HR) and oxygen levels (see picture 4 - pulse oximeter) will be taken before and after each activity. The activities tested depend on what you are able to do and we will choose them with you on the 1st visit. You will NOT be asked to do anything you don't normally do. You will NOT be asked to do any exercise.

The following week you will continue to wear the HRV monitor and instructions will be given about how to use it. You will also be given a diary to record your activities and any symptoms of post-exertional malaise (PEM) during the following five days. You will also wear an accelerometer on your wrist to record your activity levels (see picture 5). After five days of wearing the HRV monitor, accelerometer and recording your activity, the RA will return to pick up the HRV monitor, accelerometer and completed questionnaires.

Picture 1 – Heart rate variability monitor

Picture 2 - Portable metabolic chamber

Picture 3 - BP Monitor

Picture 4 - Pulse oximeter

Picture 5 - Accelerometer

On the second visit the RA will randomise you into either the control group who will receive a sham taVNS device or the intervention group who will receive a taVNS device that provides taVNS. Both devices look exactly the same so you will not know which group you are in (see picture 6). The devices fit onto the ear (see picture 7). The RA will show you how to use the device and you will have her contact details so you can ask any questions as you use the device over 3 months.

Picture 6 – tavns device

Picture 7 - fitting onto the ear

While you are using the device, you will be asked to fill out a form or an app to record how often you use it and for how long and any symptoms you have. You will also be asked to fill out a data collection form that will record your health service utilisation (GP/ Physio/ hospital), social support needed (unpaid) and participation in leisure activities for a month prior to starting the project and for a month at the end of the three months intervention phase. The PI will return after 3 months to repeat all the measures mentioned above to see if anything has changed. After a week of wearing the HRV, accelerometer and completing the followup questionnaires, the RA will return for a final time to collect the HRV monitor, accelerometer and questionnaires. If you were in the sham group she will show you how to use the taVNS as a real device to try taVNS if you want to. You can keep the taVNS devices if you want to at the end of the study.

Follow up online interviews will be carried out by the PI or RA over zoom or ms teams within a month of the end of the intervention and then an additional interview 6 months later.

If you want to withdraw your data from the study you will need to inform the PI by end of September 2025 at this point all data will be fully anonymised and entered into data analysis.

Summary of involvement

Initial visit	Research assistant takes initial measurements: - Portable metabolic unit (wearing a mask to take measurements of oxygen consumption during a few basic tasks) - Standing test (standing for up to 10 minutes)	Participant will be left with 4 questionnaires to complete. Participant will be fitted with a “heart rate variability monitor” (a small device sticking to the chest) and a “physical activity monitor” (a wrist strap). They will be asked to keep these on until the next visit.
Second visit approx. 5 days later	Research assistant takes back the heart monitor, physical activity	Participant left with vagus stimulation device.

	monitor, and checks all questionnaires completed. Research assistant then sets participant up with the vagus stimulation device and leaves them with instruction guide.	Asked to note how often they use it each day.
First post-intervention visit, after 3 months	The principal investigator will visit and repeat the measures from the first day of testing.	The heart rate variability monitor, physical activity monitor and 4 questionnaires will be left with the participant.
Second post-intervention visit, approx. 5 days later	The research assistant will return to collect the heart monitor, physical activity monitor and questionnaires. At this point they will reveal whether the vagus stimulation device was a placebo or not. If it was a placebo, the research assistant will activate it as a real device, and show the participant how to use this.	
Within a month of completing the trial	An online interview will be carried out to find out the participant's views on the intervention and the trial.	
Six months after completing the trial	An online interview will be carried out to follow-up on whether the participant has continued with the intervention, and any further comments on the trial.	

Do I have to take part?

Only if you want to.

Participation is voluntary, you may refuse to participate. You do not need to tell us why you do not want to take part. If you choose not to participate, your decision will in no way affect your future healthcare.

What are the possible disadvantages and risks of taking part?

During the assessment you will only be asked to complete activities that you do as part of everyday life. You will not be asked to exercise. We will ensure the appropriate medical cleaning procedures are used for all the equipment you will be using. Due to the lessons learnt from Covid19 we will also ensure that all researchers wear a mask while visiting you as required by the Department of Health and the Chartered Society of Physiotherapy.

Carrying out the 10 min stand test for people with orthostatic intolerance (OI) can cause dizziness and there is a risk of falls. Therefore, this test will be carried out by a qualified physiotherapist who has conducted this test with many people with OI and has been qualified for over 15 years. If you have any difficulties with this test she will stop the test and monitor you until normal values are achieved. Any meaningful results could be shared with your GP with your consent.

Following two international surveys, the research team recorded the following difficulties with taVNS: skin irritation at the site of stimulation (35.3%), headache (14.7%), insomnia (8.6%) and fatigue (8.6%) (Leslie et al., 2024). In terms of aggravating ME symptoms, 7 respondents (6%) reported they felt that using taVNS made them worse. One person reported it caused a crash. If you have any difficulties with taVNS then you can take the device off straight away and contact the researchers.

It is possible when we are discussing the study in the online interviews that you might not want to discuss all aspects of your personal experience and that is fine. If you experience any distress with this discussion we can guide you to support services that might be able to help you. In addition, we can provide a letter to your GP to help you explain your difficulties.

Are there any benefits of taking part in this study?

Following two international surveys, the research team recorded the following benefits of taVNS: improvements in: PEM, pain, gut problems, urinary problems and mental health issues. There were also significant improvements in the ability to leave the house. 56% reported beneficial effects of taVNS, with 16% reporting very beneficial effects. 67% said they would recommend it and 4% said they would not recommend it.

For people with ME, taking part will identify if you have abnormal physiological responses to activities and also you will be able to try taVNS for free. We will make every effort to prevent any adverse effects by screening and making sure we monitor your use of taVNS very closely. For everyone with ME, this is important information that we need to identify to help understand the effects of taVNS for people with ME. You will be helping people with ME in the future and help clinicians learn if there is a way to help people with ME. Finally, you will be given £100 for your involvement in the trial.

Are there any costs involved?

No

Withdrawal options and your rights

Your participation in this study is entirely voluntary and refusal will not affect any health care. You are free to withdraw without giving a reason, without your medical care and legal rights being affected. If you want to withdraw your data from the study you will need to inform the PI by end of September 2025 at this point all data will be fully anonymised and entered into data analysis.

Data protection & confidentiality

The study complies with Government & the University of Liverpool's data protection policy as well as the University's research ethics requirements. Information to identify you are: your gender and age. All information provided will be kept strictly confidential. The information from the study will be kept in a password-protected university computer that only the research team will have access to.

By the end of September 2025 all data will be fully anonymised and stored in the university secure databases. This anonymised data will be available for future use by researcher's conducting similar studies. The data from this study will be retained for ten years. Information will be kept on the University of Liverpool secure databases and will not be stored on the cloud.

The University processes personal data as part of its research and teaching activities in accordance with the lawful basis of 'public task', and in accordance with the University's purpose of "advancing education, learning and research for the public benefit. Under UK data protection legislation, the University acts as the Data Controller for personal data collected as part of the University's research. The Principal Investigator/Supervisor acts as the Data Processor for this study, and any queries relating to the handling of your personal data can be sent to Dr Nicola Clague-Baker – nicola.baker@liverpool.ac.uk.

How will my data be collected?	On the first day of assessment, 3 months follow-up and 2 interviews one at 3 months and one at 6 months after that.
How will my data be stored?	All the anonymised electronic data will be stored on the secure university databases and the anonymised paper forms will be securely stored in the physiotherapy department in locked filing cabinets and then archived after a year.
How long will my data be stored for?	Your anonymised data will be stored for 10 years
What measures are in place to protect the security and confidentiality of my data?	All anonymised paper forms will be securely stored in a locked filing cabinet in a locked room only accessed by the PI and the research team. The anonymised digital data will be securely stored on the university password protected databases only accessed by the research team.
Will my data be anonymised?	Yes once you have consented onto the study you will be assigned a number and all forms will then be given a number rather than your name.
How will my data be used?	Your anonymised data will be used to produce results for funding applications for larger studies and for journal articles and conference presentations. It will be stored securely for 10 years. The anonymised data will also be available for future use by researchers conducting similar studies.
Who will have access to my data?	The PI and research team will have access to your anonymised data. By the end of

	September 2025 all data will be fully anonymised and stored in the university secure databases. This anonymised data will be available for future use by researchers conducting similar studies.
Will my data be archived for use in other research projects in the future?	Yes the anonymised data will be available for future use by researchers conducting similar studies.
How will my data be destroyed?	The data will be erased from the University databases with the assistance of the IT department. After 10 years the data will be deleted from the university databases with the assistance of the University's confidential waste disposal service. This data management plan was developed to ensure that data of this research is managed and shared in a robust and professional manner. The plan was formulated with adherence to University of Liverpool Research Data Management, the United Kingdom Research and Innovation Data Policy

What if things go wrong? Who to complain to.

If you have a concern about any aspect of this study, you should ask to speak with the researchers, who will do their best to answer your questions, or contact the Principal Investigator, Dr Nicola Clague-Baker (Nicola.Baker@liverpool.ac.uk), Tel. 07912950671. If you are not satisfied with the response you receive from the investigator, then there is a formal university complaints procedure. This involves contacting the Research Ethics and Integrity Office at ethics@liv.ac.uk. When contacting the Research Ethics and Integrity Office, please provide details of the name or description of the study (so that it can be identified), the researcher(s) involved, and the details of the complaint you wish to make.

The University strives to maintain the highest standards of rigour in the processing of your data. However, if you have any concerns about the way in which the University processes your personal data, it is important that you are aware of your right to lodge a complaint with the Information Commissioner's Office by calling 0303 123 1113.

What will happen with the results of the study?

The results will be analysed and discussed by the research group. The results of the study may also be presented in research reports, scientific conferences and/or journals and be made available to people with ME via the PhysiosforME website. The results may act as baseline information that guides future research by other investigators.

Who has reviewed this study?

All research involving human subjects must receive approval from the University of Liverpool Ethics Committee before it can go ahead. Approval does not guarantee that you will not come to any harm if you take part. However, approval means that the committee is satisfied that your rights will be respected, that the study carries no more than minimal risk, and that you have been given sufficient information on which to make an informed decision.

Who is organising and funding the research?

This study is being conducted by a team of experts at the University of Liverpool, University of Manchester, University of Exeter, Monash University and Physios for ME. The Chartered Society of Physiotherapy and the ME Association are funding the study.

Further information/Key contact details

Principal Investigator: Dr Nicola Clague-Baker - Nicola.Baker@liverpool.ac.uk

Research Assistant: Karen Leslie – Karen.Leslie@liverpool.ac.uk

Thank you.