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Observation of genotype-phenotype interaction effects on white matter in Alzheimer Disease and Bipolar Disorder

Submission date
15/01/2012

Recruitment status
No longer recruiting

Registration date
27/01/2012

Overall study status
Completed

Last Edited
16/01/2019

Condition category
Nervous System Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The brains of humans consist of grey matter (GM), which contains the nerve cells, and white matter (WM), which contains the nerve fibres and myelin (a fatty sheath which is wrapped around the nerve fibres). White matter is very important for the brain to function, as it helps signals to move between nerve cells and around the brain much more quickly. WM in the brain is vulnerable to a wide range of diseases and injuries. For example, classic diseases of the grey matter, such as Alzheimer's, have been found to lead to damage to the white matter. Additionally, brain scans of people suffering from bipolar disorder have shown more abnormalities in the white matter than the general population. The exact cause of WM damage is still relatively unknown, but recent studies have suggested that genetic factors may make a significant contribution. This study aims to investigate how genetic variation in the gene NRG-1 might be involved in white matter damage in patients with Alzheimer's disease and bipolar disorder, in order to provide further information about the causes of both disorders.

Who can participate?
Adults over 64 years of age who have been diagnosed with Alzheimer's disease or bipolar disorder, and age-matched healthy controls.

What does the study involve?
Participants attend the study centre for three separate visits. On the first visit, patients are interviewed about their health, which is then confirmed using their medical records. On the second visit, participants have a sample of blood taken, and complete a number of questionnaires. On the third visit participants have a brain scan completed in an MRI scanner. The results of these tests are then compared to assess possible white matter damage in the three groups.

What are the possible benefits and risks of participating?
A benefit is that participants will have access to the results of the tests free of charge. There are no risks of participating.

Where is the study run from?
Hospital Santiago Apostol (Spain)

When is the study starting and how long is it expected to run for?
June 2010 to June 2013

Who is funding the study?
Saiotek Research Funding Program (Spain)

Who is the main contact?
Dr Ariadna Besga

Contact information

Type(s)
Scientific

Contact name
Dr Ariadna Besga

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Hospital Santiago Apostol
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Additional identifiers

Protocol serial number
HS/PI2010001

Study information

Scientific Title
Observation of genotype-phenotype interaction effects on white matter in Alzheimer Disease and Bipolar Disorder: a cross-sectional cohort study

Study objectives
1. Neuregulin 1 (NRG-1) might be involved in white matter damage in Bipolar Disorder (BD) and Alzheimers Disease (AD)
2. It is possible to discriminate BD and AD from healthy controls using diffusion imaging and machine learning techniques

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee CEIC Hospital Santiago (Vitoria, Spain), 06/25/2010, ref: HS/PI2010001

Primary study design
Observational

Study design
Cross-sectional cohort study

Study type(s)
Screening

Health condition(s) or problem(s) studied
1. Alzheimer Disease
2. Bipolar Disorder

Interventions
The study involves three visits per patient.

Visit 1: The baseline study visit lasts about two hours and includes: interview of patient, demographic data, diagnoses, medications used, and baseline use of health and social services. The diagnoses and medications are confirmed from medical records provided by the couples. At the beginning of the visit the patients and caregivers are given written and oral information of the study and informed consent for participation will be obtained from each subject or an appropriate surrogate (in the case of patients with AD).

Visit 2 (Week 1): The visit 2 lasts about two hours and includes: Collect blood sample for pharmacogenomic analysis and an evaluation of cognitive, functional, psychological and social domains by:
1. Minimental State Examination (MMSE)
2. Index of Independence in Activities of Daily Living (Katz, Lawton Barthel)
3. Cambridge cognitive examination (CAMCOG)
4. Clinical Dementia Rating (CDR)
5. Global deterioration scale (GDS)
6. Functional Assessment Staging (FAST)
7. Wisconsin (WCST) Trail Making, Stroop, Clock drawing test
8. Positive and negative syndrome scale (PANSS)
9. Young mania rating scale (YMRS)
10. Hamilton rating scale for depression (HDRS)
11. Neuropsychiatric Inventory (NPI).
All caregivers are assessed by the Zarit burden scale.

Visit 3 (Week 2): Image Acquisition consisting of volumetric and diffusion tensor imaging obtained in onsite MRI scanner.

Imaging data will be processed using FSL software for the computation of Fraction of Anisotropy (FA) and spatial normalization. Image analysis methods would detect white matter (WM) anomalies. Moreover, machine learning techniques for feature extraction and classification will be applied to detect locations of discriminative features in FA data. Results of machine learning on image data will be correlated with genetic data for assessing genotypic influence on WM effects.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Correlation between neuregulin 1 (NRG-1) expression and white matter effects in AD and/or BD.

Key secondary outcome(s)
Machine learning based classification of AD / BD / healthy controls using imaging and genetic data.

Completion date
01/06/2013

Eligibility

Key inclusion criteria
All participants:
1. Aged over 64 years
2. Fluency in Spanish

Alzheimer's Disease:
Participants must fulfil the NINDS-ADRDA criteria for probable Alzheimer's disease.

Bipolar Disorder:
Participants must fulfill the DSM-IV’s criteria for bipolar disorder.

Health Controls:
Participants must not have previous memory complaints.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Key exclusion criteria
Significant neurological disease other than AD and BD

Date of first enrolment
01/06/2010

Date of final enrolment
01/06/2013

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Santiago Apostol
Calle Olaguibel 29
Vitoria
Spain
01004

Sponsor information

Organisation
Hospital Santiago Apostol (Spain)

ROR
https://ror.org/023pqj155

Funder(s)

Funder type
Government

Funder Name
Basque Government (Spain) - Saiotek Research Funding Program (code SA-2010/00168)

Funder Name
Spanish Ministry of Science (MICINN) (Spain) - Non-Oriented Research Program (code TIN2011-23823)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2016		Yes	No
Results article	results	16/06/2017		Yes	No