ISRCTN11906973 https://doi.org/10.1186/ISRCTN11906973

Feasibility study of HD-DRUM - a novel drumming training app for people with Huntington's disease

Submission date
03/05/2022

Recruitment status
No longer recruiting

Registration date
09/05/2022

Overall study status
Ongoing

Last Edited
02/08/2024

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Huntington's Disease (HD) is an inherited disease that causes cell loss in brain regions important for learning and planning movements and doing two things at once (multitasking). HD leads to a worsening of these abilities. There is no cure for HD and there are currently no NHS services that can alter the progression of movement and thinking changes. Also, the current COVID-19 pandemic has highlighted the urgent need for support that can be accessed at home when clinic visits are not possible.
This project will test a new movement and rhythm training tool that people with HD can use at home. This involves learning drumming patterns that gradually increase in difficulty. Drumming requires key abilities of concentration, planning and making movements and multi-tasking (e.g. listening and drumming). HD affects all of these abilities as they rely on brain regions impaired by the disease. The drumming tool will train these key abilities.
The training is based on many studies in HD mice showing that movement symptoms can be delayed when mice have access to an enriched environment with more for them to do and think about. Movement and thinking training was also shown to help people with Alzheimer's and Parkinson's disease and can make brain changes including the strengthening of connections. Importantly, I found that two months of Bongo drumming improved concentration and multi-tasking abilities in people with HD and strengthened their brain connections. However, these pilot findings were just in a small number of people and need to be tested in larger groups. Further, we have since developed a digital drumming training, the HD-DRUM app, that allows people to always practise at the level that is best for them, i.e., neither too easy nor too hard. The app also allows to record training improvements, to see if people are training when they should be, and to make it available to everyone interested in using it.

Who can participate?
Adults over 18 years, with HD.

What does the study involve?
This feasibility study will test how easy it is for people who have not yet developed movement symptoms or have only mild-moderate changes to use HD-DRUM at home for three months (15

min per day, 5 days a week). Half of them (n = 25) will be using HD-DRUM while continuing their standard care and the other half (n = 25) will receive standard care only so that the two groups can be compared. Further a group of age, sex and education-matched healthy participants (n = 25) will also be using HD-DRUM for 3 months at home.
Everybody will have some movement and thinking tests and brain scans at the beginning and end of the study. These tests will inform about the number of participants needed for a future bigger randomised controlled (RCT) trial for studying the effects of HD-DRUM on movement and thinking and the brain. In addition, the comparison between people with HD and healthy controls will allow us to identify any disease-related differences in thinking, movement, and the brain before and after the training. This will help us to identify who may benefit most from the training and whether patients recruit different brain regions to learn drumming patterns than healthy participants.

What are the possible benefits and risks of participating?
In the future, HD-DRUM may be able to provide a remotely accessible training tool to help improve movement and thinking in HD without the risk of harmful side-effects. Even a small delay in symptoms starting due to the strengthening of brain connections and function would have direct and significant benefits for the quality of life of people with HD and their families.

Potential risks – Cognitive assessments and HD-DRUM training
For the cognitive assessments and HD-DRUM training intervention, there are no obvious ethical or safety concerns. The proposed cognitive assessments are standard neuropsychological assessment that have been widely used in the Enroll-HD study to assess HD patients. Further we did not observe any safety issues in our pilot work on drumming training and computerised cognitive training in people with HD. However, there is a small risk associated with any psychological assessment and intervention to cause distress or harm: all study and intervention material will therefore be co-produced and reviewed by stakeholders in order to minimise risk of distress. HD-DRUM implements an adaptive training schedule that will avoid distress due to over- or underchallenge.

Potential risks – MRI assessments
MRI scanning is non-invasive and has no known significant adverse health effects when appropriate screening and safety measures are in place and implemented and CUBRIC Standard Operating Procedures will be followed. MRI scans involve a strong magnetic field so that participants with certain mechanical or electronic devices cannot be scanned (e.g. pacemakers, artificial heart valves, neurostimulators). All participants will therefore be carefully screened to ensure that MRI scanning will be safe for them. Rarely, someone finds the scanner too claustrophobic: all participants will be asked about this and will also be given the opportunity to lie in a mock scanner (without a magnetic field) to experience what the scanning will be like. As MRI scanning is noisy all participants will be provided with ear protection. Verbal contact will be maintained between the investigators and the participant through the use of intercom, and a call button will be given to the participant to enable them to stop the scanning procedure at any time. A few people have reported minor side effects during MRI scanning including dizziness, mild nausea, a metallic taste in the mouth, and the sensation of seeing flashing lights. These side effects, if experienced, resolve after leaving the magnet and participants will be warned at the beginning of the MRI scanning session of these rare side effects. In some circumstances, the changes in the magnetic field in the MRI scanner could make an electric current flow through some of the volunteer’s body, causing peripheral nerve stimulation, this is rare and not harmful but may be uncomfortable. If two parts of the volunteer’s body were touching (for instance legs crossed) then in very rare occasions it is possible that an induced current may cause skin heating. Volunteers are instructed to lie with arms to their sides, and legs uncrossed, which stops this from happening.

It will also be explained to participants that the researchers do not have expertise in MRI diagnosis, as they are not medical doctors. Participants should not regard the research scans as medical screening procedures and if they had any health concerns, they should contact their medical practitioner in the normal way. In the unlikely event of an unexpected finding, a neurological consultant will be asked to examine the scans, and if appropriate to report back to the participants' GP.

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

When is the study starting and how long is it expected to run for?
August 2020 to April 2026

Who is funding the study?
Health and Care Research Wales (UK)

Who is the main contact?
Dr Claudia Metzler-Baddeley
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Contact information

Type(s)
Principal Investigator

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
310261

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 310261

Study information

Scientific Title
Feasibility randomised controlled pilot study of HD-DRUM - a novel motor activity (drumming) training app for people with Huntington's disease

Acronym
HD-DRUM

Study objectives
The adherent use of HD-DRUM is feasible in individuals with presymptomatic/early-moderate manifest Huntington's disease (HD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/07/2022, Wales Research Ethics Committee 2 (Castlebridge 4, 15-19 Cowbridge Road East, Health & Care Research Wales Ethics Service, Cardiff, CF11 9AB, UK; +44 (0) 2922941119; Wales.REC2@nhs.wales.uk), ref: 22/WA/0147

Study design
Two-arm feasibility randomized controlled pilot study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home

Study type(s)
Other

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
Improving cognitive and motor symptoms with drumming in people with Huntington's disease

Interventions
The study will take place at the Cardiff University Brain Research Imaging Centre (CUBIRC) and at participants' homes. Half of the participants (n = 25) will be randomised to receive HD-DRUM at home while the other half (n = 25) will be a non-intervention standard medical care control.

Randomisation either with REDCap tool or Minim computer software. Participants in the HD-DRUM motor activity training group will be given a tablet with the HD-DRUM drumming app and written and video instructions installed. They will be asked to use HD-DRUM five times per week for 15 min for 12 weeks. The researchers will be in weekly contact with them to see how they are progressing and to record any problems/barriers. Control participants will receive no intervention apart from their routine medical care but will have the opportunity to try HD-DRUM after study completion. They will also be contacted on a weekly basis to control for social contact with the researchers. All participants will undergo two cognitive and MRI assessments at CUBRIC, before and after the 12 weeks study period.

Brain morphology and microstructure of cortico-striatal-thalamic and cerebellar networks will be assessed at baseline and at 3 months follow-up to assess training-induced brain plasticity mechanisms.
Informed consent, specific to MRI scanning will be conducted prior to each scan. The MRI scanning procedure will be carefully explained and discussed with the participant and the participant will have the opportunity to experience lying in a simulated MRI scanner ('mock scanner'), if they feel this may be helpful. Research visits to conduct MRI scans will be arranged prior to beginning the HD-DRUM training intervention and again after the 12 weeks intervention for both intervention and control groups, in order to address the mechanism. Prior to scanning, all participants will be screened for contradictions to MRI and the procedure will be carefully explained to them. An MRI scan will then be conducted by a fully trained MR Operator at CUBRIC. MRI data acquisition will take about 60 min.
MRI scanning will be done on the National Microstructural Imaging Facility, a 3 Tesla MRI Siemens Connectom system with ultra-strong (300mT/m) gradients that is only available in CUBRIC within the UK. Ultra-strong gradients allow the acquisition of diffusion-weighted data with high b-values for the estimation of intracellular diffusion properties. These were shown to be more sensitive to WM microstructure than standard diffusion tensor imaging indices. In addition, patients will be offered an optional high-resolution anatomical scan on the 7 Tesla MRI Siemens Magnetom system to gain high-resolution images of the basal ganglia and the cerebellum.
All MRI protocols have been piloted in individuals with HD and healthy participants and were well-tolerated. Our previous research has identified microstructural differences in HD patients compared with healthy controls. Importantly, we found drumming training-induced increases in an estimate of white matter myelin. MRI data acquisition time on the Connectom scanner will be ~60 min and optional additional scanning on the 7T Magnetom will be ~30 min.

Intervention Type
Behavioural

Primary outcome measure
1. Feasibility of recruitment will be assessed by recording the number of participants enrolled and consented into the study per clinic per month.
2. Retention will be measured by the number of participants who complete the study. Number and study and non-study-related reasons for drop-out will be recorded.
3. Acceptability will be measured with a semi-quantitative self-report questionnaire asking participants to rate how engaging/motivating/frustrating the training was, whether the training frequency, duration, and difficulty was appropriate, whether they perceived any beneficial /detrimental training effects, what they liked/disliked and what aspects could be improved. This information will provide feedback for any adjustments that may need to be made to HD-DRUM

in preparation for a future RCT.
4. Adherence to the training will be automatically tracked with HD-DRUM by recording the frequency and duration of training sessions.

Secondary outcome measures

1. Computer and Paper based cognitive and motor tasks
Training-induced transfer effects to untrained motor and cognitive tasks will be estimated with paper and pencil and computerised tasks to test motor and cognitive functions at baseline and follow-up study visits. These include tasks from the core-assessment protocol of the ENROLL-HD study and computerised tasks from the Psychology Experiment Building Language (PEBL) Test library. The pace of cognitive assessments will be led by the participant although it is not expected that the completion of the cognitive tasks will exceed 2 hours. The following tasks were chosen for the purpose of identifying the best clinical outcome measure for a future RCT.
1.1. Motor functions will be assessed with the Motor Score and the Diagnostic Confidence Index from the United Huntington's Disease Rating Scale (UHDRS) and with a computerised finger tapping task from PEBL.
1.2. Everyday functioning will be assessed with the Total Functional Capacity, the Functional Assessment Scale and the Independence Scale from UHDRS.
1.3. Cognition will be assessed with the Symbol Digit Modality Test, Stroop word reading, Stroop colour naming and interference, letter and category fluency and Trail Making A & B from the core-assessment of ENROLL-HD. Executive functions of distractor suppression (Flanker task), updating (n-back), attention switching (complex span) and dual tasks will be assessed with PEBL.

2. MRI morphology and microstructure
Brain morphology and microstructure of cortico-striatal-thalamic and cerebellar networks will be assessed at baseline and at 3 months follow-up to assess training-induced brain plasticity mechanisms.
MRI scanning will be done on the National Microstructural Imaging Facility, a 3 Tesla MRI Siemens Connectom system with ultra-strong (300mT/m) gradients. MRI data acquisition time on the Connectom scanner will be ~60 min and optional additional scanning on the 7T Magnetom will be ~30 min:
2.1. T1-weighted anatomical images [magnetization prepared-rapid gradient echo sequence, 1x1x1 mm3 resolution, field-of-view: 256 x 256, repetition time (TR) = 2300 ms, echo time (TE)= 2 ms, TI = 857 ms, flip angle: 9] as reference images for all microstructural maps and to gain volume and cortical thickness measurements60.
2.2. Multi-shell diffusion-weighted data [2x2x2 mm^3 resolution; TE/TR = 59/3000 ms; δ/Δ: 7/24 ms; b-values = 0 (14 volumes), 500 (30 directions), 1200 (30 directions), 2400 (60 directions), 4000 (60 directions), and 6000 (60 directions) s/mm^2] to fit multicompartment models such as the Composite Hindered And Restricted Model of Diffusion (CHARMED)61 and the Neurite Orientation Density and Dispersion (NODDI)62 model yielding maps of the restricted signal fraction (Fr), estimating axon density, of the orientation dispersion index (ODI), estimating neurite complexity, and of the isotropic signal fraction (ISOSF), estimating free water.
2.3. Quantitative Magnetization transfer (MT)-weighted data [1.72x1.72x1.72 mm^3 resolution, turbo flash sequence, turbo factor 4, non-selective excitation MT pulse duration: 15.36 ms, 11 MT-weighted volumes and 1 volume without MT-weighting, 11 Frequency offsets (Hz) and 11 flip angles (degrees): 47180 (628); 56360 (332); 12060, (628); 1000 (332);1000 (333); 2750 (628); 2770 (628); 2790 (628); 2890 (628); 1000 (628); 1000 (628)]63 to gain the macromolecular proton fraction (MPF) as an estimate of WM myelin.
2.4. An optional high-resolution T1-weighted anatomical scan [magnetization prepared-rapid gradient echo sequence, 0.7x0.7x0.7 mm^3 resolution, field-of-view: 256 x 256, repetition time (TR) = 5000 ms, echo time (TE)= 2.45 ms, TI1 = 900 ms, T12 = 2750 ms; flip angle1: 5, flip angle2 =

3] at 7Tesla (gradient strength 70mT/m) on the Siemens Magnetom MRI scanner to obtain high-resolution images of the basal ganglia and cerebellum regions as well as susceptibility and R2* maps to characterise basal ganglia tissue properties of myelin and iron.

Overall study start date
01/08/2020

Completion date
30/04/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 06/02/2024:
Individuals over the age of 18 years with premanifest or early/moderate manifest HD as confirmed by genetic testing for the presence of the mutant huntingtin allele with a Total Functional Capacity score between 9 and 13, sufficient motor control to perform drumming and on stable medication for a minimum of four weeks prior to enrolment.

Previous inclusion criteria:
Individuals over the age of 18 years with premanifest or early/moderate manifest HD as confirmed by genetic testing for the presence of the mutant huntingtin allele with sufficient motor control to perform drumming and on stable medication for a minimum of four weeks prior to enrolment. They will have participated in at least two cognitive testing sessions for the ENROLL-HD registry to reduce the burden (cognitive data collected within a month prior to pilot will be used as baseline data) and practice effects of repeated testing.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
50

Key exclusion criteria
A history of any other neurological condition than HD and an inability to provide consent.

Date of first enrolment
01/01/2023

Date of final enrolment
30/03/2025

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
Cardiff University Brain Research Imaging Centre (CUBRIC)
Maindy Road
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CF24 4HQ

Sponsor information

Organisation
Cardiff University

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Sponsor type
University/education

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ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Government

Funder Name
Health and Care Research Wales

Alternative Name(s)
Health & Care Research Wales, Ymchwil Iechyd a Gofal Cymru, Health Care Research Wales, HCRW

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 06/02/2024:
A paper on intervention design has been published (http://dx.doi.org/10.2196/48395) and the study protocol paper is currently under review (https://doi.org/10.1101/2023.11.15.23298581). Publications on cross-sectional HD-related differences in grey and white matte microstructure and clinical outcome measures are in planning and preparation. Results of RCT with regards to primary feasibility and secondary clinical and brain microstructure measurements are planned after study completion. The app is currently being deployed in a feasibility RCT with people with HD.

Previous publication and dissemination plan:
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/06/2027

Individual participant data (IPD) sharing plan
Data will be stored and managed on RedCap. Anonymised data can be obtained on request from the principal investigator Dr Claudia Metzler-Baddeley (metzler-baddeleyc@cardiff.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	Intervention design	06/10/2023	06/02/2024	Yes	No

Protocol (preprint)	16/11/2023	06/02/2024	No	No
Protocol article	31/07/2024	02/08/2024	Yes	No