ISRCTN11391023 https://doi.org/10.1186/ISRCTN11391023

A new diagnostic for vestibular balance dysfunction

Submission date 25/09/2024	**Recruitment status** Recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 16/12/2024	**Overall study status** Ongoing	
Last Edited 16/12/2024	**Condition category** Ear, Nose and Throat	

Plain English summary of protocol

Background and study aims
The vestibular system is the part of the inner ear used to maintain balance. When it goes wrong this can lead to dizziness, loss of balance and blurred vision. It is therefore important to be able to test vestibular function accurately. The purpose of this research is to develop a faster, better vestibular test called electrical vestibular stimulation (EVS). EVS involves a very small electrical stimulus delivered behind the ears. This causes an eye movement which we record with a camera. This study will compare the accuracy of EVS with three other existing diagnostic tests: caloric irrigation, vestibular-evoked myogenic potentials (VEMPs) and the video head impulse test (vHIT).

Who can participate?
Patients aged 18 years and over diagnosed with unilateral vestibular schwannoma (VS), Ménière' s disease, and patients attending ENT clinic with suspected but undiagnosed peripheral vestibular disorders. Healthy control volunteers over 18 years old will also participate in the study as controls.

What does the study involve?
The study will involve a single visit to the School of Sport, Exercise & Rehabilitation Sciences, University of Birmingham. It will last about 3 ½ hours (including breaks) during which the participant will experience the following tests of vestibular function, all of which are non-invasive.
1. Electrical Vestibular Stimulation (EVS)
EVS is a safe and painless method of testing inner ear function. Two electrodes will be placed on the skin immediately behind your ears. A very small current (up to ~5 mA and 30 s duration) is then passed between the electrodes to produce eye movements. You may feel this current on your skin as a tingling sensation, but it should not be painful. All volunteers will be given an initial test of the stimulus before being asked if they are happy to continue. We record the eye movement in darkness using an infrared camera. This test lasts about 30 minutes.
2. Caloric Irrigation
Caloric irrigation is an established test of inner ear function which you may have experienced previously in clinic. It involves either cool (30O oC) or warm (44O oC) water being poured into the external ear canal while you lie on a couch. Calorics evoke a spinning sensation and an eye

movement which we will record by camera. This test lasts about 40 minutes.
3. Video Head Impulse Testing (vHIT)
vHIT involves very small rotations of the head. The experimenter will hold your head with their hands on either side and produce small fast rotations of the head. The resulting eye movement will be measured using small lightweight goggles with cameras. This test lasts 5-10 minutes.
4. Vestibular-Evoked Myogenic Potentials (VEMPs)
VEMPs are a technique for assessing the function of the otolith organs (a part of the vestibular system). Small recording electrodes are placed on the skin over the neck muscles or around the eyes. Very brief tones are then delivered through headphones or bone-conducted vibrations. This test lasts about 45 minutes.

What are the possible benefits and risks of participating?
There is unlikely to be any direct benefit for the participants. The main purpose of the project is to help with the diagnosis of future patients once EVS has been fully validated.
Caloric irrigation, VEMPs and vHIT are regularly used in hospital clinics. Caloric irrigation can exacerbate any pre-existing outer ear problems such as a perforated eardrum. To avoid such issues, we will carefully examine the outer ear using an otoscope. Caloric irrigation can cause a spinning sensation, and this is occasionally accompanied by feelings of dizziness or nausea. However, this usually subsides within a minute or two of stopping the test.
Since calorics can induce a strong spinning sensation, exclusion criteria will include uncontrolled heart disease or mental illness. vHIT involves small manual rotations of the head. Anyone with neck pain/damage will be excluded from vHIT. VEMPs involve bone/air-conducted sound while recording muscle activity and carry no specific risks
EVS itself is a safe technique which has been applied to humans for many years for research. We use a CE-marked stimulator approved for use on human participants. EVS can sometimes cause discomfort at the site of the stimulating electrode behind the ear. However, this is usually alleviated by repositioning the electrode. All participants will be given a test stimulus at the beginning of the session to check that they are happy to continue.
Since these interventions all carry low risk, it is unlikely that any patient will experience any lasting ill effects (other than their existing illness).

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

When is the study starting and how long is it expected to run for?
January 2023 to September 2027

Who is funding the study?
Medical Research Council (UK), Development Pathway Funding Scheme (MRC DPFS), grant reference MR/X013944/1

Who is the main contact?
Dr Raymond Reynolds, r.f.reynolds@bham.ac.uk

Contact information

Type(s)

Contact name
Dr Raymond Reynolds

ORCID ID
https://orcid.org/0000-0002-5031-3473

Contact details
School of Sport, Exercise and Rehabilitation Sciences
University of Birmingham
Edgbaston
United Kingdom
B15 2TT
+44 (0)121 414 4107
r.f.reynolds@bham.ac.uk

Type(s)
Scientific

Contact name
Mr Richard Irving

ORCID ID
https://orcid.org/0000-0003-0013-719X

Contact details
ENT Department
Queen Elizabeth Hospital Birmingham
University Hospital Birmingham NHS Foundation Trust
Mendelsohn Way
Birmingham
United Kingdom
B15 2PR
+44 (0)121 371 4928
Richard.Irving@uhb.nhs.uk

Additional identifiers

Integrated Research Application System (IRAS)
331453

Central Portfolio Management System (CPMS)
58768

Protocol serial number
MR/X013944/1

Study information

Scientific Title
Electrical vestibular stimulation as a diagnostic for vestibular dysfunction

Study objectives

The study hypothesis is that the new test is as effective as the leading alternative vestibular diagnostic tests (caloric irrigation, vHIT and VEMPS) in patients with a known unilateral peripheral deficit while being more convenient and patient-friendly.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 07/11/2023, London - City & East Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 1048171; cityandeast.rec@hra.nhs.uk), ref: 23/PR/0886

Primary study design
Interventional

Study design
Non-randomized study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Vestibular dysfunction

Interventions
Each volunteer will attend the laboratory of the School of Sport, Exercise & Rehabilitation Sciences at The University of Birmingham. During each visit the researchers will perform the following diagnostic vestibular tests:

Electrical Vestibular Stimulation
EVS is a safe and painless method of testing inner ear function. Two electrodes will be placed on the skin immediately behind your ears. A very small current (up to ~5mA and 30s duration) is then passed between the electrodes to produce eye movements. You may feel this current on your skin as a tingling sensation, but it should not be painful. All volunteers will be given an initial test of the stimulus before being asked if they are happy to continue. The researchers record the eye movement in darkness using an infrared camera. This test lasts approximately 30 minutes.

Caloric Vestibular Stimulation
Caloric stimulation is a very commonly used standard clinical test of vestibular function. Supine participants will undergo cold (~30 oC) and warm (~44 oC) water irrigation of the external ear canal. The researchers will conduct the procedure in accordance with the guidelines of the British Society of Audiology, complying with their exclusion criteria (uncontrolled hypertension, unstable angina, myocardial infarction within 6 months, psychotic/neurotic disorders, and eye or ear surgery within 6 months). Irrigation is achieved using a commercially available device approved for human clinical use. Eye movements evoked by caloric irrigation will be recorded by camera. A total of 20 trials will be performed, which will take ~40 minutes.

Video Head Impulse Testing
vHIT will be performed using commercially available diagnostic equipment supplied by

Interacoustics (EyeSeeCam). Unlike caloric irrigation, which assesses the very low frequency canal response of the horizontal canal, vHIT assesses the high-frequency response of all canals. The test involves very small manually imposed head in the plane of the semicircular canal being tested. The resulting eye movement is recorded by lightweight goggles. The test takes approximately 10 minutes.

Vestibular-Evoked Myogenic Potentials (VEMPs)
VEMPs assess the function of the otolith system, part of the vestibular system. Small recording electrodes are placed on the skin over the neck muscles or around the eyes. Very brief tones are then delivered through headphones or bone-conducted vibrations. This test lasts approximately 45 minutes.

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
Asymmetry in vestibular function determined using EVS and the other vestibular tests at a single timepoint

Key secondary outcome(s)
The diagnostic utility of EVS in a group of patients with suspected vestibular deficit prior to definitive diagnosis, determined by comparing EVS symmetrical vestibular measurements against caloric irrigation, vHIT and VEMPS values obtained at a single visit. These patients will then be followed to determine their diagnosis for a minimum of 3 years.

Completion date
30/09/2027

Eligibility

Key inclusion criteria
1. Confirmed unilateral vestibular schwannoma
2. Confirmed unilateral Meniere’s disease
3. Suspected peripheral vestibular dysfunction (patients attending ENT clinic pre-diagnosis)
4. Understand verbal and written English
5. At least 18 years old

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit

18 Years

Sex
All

Key exclusion criteria
1. Other afflictions which may affect the control of balance and vestibular function e.g. neurological conditions such as stroke, Parkinson's disease, cerebellar ataxia, dementia.
2. Electronic implants (including cochlear implants, pacemakers and bone-anchored hearing aids)
3. Uncontrolled heart disease or uncontrolled mental illness
4. Any patient with eardrum perforation or other damage/infection of the outer ear will be excluded from caloric irrigation
5. Any patient with severe tinnitus will be excluded from air-conducted VEMPs
6. Any patients with neck pain will be excluded from vHIT

Date of first enrolment
20/03/2024

Date of final enrolment
30/04/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Birmingham
School of Sport, Exercise and Rehabilitation Science
Edgbaston
United Kingdom
B15 2TT

Study participating centre
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2WB

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository. Both raw and analysed data will be stored in the University of Birmingham BEAR Research Data Storage system. This data will comprise fully anonymised eye movement kinematics from the various diagnostic tests, along with calculated parameters such as vestibular asymmetry. Anonymised data will be shared at a later date on publicly available databases when the data is submitted for publication towards the end of the project period subject to any IP constraints.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Participant information sheet	Healthy controls version 2.0	26/03/2024	02/12/2024	No	Yes
Participant information sheet	Patients version 2.0	26/03/2024	02/12/2024	No	Yes