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An observational study of factors influencing age of onset of Alzheimer's disease and disease progression

Submission date
30/08/2017

Recruitment status
Recruiting

Registration date
03/11/2017

Overall study status
Ongoing

Last Edited
13/07/2020

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Alzheimer's disease (AD) is a neurodegenerative condition that results in reduced memory and thinking skills and affects everyday activities, eventually leading to loss of independence. The disease affects approximately 850,000 people in the UK at an estimated cost of 26.3 billion per year, representing a significant personal and economic burden. The most important risk factor for Alzheimer's disease is increasing age, however the condition is also diagnosed in people in their forties and fifties. Early onset Alzheimer's disease (EOAD) is defined as presenting before the age of 65 and late onset Alzheimer's disease (LOAD) after age 65. Currently little is done to understand why patients present with Alzheimer's disease at different ages. It is presumed that very early onset (<55) is associated with genetic mutations (changes in the DNA sequences), however genetic testing is not routinely conducted. Similarly nothing is used to understand why an individual develops late onset Alzheimer's disease. There are no tests available to predict disease course (whether a patient may be likely to decline slowly or rapidly). These factors are important so that advance planning may be conducted more effectively. The aim of this study is to recruit patients with different age of onset; 45-54, 55-64, 65-74 and 75-84 in order to determine if there are blood-based markers or information from their clinical history that may be associated with the age their Alzheimer's disease is diagnosed. Disease progression will be followed from clinical records in order to see if there are blood tests or information within health records that could predict whose condition will progress quickly or slowly. An imaging sub-study, involving 100 participants, aims to look at how good MEG brain imaging is in aiding a specific diagnosis and in predicting how someone's disease will progress.

Who can participate?
Participants aged 45-84 who have a diagnosis of Alzheimer's disease or other form of dementia, Mild Cognitive Impairment (MCI) as well as age and sex matched healthy participants.

What does the study involve?
Participants are asked to attend a one off appointment to provide written consent to indicate they are happy to participate, complete a short health and lifestyle questionnaire and provide one blood sample. The appointment time is approximately 30 minutes. Participants are asked to

allow access to their electronic healthcare records for 10 years to record other conditions that they currently have, or develop over time, and to follow how their condition progresses. In the one-off appointment for healthy participants, they are asked to complete a memory test in order to compare their scores to those obtained from those with Alzheimer's disease, dementia and MCI. The appointment time for healthy controls is therefore approximately 40 minutes. Some participants are invited to have an MEG brain scan in order to see if this type of scan is a good way of confirming diagnosis and also may be used to predict how someone's condition will develop.

What are the possible benefits and risks of participating?
There are no direct benefits from taking part in this study although the information gained may help toward the understanding of the factors associated with the age of onset of Alzheimer's disease and disease progression. This knowledge will benefit research into treating the condition and ultimately benefit patients with Alzheimer's disease in the future. There are no major risks associated with taking part in this research as the main part of this study involves providing a blood sample and completing a questionnaire about your general health. There is a small chance of very mild discomfort and developing bruising after blood sampling but a fully trained phlebotomist, research nurse or clinician will carry out this procedure to minimise this risk.

Where is the study run from?
The study is being run from Ulster University's Northern Ireland Centre for Stratified Medicine based at the Altnagelvin hospital site (UK) with the Western Health and Social Care Trust (UK).

When is the study starting and how long is it expected to run for?
May 2017 to October 2029

Who is funding the study?
1. European Union Regional Development Fund (ERDF) EU Sustainable Competitiveness Programme for N. Ireland & the Northern Ireland Public Health Agency (HSC R&D) (EU)
2. EU's INTERREG VA programme, managed by the Special EU Programmes Body (SEUPB) (EU)

Who is the main contact?
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Type(s)
Public

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Additional identifiers

Integrated Research Application System (IRAS)
223348

Protocol serial number
17/NI/0132 223348, IRAS Project ID: 223348

Study information

Scientific Title
Stratification in Alzheimer's disease

Study objectives
The aim of this study is to determine if there are genetic, biochemical, environmental factors or co-morbidities associated with age of Alzheimer's disease onset in individuals aged 45-54, 55-64, 65-74 and 75-84, and also to determine if there are shared features associated with the level of deterioration within and between patients with different age of onset.

Ethics approval required
Old ethics approval format

Ethics approval(s)
HSC REC B, 24/08/2017, ref: 17/NI/0132

Primary study design
Observational

Study design
Observational longitudinal case-control study

Study type(s)
Quality of life

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

Interventions
This study gathers data from participants who have a diagnosis of Alzheimer’s disease aged 45-54, 55-64, 65-74 and 75-84, as well as age and sex matched controls and those with a diagnosis of MCI or other form of dementia to allow for differential diagnostic biomarkers to be identified within each strata.

Participants with a diagnosis of MCI, Alzheimer's disease or 'other' dementia are identified by memory clinic colleagues within the Western Trust, or respond to advertising materials directly and are invited to participate in the research. After informed consent is received participants are asked to complete a health and lifestyle questionnaire and provide a blood sample, in an appointment lasting approximately 30 minutes.

A range of biological markers (genetic, protein, metabolomic, microbiome) as well as co-morbidities, lifestyle data, sociodemographic measures and educational history are assessed in an effort to generate a wide-ranging database of factors that may influence age of Alzheimer's disease onset. Permission to follow up on participant memory clinic, and other relevant healthcare records, for ten years, in order to determine markers that may be associated with speed of cognitive decline is asked.

A sub-study will determine if Magnetoencephalography (MEG) scanning and other brain imaging techniques aid in accuracy of diagnosis and prediction of disease progression.

Intervention Type
Other

Primary outcome(s)
1. A comprehensive database of blood-based biomarkers, comorbidities and medical history associated with age of Alzheimer's disease onset is asessed using blood based-biomarkers, information from a health and lifestyle questionnaire and from electronic patient notes at baseline (time of recruitment)
2. To assess whether MEG imaging analysis increases specificity of diagnosis and has predictive value with respect to disease progression is measured using magnetoencephalography (MEG) imaging within 6 weeks of baseline (time of recruitment). Predictive value will be measured from 10 year follow up of patient notes.

Key secondary outcome(s)
1. Markers common to age of onset is measured using genetic, proteomic, metabolic and microbiome analysis of blood samples provided at baseline (time of recruitment)
2. Markers associated with rate of cognitive decline is measured using using genetic, proteomic, metabolic and microbiome analysis of blood samples provided at baseline (time of recruitment) correlated with follow up analysis of patient clinical notes annually for 10 years to assess speed of Alzheimer's disease progression

Completion date
01/10/2029

Eligibility

Key inclusion criteria
Inclusion criteria for age of onset Alzheimer's disease patients:
1. Male and female participants
2. Aged between 45-84
3. Diagnosis of Alzheimer's disease (50 aged 45-54, 50 aged 55-64, 50 aged 65-74, 50 aged 75-84)

Inclusion criteria for 'other dementia' group in age of onset study:
1. Male and female participants
2. Aged between 45-84

3. With an ‘other’ diagnosis of dementia (i.e. NOT Alzheimer’s disease) including but not limited to: Vascular Dementia (VaD), Frontotemporal dementia (FTD), Dementia with Lewy Bodies (DLB)

Inclusion criteria for MCI group in age of onset study:
1. Male and female participants
2. Aged between 45-84
3. A diagnosis of Mild Cognitive Impairment (MCI)

Inclusion criteria for apparently healthy cohort in age of onset study:
1. Men and women
2. Aged between 45-84 (50 aged 45-54, 50 aged 55-64, 50 aged 65-74, 50 aged 75-84)

Inclusion criteria for imaging sub study:
1. Men and women
2. Aged 45-84
3. Diagnosis of MCI, Alzheimer’s disease, other dementia and healthy controls (25 per group)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
45 Years

Upper age limit
84 Years

Sex
All

Key exclusion criteria
Exclusion criteria for all age of onset participants:
Participants with a bleeding disorder, for which, blood sampling would not be advisable.

Exclusion criteria for imaging sub study:
1. Participants with a bleeding disorder, for which blood sampling would not be advisable
2. Pregnancy
3. Previous head or neck surgery
4. Suffer from epilepsy or migraine
5. Active implants (pacemaker, neurostimulator, insulin pump, ossicular prosthesis)
6. May have metal fragments in the body
7. Have jewellery/piercings that cannot be removed
8. Suffer from claustrophobia

Date of first enrolment
01/11/2017

Date of final enrolment
01/10/2029

Locations

Countries of recruitment
United Kingdom

Northern Ireland

Study participating centre
Clinical Translational Research and Innovation Centre (C-TRIC)
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Sponsor information

Organisation
Ulster University

ROR
https://ror.org/01yp9g959

Funder(s)

Funder type
Government

Funder Name
European Union Regional Development Fund (ERDF) EU Sustainable Competitiveness Programme for N. Ireland & the Northern Ireland Public Health Agency (HSC R&D)

Funder Name
EU INTERREG VA programme, managed by the Special EU Programmes Body (SEUPB).

Results and Publications

Individual participant data (IPD) sharing plan

The current data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No