ISRCTN18150075 https://doi.org/10.1186/ISRCTN18150075

Imaging lithium in Alzheimer's disease

Submission date
21/11/2025

Recruitment status
No longer recruiting

Registration date
02/12/2025

Overall study status
Completed

Last Edited
17/02/2026

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
Lithium has long been used as a treatment for mood disorders and evidence suggests that it has neuroprotective effects (it protects the brain from harm), increasing grey matter volume and lowering the risk of dementia. In Alzheimer’s disease, early reports suggest that lithium slows the progression of the condition, even at low doses. Researchers have developed a way of safely measuring the levels of lithium in the brain. This may be very useful in future studies looking to use lithium as a treatment for Alzheimer’s disease. Using this advanced magnetic resonance imaging (MRI) scan, they will measure where lithium goes to in the brain. The lithium images will be combined with standard MRI scans to better understand the effects of lithium on the brain at different doses. This study will also see if these effects differ between healthy people and those with dementia. This will guide the choice of dose for future treatment trials and help understand how easy it is for people with dementia to undergo lithium brain scanning.

Who can participate?
Adult patients with Alzheimer’s disease and adult healthy volunteers.

What does the study involve?
Participants will each take lithium at two different doses for one week per dose (two weeks of taking lithium in total) and have 3 MRI scans, each one week apart.

What are the possible benefits and risks of participating?
Benefits: While there are no direct benefits from participating in this research, this study may lead to future trials investigating novel treatments for dementia. People with Alzheimer's disease are often motivated to participate in medical research as they want to contribute to work to improve the lives of people with dementia in future.

Risks:
- Lithium administration and monitoring: This study involves the administration of low-dose oral lithium to participants in order to assess whether it can be detected after administration in the brain using MRI. Lithium carbonate (Priadel) is generally well tolerated and has been used extensively in the treatment of mood disorders for more than 70 years. Nonetheless, participants will be exposed to a greater risk by taking the medication than they would were they not participating in the study - namely the risk of side effects from short term lithium administration. The majority of side effects from lithium are dose-dependent (and therefore less

likely with the doses used in this study) and normally mild, tolerable and transient. The risk of side-effects will be minimized by using as low dose as is feasible. A study physician will review subjects and will assess any occurrence of side effects and offer advice and management if needed. No severe or potentially life-threatening adverse events are expected.
- MRI scan process: MRI scanning does not involve ionising radiation and is generally well tolerated, without side effects. MRI scanning does involve a high magnetic field, which can present risks to people with metallic implants. However, risks are minimal provided that they have no contraindications to MRI as listed in the exclusion criteria. Potential risks associated with metallic implants will be mitigated by administration of MRI safety questionnaires at screening and MRI visits and careful screening assessment. The MRI scanning procedure can be uncomfortable as the scanner is loud and participants need to lie still an extended period. To mitigate these issues, ear defenders will be provided, the participant will be monitored in case they want to leave the scanner, and the scan procedure will be limited to no more than one hour.

Where is the study run from?
Newcastle Magnetic Resonance Centre, UK.

When is the study starting and how long is it expected to run for?
August 2025 to April 2026

Who is funding the study?
Alzheimer's Research UK

Who is the main contact?
Dr David Cousins,

Contact information

Type(s)
Scientific, Public, Principal investigator

Contact name
Dr David Cousins

ORCID ID
https://orcid.org/0000-0001-5682-7507

Contact details
Director, Newcastle Magnetic Resonance Centre
Honorary Consultant Psychiatrist, Regional Affective Disorders Service Chair
Campus for Ageing and Vitality
Newcastle upon Tyne
United Kingdom
NE4 5PL
+44(0)191 208 1152
david.cousins@ncl.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)

306317

Central Portfolio Management System (CPMS)
67648

Alzheimer's Research UK grant code
ARUK-PPG2020A-031

Study information

Scientific Title
A 7Li-MRI study of brain lithium distribution in Alzheimer’s disease and healthy controls

Acronym
ILiAD

Study objectives
This is a basic science imaging study involving procedures with human participants and is not a clinical trial. The aim of the study is to investigate whether 7Li can be detected in vivo in the brain in patients with Alzheimer's disease and healthy subjects following a short course (two weeks total) of lithium carbonate.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 16/07/2025, London-Chelsea Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8197; chelsea.rec@hra.nhs.uk), ref: 25/LO/0443

Primary study design
Interventional

Allocation
N/A: single arm study

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Single

Purpose
Basic science

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Dementia and Neurodegeneration, Primary sub-specialty: Dementia; Health Category: Neurological; Disease/Condition: Other degenerative diseases of the nervous system

Interventions
This study is a feasibility study and will follow a longitudinal design using serial 7Li-MRI and structural MRI sequences.

Participant recruitment:
This study will recruit up to 20 subjects: 12 participants with a diagnosis of mild-moderate Alzheimer's disease (diagnosis made by two independent clinicians based on McKhann criteria; MMSE score 16-24) and 8 healthy volunteers (matched on age and sex).

Study design:
The study will proceed in 2 phases.

In study phase 1:
Up to 4 people with Alzheimer's disease will be recruited to complete study phase 1.

- At visit 1, potential participants will attend for informed consent and screening visit. Consenting participants will undergo baseline assessment including a physical assessment, cognitive assessment and blood tests for lithium initiation (renal function, thyroid function, calcium and full blood count).

If suitable for the study, at visit 2, participants will undergo a standard MRI of brain structure including high resolution hippocampal acquisition. Participants will then receive a lower dose of lithium (100mg Priadel once daily) for a period of one week.

- After week one, at visit 3, they will return for an assessment comprising measurement of serum lithium level, rating of lithium side-effects using a validated rating scale (LISERS), and an MRI scan including standard MRI and 7Li-MRI. At the end of this visit, the dose of lithium will be increased (200mg Priadel once daily), continuing for a further week.

After week two, at visit 4, participants will return for repeat investigations (structural MRI, 7Li-MRI, blood sampling and side-effects ratings). Lithium will then be stopped. After a week, participants will be contacted to check on their ongoing wellbeing.

The 7Li-MRI will the analysed to determine if appreciable signal is detected. If it is, the study will proceed to phase 2a. If insufficient signal is detected at the initial low doses, the study will proceed to phase 2b.

In study phase 2a:
- Additional participants (up to 8 patients with Alzheimer's disease and 8 healthy controls) will be recruited for the study, with procedures and doses as per study phase 1.

In study phase 2b:
Additional participants (up to 8 patients with Alzheimer's disease and 8 healthy controls) will be recruited for the study, with procedures as per study phase 1.

- The doses of lithium will be adjusted to 200 mg once daily for the first week, and 300 mg once daily for the second week.

Study conduct:
The study will be conducted in the North East of England by experienced clinical academics making use of established clinical research networks and Newcastle University's Centre for Neuroscience research register to support recruitment. On the basis of previous studies, a recruitment rate of two dementia participants per month is anticipated. MRI scans will be undertaken at Newcastle Magnetic Resonance Centre using a 3T Philips Achieva equipped for multinuclear imaging. 7Li-MRI will be achieved using a CE-marked 1H/7Li dual-tuned radio-frequency coil manufactured by Rapid Biomedical (Rimpar, Germany) and used in our previous studies of bipolar disorder. Clinical assessment and diagnosis will be undertaken by senior psychiatrists; the cognitive assessment and the side-effect ratings will be undertaken by research assistants, psychiatric trainee doctors and psychology interns. Involvement with the study will comprise a total of two weeks of lithium administration, enabling the investigation of each dose of lithium at steady state whilst maximising the likelihood of tolerability and participant retention to the completion of the study. The study team will oversee prescription and monitoring of the lithium for the duration of the study.

Data analysis:
The primary analysis will explore brain 7Li distribution with respect to dose and disease state. Established data processing workflows, developed and published by our group will be implemented by a member of the research team at Newcastle Magnetic Resonance Centre. The analysis permits the quantification of 7Li-MRI signal intensity (proportional to 7Li concentration) in regions of interest, per-participant and group-wise. Standard processing pipelines (such as voxel-based morphometry and FreeSurfer cortical/subcortical segmentation with thickness estimation) for T1W (structural) image analysis, in which we have substantial experience and expertise, will be used for within group and between group comparisons of the effects of lithium on grey matter volume and density. Combined analysis of 7Li-MRI and T1W data will follow our previous multimodal strategy.

Intervention Type
Other

Primary outcome(s)
1. Brain lithium levels measured using 7Li-MRI Signal intensity at 1 and 2 weeks post-lithium initiation

Key secondary outcome(s)

Completion date
30/04/2026

Eligibility

Key inclusion criteria
Healthy subjects
1. Aged 50-80 years old
2. No history of past or present major psychiatric or neurological disorders or mild cognitive impairment

Patients only
1. Aged 50-80 years old
2. Diagnosis of Alzheimer’s disease – made by two independent clinicians based on McKhann

criteria
3. Mild-moderate disease severity (Mini- Mental State Examination score 16-24)
4. No history of bipolar disorder, major depression or other neuropsychiatric conditions aside from Alzheimer’s disease

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
50 Years

Upper age limit
80 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Presence of contraindications to lithium treatment (such as renal failure, epilepsy or psoriasis)
2. Presence of contraindications to magnetic resonance imaging (such as pacemakers and other incompatible implants, claustrophobia)
3. Current treatment with lithium, non-steroidal anti-inflammatory drugs or ACE inhibitors
4. Lack of sufficient understanding of the nature of the study and any hazards of participating in it
5. Lack of ability to communicate satisfactorily with the investigator and to participate in, and comply with the requirements of, the entire study
6. Lack of willingness to give written consent to participate after reading the information and consent forms, and after having the opportunity to discuss the study with the investigator or his delegate
7. Lack of capacity to provide informed consent, as judged by an investigator

Date of first enrolment
08/09/2025

Date of final enrolment
10/04/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Nicholas Hospital (newcastle upon Tyne)
Jubilee Road, Gosforth
Newcastle upon Tyne
England
NE3 3XT

Sponsor information

Organisation
Cumbria Northumberland Tyne and Wear NHS Foundation Trust

ROR
https://ror.org/01ajv0n48

Funder(s)

Funder type
Government

Funder Name
Alzheimer’s Research UK

Alternative Name(s)
Alzheimer's Research Trust, AlzResearchUK, AlzheimersResearch UK, ARUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available