ISRCTN14435750 https://doi.org/10.1186/ISRCTN14435750

Study of hallucinations in Parkinson's disease, eye disease and dementia- trial feasibility

Submission date
22/01/2018

Recruitment status
No longer recruiting

Registration date
30/01/2018

Overall study status
Completed

Last Edited
20/03/2019

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
An estimated 2 million people in the UK see things that are not actually there- termed visual hallucinations. The number of people affected will rise as the population ages. The hallucinations occur most often in people with Eye disease, Parkinson's disease or Dementia, and can cause significant distress to affected individuals. They also have implications for the NHS, for example triggering hospital admission or the move to a care setting from independent living. Yet despite a clear need for help, to date, there have been no clinical studies on the best way to treat visual hallucinations. The aim of this study is to collect patients' views on treatment and other information to help design future treatment trials.

Who can participate?
Adults aged 60 that have diagnosed dementia, idiopathic Parkinson's disease, or eye disease (such as age-related macular degeneration) that have experienced visual hallucinations in the last 2 weeks before study entry.

What does the study involve?
Taking part in the study involves completing questionnaires and assessments approximately every two weeks and telephone contact in between these times to check on your progress. The assessments take place at a time and place that is convenient for participants, such as their home. This study involves two stages. Stage 1 does not involve any medication and compares two non-medication strategies that other people have found helpful for the treatment of visual hallucinations. Stage 2 is entirely optional and involves comparing the effects of two medications. Participants are given one medication based on your currently prescribed medication. Stage 2 entry involves taking a blood sample and testing your heart (ECG), to make sure it is safe for you to take the medication. Stage 2 also involves 2 electroencephalography (EEG) exams to measure brain activity. EEG uses a set of electrodes placed on your scalp in an elasticated cap. To ensure good electrical conduction researchers lightly scrub the scalp under the electrode and place a small amount of gel between the electrode and the scalp. This is a simple non-invasive procedure and usually takes around 30 minutes to carry out. The visits in Stage 2 take place at the lead research centre. The study lasts approximately 6 weeks, if you only take part in Stage 1. If you enter Stage 2, the entire study period lasts approximately 8 weeks.

What are the possible benefits and risks of participating?
There are guarantee of any direct benefit to participants. However, participants may find that their hallucinations are reduced in terms of frequency and duration. The information that researchers get from this study will help to understand how to design future studies to investigate new treatments for visual hallucinations. As such, the main benefit of taking part is the contribution to help develop better treatments for visual hallucinations in future. Some people may find it distressing to talk about visual hallucinations. Some people do not want others to find out they have hallucinations. Researchers make sure participants have the opportunity to talk to us alone when we ask about these experiences. Visits may be quite long for some people there will be breaks as needed to minimise any tiredness. There is also a possibility that researchers find out that participants may have medical problems they do not know about, such as early problems with your vision or memory. If so, one of the doctors on the study discusses these findings with you. Participants provide researchers with permission to contact their GP's to let them know what has been found in case there are other things that need to be done. The main physical risks and discomforts of participating in the study are limited to giving the blood sample (if taking part in optional Stage 2) and are the same as those for any other blood sample taken. There may be minor bruising or irritation. EEG is a very safe technique and very few people report any side effects. However, some people may experience temporary redness under electrodes on the scalp or mild discomfort during electrode set-up. On rare occasions people may experience a headache from the EEG cap or may have an allergic reaction to the gel. We will provide facilities to remove most of the gel at the end of test but it is recommended you wash your hair when you get home.

Where is the study run from?
1. South London and Maudsley NHS Foundation Trust (UK)
2. King's College London (UK)

When is the study starting and how long is it expected to run for?
October 2017 to November 2018

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
36612

Study information

Scientific Title
Study of HAllucinations in Parkinson's disease, Eye disease, and Dementia- Trial Feasibility (a randomised controlled 2-stage interventional trial

Acronym
SHAPED-TF

Study objectives
The overall objective is to obtain feasibility data from which to design future large-scale clinical trials for the treatment of visual hallucinations. As such the study is not powered to detect treatment effects for medication, with the primary objectives to understand factors underlying the decision to take medication.

Primary objectives:
1. To obtain evidence of hallucination phenomenology in a trial setting (frequency, duration, types of hallucination and emotional impact) to inform the design of future trials
2. To obtain patient views on:
2.1. Clinically meaningful endpoints to inform the design of future trials (e.g. cessation of hallucinations or reduction of hallucination duration
2.2. The practicality and adverse consequences of non-drug treatment approaches for visual hallucinations
2.3. Factors influencing the decision to take medication as part of routine clinical care

Secondary objectives:
1. Provide effect size estimates for non-drug treatments to inform future trials of: therapeutic effect, quality of life, treatment satisfaction, wellbeing, carer wellbeing and cost-effectiveness (Phase 1)
2. Provide proof-of-concept mechanism data for donepezil and ondansetron using EEG measures of cortical excitability (Phase 2)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Camden and Kings Cross Committee for the National Research Ethics Service, 04/12/2017, ref: 17/LO/1971

Study design
Randomised; Interventional; Design type: Treatment, Drug, Education or Self-Management

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Dementias and neurodegeneration, Primary sub-specialty: Dementia; UKCRC code/ Disease: Neurological/ Extrapyramidal and movement disorders, Neurological/ Other degenerative diseases of the nervous system

Interventions
SHAPED-TF is designed in two phases:
Phase 1:
Investigates the efficacy and tolerability of non-drug approaches to treating visual hallucinations. All patients entering SHAPED-TF are randomised into two non-drug treatments (eye movements or lighting changes) for two weeks. Phase 1 randomisation iscarried out centrally by the SHAPED-TF randomisation service. A permuted-block procedure is used to reduce the risk of chance imbalances between treatments with respect to clinical diagnosis.

Phase 2:
Participants that have not responded to non-drug treatments in Phase 1 are offered cholinergic modulation (Ach-Phase 2). Some patients may already be prescribed a cholinesterase inhibitor as part of their routine clinical care for another indication (e.g. cognitive decline). The fact that they continue to have visual hallucinations suggests cholinergic modulation is either not effective for them or has reached its maximal therapeutic effect. These participants are offered 5HT modulation (5HT-Phase2) as an adjunct to their current cholinesterase inhibitor. Some patients may have been prescribed a cholinesterase inhibitor previously and were not able to tolerate it or their visual hallucinations did not improve. These patients are also be offered 5HT modulation (5HT-Phase2).
1. Ach-Phase2 – patients not prescribed a cholinesterase inhibitor will be prescribed:
1.1. Donepezil 5mg for 2 weeks.

2. 5HT-Phase2 – patients currently prescribed a cholinesterase inhibitor (or previously prescribed but with side-effects or a lack of therapeutic response) are prescribed:
2.1. Ondansetron 8mg for 2 weeks.

After completing 2 weeks of cholinesterase or serotonergic modulation, participants are followed for a further two weeks before exiting the study.

Intervention Type
Other

Primary outcome(s)
1. Hallucination phenomenology is measured using the North East Visual hallucination Interview (NEVH-I) as adapted for SHAPED-TF to record the frequency, duration and emotional impact of visual hallucinations at all time points
2. Patient views are measured using semi-structured questionnaires through interviews at various time-points. The semi-structured questionnaire about general views is administered at baseline and the semi-structured questionnaire about the non-medication strategy is administered at week 4. The semi-structured questionnaire about the medication is administered at week 6 (for those taking part in Stage 1 and Stage 2), and the semi-structured questionnaire about all the strategies in the study is administered at the last time-point (week 6 if only taking part in Stage 1, and week 8 if taking part in Stage 1 and Stage 2).

Key secondary outcome(s))
In order to inform future trials, we will obtain effect size estimates for the two non-drug treatment approaches across various domains. These will include changes in hallucination phenomenology (hallucination frequency, duration and emotional impact in the groups) as measured by the NEVH-I at all time-points, and in therapeutic effect, quality of life, treatment satisfaction, wellbeing, carer wellbeing and cost-effectiveness:
1.1. Disease specific quality of life is measured using the disease-specific quality of life (DQoL) questionnaire administered at two time points: baseline and either week 4 (if only taking part in Stage 1) or week 6 (if taking part in Stage 1 and Stage 2)
1.2. Changes in treatment satisfaction are measured using the “general” treatment of “hallucinations” satisfaction questionnaires (“Hall”TSQ) administered at baseline and week 4 and week 6 (if taking part in Stage 2) and at the last time-point (week 4 if only taking part in Stage 1, and week 8 if taking part in Stage 1 and Stage 2)
1.3. Overall well-being in participants and study partners is measured using the 12-item well-being questionnaire (W-BQ12) at two time points: baseline and either week 4 (if only taking part in Stage 1) or week 6 (if taking part in Stage 1 and Stage 2)
1.4. Depression is measured using the geriatric depression scale (GDS) at two time points: baseline and either week 4 (if only taking part in Stage 1) or week 6 (if taking part in Stage 1 and Stage 2)
1.5. Health and social care service use information is assessed using the Client Service Receipt Inventory (CSRI) as adapted for SHAPED-TF, administered at two time points: baseline and either week 4 (if only taking part in Stage 1) or week 6 (if taking part in Stage 1 and Stage 2)
1.6 The EuroQol-5 dimension (EQ-5D) will also be used to provide a descriptive profile and single index value for health status, administered at baseline and either week 4 (if only taking part in Stage 1) or week 6 (if taking part in Stage 1 and Stage 2)
2. Proof of Mechanism EEG measures of cortical excitability is indicated by a reduction in alpha power as measured by an EEG administered at week 4 and week 6 (if taking part in Stage 2)
2.1. Reduction in a visual cortical excitability is measured using the occipital alpha power at week 4 and week 6 (if taking part in Stage 2)

2.2. Mechanisms of drug treatment (a cholinesterase inhibitor + 5HT modulation (ondansetron); ondeansteron only; a cholinesterase inhibitor only) is measured by a change in EEG alpha power from week 4 to week 6
2.3. Previous side effects or a lack of therapeutic response to a cholinesterase inhibitor is measured from a clinical screening semi-structured interview at baseline

Completion date
31/03/2019

Eligibility

Key inclusion criteria
1. 60+ years old
2. Sufficient fluency in English to participate in the interviews
3. Clinical diagnosis of dementia, eye disease or Parkinson's disease.
4. Experience of visual hallucinations every two weeks over the 4 weeks prior to trial entry.
5. MMSE > 13

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
10

Key exclusion criteria
Exclusion Phase 1
1. Visual hallucinations accounted for by schizophrenia, epilepsy or narcolepsy
2. Participation in an interventional clinical trial in the previous 28 days.
3. Patients with dementia without a study partner.

Exclusion Phase 2
1. If prescribed a cholinesterase inhibitor as part of routine clinical care, contraindications or cautions to ondansetron (Congenital long QT syndrome; Adenotonsillar surgery; subacute intestinal obstruction; susceptibility to QT-interval prolongation (including electrolyte disturbances - see current summary of Product Characteristics)).
2. If not prescribed a cholinesterase inhibitor as part of routine clinical care, contra-indications or cautions to donepezil (Asthma; chronic obstructive pulmonary disease; sick sinus syndrome; supraventricular conduction abnormalities; susceptibility to peptic ulcers - see current Summary of Product Characteristics).

Date of first enrolment

01/02/2018

Date of final enrolment
28/02/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
South London and Maudsley NHS Foundation Trust
-
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Study participating centre
King's College London
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Sponsor information

Organisation
King's College London

Organisation
South London and Maudsley NHS Foundation Trust

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

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 at a later date.

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?
HRA research summary			28/06/2023	No	No