ISRCTN17419165 https://doi.org/10.1186/ISRCTN17419165

Permeability of the blood-brain barrier in Alzheimer's disease

Submission date
08/04/2024

Recruitment status
No longer recruiting

Registration date
21/05/2024

Overall study status
Ongoing

Last Edited
18/08/2025

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
The causes of Alzheimer's disease (AD) are poorly understood. Infections can cause symptoms to worsen for people with AD. Infections activate the immune system in the blood, a process called inflammation. Inflammation can send signals to the brain that cause damage to nerve cells, leading to worsening memory. How this signal enters the brain could explain why some people with AD decline faster than others.

The blood-brain barrier is a lining around the blood vessels in the brain. It is an important structure that protects the brain from inflammation in the blood. However, several studies have shown that the blood-brain barrier may be leakier in people with AD.

Using a brain scan technique we can measure how leaky the blood-brain barrier is. We do this by measuring the movement of an injected dye from the blood into the brain. Our team will recruit 50 people with AD and 20 people without dementia into a research study. Participants will have blood and urine tests to measure their levels of inflammation. We will explore how leaky the blood-brain barrier is in people with AD. We will also study how blood-brain barrier leakiness and inflammation contribute to how quickly people with AD decline over two years.

This research will improve our understanding of the factors that cause worsening symptoms for people with AD. It will also help to identify whether our brain scan could predict those people with AD whose symptoms may decline faster.

Who can participate?
Patients with AD, and healthy participants, aged over 50 years.

What does the study involve?
Participants will undergo a brain scan, clinical assessments and provide blood and urine samples. Participants with AD will be reviewed once yearly for two years.

What are the possible benefits and risks of participating?
We do not expect there to be any direct benefits to participants by taking part in this study. However, participants may feel satisfaction in knowing that their participation in the study will

improve our current understanding of the causes of Alzheimer’s disease. The MRI brain scan that participants undergo will be reviewed by a radiologist and they will be informed of any important findings, if they chose.

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

When is the study starting and how long is it expected to run for?
November 2023 to February 2028

Who is funding the study?
Alzheimer's Society (UK)

Who is the main contact?
claire.firth@southernhealth.nhs.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
330286

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 59059, IRAS 330286

Study information

Scientific Title
Blood-brain barrier permeability, inflammation, and clinical progression in Alzheimer's disease

Study objectives
Blood-brain barrier permeability will be altered in people with Alzheimer’s disease, and when combined with markers of inflammation, will predict the rate of clinical progression over two years.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 13/11/2023, Wales Research Ethics Committee 7 (Castlebridge 4, 15-19 Cowbridge Rd E, Cardiff, CF11 9AB, United Kingdom; +44 2922 940968; Wales.REC7@wales.nhs.uk), ref: 23/WA/0308

Study design
Observational cohort study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Alzheimer's disease, dementia

Interventions
At the start of the study, all participants will be given information about the study by a researcher. The researcher will also answer any questions about the study. If they are happy to take part, the participant will be asked to sign a consent form. All participants will have a clinical assessment that involves talking to a nurse or doctor, having a brief physical examination, and completing some memory tests. They will also be asked to provide a blood and urine sample. For people with AD, their study partner will also be asked some questions about what symptoms are present and how severe they are. Participants will be offered breaks and refreshments if they feel tired. On the same day, or within 1 week if required, all participants will attend Southampton General Hospital for an MRI brain scan. This scan will involve injection of a small amount of dye into a vein. The participant will need to lay in a scanner for about 45 minutes. Participants will be offered headphones with music and an eye mask for comfort. In total, all procedures during this study visit will be completed within 5 hours (including transport for 30 minutes to the brain scan).

All participants with AD will then be assessed again after one and two years, with the same format as above apart from the brain scan. These study visits will be completed within 3 hours. The purpose of these visits is to measure any changes that have happened in memory, thinking, and other symptoms of dementia. We will calculate how quickly symptoms have become worse after one and two years. Travel expenses (including taxis) will be offered to all participants for

all visits. The blood and urine tests taken at the study visits will be used to measure how inflammation changes over two years. The brain scan includes measurement of the amount of dye that moves from the blood into the brain. We will use information from the memory tests, brain scan, blood test, and urine test to answer our study aims.

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
Blood-brain barrier permeability is measured using dynamic contrast-enhanced MRI at baseline

Key secondary outcome(s))
1. Inflammation is measured using single molecule array assays on plasma and mass spectrometry on urine, at baseline, 1 year and 2 years
2. Cognition is measured using the Addenbrooke's Cognitive Examination (ACE) and Montreal Cognitive Examination (MoCA), at baseline, 1 year and 2 years

Completion date
22/02/2028

Eligibility

Key inclusion criteria
1. Age > 50 years old, no upper limit.
2. Able and willing to give informed consent for participation in the study at baseline.
3. AD participants: meet international consensus criteria for a diagnosis of AD dementia or mild cognitive impairment secondary to AD.
or
Control participants: no cognitive impairment and a MoCA score greater than, or equal to, 26 at baseline.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 years

Sex
All

Key exclusion criteria

1. Lack capacity to provide informed consent at baseline or decline to participate.
2. Not proficient in English language.
3. Absence of a reliable study partner (AD participants only).
4. Diagnosis of mixed dementia or another central nervous system disease (e.g. multiple sclerosis, stroke).
5. Intercurrent acute kidney injury, infection, or delirium.
6. History or presence of major psychiatric disorder or alcohol/substance misuse, within the last two years.
7. Diagnosis of any severe inflammatory disorder (e.g. rheumatoid arthritis, periodontitis, inflammatory bowel disease, chronic/recurrent gingivitis).
8. Use of non-topical steroids or cytokine modulators.
9. Previous brain imaging showing confluent white matter changes reflective of gross cerebrovascular disease.
10. Impaired renal function that absolutely contraindicates contrast-enhanced MRI (eGFR < 40).
11. Any contraindication for MRI (e.g. claustrophobia, implanted MR-unsafe metalwork, known hypersensitivity to contrast agent).

Date of first enrolment
22/12/2023

Date of final enrolment
01/10/2025

Locations

Countries of recruitment
United Kingdom

England

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

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
University of Southampton

ROR
https://ror.org/01ryk1543

Funder(s)

Funder type
Charity

Funder Name
Alzheimer's Society

Alternative Name(s)
alzheimerssoc

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

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 a publicly available repository (University of Southampton Institutional Repository https://eprints.soton.ac.uk/). Data will include anonymised clinical information, DCE-MRI data, and inflammation data. The decision to supply research data to a potential new user will be made by the chief investigator in conjunction with the Legal Services Team at the University of Southampton. The University's current policy is for data sharing requests to be forwarded to the University's Legal Services Team for prior background checks, and in case the chief investigator is no longer available. If research data is shared, then external users will be bound by data sharing agreements.

IPD sharing plan summary

Stored in publicly available repository, Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes