ISRCTN10751858 https://doi.org/10.1186/ISRCTN10751858

Using a combination of brain imaging techniques and biomarkers for early diagnosis of dementia

Submission date
12/02/2018

Recruitment status
No longer recruiting

Registration date
15/02/2018

Overall study status
Completed

Last Edited
15/02/2018

Condition category
Mental and Behavioural Disorders

[X] 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) has been recognized as an epidemic with approximately 50 million people suffering worldwide, and about half a million people in Iran are estimated to have AD. AD is a chronic disease that affects the brain functions, such as memory, and worsens over time. By the time patients currently receive the diagnosis, their disease has already progressed irreversibly. Early diagnosis is therefore the mainstay of focus in scientific research globally as it is believed that earlier diagnosis and earlier clinical interventions offer the best hope. In diagnosing AD, researchers have tended to look for signs in some regions of the brain, such as hippocampus. However, to detect the first disruptions to brain circuitry, techniques that probe the activity of thousands or millions of networked neurons are needed. This provides the biggest clues to detect the steady cognitive decline that is symptomatic of the disease. This study aims to combine brain imaging techniques with high spatial resolution (fMRI) and techniques with high temporal resolution (EEG) to monitor and characterize activity of large-scale network of brain areas across both space and time.

Who can participate?
Adults aged 65-80 with either mild Alzheimer's dementia, mild cognitive impairment or are healthy.

What does the study involve?
Participants undergo a screening assessment to assess their cognitive functions. It includes a variety of different assessments. Participants undergo a second assessment meeting within 12 weeks from the initial screening which includes a rapid visual categorization task in the scanner. They also undergo EEG (a record of brain activity) and MRI imaging. The third assessment is one week after the second screening assessment which includes a rapid categorization task and undergoing EEG and MRI imaging Participants are asked to undergo a lumbar puncture to take a measurement of the spinal fluid biomarkers.

What are the possible benefits and risks of participating?
The study has a great potential to tell us where to look for earliest signs of the disease, and to

help us find where to target for stopping the disease progression. However we are confident that through participation in this study, trial participants are more likely to learn more about their cognition. Participants are also be seen more often and may feel more supported as a consequence of their involvement. The most likely benefits from this study will be experienced by others in the future, if the ICA test becomes part of standard care. The risks of participating in the study are generally low. There is a small chance participants will experience anxiety or fatigue. Prior exploratory testing suggests that the rapid categorisation task (ICA) has a very low risk of epileptic seizure activity. A lumbar puncture is generally a safe procedure and serious side effects are uncommon. The most common side effects are: headaches, which can last for up to a week, swelling and lower back pain where the needle was inserted. These are the most common risks that are widely accepted as associated with a lumbar puncture.

Where is the study run from?
Royan Institute (Iran)

When is the study starting and how long is it expected to run for?
September 2017 to February 2019

Who is funding the study?
Cognetivity Limited (UK)

Who is the main contact?
1. Dr Seyed Mahdi Khaligh-Razavi (Public)
Seyed@cognetivity.com
2. Dr Chris Kalafatis (Public)
chris@cognetivity.com

Contact information

Type(s)
Public

Contact name
Dr Seyed Mahdi Khaligh-Razavi

Contact details
Royan Institute
Banihashem Square
Banihashem Street
Ressalat Highway
Tehran
Iran
19395-4644
+98 21 22306485
Seyed@cognetivity.com

Type(s)
Public

Contact name
Dr Chris Kalafatis

ORCID ID
http://orcid.org/0000-0002-7171-5391

Contact details
Cognetivity Limited
3 Waterhouse Square
138 Holborn
London
United Kingdom
EC1N 2SW
+44 7824 425 854
chris@cognetivity.com

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CGN-1701

Study information

Scientific Title
Employing combined neuroimaging techniques and CSF biomarkers to characterise spatiotemporal dynamics in Dementia and Mild Cognitive Impairment

Study objectives
Task-based multimodal neuroimaging (EEG-fMRI) can be used to differentiate MCI, AD and healthy individuals. Participants at different stages of cognitive impairment will show distinct spatiotemporal brain dynamics that can be diagnostic of the disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Research Ethics Committee Royan Institute, 08/08/2017, ref: IR.ACECR.ROYAN.REC.IR.ACECR.ROYAN.REC.1396.98

Study design
Interventional non-randomised study

Primary study design
Interventional

Secondary study design

Non randomised study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Alzheimer's Dementia, Mild Cognitive Impairment, Mild Cognitive Disorder

Interventions
All study participants including healthy controls undergo the following interventions.

At screening assessment participants undergo the following assessments:
1. Rapid categorisation task- 5-6 minutes on one occasion
2. Addenbrooke's Cognitive Assessment - once only with approximate duration of 30 minutes
3. Montreal Cognitive Assessment - once only with approximate duration of 20 minutes
4. Geriatric Depression Scale - once only with approximate duration of 10 minutes
5. Neuropsychiatric Inventory - once only with approximate duration of 15 minutes
6. Bristol Activities of Daily Living Scale - once only with approximate duration of 15 minutes

The second assessment meeting takes place within up to 12 weeks from initial screening assessment and entail rapid categorisation task that lasts 5-6 minutes. This is expected to be taken up to six times in 30 minutes along with each trial participant is undergoing the EEG or f-MRI imaging. The sequence of MRI and EEG are randomised. The minimum duration between EEG and f-MRI imaging will be at least one week.

The third assessment meeting takes place approximately one week from the second screening assessment and entails a rapid categorisation task that lasts 5-6 minutes. This is expected to be taken up to 6 times in 30 minutes along with each trial participant is undergoing the EEG or f-MRI imaging. The sequence of MRI and EEG is randomised. If a trial participant has undergone an f-MRI on second assessment, he/she undergoes the EEG and vice-versa.

On third assessment the trial participants are asked to undergo a lumbar puncture for Cerebrospinal Fluid Biomarker measurement. The lumbar puncture takes around 30 to 45 minutes and the patient is expected to remain lying down at the hospital for at least another hour under nurse monitoring. Participants who wish not to consent to a Lumbar Puncture are not excluded from the study and undergoes the remaining study assessments.

Intervention Type
Device

Primary outcome measure
1. BOLD responses are measured using fMRI in <12 weeks after screening (i.e. baseline)
2. Neural activity on the skull is measured using electroencephalography (EEG) in <12 weeks after the first screening (i.e. baseline) session, and this will be one week before or after the fMRI

session (in random order)
3. Level of amyloid beta and cis-p-tau-a is measured from the CSF samples for MCI patients at any time, up to three months after the baseline
4. Level of cognitive performance is measured using MoCA, ACE-R, and ICA at the baseline

Secondary outcome measures
There are no secondary outcome measures.

Overall study start date
01/09/2017

Completion date
01/02/2019

Eligibility

Key inclusion criteria
Control group:
1. Addenbrooke's Cognitive Examination (Revised/III) score of above 84
2. Bristol Activities of Daily Living Scale score of "unimpaired" or "mildly impaired"
3. Capacity to understand the information about the study and to give consent to participate
4. Males and females aged between 65-80 years
5. Not currently on medication that may interfere with the study results
6. In good general health
7. Matched for age and education

MCI group
1. A clinical diagnosis of MCI according to ICD-10 criteria, diagnosed by an Old Age Psychiatrist
2. Mini Mental State Examination (MMSE) <28 and > 24
3. Males and Females aged 65-80 years
4. Capable of indicating informed consent for participation

Mild-AD group
1. A clinical diagnosis of Mild-AD according to ICD-10 criteria, diagnosed by an Old Age Psychiatrist
2. Mini Mental State Examination (MMSE) <24 and > 19
3. Males and Females aged 65-80 years
4. Capable of indicating informed consent for participation

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants

30 patients with Mild Alzheimer's Dementia, 30 patients with Mild Cognitive Impairment, 30 Healthy Controls

Key exclusion criteria

Control group
1. Presence of significant cerebrovascular disease ie. History of CVA
2. Major medical co-morbidities e.g. Congestive Cardiac Failure, Diabetes Mellitus with renal impairment
3. Major psychiatric disorder eg. Chronic psychosis, recurrent depressive disorder, generalized anxiety disorder
4. The use of cognitive enhancing drugs e.g. cholinesterase inhibitors
5. A concurrent diagnosis of epilepsy
6. A history of alcohol misuse
7. A history of illicit drug use
8. A history of severe visual impairment, e.g. macular degeneration, diabetic retinopathy, as determined by the clinical team
9. A history of repeated head trauma

MCI group
1. Patients who fulfill criteria for a diagnosis of Mild AD
2. Major medical co-morbidities e.g. Congestive Cardiac Failure, Diabetes Mellitus with renal impairment
3. Major psychiatric disorder eg. Chronic psychosis, recurrent depressive disorder, generalized anxiety disorder
4. The use of cognitive enhancing drugs e.g. cholinesterase inhibitors
5. A concurrent diagnosis of epilepsy
6. A history of alcohol misuse
7. A history of illicit drug use

Mild-AD group
1. Patients who fulfill criteria for a diagnosis of Moderate AD or Other Mild Dementias
2. Major medical comorbidities e.g. Congestive Cardiac Failure, Diabetes Mellitus with renal impairment
3. Major psychiatric disorder eg. Chronic psychosis, recurrent depressive disorder, generalized anxiety disorder
4. A concurrent diagnosis of epilepsy
5. A history of alcohol misuse
6. A history of illicit drug use
7. A history of severe visual impairment, e.g. macular degeneration, diabetic retinopathy, as determined by the clinical team
8. A history of repeated head trauma
9. MMSE scores less than 19
10. Presence of Sleep Apnoea

Date of first enrolment

01/03/2018

Date of final enrolment

01/10/2018

Locations

Countries of recruitment
Iran

Study participating centre
Royan Institute
Banihashem Square
Banihashem Street
Ressalat highway
Tehran
Iran
19395-4644

Sponsor information

Organisation
Cognetivity Limited

Sponsor details
3 Waterhouse Square
138 Holborn
London
United Kingdom
EC1N 2SW
+44 7824 425 854
team@cognetivity.com

Sponsor type
Industry

Website
www.cognetivity.com

Funder(s)

Funder type
Industry

Funder Name
Cognetivity Limited

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal. No such additional docs are currently available for publication/pre-print.

Intention to publish date
02/02/2020

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