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The role of the immune system in early Lewy Body and Alzheimer's disease

Submission date	Recruitment status	[_] Prospectively registered
01/06/2022	Recruiting	[X] Protocol
Registration date	Overall study status	[_] Statistical analysis plan
28/06/2022	Ongoing	[_] Results
Last Edited	Condition category	[_] Individual participant data
03/12/2025	Mental and Behavioural Disorders	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Inflammation is the process by which the immune system (white blood cells and other proteins) work to protect the body from things that may harm it. Whilst this is important to protect the body, in some instances, the inflammation itself can be too extreme or continue for too long and become harmful rather than helpful. There is now increasing evidence that neuroinflammation (inflammation in the brain) is associated with conditions that affect memory, such as dementia or mild cognitive impairment. This study will collect blood, urine, saliva, and spinal fluid samples in people with mild cognitive impairment, Alzheimer's disease and Lewy body dementia as well as similarly aged healthy volunteers to look for evidence of inflammation and other biological markers. These immune changes will be explored to identify what differences there are between those with memory difficulties and those without, the impact on symptoms and their progression, and how the immune markers change over time.

Who can participate?
People aged 50 and over with early memory problems and without significant medical, psychiatric, or inflammatory illnesses, along with healthy controls

What does the study involve?
Participating in this research involves a number of different steps. We hope that everyone will be able to complete all steps, but we realize that this may not always be possible. The steps include: A medical assessment, psychology tests (on paper or a computer), a blood test, a urine sample, and a sample of your saliva, all participants with capacity to consent will be offered the option to undergo cerebrospinal fluid sampling by a lumbar puncture, follow-up visits involving physical examination and cognition (thinking and memory tests); we hope to see you again for follow-up visits at 18 months and once a year for up to 3-years. The practicality of these visits will be discussed on an individual basis.

What are the possible benefits and risks of participating?
This is not a trial of any drug or other treatment and there is no direct benefit to you from taking part in this study. However, if you do take part, you will be making a significant contribution to medical knowledge and especially to the challenge of better understanding dementia and other illnesses that lead to a deterioration of the brain. If you decide to take part in this study, we

would cover your travel expenses or arrange transport if required. The tests are safe but could be tiring. We will give you as much time as you need to complete the psychology tests. The blood test is an ordinary blood test and will be done by a trained member of staff. For the lumbar puncture, we use a local anaesthetic to minimise the pain of the procedure, but it can sometimes still be uncomfortable during the test. Some people experience a headache after the procedure that can last up to a week.

Where is the study run from?
Addenbrookes Hospital (United Kingdom)

When is the study starting and how long is it expected to run for?
January 2021 to December 2027

Who is funding the study?
Medical Research Council (United Kingdom)

Who is the main contact?
Dr Peter Swann
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Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
297391

Central Portfolio Management System (CPMS)
50597

Study information

Scientific Title
Immune profiling in early cognitive disorders

Acronym
IMPRINT v1

Study objectives
There is a specific innate immune signature in early Alzheimer's disease (AD) and dementia with Lewy bodies (DLB). This signature is associated with accelerated disease progression. The signature profile changes as the disease progresses.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/12/2021, North West - Preston Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 (0)207 1048206; mark.thompson@hra.nhs.uk), ref: 21/NW/0314

Study design
Non-randomized interventional cohort study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Dementias and Neurodegeneration

Interventions
IMPRINT is a longitudinal study of early neurodegenerative cognitive disorders, with patients and healthy control volunteers. We will undertake blood, saliva, urine and CSF sampling together with clinical and cognitive assessment at baseline and 18 months later in people with early AD and DLB, including the prodromal (i.e. mild cognitive impairment; MCI-AD and MCI-DLB) and mild dementia stages, as well as in similarly aged healthy controls. Further clinical and cognitive follow-up, up to 3 years, will be undertaken to determine the impact on longer-term disease progression.

Demographic/clinical interview: Participants will be interviewed on socio-demographic and lifestyle factors, and family history of AD/dementia in first-degree relatives, medical history and medication.

Clinical assessment: Participants will be assessed with a physical examination of movement, coordination and reflexes as well as using clinician-administered scales. Participants will also complete self-reported scales of depression, anxiety, mood, sleep quality and language abilities.

Neuropsychological assessment: Participants will be assessed on memory, attention, vision and language using paper and pencil or computer assessment.

Venepuncture: Up to 80 ml (4 tablespoons) of blood will be taken. This will be used for routine blood tests (haematology, clinical chemistry and coagulation parameters), and for genetic, chemical and biomarker analysis.

Saliva: Saliva will be collected in a resting, unstimulated state by drooling into a 50 ml collection vial with the head tilted forward, allowing the saliva to accumulate in the mouth. 5-20 ml will be collected following a one-hour period of not eating or drinking.

Urine: 20-30 ml of midstream urine will also be collected in sterile containers.

CSF: Lumbar puncture will be offered to participants who can decide for themselves (i.e. have the capacity to consent). Up to 10 ml of CSF will be taken. This will be used for biomarker analysis and will be performed using a small caliber needle in either a sitting or lying on the side position. CSF is obtained via gravity flow into polypropylene tubes.

Intervention Type
Other

Primary outcome(s)
Comparison of blood and cerebrospinal fluid (CSF) immune signatures to include proportions of immune cell subsets (monocytes, dendritic cells, granulocytes, and lymphocytes) measured by the mass cytometry time of flight in between groups (mild cognitive impairment [MCI] with Lewy body and dementia with Lewy bodies, MCI-Alzheimer’s disease [AD] and AD and controls) at baseline

Key secondary outcome(s))
1. Association between baseline immune signatures and:
1.1. Change in cognitive decline over time (ACE-III and other measures) Addenbrookes measured using the Cognitive Examination revised (ACE-R) test, ACE-III test, Montreal Cognitive

Assessment test, Rey Auditory Verbal Learning Task, Trails A&B test at baseline and 18 months
1.2. Change in functional decline over time measured using the Bristol Activities of Daily Living Scale at baseline and 18 months
1.3. Progression from mild cognitive impairment to dementia measured using the Clinical Dementia Rating Scale at baseline and 18 months
1.4. Progression in non-cognitive symptoms:
1.4.1. Baseline and motor function measured using the Unified Parkinson’s disease rating scale part III scores at baseline and 18 months
1.4.2. Baseline and neuropsychiatric symptoms measured using the Neuropsychiatric inventory total and subscale scores, hospital anxiety and depression scale, geriatric depression scale, Pareidolia noise test and Feeling of Presence scores at baseline and 18 months
1.4.3. Other symptoms, including smell measured using the Brief Smell Identification Test (B-SIT), colour discrimination measured using the Farnsworth D-15 colour test, fluctuations measured using the Dementia cognitive fluctuations scale and Clinician Assessment of fluctuations at baseline and 18 months
1.5. Difference in proportions of immune cell subsets, including monocytes, dendritic cells, granulocytes, and lymphocyte subsets, measured using the mass cytometry time of flight at baseline and 18 months, and the association between these differences and the above scales

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. Diagnosis of:
1.1. Early Alzheimer's disease (including MCI or mild AD dementia)
1.2. Lewy body disease (including MCI-Lewy body type or mild DLB)
2. Cognitively normal for age and education with MMSE >26
3. Sufficient grasp of the English language to permit meaningful cognitive testing

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Severe dementia so as to be unable to comply with study procedures or MMSE< 12
2. Concurrent major psychiatric illness, severe physical illness or comorbidity that may limit ability to fully participate, including inflammatory medical conditions or taking

immunosuppressants (including oral steroids).
3. Absence of reliable informant (for patients)
4. Women who are pregnant or who are breastfeeding
5. Severe impairment of vision or hearing that would make assessments difficult
6. REM sleep behaviour disorder and/or late onset depression/anxiety (healthy control group only)

Date of first enrolment
22/06/2022

Date of final enrolment
30/06/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Cambridge
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Study participating centre
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Sponsor information

Organisation
Cambridgeshire and Peterborough NHS Foundation Trust

ROR
https://ror.org/040ch0e11

Organisation
University of Cambridge

ROR
https://ror.org/013meh722

Funder(s)

Funder type
Government

Funder Name
Medical Research Council; Grant Codes: MR/T033371/1

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in the non-publicly available Dementia Platform's UK repository, where researchers can apply for access

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		21/11/2025	03/12/2025	Yes	No
HRA research summary			28/06/2023	No	No