CLEAR-HD

Cortical Layer Examination At high Resolution in Huntington's Disease

Information Sheet and Informed Consent Form

Control Participant

Version 6.0, 13th July 2021 (IRAS number: 252676)

I. **Part I**

1. Invitation Paragraph

You are being invited to participate in a research study named Cortical Layer Examination at high Resolution in Huntington's disease (CLEAR-HD). Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

2. What is Huntington's Disease?

Huntington's disease (HD) is an inherited neurodegenerative disease. A faulty gene causes the build-up of a toxic protein - mutant huntingtin - which damages brain cells, leading to problems with movement, thinking and behaviour. The faulty gene can be passed down within families, a person whose parent has HD is born with a 50-50 chance of inheriting the faulty gene. Anyone with a family history of HD can choose to have a predictive genetic test, which means they can find out whether they have the faulty gene or not, and therefore, whether they will go on to develop the disease or not.

3. What is the purpose of the study?

The purpose of this research study is to use novel high-resolution brain imaging techniques to assess whether subtle brain changes can be seen in HD gene carriers who show no clinical signs of HD and are completely well. This will allow us to guide the use of any potential future treatments, so that they can be given at the earliest and most effective time in order to prevent or treat HD disease progression.

To study whether these changes can be identified, we will carry out a number of assessments. We will look at images of the brain using safe and non-invasive techniques. To look at brain structure we will use a technique called Magnetic Resonance Imaging (MRI) and to look at brain function we will use a technique called Magnetoencephalography (MEG).

This information sheet describes the research study and what you can expect if you decide to participate. Please read this information sheet carefully. Ask the person who presents the form to

you, or contact the study team (details on page 14), with any questions you may have before deciding whether to participate in this study.

4. **Why am I being invited to take part?**

We are inviting you to participate in the CLEAR-HD study as a healthy control because you are known not to carry, or be at risk of carrying the faulty gene that causes HD.

5. **Do I have to take part in this study?**

Your participation in this study is completely voluntary. You are free to choose whether or not to participate in this study. If you decide to participate, you can change your mind and withdraw from this study at any time, for whatever reason. You are not required to give any reason for your decision on whether or not to participate in this study or, if you decide to participate, for your decision to withdraw from this study. Deciding not to participate in this study, or deciding to withdraw from this study will not affect the current or future care that you would otherwise expect to receive.

6. **What will happen to me if I take part in this study?**

Telephone call

A member of the research team will arrange to speak to you on the telephone to discuss your interest in participating in the study. During the phone call, the researcher will provide you with information about the study and give you the opportunity to ask any questions. If you need time to consider participating in the study, the researcher can arrange to contact you at an agreed later date.

Study Visit

If you agree to take part, you will be asked to attend one study visit. This will take place at the Royal London Hospital for Integrated Medicine and the Wellcome Centre for Human Neuroimaging. The visit will last from approximately 9:15am until 4:00pm. We will begin the visit by explaining the study in detail and if you would like to participate we will invite you to sign a consent from. We will then take a medical history and conduct a clinical examination including some tests assessing mood, thinking and behaviour.

Following this we will show you how to play the computer game task that we will use during the MEG scanning and we will give you some time to practice it. There is then a MEG scan lasting 60-90mins during which time we will ask you to play the computer game task. There will be a short break before we then take a medical history and conduct a clinical examination including some tests assessing mood, thinking and behaviour. We will take a 20 ml blood sample from your arm (approximately 2 tablespoons). After this there will be a lunch break. A high-resolution 7-Tesla MRI scan will then be performed and this will last 60-75 mins. A subset of patients will be asked to play some computer games during the scan. Once this scan is finished we will ask you to complete a short questionnaire based on your experience during the study and assessments. The study visit is then finished.

7. Who is organising, sponsoring and funding CLEAR-HD?

This research is organised by Dr Peter McColgan, NIHR Academic Clinical Lecturer at the UCL Huntington's Disease Centre and the study is being funded by the European Huntington's Disease Network.

UCL is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. In accordance with the UCL Records Retention Policy, research data are retained by UCL in their capacity as sponsor for 20 years after the research study has ended. Data is then securely destroyed.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting Dr Mitsuko Nakajima, clinical research fellow and PhD candidate at UCL, who is conducting CLEAR-HD with Dr Peter McColgan (Principal Investigator).

Part 2 below gives you more information about the conduct of CLEAR-HD

II. PART 2

1. How many participants will be involved?

Up to 60 participants will be included in this study – half of the participants will carry the HD gene, but not show any signs of the disease and half of the participants will be control participants. A control participant is a person who does not carry, and is not at risk of carrying the genetic mutation that causes HD.

2. Procedures and Study Visits

The study consists of one visit at the Royal London Hospital for Integrated Medicine / Wellcome Centre for Human Neuroimaging, both in Queen Square, central London. You may be offered an overnight stay in a nearby hotel depending on how far you have to travel and there will be plenty of time for refreshments, lunch and breaks.

Magnetoencephalography (MEG) scan

MEG is a painless and safe technique that measures magnetic fields produced by brain cell activity. MEG does not use any ionizing radiation or x-rays and there are no known side-effects or cumulative risks. The scanner is situated within a magnetically shielded room to stop interference from external magnetic fields. Some people find the enclosed space of the shielded room (the size of a large elevator) uncomfortable. You will be able to communicate with the study staff all times during the scan and if you feel like to need to stop or take a break this can be accommodated right away.

Huntington's disease (HD) Core Assessment Battery

We will ask questions about your medical history, your current health and treatments (including medications) you are then taking. We will measure your height and weight. We also will conduct tests to see how well you move, think, remember things, perform daily tasks, and behave – all behaviours, which may be affected by HD. The examination should take approximately 60 minutes. If you have had an Enroll-HD visit within 6 months of this visit we will not repeat these assessments at this Clear-HD visit. We will also take a small blood sample (approximately 20 mls) for measuring the neurofilament light chain (NfL), a relatively new biomarker for HD.

High-resolution 7T MRI scan

. We are using the high-resolution 7 Tesla MRI (also referred to as "*7T*" or "*ultra-high field MRI*") scanner, which uses stronger magnets. This is because it allow us to obtain more detailed images of the brain. The magnet is significantly stronger than the standard MRI scanners, such as those used in hospitals, and the experience will be quite different. Some people scanned in 7T MRI scanners may experience transient sensation, such as a mild dizzy sensation, disorientation, or metallic taste as they are moved into and out of the scanner. This is normal and the sensation starts to go away as

soon as you are in the scanner. In order to minimise and avoid these effects, movement into the scanner is done slowly by an advanced MRI operator. The scan lasts up to 60-75 minutes.

. The MRI scanner is like a tunnel about 1.5 metres long, surrounded by a large circular magnet. You lie on a couch, which then slides into the scanner. The scanner will produce loud noises; this is normal and should not worry you. However, you will be provided with earplugs and/or headphones. During the MRI, the operator will be able to speak to you, hear you, and observe you at all times through a window and a 2-way microphone communication system.

MRI is a painless and safe technique that can provide detailed pictures of the brain. It uses a magnetic field and radio waves, together with an advanced computer system to build up a series of images, each one showing a thin slice of the area being examined. It does not use any ionizing radiation or x-rays, and in general, MRI causes no known short-term or long-term tissue damage of any kind. However, the powerful magnetic field of the MRI scanner can attract certain metallic objects, causing them to move suddenly and with great force towards the centre of the MRI machine. This may pose a risk to anyone in the way of the object. Therefore, great care is taken to prevent such objects such as watches, jewellery, hair pins and items of clothing that have metallic threads or fasteners from entering the MRI room. Before visiting the facility, research staff will ask about the presence of metallic implants (such as pace-makers, pins, screws, plates, clips). They will also ask about tattoos, as research suggests that heating and pulling can occur with older tattoos, which may contain small quantities of metal. Therefore, participants with tattoos are sometimes excluded from MRI scans unless special precautions are taken. Similarly, permanent make-up (e.g. eye-liner, eye-brows) may contain metal, which cause burns as well as distort the quality of the images. For these reasons, participants who have had these procedures recently may be excluded from the study.

Female participants: Although there is no evidence to suggest that MRI si harmful to unborn babies, as a precaution, the Department of Health advises against scanning pregnant women unless there is a clinical benefit. We do not test for pregnancy as a routine, so if you think you may be pregnant, you should not take part in this study.

3. **What will I have to do on the day?**

Day Schedule (approximate times):

Time	Event	Location
09:15 – 09:30	Meet the research team	WCHN
09:30 – 10:00	Study explanation & consent	WCHN
10:00 – 11:30	Magnetoencephalography (MEG) scan	WCHN
11:30 – 11:45	Break	
11:45	Reconvene at RLHIM	RLHIM
11:45 – 12:45	Huntington's disease (HD) Core Assessment Battery, AMI questionnaire	RLHIM
12:45 – 13:45	Lunch break	
13:45	Reconvene at WCHN	WCHN
13:45 – 14:30	Preparation for 7T MRI	WCHN
14:30 – 16:00	7T MRI	WCHN
16:00 – 16:15	Questionnaire	

Table 1. Visit day timetable. Abbreviations: WCHN - Wellcome Centre for Human Neuroimaging; RLHIM – Royal London Hospital for Integrated Medicine

Your study will begin at 09:15-09:30am at the Wellcome Centre of Human Neuroimaging (WCHN, 12 Queen Square). One of our research team will meet you at the entrance. As part of our COVID-19 safety procedure, we will check your temperature, and ask you to wash your hands and change the face masks to the ones provided.

After entering the building, we will take you to a testing room. There, we will explain the study. You will be asked to sign the imaging facility's COVID-19 rules, and the imaging questionnaire.

Thereafter we will take you to the Magnetoencephalography (MEG) room. Because the device measures small magnetic fields you will be asked not to wear metallic items (clothing with zips, metal buttons etc) on the day of your scan. Once you have removed any metal you are wearing or carrying, you will be asked to sit with your head inside the scanner. Before scanning, you will be shown exactly what you have to do, and given time to practise. The game involves looking at simple pictures on a screen or listening to sounds, and responding using a simple keypad. Having practised, and having asked any questions, you will then be asked to play the same game while your brain is being scanned.

There are four separate parts to the game, with a short break in between. Overall, this session will last approximately 1.5 hour.

After the MEG scan, there will be a short break (~15 minutes), and we will move from WCHN to Royal London Hospital for Integrated Medicine (RLHIM). There, we will complete the Huntington's disease (HD) Core Assessment Battery and blood test. This takes approximately 1 hour. Afterwards, there will be a 45 minutes – 1 hour lunch break. Please keep your receipt, as we can request UCL to reimburse you up to £7.

After lunch, we will reconvene at the WCHN reception for the MRI scan. First we will show you round to the changing room. For your comfort and safety we will ask you to change into a 'pyjama-style' top and trousers, which are available in a range of sizes. You may keep your underwear and socks on, but if you are wearing a bra with metal underwire or clips, we will ask you to remove that too. Please don't wear clothing made of fabric containing metallic threads or fabric that has been impregnated with silver (marketed as anti-microbial/bacterial or anti-odour/stink). Lockers are provided for your personal belongings and clothing. You will be asked to remove all metal objects, such as dentures, watches, jewelleries, body piercings, bank cards, smartphones. Footwear will also be removed. If you are wearing eye make-up, we will ask you to remove it. This is because some types of eye-shadow and mascara contain materials that can interact with the magnetic field. You may wish to bring your own make-up remover and your make-up bag. With a subset of volunteers, we will then go to a Testing Room to practice the game that you will play inside the scanner, which consists of looking at a computer screen and responding using a simple keypad.

Once we are ready, the radiographer will escort you to the scanner room, and you will be shown exactly what you have to do. The research team will introduce you to the scanner environment. You will be given earplugs to wear, and asked to get onto the scanner table and lie down. A small device will be placed on your finger to monitor your pulse and/or an elastic belt to monitor breathing. A "head coil" will then be placed over your head. This is special type of helmet that covers your head and face, but still allows you to see open ends of the scanner via mirrors. The research team will ensure you are comfortable before moving you inside the scanner. You will be able to contact the radiographer or operator from inside the MRI machine at all times using a hand-held "squeeze bulb", and they will talk to you between scans while you are inside the scanner. The scan involves taking detailed anatomical images of your brain – a structural scan. While structural images of your brain are made, you will be asked to relax and keep still. You may have another type of scan, known as a functional MRI (fMRI) scan, during which you will play the games you practised before entering the

scanner, and using the keypad to respond. After scanning, we will ask you questions about your experience of the scan. The MRI scan will last approximately 1.5 hours.

4. What must I keep in mind during this study?

During the time of this study, you are being asked to follow all instructions that the study physician and study team give you. If you are not feeling well or if you have had medications since your referral to us for the study or the telephone call to arrange your study visit you should inform the study team as soon as possible.

5. How will my information be stored?

The information collected about you during this study will be entered via secure internet connections into a confidential database that is located on a secure server through the study sponsor, University College London. In addition, data will be held at a data storage facility selected for this study. This facility, called a hosting facility, follows security procedures to make sure the information is safe and secure. Access will be restricted to authorised personnel.

The information collected from you and entered in a secure database will not be associated with, or identified by, your name or other information that could directly identify you. Only the study site staff will be aware of your identity and have the key to the code that links your information to you.

More information regarding the safeguards we have in place to protect personal information can be found at the following link: https://www.ucl.ac.uk/legal-services/privacy/participants-health-and-care-research-privacy-notice.

6. How will my information be used and shared?

UCL will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from UCL and regulatory organisations may look at your medical and research records to check the accuracy of the research study. UCLH will pass these details to UCL along with the information collected from you. The only people in UCL who will have access to information that identifies you will be people who need to contact you to audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

The coded information collected from you during this study may be used by the UCL research team members and collaborators in the Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany to check the quality of the information collected from you during this study and design and guide future research studies.

The research team and the study sponsor (UCL) may publish the results of their research, including coded information, in medical journals or present such results at meetings. However, your name, address or any other information that could directly identify will not be published.

The information collected from you during this study will be used only for research purposes and will not be sold.

You can change your mind at any time about the storage and use of the information collected from you during this study. Just contact the research team, and let him or her know that you no longer want the information collected from you during this study stored and such information will be deleted.

The information collected from you and entered in the database will not be associated with, or identified by, your name or other information that could directly identify you. Only the study site staff will be aware of your identity and have the key to the code that links your information and biological samples to you.

Whilst we do not want to cause alarm, we are required by the body governing Research Ethics Committee to let participants know what will happen to their samples and/or data if they were to lose capacity during the course of the study (or thereafter). Should you lose the capacity to consent during your participation, you will be withdrawn from the study by the research team, and we would like to ask your permission in advance to retain any information collected prior to your withdrawal for use in HD research.

7. What discomforts and risks are involved?

Any adverse medical events arising from your participation in this study will be followed up and treated as necessary by the study team.

MEG scan

MEG is a painless and safe technique, there are no known side-effects or cumulative risks.

7T MRI scan

Some subjects find MRI scanning uncomfortable because of the enclosed space and the need to stay still during the scanning process. Appropriate steps will be taken to make you feel as comfortable as possible. A 2-way communication system will also allow you to speak to the MRI operator during the scan. A safety assessment will be performed by trained personnel to ensure that it is safe to perform an MRI. As long as this questionnaire is correctly completed, MRI is safe. Some participants may feel temporarily dizzy as they move into or out of the 7T MRI scanner. This is caused by the change in magnetic field and is not harmful in anyway. This sensation normally resolves after a few minutes.

Assessments and questionnaires

When completing the clinical, behavioural and cognitive assessments for CLEAR-HD, you may experience low mood or psychological discomfort (such as stress or anxiety). If at any time you feel you could benefit from treatment or support, you may request to be referred for appropriate care. In the course of doing these questionnaires or tests you may also feel tired and/or irritable. If this happens please tell your doctor or a member of the research staff and ask them to allow you time to rest or stop the testing all together.

Collection of private / personal information

We take great care to protect your personal information and all procedures are in compliance with the General Data Protection Regulation (GDPR). However, there is a slight risk of accidental disclosure of information, or breach of computer security.

Unexpected findings

We do not expect to find anything of medical significance for individual research participants as part of this study. The results of the tests will not routinely be conveyed to you. However, occasionally the clinical examination or MRI scan can reveal an unexpected finding of possible medical importance. If this happens, we will let you know and inform your General Practitioner (GP) who will be able to take any necessary action through the usual NHS care pathways.

8. What are the benefits of taking part in CLEAR-HD?

You will not have any direct benefits from participating in this study. The results of this study may contribute to new knowledge of HD. If you would like a summary of the results of this study once it is completed please contact Dr Mitsuko Nakajima.

9. Is there any payment or cost?

Your expenses, including meals and hotel (if applicable) incurred within the scope of your participation in this study will be covered. You will need to provide receipts for your expenses. We can help book travel and accommodation so you don't have to pay upfront. Please consult the study team before spending your own money, to make sure the expense will be refunded, as some items like train fares and hotel accommodation have limits on how much can be reimbursed.

10. What happens if I am injured or something goes wrong?

If you wish to complain, or have any concerns about the way you have been approached or treated as part of this study, you should contact a member of the research team, who will do their best to address your concerns. The National Health Service or UCL complaints mechanisms are available to you. Please ask a member of the research team if you would like more information on this.

UCL Hospitals Foundation Trust will provide medical care for any emergency medical problem that you may experience as a direct result of your participation in this research. You will not have to pay for this emergency care.

We will not routinely inform your GP of your participation in this study. We will only notify your GP that you are taking part in this study where there is a clinical need, for example, if we identify an unexpected finding and there is a medical need, as described above.

If you have health insurance, it is up to you to find out whether participation in this study may affect your insurance cover.

In the unlikely event that you are harmed by taking part in this study, compensation may be available. University College London (UCL) holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, if this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the clinical study. University College London does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

If you have concerns about any aspect of this study, you should call 020 3108 7480 and ask to speak to the researchers who will do their best to answer your questions.

If you remain unhappy and wish to complain formally, you can do this by contacting the Patient Advice and Liaison Service on 020 3448 3237 or write to UCLH Patient Advice and Liaison Service at the following address; PALS, Box 25, National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, or email: pals@uclh.nhs.uk

11. Will my information or samples be used for commercial purposes?

Successful research by us and others using your coded information collected in the course of this study could result in a commercial test or therapeutic product with significant value, such as a product for the treatment of HD. You will not receive any financial benefit from such a result.

12. Who has reviewed this study?

CLEAR-HD has been reviewed by the Health Research Authority and the London Queen Square Research Ethics Committee.

13. Could the study end early?

You may be withdrawn from this study if you do not follow the directions of this study or if your medical condition changes so that staying in this study might risk your health or this research. Your participation in this study may also end if the sponsor (UCL) or Principal Investigator (Dr Nakajima) decides to terminate the study for safety or other reasons.

14. How do I get in touch with the study team?

For more information concerning this research or if you believe that you have suffered a research related injury, please contact:

Dr Mitsuko Nakajima
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Queen Square
London WC1N 3BG

Telephone 020 3108 7204

Research Team Telephone 020 3108 7480