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A trial of stimulating the vagus nerve at the ear for people with myalgic encephalomyelitis /chronic fatigue syndrome (ME/CFS)

Submission date
15/08/2024

Recruitment status
No longer recruiting

Registration date
20/08/2024

Overall study status
Ongoing

Last Edited
14/03/2025

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Myalgic Encephalomyelitis (ME), often called Chronic Fatigue Syndrome, is a condition that causes extreme tiredness that doesn't get better with rest, along with other symptoms like muscle pain, headaches, and problems with concentration. It can significantly impact daily life, but the exact cause is not fully understood. ME affects over 250,000 people in the UK. The main feature is post-exertional malaise (PEM) – a worsening of symptoms after seemingly trivial activity. These symptoms are particularly associated with the autonomic nervous system (ANS). The ANS regulates involuntary physiological processes (such as heart rate and digestion).

Some people with ME (PwME) use Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) to manage their symptoms. TaVNS involves stimulating the Vagus nerve which is one of the main parts of the ANS. The stimulation occurs via electrodes applied to the ear. This is the area of skin connected to the vagus nerve. The electrodes produce a gentle tingling/pins and needles sensation which stimulates the nerve and in turn the ANS. To date, there have been only two small studies of taVNS in PwME and neither measured the effect on the ANS.

Aim: To undertake a feasibility trial of taVNS to see if a larger trial to test whether taVNS works for PwME is possible and how to conduct it.

Who can participate?
40 PwME will be recruited from ME support groups and online ME forums_

What does the study involve?
After informed consent, participants will be randomly divided to either receive taVNS or treatment with a sham taVNS device. They will be assessed before and after 3 months treatment. We will mainly test whether a full trial can be conducted by assessing recruitment and drop-out rates; the safety (any side effects of taVNS treatment), what participants think of the treatment and taking part in the trial (via interviews after treatment is complete), and whether the things we measure (outcomes) produce good quality data.

What are the possible benefits and risks of participating?
Benefits:
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

Risks:
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.

Where is the study run from?
University of Liverpool (UK)

When is the study starting and how long is it expected to run for?
June 2024 to March 2026

Who is funding the study?
University of Liverpool (UK)

Who is the main contact?
Dr Nicola Baker, nicola.baker@liverpool.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
UoL001879

Study information

Scientific Title
A phase II feasibility trial of transcutaneous auricular vagus nerve stimulation for people with myalgic encephalomyelitis

Study objectives
Aim: To conduct a feasibility trial of taVNS in PwME.
Objectives:
1. Establish the acceptability, adherence, recruitment & retention rates, sample size and outcome measures for a larger study.
2. Understand PwME's experience of using taVNS and participating in the trial.
3. Evaluate the safety of taVNS by monitoring adverse events.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 31/07/2024, University of Liverpool - Central ethics committee (University of Liverpool, Liverpool, L69 3BX, United Kingdom; +44 151 794 8290; ethics@liverpool.ac.uk), ref: 14301

Study design
Phase II interventional randomized controlled feasibility trial

Primary study design
Interventional

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Myalgic Encephalomyelitis (ME)

Interventions
People with ME will be recruited from ME support groups and online ME forums. After informed consent, participants will be randomly divided to either receive transcutaneous auricular vagus nerve stimulation (taVNS) or treatment with a sham taVNS device. They will be assessed before and after 3 months treatment. We will mainly test whether a full trial can be conducted by assessing recruitment and drop-out rates; the safety (any side effects of taVNS treatment), what participants think of the treatment and taking part in the trial (via interviews after treatment is complete), and whether the things we measure (outcomes) produce good quality data. These include measures of ANS function, PEM, fatigue and activity levels.

Intervention Type
Device

Phase
Phase II

Drug/device/biological/vaccine name(s)
Nurosym

Primary outcome(s)
Feasibility outcomes:
1. Acceptability (followup interviews at 3 months after baseline and 6 months later)
2. Recruitability (recruitment rate measured at screening and initial assessment)
3. Suitability of outcome measures (completion of outcome measures at baseline and 3 months after baseline plus discussion at interview)
4. Calculation of sample size (based on outcomes of primary OM - heart rate variability measured with firstbeat devices at baseline and 3 months later) for a definitive study

Key secondary outcome(s))
Measured at baseline and 3 months later:
1. Accelerometer (Axivity AX3) - measures activity levels over 5 days
2. Portable metabolic measures (cortex) - Vo2, Vco2, RER
3. 10 min stand test measuring BP, Heart rate and pulse oximetry
4. Funcap questionnaire - measures functional activity
5. EQ5D questionnaire - measures QOL, COMPASS questionnaire measures autonomic nervous

system
6. Health utilisation questionnaire specifically designed for this study

Completion date
01/03/2026

Eligibility

Key inclusion criteria
1. Adults with ME (as defined by the International Consensus Primer criteria for ME)
2. Mild to severe ME
3. Live in the Liverpool and Manchester region. The geographical restriction is to make the logistics and costs of visiting participants in their own home feasible

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
40

Key exclusion criteria
1. Previous or ongoing use of taVNS (as this study is evaluating first-time use of taVNS)
2. Inability to stand (as this is part of the assessment procedure)
3. Contraindications to Tavns

Date of first enrolment
01/09/2024

Date of final enrolment
20/02/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Liverpool
Physiotherapy department
Liverpool
United Kingdom
L69 3BX

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
University/education

Funder Name
University of Liverpool

Alternative Name(s)
The University of Liverpool, , Universidad de Liverpool, UoL

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available later

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2	26/07/2024	16/08/2024	No	Yes