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A novel targeted treatment for reducing anxiety in joint hypermobility

Submission date	Recruitment status	[X] Prospectively registered
28/01/2019	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
20/02/2019	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
06/10/2021	Mental and Behavioural Disorders	[ ] Record updated in last year

Plain English Summary
Background and study aims
Our body state influences the way we feel and react: strong emotion such as anxiety is made more intense by the feeling of our heart racing. The way in which people differ physically can affect how much their body reacts and how likely they are to experience anxiety symptoms. Some of these differences can be related to flexible 'hypermobile' joints. Hypermobility can affect up to a quarter of the population. More people who are hypermobile experience problems with anxiety or panic than you would expect by chance. Although the link between anxiety and hypermobility has been known for some time, to date no specific targeted treatments exist. The study team's previous work shows that some hypermobile people have heightened fight or flight nervous systems responses and seem particularly sensitive to changes in bodily sensations. The difference between symptoms and signs of these bodily changes predicts anxiety level and also explains how brain activity in a key emotion processing area is linked to anxiety. The aims of the study are as follows. Having refined a new non-drug therapy which aims to alter unpleasant feelings caused by the way we respond to changes in body such as fast heart beats we will test whether the therapy works in practice by comparing it to another non-drug therapy and then use information from brain scans before and after treatment to predict why people respond to the treatment, in order to help doctors and patients to pick treatments based on good evidence in the future.

Who can participate?
Adults with lived experience of anxiety and joint hypermobility

What does the study involve?
The study involves a telephone pre-screening interview to check inclusion and exclusion criteria for the study and then a face-to-face baseline assessment to confirm these criteria. If the participant is eligible to continue in the study after appropriate consent they receive 10 weekly sessions of therapy (random chance of either therapy) and complete research assessment questionnaires and tasks. A sub-group are randomly allocated to a brain scan before and after treatment.

What are the possible benefits and risks of participating?
All participants are compensated for their time spent undertaking research assessments and

tasks. This research is designed to help with symptoms of anxiety and it may be beneficial in treating anxiety that you experience. The results of this study will inform the evidence base for treatment of anxiety and hypermobility for patients in the future. There are no specific disadvantages to taking part in the study and if participants decide not to take part their usual NHS treatment will not be affected in any way. However, undergoing any psychological therapy poses a potential burden of time and also may involve discussing personal issues in an in-depth way, which some people may find emotionally triggering. If this is the case the participant will have the opportunity to discuss this with your therapist. The research tests are not for diagnostic purposes and the examination should not be considered an alternative to a proper medical consultation. However, sometimes the joint examination, related assessments (heart rate and blood pressure), questionnaires or brain scans may suggest a clinically significant issue. If this is the case or the participant needs further tests, their GP will be contacted in the first instance. The GP will then contact the participant if further tests are required.

Where is the study run from?
The study is run from Department of Neuroscience at Brighton and Sussex Medical School in Brighton, East Sussex, UK and is supported by Sussex Partnership NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2019 to December 2021

Who is funding the study?
The study is funded by an MQ Versus Arthritis Fellowship to Dr Jessica Eccles

Who is the main contact?
Dr Jessica Eccles
j.eccles@bsms.ac.uk

Study website
https://www.mqmentalhealth.org/research/profiles/new-anxiety-treatment-h

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
40233

Study information

Scientific Title
A novel targeted treatment for reducing anxiety in joint hypermobility: a proof of concept study

Acronym
ADAPT

Study hypothesis
Hypothesis 1a: Reduced autonomic trait prediction error in active treatment group will predict anxiety reduction (T1).
Hypothesis 1b: Neuroimaging will reveal changes in fronto-insula-limbic connectivity (intervention compared to comparator), which will relate to reduced autonomic trait prediction error.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London – Bloomsbury REC, Health Research Authority, 3rd Floor Barlow House, 4 Minshull Street, Manchester, M1 3DZ, Tel: +44 (0)207 104 8345 / 0207 104 8127, Email: nrescommittee.london-bloomsbury@nhs.net, 04/01/2019, ref: 18/LO/1920

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

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

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

Condition
Anxiety in patients with joint hypermobility

Interventions
Randomisation will be performed with minimisation (gender, age) by sealedenvelope.com.

The two treatment arms are ADAPT, a novel hypothesis driven non-drug therapy to reduce anxiety in hypermobility, and the comparator therapy is Emotion-Centred Supportive Therapy.

Each therapy will consist of the same quantity of face-to- face contact and will include 10 (weekly) sessions. There is no extended follow up.

Intervention Type
Other

Primary outcome measure
Anxiety levels as measured by Beck Anxiety Inventory (BAI) at T1 (end of therapy)

Secondary outcome measures
1. Autonomic trait prediction error (measured from z score of objective signs of orthostatic intolerance (heart rate rise on active stand test) – subjective symptoms of orthostatic intolerance (orthostatic intolerance subscale of Autonomic Symptoms and Quality of Life Questionnaire (ASQoLS) at T0 (baseline assessment) to T1 (end of therapy)
2. Interoception measures, including:
2.1. Interoceptive sensibility as described by score on awareness subscale of Porges Body Perception Questionnaire, at T0 and T1
2.2. Interoceptive accuracy as defined by performance on the heart beat tracking and heart beat discrimination tasks, at T0 and T1
2.3. Interoceptive awareness as defined by correlation between accuracy and Visual Analogue Scales of confidence in accuracy, at T0 and T1
3. Functional neural datasets – significant changes in activation between T0 and T1

Overall study start date
01/01/2019

Overall study end date
01/12/2021

Eligibility

Participant inclusion criteria
1. Age: All adults aged 18 years or over
2. Capacity: All participants must be able to give informed consent

3. Joint hypermobility: Diagnosis of hypermobile Ehlers Danlos Syndrome/Hypermobility Spectrum Disorder/Joint Hypermobility Syndrome OR Score of 2 or more on Hakim and Grahame 5-point questionnaire to detect Joint Hypermobility
4. Anxiety: Self-reported lived experience of Anxiety disorder AND a score of 16 or more on Beck Anxiety Inventory endorsing moderate anxiety level AND Anxiety should be the primary psychiatric problem
5. Medication use: All participants should be on a stable dose of medication for 3 months OR Medication free AND willing to consider omitting medication that directly affects heart rate (e.g. beta blockers) during the trial
6. Language: All participants must have a good level of both written and spoken English as therapies and assessments will be conducted in English
7. MRI safety: For Phase II (ADAPT TRIAL) only all participants must be MRI safe (i.e no non-removable metal work in body) and be able to lie flat comfortably for one hour

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 90; UK Sample Size: 90

Total final enrolment
50

Participant exclusion criteria
1. Age: Participants under the age of 18
2. Capacity: Unable to give informed consent
3. Joint hypermobility: No diagnosis of hEDS/HSD/JHS AND score of 1 or less on Hakim and Grahame 5 point questionnaire to detect Joint Hypermobility
4. Anxiety: No Self-reported lived experience of anxiety disorder OR a score of 15 or less on Beck Anxiety Inventory OR anxiety is not the primary psychiatric problem
5. Other psychiatric disorder: Presence of major psychiatric disorder (other than co-morbid depression) e.g. Bipolar Affective Disorder, Schizophrenia or Psychosis OR Personality Disorder (e.g. Emotionally Unstable Personality Disorder) OR diagnosed Neurodevelopmental disorder such as Attention Deficit Hyperactivity Disorder or Autism Spectrum Condition OR Neurological disorder
6. Medication use: Not on a stable dose of medication (or medication free) for 3 months
7. Language: Poor level of both written and spoken English
8. MRI safety: For Phase II (ADAPT TRIAL) only MRI incompatability (i.e. non-removable metal work in body) OR be unable to lie flat comfortably for one hour
9. Psychological therapy: Currently receiving another modality of talking therapy

Recruitment start date

27/02/2019

Recruitment end date
01/08/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Sussex (lead centre)
Department of Neuroscience
,Brighton and Sussex Medical School
Trafford Centre, Falmer
Brighton
United Kingdom
BN1 9RY

Study participating centre
Mill View Hospital
Research and Development
Sussex Education Centre
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Sponsor information

Organisation
University of Sussex

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Sponsor type
University/education

ROR
https://ror.org/00ayhx656

Funder(s)

Funder type
Charity

Funder Name
MQ: Transforming Mental Health; Grant Codes: MQ17-18 Eccles

Alternative Name(s)
Mental Health Research, MQ: Transforming Mental Health, MQ

Funding Body Type
Government organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Planned publication in a high-impact peer reviewed journal by May 2022
2. Talks at local and national patient and public involvement events
3. Talks at local, national and international scientific conferences
4. Study protocol and analysis plan will be submitted for publication shortly and certainly before the last recruit

Intention to publish date
01/06/2022

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?
Protocol article	protocol	21/09/2021	06/10/2021	Yes	No
HRA research summary			28/06/2023	No	No