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Understanding Brain Inflammation in Cognitive Problems (BRIC)

Submission date
28/03/2024

Recruitment status
Recruiting

Registration date
09/07/2024

Overall study status
Ongoing

Last Edited
22/08/2024

Condition category
Nervous System Diseases

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

Plain English Summary
Background and study aims
There is evidence that brain inflammation can be involved in a wide range of brain diseases. In this study the researchers are interested in how brain inflammation might play a role in cognitive (thinking) problems. They can measure inflammation in the body using blood tests and specialised brain scans to answer important questions such as:
1. Are cognitive problems associated with brain inflammation?
2. Is brain inflammation associated with the progression of cognitive problems?

Who can participate?
People aged 60 years and over with specific cognitive problems, along with people aged 60 years and over without cognitive problems

What does the study involve?
All participants will have a clinical assessment and blood samples. Some participants will also have a brain scan. The clinical assessment will help the researchers to understand the problems people are experiencing, and if their problems are progressing over time. The brain scan will allow the researchers to measure inflammation in the brain. The blood samples will show how inflammation in the rest of the body affects the brain. Participants will have a further clinical assessment and blood samples annually for 2 years. Participants who had a brain scan will be offered a repeat brain scan after 2 years. The findings of this study could identify brain inflammation as a new treatment target for people with cognitive problems.

What are the possible benefits and risks of participating?
There is no direct benefit from taking part in this study. However, the information from this study may help improve the future treatment of people with cognitive problems.
Participants will have a brain scan looking at inflammation in the brain. This scan uses radiation to form images of the brain. Radiation may cause cancer many years or decades after the exposure. The radiation dose is around four times the amount of radiation received each year from natural background radiation in the environment. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during their lifetime. Taking part in this study will increase the chances of this happening to about 50.04%.

MRI is not safe for people with certain implants, such as cochlear implants and pacemakers. Participants will complete a questionnaire before the scan to ensure there is no reason why they cannot have an MRI scan.
The PET scan involves a small amount of radioactive dye being injected into a vein (usually in the arm or hand). This will feel similar to having a blood test.
PET-MR and MRI scans can be very noisy, but this gives a lot of important information about the brain.

Where is the study run from?
Newcastle University (UK)

When is the study starting and how long is it expected to run for?
February 2020 to September 2029

Who is funding the study?
1. Medical Research Council (UK) (grant number MR/W000229/1)
2. Lewy Body Society (UK)

Who is the main contact?
Dr Paul Donaghy, paul.donaghy@ncl.ac.uk

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
305370

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 305370, CPMS 54263

Study information

Scientific Title
Understanding Brain Inflammation in Cognitive Problems (BRIC)

Acronym
BRIC

Study hypothesis
1. Mild cognitive impairment with Lewy bodies (MCI-LB)/mild dementia with Lewy bodies (DLB) will be associated with increased 18F-DPA714 binding, which will be associated with more rapid disease progression.
2. 18F-DPA714 binding will decline over time in MCI-LB/mild DLB.
3. MCI-LB/mild DLB will show an altered peripheral inflammatory profile at baseline compared to controls.
4. Alterations in immunosenescent markers at baseline will be associated with more rapid disease progression in MCI-LB/mild DLB.
5. More frequent occurrence of peripheral pro-inflammatory events (e.g. infections, surgery) will be associated with increased pro-inflammatory cytokines and more rapid disease progression in MCI-LB/mild DLB.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 15/11/2022, Wales REC 7 (St David's Park, Carmarthen, SA31 3HB, United Kingdom; +44 (0)2922 941107; Wales.REC7@wales.nhs.uk), ref: 22/WA/0312

Study design
Longitudinal observational case-control study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital, University/medical school/dental school

Study type(s)
Other

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

Condition
Dementia with Lewy bodies

Interventions
At the initial baseline assessment, consent and clinical assessment will be carried out over two visits, each taking 1-2 hours. This will include a blood test. Most participants will have brain scans (a combined PET and MRI scan, or separate PET and MRI scans on different days, each taking 1-1.5 hours).

Follow-up will take place annually for 2 years. After 1 year, the researchers will contact study volunteers to see if they are happy to have an appointment to repeat some of the assessments, have a blood sample and repeat the questionnaires with a relative/friend, taking 1-2 hours.

After 2 years, the researchers will contact study volunteers to see if they are happy to have repeat brain imaging, clinical assessment, questionnaires and a repeat blood sample, taking 1-2 hours.

Intervention Type
Other

Primary outcome measure
Brain Mitochondrial Translocator Protein (TSPO) is measured by 18F-DPA714 binding (mean cortical and regional) at baseline and 2 years

Secondary outcome measures
1. Peripheral blood inflammatory profile is measured by flow cytometry of cells and analysis of inflammatory markers at baseline, 1 year and 2 years
2. Cognition is measured using the Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) at baseline, 1 year and 2 years
3. Global functional impairment is measured using the Clinical Dementia Rating Scale Sum of Boxes at baseline, 1 year and 2 years

Overall study start date
01/02/2020

Overall study end date
01/09/2029

Eligibility

Participant inclusion criteria
MCI-LB/DLB group:
1. Age ≥60 years
2. Fulfil criteria for probable MCI-LB (McKeith et al., 2020) or DLB (McKeith et al., 2017)
3. Capacity to consent to participation in the study
4. MMSE ≥20
5. If on cholinesterase inhibitors and/or memantine, stable dose for 3 months

Control group:
1. Age ≥60 years

2. MMSE ≥27
3. No evidence of mild cognitive impairment or dementia

Participant type(s)
Healthy volunteer, Patient

Age group
Adult

Lower age limit
60 Years

Upper age limit
120 Years

Sex
Both

Target number of participants
110

Participant exclusion criteria
1. Active systemic inflammatory disease
2. Active autoimmune disease
3. Taking immune system modifying medications (e.g., oral steroids or tumour necrosis factor inhibitors)
4. Taking incretin analogues (e.g., liraglutide), minocycline or other microglial suppressing agents
5. History of clinical stroke
6. Current major depression
7. History of bipolar disorder, non-organic psychosis (e.g., longstanding schizophrenia) or recurrent severe depression
8. Chronic migraine

Recruitment start date
14/02/2024

Recruitment end date
14/08/2027

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital,

Freeman Road,
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Southern Health NHS Foundation Trust
Tatchbury Mount Hospital
Calmore
Southampton
United Kingdom
SO40 2RZ

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

Sponsor details
Newcastle Joint Research Office
Level 1, Regent Point
Regent Farm Road
Gosforth
Newcastle upon Tyne
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United Kingdom
NE3 3HD
+44 (0)191 233 6161
nuth.nuthsponsorship@nhs.net

Sponsor type
Hospital/treatment centre

Website
https://www.newcastle-hospitals.nhs.uk/contact-us/

ROR
https://ror.org/05p40t847

Funder(s)

Funder type

Government

Funder Name
UK Research and Innovation Medical Research Council

Alternative Name(s)
UKRI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Lewy Body Society

Results and Publications

Publication and dissemination plan
The results from this research will be shared with the wider research community through publication in high-impact journals in the fields of clinical medicine and medical imaging, and presentation at international conferences. The researchers will seek to disseminate their findings to the public through local, regional and/or international meetings.

Intention to publish date
01/03/2028

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository (https://www.dementiasplatform.uk/)

IPD sharing plan summary
Stored in non-publicly available repository