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Life-style and multi-omics to approach cognitive decline and dementia

Submission date
11/05/2023

Recruitment status
Recruiting

Registration date
16/05/2023

Overall study status
Ongoing

Last Edited
30/05/2023

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
Cognitive impairment and dementia are serious public health problems that affect not only the patients who suffer from them but also their caregivers and family members. It is estimated that between 5 and 8% of the general population aged 60 years old and over suffers from dementia, currently highlighting around 50 million people, and it is expected to reach 82 million in 2030 and 152 million in 2050. Although age is the main risk factor for cognitive decline and dementia, these are not inevitable consequences of aging. In fact, certain pathologies related to lifestyles, such as obesity and type 2 diabetes, are important risk factors for the development and progression of cognitive decline and dementia. Therefore, identifying the biological alterations that precede the onset of dementia, as well as their interaction with modifiable lifestyle factors, may contribute not only to a better understanding of the pathophysiology of cognitive impairment and dementia but also to a more accurate and effective approach to the disease. This study is specifically designed to address the relationship of diet and other lifestyle factors with the biological mechanisms related to cognitive decline and the onset of dementia, in a metabolic approach to this disease. Data on lifestyle, metabolism, microbiota and several molecular information will be integrated to achieve a holistic and detailed vision of the progression of diseases required to carry out a truly personalized precision medicine.

Who can participate?
Patients aged between 45-80 years old with subjective cognitive decline or mild cognitive impairment

What does the study involve?
Participants will be followed for a long time with regular visits every 2 years. These volunteers will attend their visits with clinicians and nutritionists in Spain, starting in 2023 with an expected follow-up up 10 years. The results of this study are aligned with one of the main challenges in health, which is healthy aging and well-being. Not in vain, the WHO has proclaimed the years 2021-2030 as the Decade of Aging, a strategy that allows joining efforts between governments, civil society, international organizations, professionals, academic institutions, the media and the sector around international, catalytic and collaborative action to improve the lives of older people, their families and the communities in which they live.

What are the possible benefits and risks of participating?
It is expected that the results of the project will have a notable social impact, not only on subjects with cognitive impairment but also on those individuals at risk, and that it will also allow citizens to be empowered in their health management decisions, thus improving processes and health care outcomes, reducing associated costs. The identification of mechanisms underlying the development of the disease will contribute to a better knowledge of it, favoring the strategies of health professionals to address the disease, in addition to allowing the identification of possible targets for the design of future preventive strategies. and/or therapeutics for community application but also for the advancement of precision medicine. Beyond the current and future knowledge that this project may generate in the field of research and health care, it has been designed to generate a direct impact on society. For this, the professionals of the Dementia Unit of the HUSJR and the Primary Care Centers will play a fundamental role in the dissemination and empowerment of patients and the target population. Also, the research team will use the usual dissemination channels of the institutions to which the members belong (hospitals, primary care centers, universities, research centers and institutes, etc.) to disseminate knowledge among its professionals. Finally, since civil society is the essential recipient of the knowledge generated, it will be communicated in non-scientific language through the national and international CSOs with which researchers collaborate.

Where is the study run from?
Universitat Rovira i Virgili (Spain)

When is the study starting and how long is it expected to run for?
January 2023 to December 2033

Who is funding the study?
Institute of Health Carlos III (Spain)

Who is the main contact?
Mònica Bulló Bonet, monica.bullo@urv.cat

Contact information

Type(s)
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
003/2023

Study information

Scientific Title
A comprehensive life-style and multi-omics integrative approach to study metabolic processes related to cognitive function, cognitive decline and progression to dementia

Study objectives
Early metabolic abnormalities, partly influenced by dysregulation of circulating metabolites, non-coding RNAs and gut microbiota metabolism, are related to cognitive function and precede cognitive impairment and dementia progression. Some of these metabolic disturbances are influenced by nutrition and other life-style factors and therefore they can potentially be modifiable with appropriate community policies.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/03/2023, Ethical Committee for Research with Medicines (CEIM) of Pere Virgili Health Research Institute (Institut d'Investigació Sanitària Pere Virgili [IISPV]),(Avda, Josep Laporte, 2. Planta 0 – E2 color taronja 43204 Reus, Spain; +34 977 779946; ceim@iispv.cat) Ref. CEIM: 217/2022

Study design
Prospective observational cohort study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Community, Hospital

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Subjective cognitive decline and mild cognitive impairment

Interventions
A prospective observational cohort study will be conducted on over 300 men and women, aged 45-80 years, with subjective cognitive decline (SCD) or mild cognitive impairment (MCI), who attend the Unit of Dementia at the University Hospital Sant Joan (HUSJR). SCD will be considered when normality in all cognitive tests or deficient performance (less than percentile 10 according to NEURONORM) in maximum 2 tests of two different cognitive functions. MCI will

be considered when performance in deficient percentiles (less than percentile 10 according to NEURONORM) in 2 variables within the same function or at least 3 in more than one cognitive function. The Institutional Ethical Committee approved the study protocol and all participants will give their informed consent to the experimental protocol before being included in the study.

Participants recruitment and visits. Participants' eligibility for the study will be determined by a review of the clinical records and by a formal visit by the physicians at the Unit of Dementia.

- Screening visit: The visit will serve to identify inclusion/exclusion criteria more comprehensively. An informed consent form will be given to the volunteer for signing after a detailed explanation of all procedures and the anticipated time commitment.
- Baseline visit: Questionnaires, measurements and sampling will be administered and collected at the baseline visit. This visit will be scheduled according to the routine clinical protocol to facilitate patient participation.
- Follow-up visits: Subjects will be followed during the study duration as part of the clinical routine. Biological samples (blood, urine, feces, saliva), lifestyle data (including sleep patterns and physical activity) and neuropsychological tests will be collected at baseline and every 2 years during the follow-up.

A battery of neuropsychological tests assessing orientation, attention, language, praxis, learning memory and executive function will be administrated. This battery will include the Mini-Mental State Examination (MMSE), the Spanish version of the Yesavage abbreviated questionnaire (GDS), the Hospital Anxiety and Depression Scale (HADS), the Rami Cognitive reserve questionnaire (CRQ), the Subjective Cognitive Impairment Questionnaire (SCD-Q), the Activities of Daily Living (ADL) scale, Direct and inverse digits (Test Barcelona), WAIS-III, TMT-A and TMT-B, Symbol Digit Modality test, Boston Naming Test (abbreviated version), a semantic and phonological verbal fluency test, Rey–Osterrieth complex figure, Barcelona-II), Free and cued selective reminding test (Buschke), and the Clock Drawing Test.

Intervention Type
Not Specified

Primary outcome measure
Cognitive decline measured by a battery of neuropsychological tests assessing orientation, attention, language, praxis, learning memory and executive function (Mini-Mental State Examination (MMSE), the Spanish version of the Yesavage abbreviated questionnaire (GDS), the Hospital Anxiety and Depression Scale (HADS), the Rami Cognitive reserve questionnaire (CRQ), the Subjective Cognitive Impairment Questionnaire (SCD-Q), the Activities of Daily Living (ADL) scale, Direct and inverse digits (Test Barcelona), WAIS-III, TMT-A and TMT-B, Symbol Digit Modality test, Boston Naming Test (abbreviated version), a semantic and phonological verbal fluency test, Rey–Osterrieth complex figure, Barcelona-II), Free and cued selective reminding test (Buschke), and the Clock Drawing Test) at baseline and every 2 years during the follow-up.

Secondary outcome measures
Secondary outcome measures are assessed at baseline and follow-up:
1. Circulating and fecal metabolites measured using (multi-omics platform) gas chromatography-high-resolution mass spectrometry (GC-HRMS), liquid chromatography (LC)-HRMS and proton nuclear magnetic resonance (H-NMR)
2. Non-coding RNA measured using rt-PCR/RNAseq
3. Gut and salival microbiota measured using 16S, metagenomics
4. Markers of vulnerable aging i.e., inflammation, oxidation, and other specific markers

measured with appropriate methodologies accordingly i.e., ELISA, MAGPIX)
5. Brain metabolism and structure measured using 18F-FDG-PET, CT-scan, NMR
6. Lifestyle, environmental factors and cognitive tests measured using specific questionnaires such as food frequency questionnaire (FFQ), healthy lifestyle scoring (HLS), quality of life (QoL), and actigraphy with ActiGraph ActiLife
7. Genetics and epigenetics tags measured using RT-PCR, methylation kit, sequencing-Illumina
8. Proteomic and transcriptomic analyses measured using external platforms and services

Overall study start date
01/01/2023

Completion date
31/12/2033

Eligibility

Key inclusion criteria
1. Men and women aged between 45-80 years old
2. Mini-Mental State Examination (MMSE) ≥ 26, hospital anxiety scale ≤ , hospital depression scale ≤ 11

Participant type(s)
Patient

Age group
Mixed

Lower age limit
45 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
300 initially, expected to extend up to 1000

Key exclusion criteria
1. Mini-Mental State Examination (MMSE) <26 or inability to give informed consent
2. Diagnosis of dementia
3. Presence of depressive symptoms (Geriatric Depression Scale ≤5)
4. Major medical or psychiatric condition
5. Evidence of impairment due to psychoactive drugs
6. Alcohol or drug abuse
7. Inability to perform imaging studies (i.e.CAT, MR)
8. Other conditions under the neurologist criteria

Date of first enrolment

01/06/2023

Date of final enrolment
31/12/2030

Locations

Countries of recruitment
Spain

Study participating centre
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Sponsor type
Research organisation

Website
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ROR
https://ror.org/01av3a615

Funder(s)

Funder type
Government

Funder Name
Instituto de Salud Carlos III

Alternative Name(s)
SaludISCIII, InstitutodeSaludCarlosIII, Instituto de Salud Carlos III | Madrid, Spain, Carlos III Institute of Health, Institute of Health Carlos III, Carlos III Health Institute, ISCIII

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Results and Publications

Publication and dissemination plan
1. Planned publication in a high-impact peer-reviewed journal
2. Press Releases on the project start
3. Information on the study is displayed on the websites of the researcher's related institutions and patient organisations
4. Set of materials developed (e.g. leaflets, posters, news, videos etc.) for dissemination at conferences and social media
5. Personal training and supervision plans for the early career researcher
6. Compiled Press Releases on selected results

Intention to publish date
31/12/2034

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the study PI, Mònica Bulló, monica.bullo@urv.cat. All available data can be shared under the request following the data sharing rules. The timing for availability is undefined. Written informed consent is required for all participants before starting the study. Data anonymization is encoded as requested by the Institutional Data Protection Office.

IPD sharing plan summary
Available on request