Title of Study: Cholinergic ResponsE in Early lewy body Disease (CREED) study

Participant's Information Sheet

For research involving the NHS:
IRAS ID: _____
Participant ID: _____

Invitation and Brief Summary
You are being invited to take part in a research study. Before you decide whether you wish to take part it is important that you understand why the research is being done and what it will involve. Please read this information carefully and discuss it with others if you wish. Take time to decide whether you wish to take part. If you do decide to take part, you will be asked to sign a consent form. However, you are free to withdraw at any time, without giving any reason and without any penalty or loss of benefits.

Why have I been invited to take part?
You are invited to participate in this research study because you are diagnosed with or suspected to have cognitive impairment or dementia related to Parkinson 's disease or Dementia with Lewy Bodies as you have reported cognitive problems. Cognitive impairment/dementia is a condition in which a person has problems with cognitive ability, for example memory and thinking. The impairment is worse than would normally be expected for a healthy person of their age. The diagnosis is mild cognitive impairment if it is not severe enough to interfere with daily activities and dementia if it does. Collectively, the conditions are known as Lewy Body Disease.

What is the purpose of the research?
In people with Lewy Body Disease, a chemical in the brain called Acetylcholine frequently is reduced and this leads what is known as cholinergic dysfunction. Lewy Body Disease may be treated by preventing the breakdown of Acetylcholine in the brain by using a group of drugs called Cholinesterase inhibitors (donepezil is one of them). However, not all people with Lewy Body Disease will response and benefit from long-term treatment with a cholinesterase inhibitor. The purpose of this research study is to identify from several tests the best way of predicting response to treatment and hence identifying people that will benefit the most from treatment with a cholinesterase inhibitor. The knowledge that we obtain may also help to treat other types of dementias and develop new drugs that better treat this cholinergic dysfunction.

What does taking part involve?
If you had not been diagnosed with Lewy Body Disease, you will first undergo a screening assessment to ascertain if you can continue to be enrolled. The study design is a double-blind randomised placebo-controlled crossover trial. This means you will be randomly assigned (like flipping a coin) to receive either donepezil (a cholinesterase inhibitor) or a placebo for a certain period of time followed by a period when no drug would be given before switching over the other treatment group. For example, if you are given donepezil in the initial period, you will receive placebo in the later stage and vice versa. Both donepezil and placebo will look the same; hence, both you and the researchers will not know at any point

during the study whether you are receiving active treatment or placebo. The study will be divided into several phases. In the initial phase, a researcher will conduct an interview (usually at your home) and ask questions about your thinking abilities, mood, daily function and movement as well as do some thinking and memory tests. You will also be invited to have an electroencephalography (EEG or brain wave test) in the hospital. This is to establish how you are at the start of the study. You will then be assigned active treatment or placebo for 8 weeks before stopping treatment for 4 weeks. You will then receive the other treatment for 8 weeks as described above. At the end of each 8-week treatment period, we will conduct an interview (usually at your home, taking less than two hours) and a series of test, which will be described in the following section. We will schedule these tests to be carried out in a single day in the hospital. Some tests will be carried out in the morning and some in the afternoon, with plenty of time for breaks in between. Alternatively, if you prefer the tests to be scheduled over several shorter visits, we can arrange that as well. One final follow-up will be conducted 6 months after the second 8-week treatment period. This final follow-up will only involve an interview at your home with no additional tests. The study flowchart summarises the activities involved in this study.

Electroencephalography (EEG)
This is a record of brain waves, which will be conducted in the laboratory in hospitals and should take approximately 45 minutes. You will be asked to wear a cap on your head with wires attached to it. The wires function as sensors, which will record your brain waves into a computer programme. You will be asked to open and close your eyes for a few minutes throughout the recording and perform a simple task on the computer (like pressing on a right or left button to indicate where majority of arrows are pointing on the computer screen). The procedure is usually well tolerated. Some people experience redness on the scalp, which will be temporary, but it should not cause any pain.

Short latency afferent inhibition (transcranial magnetic stimulation)
This procedure involves stimulating brain activity using a magnetic coil with a concurrent electrical nerve stimulation of one of your hands. A magnetic coil (look like a small metal detector) will be placed on top of your head. Magnetic stimulation is usually well tolerated and should not cause any pain. There may be twitching of the muscles of the neck or jaw during the procedure. Occasionally, people who underwent the procedure may complain of headache, discomfort at the scalp or dizziness later but this is usually mild and short lasting. Very rarely, the procedure had been reported to have caused seizure or hearing disturbance although this seems to have only happened in people who have prior history of seizures. The electrical nerve stimulation of the hand is usually well-tolerated. There may be some discomfort at the stimulation site during the procedure.

Magnetic resonance imaging (MRI)
This is a type of brain scan, which will take around 45 minutes. This brain scan is considered a very safe test. The only possible risk is that it may affect implanted medical devices such as a heart pacemaker. The technician routinely completes a checklist before the scan to ensure you are suitable to undergo the scan.

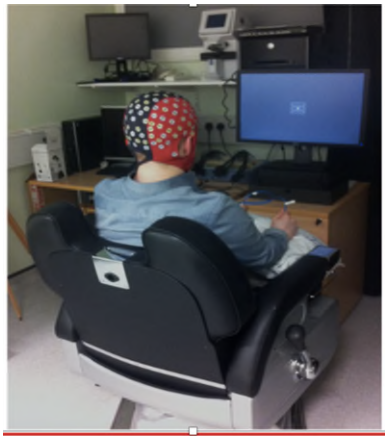
You will be asked to remove all jewellery and loose metal before you go into the scanner. You will be asked to lie still on your back in the scanner. There is padding to make you more

comfortable and you can have a blanket if you feel cold. The scanner can be noisy so you can have protective earplugs or earphones. There is an intercom system and an emergency buzzer if you need to contact anyone during your scan. Experienced staff will be with you at all times.

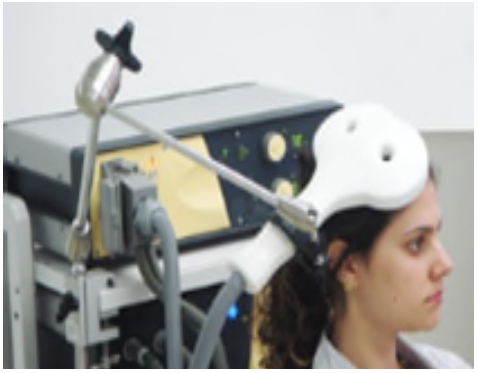
You may be asked to perform several tasks such as looking at some pictures and pushing buttons to answer questions (similar to the EEG task) while your brain scan is being recorded.

Body sensors

This is a wearable device will be attached to you lower back (just above the hip) and secured with an adhesive. The sensors will be worn for seven days at home and will record information on your activity, gait and sleep. The sensors are usually well tolerated and will not interfere with your activities.



Electroencephalography



Transcranial Magnetic Stimulation

Body sensor

Magnetic Resonance Imaging

Gait assessment

Magnetic Resonance Imaging

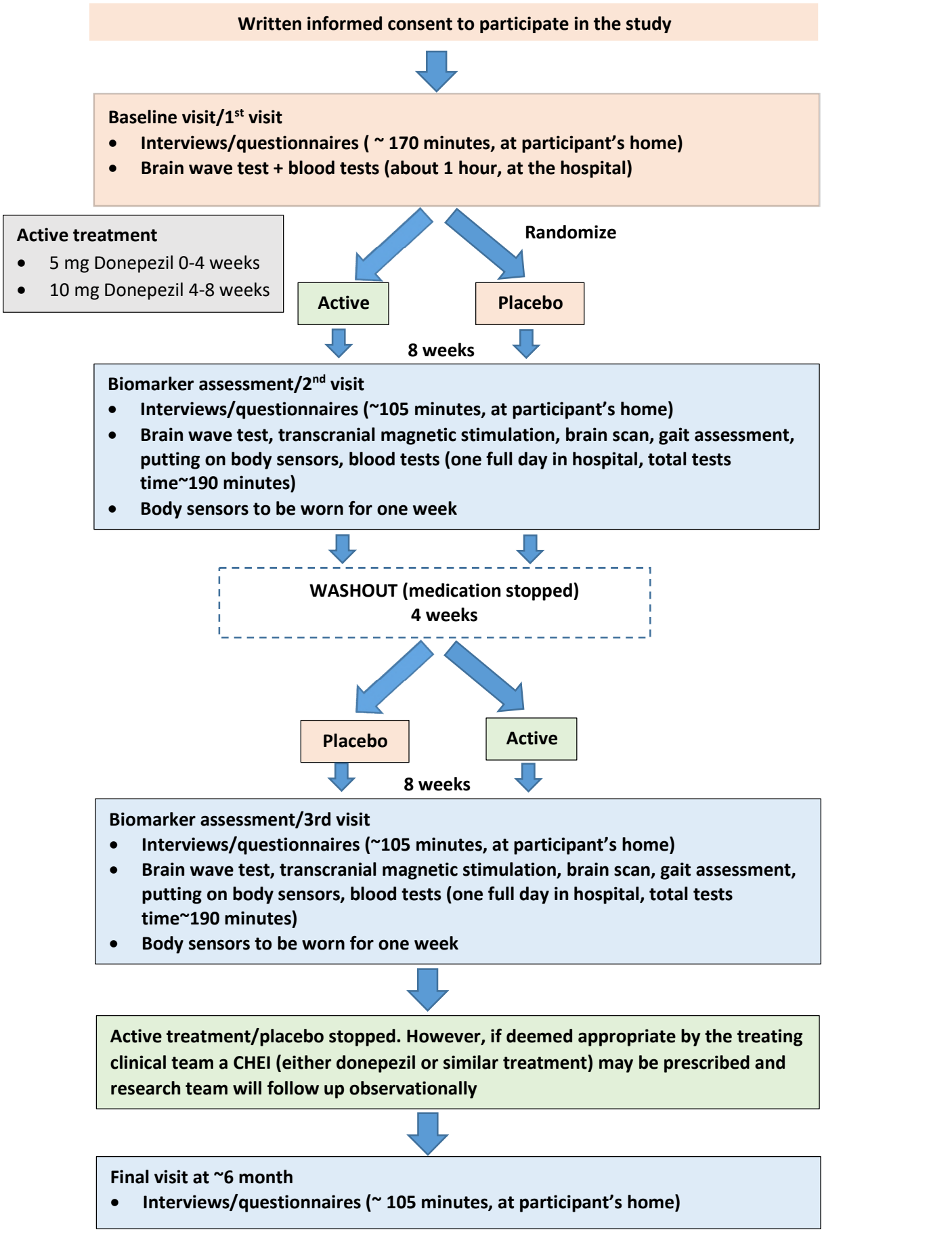
Gait assessment

Gait assessment

This is an assessment of your gait, which will be carried out in the laboratory in hospital. You will be asked to walk on a walkway at a preferred and fast speed in addition to walking while performing mental tasks. We will ask your permission to obtain a video recording of your gait for further analysis. Your facial features will be recognisable from the video. A video helps us to verify the data ad if you agree, we may use it for presentations at conferences or seminars. However, this is not an essential aspect of the assessment and if you would rather not have your video taken this is not a problem.

Blood tests

Approximately 20 mL (one and a half tablespoon) of blood will be drawn from your vein using a sharp needle by a trained member of the study team to check for the levels of donepezil in your blood. The blood samples will also be tested for presence of genes that may have contributed to you developing Lewy Body Disease. In addition, you may agree for your blood samples to be stored long term under the Newcastle University Human Tissue Authority License for future studies involving study of genes (genetics) or proteins (proteomics).This is optional and will not involve additional blood to be drawn. If you are agreeable to have your blood stored for study, you will be asked to provide one urine sample as well.



Study flowchart

What information will be collected and who will have access to the information collected?
If you join the study, authorised individuals may look at relevant sections of your medical notes and data collected in the study from the Newcastle University, the research group and regulatory authorities where it is relevant to this study.

They may also be looked at by representatives of regulatory authorities and by authorised people from the Trust, or other NHS bodies to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity will be disclosed outside the research site.

Our procedures for handling, processing, storage and destruction of patient's data are compliant with the General Data Protection Regulation 2018.

We will use your name and contact details [telephone number, address] to contact you about the research study. We will use your initials, sex and date of birth in our records for identification purpose. Individuals at Newcastle University may look at your research data to check the accuracy of the research study. The only individuals at Newcastle University who will have access to information that identifies you will be individuals who need to contact you to audit the data collection process.

If you agree to take party in the research study, your data will become part of a dataset, which can be accessed by other users running other research studies at Newcastle University and in other organisations. These organisations may be universities or NHS organisations. Your information will only be used by organisations and researchers to conduct research.

Your data will be held in a data repository which other researchers can request access to. This data can be combined with information about you from other sources held by researchers, the NHS or government. Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you. Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

How long will the personal information be kept?
Personally, identifiable information (name, date of birth, address, contact number) will be kept for 3 years. However, anonymised information generated by the research will be kept for up to 20 years.

What are the possible benefits of taking part?
Knowledge learnt from this study may benefit people with mild cognitive impairment or dementia in the future. The results of the tests performed may provide additional information to your doctor, which may help with decisions about your care. You may find that being on

the cholinesterase inhibitor drug that used in the trial helps with your thinking abilities and given that this drug is available in the NHS, this might mean that after the study you can have a discussion with your doctor about potentially starting this drug as part of your treatment.

What are the possible disadvantages and risks of taking part?
You will need to spend some time answering questionnaires and undergoing study procedures. The specific risk of each test is described in the previous section. In addition, it is possible to experience undesirable effects from donepezil. The known undesirable effects of donepezil include common or very common (affects up to one in 10 people): Aggression; agitation; appetite decreased; common cold, diarrhoea, dizziness, fatigue, gastrointestinal disorders, hallucination, headache, injury, muscle cramps, nausea, pain, skin reactions, sleep disorders, syncope, urinary incontinence, vomiting; Uncommon (less than one in 100): Bradycardia, gastrointestinal bleeding, hypersalivation, seizure; rare (less than one in 1000): Cardiac conduction disorders, extrapyramidal symptoms, hepatic disorders, neuroleptic malignant syndrome, rhabdomyolysis.

Expenses
If you agree to take part in this study, we would cover all your travel expenses, and we would, if you wish, arrange transport for you and a relative or friend (by taxi) to come to the hospital and go home. In case you have carer responsibility, we may pay for sitter's expenses.

Will I be informed of the results of the study?
If you wished to be informed of the results of the study, we will send you a lay summary of the results once the study is completed and the results published in a scientific journal.

Who is the sponsor and data controller for this research?
Newcastle upon Tyne Hospitals (NuTH) NHS Trust is the sponsor for this study based in the United Kingdom. Newcastle University will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that Newcastle University is responsible for looking after your information and using it properly.

The lawful basis for carrying out this study under GDPR is Task in the Public Interest, (Article 6,1e) as research is cited as part of the University's duties. The lawful basis for processing any special categories of personal data is Scientific Research (Article 9,2j).

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

You can find out more about how Newcastle University uses your information at https://www.ncl.ac.uk/data.protection/ and/or by contacting their Data Protection Officer [Maureen Wilkinson, rec-man@ncl.ac.uk].

Who is funding this research?
Newcastle NIHR Biomedical Research Centre

Has this study received ethical approval?
This study has received ethical approval from North East – Newcastle & North Tyneside 1 Research Ethics Committee on 28/2/2020.

Whom should I contact for further information relating to the research?

Dr Jahfer Hasoon jahfer.hasoon@ncl.ac.uk; 0191 2083282
Carein Todd carein.todd@ncl.ac.uk; 0191 2081405
Professor John-Paul Taylor john-paul.taylor@ncl.ac.uk; 0191 2081316

Who should I contact in order to file a complaint?
If there are any problems, the study team will do their utmost to resolve them. The NHS will provide indemnity for the study. If you have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms will be available to you. If you require further assistance the NHS Patient Advice and Liaison Service (PALS) is available to you.

PALS for Campus for Ageing and Vitality/Royal Victoria Infirmary:
Tel. 0800 0320202 or web:northoftynepals@nhct.nhs.uk

If you wish to raise a complaint on how your personal data is handled, you can contact the Data Protection Officer who will investigate the matter: Maureen Wilkinson, rec-man@ncl.ac.uk

If you are not satisfied with their response, you can complain to the Information Commissioner's Office (ICO): https://ico.org.uk/