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Transcutaneous vagal nerve stimulation for episodic aggression

Submission date
06/04/2016

Recruitment status
No longer recruiting

Registration date
26/07/2016

Overall study status
Completed

Last Edited
19/11/2018

Condition category
Injury, Occupational Diseases, Poisoning

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Some people with disabilities caused by damage or changes to the brain can get frustrated, annoyed or overwhelmed more easily. Sometimes this can be hard to control and can change behaviour. For example, it could lead to shouting, swearing or maybe even throwing or hitting something. Afterwards the person can feel bad, and so can other people who were there when it happened. This is a big problem and there are not many things that can be done to help people learn to control or reduce these behaviours. We have an idea that a particular nerve that connects the heart and the brain might be important in how these behaviours may be triggered. We think that a gadget that is currently being used to help some people with epilepsy control their seizures might also help some people who have certain kinds of problems in brain development or injury who also have with repeated episodes of aggressive behaviour, to reduce these episodes. The gadget is like an earphone and gives a very small electrical pulse to stimulate a nerve in the ear – all you'd notice is a slight tingle at the site of the electrode in the ear. We are doing a study to find out if this gadget can help people who struggle to manage their behaviour.

Who can participate?
Adults aged 18-55 with intellectual disabilities, acquired brain injury, or autism who also have repeated aggressive outbursts

What does the study involve?
Participants are asked to wear a gadget that measures their heart rate and to wear a gadget that gives a small electrical pulse, either switched on or off, for up to four months. Information is gathered from the participants' family or care-givers about how often problems with behaviour occur. At the end of the study we look at the information collected to see if there were fewer problems on the days when the gadget was switched on.

What are the possible benefits and risks of participating?
If it looks like it might be helpful, the results of the study will be used to develop a bigger study to test the gadget in a bigger group of people, and to understand more about how it works. Being in the study will mean that participants are carefully assessed by people experienced in understanding and treating behavioural symptoms associated with developmental or acquired

brain injury. This could help suggest approaches to reducing some of these symptoms. It is also possible that the stimulator could reduce some of these behavioural symptoms. Vagus nerve stimulation has been shown to be safe when used for treating epilepsy. Those wearing the stimulator will notice a tingling sensation in their left ear, where the stimulator is worn. This tingling may be mildly uncomfortable but it is not dangerous and if need be the intensity of the stimulation can be turned down. Monitoring of heart rate will be undertaken for 24 hour periods on up to 21 occasions by asking participants to wear a small heart monitor consisting of three sticky pads on the chest. These are not associated with any discomfort. Participants will have the opportunity to try one and to become used to wearing it. They will usually be fitted at home and support workers or family members will be trained to help refit them after washing or if they become dislodged.
People do not always like talking about episodes of aggressive behaviour and their mood but the conversations will be with trained researchers and we do not think there will be any risks associated with these questions.

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

When is the study starting and how long is it expected to run for?
June 2016 to May 2017

Who is funding the study?
National Institute for Health Research CLAHRC for the East of England (UK)

Who is the main contact?
Dr Howard Ring

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

1.1

Study information

Scientific Title
Transcutaneous vagal nerve stimulation for episodic aggression: a feasibility and pilot study

Study objectives
The use of transcutaneous (external) vagal nerve stimulation (tVNS) is acceptable to, and feasible in, adults with intellectual disabilities, acquired brain injury, or autism who also have repeated aggressive outbursts.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Single-case multiple-baseline single-centre trial

Primary study design
Interventional

Secondary study design
Single-case multiple-baseline trial

Study setting(s)
Community

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Developmental and acquired brain injury

Interventions
Participants will undergo four research phases lasting two - five weeks. During each phase a diary of aggressive episodes will be kept, a small heart rate monitor worn on the chest for 1-3 days, and some problem solving and emotion-recognition tests performed. The first and fourth phases will be for initial and final baseline recording. In the second (control) phase participants will wear the tVNS device for four 1-hour periods per day with the device mostly switched off. In the third (active) phase the tVNS device kept on for four 1-hour periods per day.

Intervention Type
Procedure/Surgery

Primary outcome measure
The feasibility of delivering the intervention, which will be determined as follows:
1. The number of hours for which the tVNS device was used as a proportion of the total number of hours required in the study protocol, for each participant – for the 2 weeks of sham stimulation and five weeks of active stimulation.
2. The number of daily behavioural diary entries recorded as a proportion of the total number of diary entries required in the study protocol, for each participant – for the five weeks of baseline-1, the two weeks of sham stimulation, the five weeks of active stimulation and the four weeks of baseline-2.

Secondary outcome measures
1. Heart rate variability (HRV) will be measured over three 24 hour periods during each of the second and fourth weeks of baseline-1, active and baseline-2 phases and during the second week of the sham stimulation phase. On each of these occasions it will be measured over a 15-minute rest period at the start of the 24 hour recording and as an average over the whole of the 24-hour period. It will be quantified as the ratio of low frequency to high frequency HRV components over these periods.
2. The number of aggressive episodes will be counted from the behavioural diaries completed every day through the study. Specific aspects of their presentation will be rated using The Challenging Behaviour Interview (Oliver et al. 2003), The Behaviour Problems Inventory (Rojahn et al. 2001) and the Aberrant Behaviour Checklist (Aman et al. 1985) collected in baseline-1 week 1, sham week 2, active phase week 5 and baseline-2 week 4.
3. Changes in emotional state will be assessed using the Hospital Anxiety and Depression scale, the self-report State-Trait Anger Expression Inventory-2 (STAXI-2). Emotional state will be measured in baseline-1 week 1, baseline-1 week 5, sham week 2, active week 5, baseline-2 week 4.
4. Changes in psychological (executive function and hostility bias) state will be assessed as follows:
4.1. The Dysexecutive Questionnaire (DEX; Burgess et al 1998): self-report version
4.2. Working memory capacity: Digit Span (Forwards and Backwards) from the WAIS-IV
4.3. Concept formation and switching: Wisconsin Card Sort Test (WCST) (Weigl card sort test)
4.4. Working memory control: Letter number sequencing from the WAIS-IV
4.5. Digit Span (Backwards) from the WAIS-IV
4.6. Inhibition and switching: Colour-word interference test (Stroop) from the D-KEFS ('Cat-dog' Stroop test)
4.7. Potential hostility bias: the Facial Expression of Emotion Stimuli and Tests (FEEST) to examine responses (recognition and latency) to neutral and emotional faces
Psychological state will be measured at baseline-1 week 1 and active phase week 5.

Overall study start date
01/06/2016

Completion date
31/05/2017

Eligibility

Key inclusion criteria
1. A diagnosis of an intellectual disability, autism or acquired brain injury
2. Male and female participants aged 18-55 years

3. Capacity to consent to participation in the study
4. Manifestation of at least one episode of verbal or physical aggression per week, when averaged over the preceding four weeks
5. Agreement from participants' family and/or paid carers to support the trial

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
12

Key exclusion criteria
1. The presence of a diagnosis of an affective or psychotic condition considered to underpin the aggressive episodes
2. The presence of current drug or alcohol dependence
3. A current diagnosis of epilepsy
4. Significant physical comorbidity that could interact with trial participation (for instance ongoing cardiac arrhythmias, active implants such as a cardiac pacemaker or a cochlear implant, wounds and diseased skin in the area of the tVNS electrodes)
5. Current or recent (previous 12 months) participation in a clinical trial of an investigational medicinal product (CTIMP) or medical device.
6. Pregnancy

Date of first enrolment
14/07/2016

Date of final enrolment
31/12/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

University of Cambridge
Trinity Lane
Cambridge
United Kingdom
CB2 8AH

Sponsor information

Organisation
Cambridge and Peterborough NHS Foundation Trust (UK)

Sponsor details
R&D Department
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/040ch0e11

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research CLAHRC for the East of England (UK)

Results and Publications

Publication and dissemination plan
Planned submission an account of the research together with the findings to a peer-reviewed scientific journal once the study is finished and analysed.

Intention to publish date

31/05/2018

Individual participant data (IPD) sharing plan

This study uses a single case design with a planned recruitment of just 12 individuals. There are plans to make available on request the numerical data from heart rate and cognitive measures but will not include any data that could lead to identification of the participants.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2018		Yes	No