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Virtual reality treatment for building confidence around people

Submission date
13/08/2018

Recruitment status
No longer recruiting

Registration date
14/08/2018

Overall study status
Completed

Last Edited
25/09/2023

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
The researchers are developing the delivery of psychological treatment via virtual reality (VR) for patients with psychosis. Previous work in this area has always relied on a therapist to provide the psychological treatment. This trial tests, for the first time, a fully automated virtual reality cognitive treatment for patients with severe paranoia.
Severe paranoia, seen as persecutory delusions in the context of psychosis, concerns unfounded beliefs that other people are trying to harm the person (e.g. 'People know what I'm thinking and will kill me'). Persecutory delusions are very common in schizophrenia, affecting over 70% of patients, and are highly distressing. Current treatment needs to be significantly improved.
A cognitive treatment will be delivered via VR. It is based upon a cognitive model in which the delusion is viewed as a threat belief, maintained by defence ('safety-seeking') behaviours. Defences include avoiding other people, averting gaze, and remaining vigilant. When harm does not occur, this is attributed to use of these defences instead of the absence of persecution (e.g. 'The reason I wasn't attacked was because I kept away from people'). For treatment to be successful, patients need to re-evaluate their fears and learn that they are safe enough around other people. VR offers a powerful way to do this: patients are much more likely to test out their fears in VR because they know it is a simulation but the learning that they make then transfers to the real world. A one-session VR cognitive treatment was found to produce large improvements in these distressing beliefs. To increase accessibility, the new treatment has been automated by including a virtual coach who guides patients through the therapy. The aim of this study is to compare this new automated VR cognitive therapy (VRCT) with VR mental relaxation (VRMR), to test whether VRCT is more effective at helping patients feel safer (reduced persecutory delusions) than VRMR.

Who can participate?
Patients aged 16 or over who have persistent persecutory delusions, feel under threat around others, and have a diagnosis of non-affective psychosis (e.g. schizophrenia)

What does the study involve?
Participants are randomly allocated to one of two groups. One group receives the new Virtual Reality Cognitive Therapy intervention. The other group receives the relaxation-based virtual reality intervention. All participants continue with their usual care (e.g. taking medication). Both

treatments involve around four sessions lasting 30 minutes each in VR. At the start of the study (0 weeks) and then again at 2, 4, 8, 16, and 24 weeks, participants in both groups complete assessments in order to find out if there have been any changes.

What are the possible benefits and risks of participating?
All participants have about four sessions of a VR intervention. It is hoped that this will lead to improvements in the distressing belief and their overall wellbeing. There are unlikely to be any significant risks in participating, although sometimes people get short-term motion sickness with VR (though this has not been found to occur with this VR set-up).

Where is the study run from?
1. University of Oxford (UK)
2. Oxford Health NHS Foundation Trust (UK)
3. Berkshire Healthcare NHS Foundation Trust (UK)
4. Northamptonshire Healthcare NHS Foundation Trust (UK)
5. Central and North West London NHS Foundation Trust (specifically teams in the Milton Keynes area) (UK)

When is the study starting and how long is it expected to run for?
July 2017 to December 2021 (updated 12/01/2021, previously: June 2021)

Who is funding the study?
Medical Research Council (MRC) (UK)

Who is the main contact?
Prof. Daniel Freeman
daniel.freeman@psych.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Daniel Freeman

ORCID ID
https://orcid.org/0000-0002-2541-2197

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daniel.freeman@psych.ox.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
239628

Protocol serial number
38682

Study information

Scientific Title
The THRIVE study: a randomized controlled trial comparing Virtual Reality Confidence Building with VR Mental Relaxation for people with fears about others

Acronym
THRIVE

Study objectives
The primary hypothesis is that:
1. Compared to the control condition, VRCT will lead to a reduction in delusional conviction (post treatment, 4 weeks).
The secondary hypotheses are that:
2. Compared to the control condition, VRCT will lead to reductions in distress in real world situations, overall paranoia and delusion severity, and suicidal ideation and increases in activity, well-being, and quality of life (post treatment, 4 weeks).
3. The benefits of VRCT will be maintained over time.
4. Change in delusion conviction will be mediated by changes in safety beliefs and use of defence behaviours.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford B Research Ethics Committee, 10/07/2018, ref: 18/SC/0316

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Device, Psychological & Behavioural

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Persecutory delusion

Interventions
Current intervention as of 28/04/2021:
The trial is for people who have a persecutory delusion; specifically, that they feel threatened

when with other people. It is a parallel group randomised controlled trial (i.e. each person has a 50% chance of being randomly allocated to receive one of two therapies). This allows us to see whether one treatment is more effective than the other in reducing fears about others. In total we expect 90 people to take part, with an interim check after 30 people to see whether the trial is feasible.

Assessments:
Each participant who takes part will meet with a research assistant at six different times for an assessment. These are in person, at the clinic or at home. This will happen at the beginning of the study, and then after 2, 4, 8, 16, and 24 weeks. At each assessment, participants will be asked to complete questionnaires on, for example, their fears about others and things they do to try and keep themselves safe. Participants are also be asked to wear a watch which measures activity levels, at some assessments. We expect the 'beginning', 'week 4', and 'week 24' assessments to take about an hour each. Other assessments are likely to be shorter (as only a subset of the measures will be completed at these). The measures have successfully been used in previous studies by the research team. The research assistant will not be aware of which treatment the participant is allocated, to reduce bias.

The full list of assessment measures includes: Basic demographic and clinical data (e.g. age, gender, ethnicity, clinical diagnosis). The primary outcome measure will be conviction in the persecutory delusion (using a 0–100% scale). As in the pilot, a behavioural test will assess distress in real situations. Activity levels will be assessed using actigraphy (over 7 days), complemented with a time-budget assessing meaningful activity (Jolley, 2006). The EQ-5D-5L (http://www.euroqol.org/) will assess quality of life. Suicidal ideation (Columbia Scale; Posner, 2011), overall paranoia (Revised-GPTS; Green, 2008; Freeman et al., 2019), and delusion severity (PSYRATS; Haddock et al, 1999). Additionally, wellbeing will be assessed using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) (Tennant et al., 2007) and the Questionnaire about the Process of Recovery (QPR); a tool developed in collaboration with service users, will assess client perceptions of recovery (Neil et al., 2009). We will record service use using the Client Service Receipt Inventory (CSRI; Beecham & Knapp, 1992), this will provide health economic data. For mediation, we will assess use of defence behaviours (SBQ; Freeman et al, 2001) and strength of safety beliefs (Freeman et al, 2016); this will further inform theories of persecutory delusions and allow a greater understanding of how the treatments work.

At the 'beginning' and 'week 4' assessments only, there is an additional task. We would ask participants about everyday situations that they would like to feel more confident in but at the moment do not. We would then see how they feel when briefly going into that situation (measuring distress related to the belief). This informs whether the treatments have an effect on distress in participants day to day life.

At the 'beginning' and 'week 4' assessments only, there is an additional task (the Oxford Behavioural Avoidance Task – O-BAT; Freeman et al., 2016). We would ask participants about everyday situations that they would like to feel more confident in but at the moment do not. We would then see how they feel when briefly going into these everyday situations. We will gather both an avoidance and a distress score. This informs whether the treatments have an effect on distress in participants day to day life.

VR therapy sessions:
After the first assessment, the treatment will be randomly allocated by a computer (rather like flipping a coin). A therapist will tell participants the outcome. Depending on the outcome, four sessions of either VR Confidence Building or VR Mental Relaxation will be available to the participant. The VR equipment can be set up in a place that is convenient, making the treatment

significantly more accessible. Each session, participants would try a different VR environment for approximately 25 minutes.

Virtual Reality Cognitive Therapy/Confidence Building:
This treatment aims for patients to test their fear expectations around other people in order to relearn safety. It is designed to be delivered in approximately 4 sessions of thirty minutes. Set in a virtual shopping centre, a virtual coach guides the person through the treatment, including encouraging the dropping of defence behaviours, and elicits feedback to tailor the progression of the treatment. For patients in the trial this will be called 'VR Confidence Building', since we are increasing confidence being in everyday situations around other people.

Virtual Reality Mental Relaxation:
This treatment aims for patients to feel calmer using relaxation techniques. It is explained to participants that a helpful way to counteract a fear is to have a calm mind. Participants are taken to calm VR environments to practice the relaxation techniques. The number of sessions and time in VR will be equivalent to VRCT in this control condition.

A simulator sickness questionnaire will be given at the start and end of the first session to assess for this possible (although unlikely) effect. Additionally, participant beliefs about the potential effectiveness of the intervention they are to receive will be assessed using the credibility /expectancy questionnaire (Devilly & Borkovec, 2000) at the start of the first therapy session.

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Previous intervention:
The trial is for people who have a persecutory delusion; specifically, that they feel threatened when with other people. It is a parallel group randomised controlled trial (i.e. each person has a 50% chance of being randomly allocated to receive one of two therapies). This allows us to see whether one treatment is more effective than the other in reducing fears about others. In total we expect 90 people to take part, with an interim check after 30 people to see whether the trial is feasible.

Assessments:
Each participant who takes part will meet with a research assistant at six different times for an assessment. These are in person, at the clinic or at home. This will happen at the beginning of the study, and then after 2, 4, 8, 16, and 24 weeks. At each assessment, participants will be asked to complete questionnaires on, for example, their fears about others and things they do to try and keep themselves safe. Participants are also be asked to wear a watch which measures activity levels, at some assessments. We expect the 'beginning', 'week 4', and 'week 24' assessments to take about an hour each. Other assessments are likely to be shorter (as only a subset of the measures will be completed at these). The measures have successfully been used in previous studies by the research team. The research assistant will not be aware of which treatment the participant is allocated, to reduce bias.

The full list of assessment measures includes: Basic demographic and clinical data (e.g. age, gender, ethnicity, clinical diagnosis). The primary outcome measure will be conviction in the persecutory delusion (using a 0–100% scale). As in the pilot, a behavioural test will assess distress in real situations. Activity levels will be assessed using actigraphy (over 7 days), complemented with a time-budget assessing meaningful activity (Jolley, 2006). The EQ-5D-5L (http://www.euroqol.org/) will assess quality of life. Suicidal ideation (Columbia Scale; Posner, 2011), overall paranoia (GPTS; Green, 2008), delusion severity (PSYRATS; Haddock et al, 1999) and service user-led outcomes (CHOICE; Greenwood, 2010) will be assessed. Additionally, wellbeing will be assessed using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS)

(Tennant et al., 2007) and the Questionnaire about the Process of Recovery (QPR); a tool developed in collaboration with service users, will assess client perceptions of recovery (Neil et al., 2009). We will record service use using the Client Service Receipt Inventory (CSRI; Beecham & Knapp, 1992), this will provide health economic data. For mediation, we will assess use of defence behaviours (SBQ; Freeman et al, 2001) and strength of safety beliefs (Freeman et al, 2016); this will further inform theories of persecutory delusions and allow a greater understanding of how the treatments work.

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Updated 01/04/2021:
At the 'beginning' and 'week 4' assessments only, there is an additional task (the Oxford Behavioural Avoidance Task – O-BAT; Freeman et al., 2016). We would ask participants about everyday situations that they would like to feel more confident in but at the moment do not. We would then see how they feel when briefly going into these everyday situations. We will gather both an avoidance and a distress score. This informs whether the treatments have an effect on distress in participants day to day life.

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A simulator sickness questionnaire will be given at the start and end of the first session to assess for this possible (although unlikely) effect. Additionally, participant beliefs about the potential effectiveness of the intervention they are to receive will be assessed using the credibility /expectancy questionnaire (Devilly & Borkovec, 2000) at the start of the first therapy session.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Not provided at time of registration

Primary outcome(s)
Conviction in the persecutory delusion, measured using a 0–100% scale; Timepoint(s): This is assessed at 0, 2, 4, 8, 16, and 24 weeks. The primary endpoint is 4 weeks.

Key secondary outcome(s)
Current secondary outcome measures:
1. Real world distress assessed by a brief behavioural test (added 01/04/2021: O-BAT) ; Timepoint (s): Assessed at 0 and 4 weeks
2. Overall paranoia assessed using the Revised Green Paranoid Thoughts Scale (Revised-GPTS); Timepoint(s): Assessed at 0, 2, 4, 8, 16, and 24 weeks
3. Delusion severity assessed by the PSYRATS; Timepoint(s): Assessed at 0, 2, 4, 8, 16, and 24 weeks
4. Suicide ideation assessed by the Columbia-Suicide Severity Rating Scale; Timepoint(s): Assessed at 0, 4, and 24 weeks
5. Activity levels assessed using actigraphy and a time-budget measure; Timepoint(s): Assessed at 0, 4, and 24 weeks
6. Quality of life assessed by the EQ-5D-5L; Timepoint(s): Assessed at 0, 4, and 24 weeks
7. Wellbeing assessed by the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) and the Questionnaire about the Process of Recovery (QPR); Timepoint(s): Assessed at 0, 4, and 24 weeks
8. Service use recorded using questions from the Client Service Receipt Inventory; Timepoint(s): Assessed at 0 and 24 weeks
9. Defence behaviours assessed using the Safety Behaviours Questionnaire; Timepoint(s): Assessed at 0, 2, 4, 8, 16, and 24 weeks
10. Strength of safety beliefs assessed using visual analogue scales; Timepoint(s): Assessed at 0, 2, 4, 8, 16, and 24 weeks

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Previous secondary outcome measures:
1. Real world distress assessed by a brief behavioural test (added 01/04/2021: O-BAT) ; Timepoint (s): Assessed at 0 and 4 weeks
2. Overall paranoia assessed using the Green Paranoid Thoughts Scale (GPTS); Timepoint(s): Assessed at 0, 2, 4, 8, 16, and 24 weeks
3. Delusion severity assessed by the PSYRATS; Timepoint(s): Assessed at 0, 2, 4, 8, 16, and 24 weeks
4. Suicide ideation assessed by the Columbia-Suicide Severity Rating Scale; Timepoint(s): Assessed at 0, 4, and 24 weeks
5. Activity levels assessed using actigraphy and a time-budget measure; Timepoint(s): Assessed at 0, 4, and 24 weeks
6. Quality of life assessed by the EQ-5D-5L; Timepoint(s): Assessed at 0, 4, and 24 weeks
7. Wellbeing assessed by the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS), the Questionnaire about the Process of Recovery (QPR), and CHOICE; Timepoint(s): Assessed at 0, 4, and 24 weeks
8. Service use recorded using questions from the Client Service Receipt Inventory; Timepoint(s): Assessed at 0 and 24 weeks
9. Defence behaviours assessed using the Safety Behaviours Questionnaire; Timepoint(s):

Assessed at 0, 2, 4, 8, 16, and 24 weeks
10. Strength of safety beliefs assessed using visual analogue scales; Timepoint(s): Assessed at 0, 2, 4, 8, 16, and 24 weeks

Completion date
31/12/2021

Eligibility

Key inclusion criteria
1. Participant is willing and able to give informed consent for participation in the trial
2. Male or female, aged 16 years or above
3. Persistent (at least 3 months) persecutory delusion (as defined by Freeman & Garety, 2000), held with at least 50% conviction; specifically, participants will be reporting feeling threatened when with other people
4. Primary diagnosis of schizophrenia-spectrum psychosis (non-affective psychosis)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
80

Key exclusion criteria
1. Primary diagnosis of alcohol or substance disorder
2. Photosensitive epilepsy
3. Significant visual, auditory, or balance impairment
4. Current receipt of another psychological therapy
5. Insufficient comprehension of English
6. In forensic settings
7. Organic syndrome
8. Learning disability
9. Current active suicidal plans
10. Any other factor, which in the judgement of the investigator would preclude the participant from providing informed consent or from safely engaging with the trial procedures. Reason for exclusion will be recorded in line with CONSORT guidelines.

Added 01/04/2021:
When ethical approval was received on 07/09/2020 to restart the trial following the pause due to COVID-19, this was with a continuing recruitment suspension in place for participants who were at moderate or high risk for a severe course of COVID-19. From 05/02/2021 patients who

were at moderate or high risk for a severe course of COVID-19 could join the trial if they had received the COVID-19 vaccine (subject to medical advice).

Date of first enrolment
20/08/2018

Date of final enrolment
30/04/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford Health NHS Foundation Trust
Warneford Hospital
Warneford Lane
Headington
United Kingdom
OX3 7JX

Study participating centre
Berkshire Healthcare NHS Foundation Trust
Fitzwilliam House
Skimped Hill Lane
Bracknell
United Kingdom
RG12 1BQ

Study participating centre
Northamptonshire Healthcare NHS Foundation Trust
Sudborough House
St Mary's Hospital
77 London Road
Kettering
United Kingdom
NN15 7PW

Study participating centre

Central and North West London NHS Foundation Trust (specifically teams in the Milton Keynes area)
350 Euston Road
Regent's Place
London
United Kingdom
NW1 3AX

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council; Grant Codes: MR/P02629X/1

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
Requests - accompanied by a study summary - for sharing of de-identified data will be considered by the Chief Investigator (daniel.freeman@psych.ox.ac.uk) and team. The intent is to

share data for reasonable requests. Data will be made available to external researchers subject to the constraints of the consent under which data were collected, with an appropriate data sharing agreement, and after publication of the main study report.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		21/09/2023	25/09/2023	Yes	No
Protocol article	protocol	29/01/2019		Yes	No
HRA research summary			28/06/2023	No	No