IMAP+ - Longitudinal Study on Multimodal Imaging for Early-Stage Alzheimer's Disease: Biomarkers for Detection and Progression and Physiopathological Mechanisms

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General

Identification

Detailed name	Longitudinal Study on Multimodal Imaging for Early-Stage Alzheimer's Disease: Biomarkers for Detection and Progression and Physiopathological Mechanisms
Sign or acronym	IMAP+
CNIL registration number, number and date of CPP agreement, AFSSAPS (French Health Products Safety Agency) authorisation	CNIL:1238252; CPP 2011-A01493-38

General Aspects

Medical area	Neurology Psychology and psychiatry
Health determinants	Genetic
Keywords	Genetics, early diagnosis, normal ageing, neuroimaging, PET, MRI, fMRI, neuroanatomy, molecular imaging, FDG-PET, Alzheimer's disease, biomarkers, AV45

Scientific investigator(s) (Contact)

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Unit	U1077 Neuropsychologie cognitive et neuroanatomie fonctionnelle de la mémoire humaineÉquipe/activité : Imagerie multimodale des maladies neurodégénératives
Organization	Institut national de la santé et de la recherche médicale - Inserm ; CHU Caen ; Université de Caen ;

Collaborations

Funding

Funding status	Public
Details	French Alzheimer's Association, Alzheimer's Foundation Plan [Fondation Plan Alzheimer] (Alzheimer's Plan 2008-2012), Hospital Clinical Research Programme (ANR LONGVIE 2007), Lower-Normandy Region, French National Institute of Health and Medical Research (INSERM)

Governance of the database

Sponsor(s) or organisation(s) responsible	CHU Caen
Organisation status	Public

Additional contact

Main features

Type of database

Type of database	Study databases
Study databases (details)	Longitudinal study (except cohorts)
Database recruitment is carried out by an intermediary	A selection of health institutions and services
Database recruitment is carried out as part of an interventional study	No
Additional information regarding sample selection.	Healthy subjects will be recruited from advertisements in local newspapers, on websites, during conferences, as well as posting and/or distribution in public places or through word of mouth. Subjects will be invited to attend research centres for the screening visit following recruitment. NORMA subjects will be recruited through correspondence sent to neurologists from

	the French capital, having been diagnosed with familial AD where results demonstrating causal mutation were established. Individuals that meet the selection criteria will be included in the study. Genetic analyses will be performed in Rouen and all other tests will be conducted in Caen. SCI, MCI, MA and SAND patients will be recruited from neurology departments or memory assessment services across various recruitment centres (CHU in Caen, Rennes, Rouen, Lille and Tours). Individuals should be accompanied by someone they know at baseline and subsequent visits. This person, referred to as the "accompanying party" should be quite close to the patient and know them well, i.e. spends at least one day per week with them (spouse, family member, neighbour or friend), as they will be asked questions to better identify disorders. This person should be the same where possible. Only questions regarding the patient's memory disorders, habits and daily activities will be asked. 280 subjects/patients to be included: - 40 young healthy control subjects (18-39 years old) - 40 middle-aged healthy control subjects (40-59 years old) - 40 elderly healthy control subjects (aged 60+) - 50 NORMA subjects (NORMaux Apparentés) - 40 patients with subjective cognitive impairment - 40 patients with mild cognitive impairment (Mild Cognitive Impairment - MCI) - 30 patients with probable Alzheimer's disease (AD) - 15 patients with amnesic syndrome that is not neurodegenerative (SAND).
Database objective	
Main objective	General objective: To study and compare the effectiveness of different in vivo markers to predict cognitive decline in patients at risk of developing Alzheimer's disease through neuroimaging, neuropsychology and biology measures. Secondary objectives: To study: i) Deterioration in NORMA subjects, as well as SCI, MCI, AD and SAND patients compared with healthy subjects of the same age; ii) Deterioration in E4 allele and apolipoprotein E (ApoE) carriers compared to non-carriers; iii) Cerebral and cognitive changes during normal ageing; iv) Progress and dynamics of different biomarkers during follow-up. To study the links between different deterioration profiles (intra-modality comparison and correlation), as well as differences in inter-group progression

	profiles.
Inclusion criteria	Education level equal to 7 years or higher, native language is French, signed informed consent, medical, neurological and neuroimaging tests, as well as neuropsychological diagnostic test battery. Control subjects: normal performance according to age and education level in all diagnostic battery tests. Middle-aged (40-59 years old): no memory complaints. Elderly (aged 60+): living at home, independent, no memory complaints. NORMA (aged 18+) with identified disease, carriers of mutated gene associated with familial early-onset AD, normal performance according to age and education level in all diagnostic battery tests. Patients from memory assessment centres: SCI (aged 50+), no memory complaints, normal performance according to age and education level in all diagnostic battery tests. MCI meeting current amnestic MCI criteria with memory complaints, objective episodic memory deficits, performances in other cognitive functions where memory loss could occur, standard performance for age and education level in assessments of overall cognitive ability, independent in everyday life, no dementia according to DSM-IV criteria and no probable AD according to NINCDS-ADRDA criteria. Alzheimer's patients meeting NINCDS-ADRDA criteria for probable AD with abnormal overall cognitive function and deficits in at least 2 cognitive areas identified by diagnostic battery tests; mild- to moderate-stage AD; accompanying party's signed informed consent. SAND: CHU neurology departments - major episodic memory disorder that may be related to an objective deficit in executive function and standard performance for age and education level in all diagnostic battery tests measuring instrumental function.
Population type	
Age	Adulthood (19 to 24 years) Adulthood (25 to 44 years) Adulthood (45 to 64 years)

	Elderly (65 to 79 years) Great age (80 years and more)
Population covered	Sick population
Gender	Male Woman
Geography area	National
Detail of the geography area	3/4 of patients are from the region.
Data collection	
Dates	
Date of first collection (YYYY or MM/YYYY)	2012
Date of last collection (YYYY or MM/YYYY)	2017
Size of the database	
Size of the database (number of individuals)	< 500 individuals
Details of the number of individuals	280
Data	
Database activity	Current data collection
Type of data collected	Clinical data Declarative data Paraclinical data Biological data Administrative data
Clinical data (detail)	Direct physical measures Medical registration
Details of collected clinical data	Clinical data collected through clinical records only include SCI, MCI, AD and SAND patients.
Declarative data (detail)	Paper self-questionnaire Face to face interview Phone interview
Details of collected declarative data	Neuropsychological tests include self-administered questionnaires, face-to-face interview and initial

	contact by phone.
Paraclinical data (detail)	Imaging: Anatomical MRI, fMRI at rest, active fMRI, FDG-PET and PET AV-45
Biological data (detail)	Biological components (blood and CSF): i) blood test for fibrinolysis markers (tPA, ADAMTS-4); ii) AB40 and AB42 blood tests and AB40, AB42 CSF, tau protein and its phosphorylated form, iii) ApoE genotyping; iv) potential mutated gene sequencing in NORMA subjects
Administrative data (detail)	Civil status, sex, native language, education level
Presence of a biobank	Yes
Contents of biobank	Plasma DNA
Details of biobank content	Components stored at -80°C.
Health parameters studied	Health event/morbidity
Procedures	
Data collection method	Subjects/patients attend 6 examinations lasting approx. 2 hours + one blood sample. All examinations are conducted over a period of approx. 1 month. Subjects/patients are treated by a contact person that monitors and supports them throughout the protocol. Collected data are reviewed in a multimodal meeting. Imaging data quality control results are also reported during this meeting. Collected data are reviewed during a diagnostic commission so that subject/patient results, as well as their enrolment category, can be reported on a case-by-case basis.
Classifications used	NINCDS-ADRDA and DSM IV
Quality procedure(s) used	A diagnostic commission is organised on a monthly basis to report subject/patient neuropsychological results, as well as their enrolment category, on a case-by-case basis. A multimodal meeting is organised on a monthly basis to report quality control results for imaging data. This trial is monitored by a person appointed by the CHU to ensure that exact, complete and reliable data is collected and to provide logistical support to research centres.
Participant monitoring	Yes

Details on monitoring of participants	Elderly healthy subjects, NORMA subjects, as well as SCI and MCI patients are monitored over a period of 36 months Young, middle-aged and AD patients are monitored over a period of 18 months Post-monitoring enrolment after 18 months; all participants will be asked to take all of the baseline tests again in an almost identical fashion: detailed neuropsychological evaluation, blood sample (without genotyping), 2 MRI sessions, FDG-PET at rest and PET-AV45 test. Post-monitoring enrolment after 36 months, elderly healthy subjects, NORMA subjects, as well as SCI and MCI patients will be asked to take the same tests as described for the visit at 18 months.
Links to administrative sources	No

Promotion and access

Promotion

Link to the document	http://www.hal.inserm.fr/docs/00/93/16/85/PDF/MainManuscrit_GC_RLJ_withTables-and-figures.pdf
Link to the document	http://www.em-consulte.com/article/840363/alertePM
Link to the document	http://www.hal.inserm.fr/inserm-00844867
Link to the document	http://www.ncbi.nlm.nih.gov/pubmed/23084083
Link to the document	http://www.ncbi.nlm.nih.gov/pubmed/23152610
Link to the document	http://www.ncbi.nlm.nih.gov/pubmed/24179859
Link to the document	http://www.ncbi.nlm.nih.gov/pubmed/23670109
Link to the document	http://www.nature.com/nrneurol/journal/v9/n6/pdf/nrneurol.2013.21-c2.pdf?WT.ec_id
Link to the document	http://www.ncbi.nlm.nih.gov/pubmed/23631988
Link to the document	http://www.ncbi.nlm.nih.gov/pubmed/23518010
Link to the document	http://www.hal.inserm.fr/inserm-00806868
Link to the document	http://www.ncbi.nlm.nih.gov/pubmed/22796505
Link to the document	http://www.ncbi.nlm.nih.gov/pubmed/22119654
Link to the document	http://www.ncbi.nlm.nih.gov/pubmed/22252372

Access	
Terms of data access (charter for data provision, format of data, availability delay)	Publications. Database access conditions are currently being determined.
Access to aggregated data	Access on specific project only
Access to individual data	Access on specific project only