The objective of MEMENTO is to better understand the natural history of Alzheimer’s disease and related disorders (AD) by characterizing, through the analysis of risk factors and multiple biomarkers alone or in combination, the determinants of transitions from early signs and symptoms of AD (cognitive complaints, mild cognitive impairment) to clinical dementia.

Positioning

- **MEMENTO** is a large observational study enrolling patients at an early stage before dementia and with a highly comprehensive and standardized workup (clinical, biological, imaging, socio-economics)
- **A unique platform for research**: no similar cohort at an international level
- **Collaboration with the Framingham cohort**
- **Partnerships with pharmaceutical companies** already ongoing
SCIENTIFIC NETWORK

Current collaborations

EMIF-AD (IMI call 2011): pooled cohort studies on presymptomatic AD and prodromal AD across Europe for discovery of new biomarkers for AD

Framingham cohort: determinants of dementia and associated disorders with a special focus on vascular risk factors, temporal trends in dementia, cross validation of neuroimaging biomarkers between Memento and Framingham

MELODEM (Methods in longitudinal dementia research)

Future collaborations

Mayo Clinic Study of Aging, Rochester, Minnesota, USA: To replicate in a different setting (population based study) and different country findings from Memento

Center Brain Health, New-York, USA: To set up ancillary studies to test the added value of novel biomarkers

Involved in two IMI-H2020 applications

SCIENTIFIC MANAGEMENT

Through its external scientific committee, MEMENTO involves experts in:

Basic science: Mony de Leon (New York University School of Medicine and Scientist, US)

Social sciences: Lisa Berkman (Harvard, US)

Neurology: Ronald Petersen (Rochester, US)

Biostatistics: David Clayton (MRC, UK)

Neuroimaging and biomarkers of AD: Philip Scheltens (Vrije Universiteit Amsterdam, Netherlands)
PROJECT DESCRIPTION

SCIENTIFIC OBJECTIVES

Main objective
> Identification and validation of biomarkers or combination of biomarkers that best predict the occurrence of dementia

Secondary objectives
> Provide an extensive characterization of the natural history of well phenotyped patients with potential early signs of Alzheimer’s disease
> Investigate the impact of vascular burden on cognitive health
> Document the socio-economic burden of Alzheimer’s disease and related disorders for patients, caregivers and society
> Provide for a national integrated research platform with standardized clinical, biological and imaging assessments

INNOVATIVE SCIENTIFIC FEATURES

The largest naturalistic cohort on brain health, with a rigorous prospective design
Extensive follow-up (at least 5 years)
Standardized procedures, multiple biomarkers (imaging, blood CSF) assessed with standardized acquisitions and analyses

METHODOLOGY QUALITY

Harmonization and Standardization of assessments
E-CRF and robust data-monitoring
Certification of imaging centers, centralized imaging analysis through Neurospin CATI (Saclay)
Centralized biobank and neuroimaging (CATI, Neurospin)
Inclusion Collection
Clinical data:
Cognitive testing, cognitive complaints, psychopathology, social & human sciences, vascular risk factors and history

Imaging collection:
Brain MRI (including DTI and rs-fMRI), 18F-FDG PET, Amyloid PET

Biobank:
Cerebrospinal fluid (CSF) and blood samplings

Follow-up: at least yearly
At least every year:
Cognitive testing, cognitive complaints, psychopathology, social & human sciences; vascular damages

Every 2 years:
- Brain MRI (including DTI and rs-fMRI), 18F-FDG PET, Amyloid PET
- CSF and blood samplings

Recruitment objectives: 2,323 consecutive individuals recruited

Sites:
28 Memory Research Centers in France

Inclusion criteria:
Adults; either a recently evaluated (< 6 months) cognitive performance worse than one standard deviation to the mean in one or more domains or an isolated cognitive complaint (patient aged ≥ 60 years); Non-demented; Clinical Dementia Rating Scale (CDR) ≤ 0.5

Exclusion criteria:
Guardianship; Meeting brain MRI exclusion criteria or refusing MRI; Illiteracy
DATABASE & BIOBANK CONTENTS

DATABASE

Clinical data
The database is comprehensive, with a clinical assessment of patients every 12 months, for at least 5 years
- Clinical assessment, memory tests, neurological and psychiatric assessment, socioeconomic data (burden of disease), quality of life, social sciences (social and family environment, caregiver’s assessment) etc...
- Linkage of the database with other databases as SNIIRAM is on going

Imaging collection
Imaging is performed at inclusion and every 24 months -
- Cerebral MRI
  - 3D-T12D, T2 FLAIR, 2D-T2* (GRE) + phase, 2D-T2 TSE/FSE 1 echo, Resting state (BOLD EPI), diffusion (DTI – DWI EPI)
  - Visual assessment recorded in e-CRF
  - Quality assessment of each sequence with automated test procedures and report
  - Automated analyses: brain tissues and hippocampus volumes, global and ROI-based cortical thickness, gyrification index, fold opening
- FDG PET
  - Harmonization using phantoms
  - Optimization of reconstruction parameters
  - Automatic quantitative analysis

BIOBANK

Originality
- Collection according to standardized procedures (SOPs) for the treatment, storage and transfer of the sampled biospecimens
- A duplication of all the biospecimens has been organized through the constitution of a Mirror Biobank hosted at the ICM (Institut du Cerveau et de la Moelle Epinière, Paris) to ensure the biological samples safety
- Repeated measures are performed to ensure the biospecimens quality

Scientific objective
- Developing novel blood-based biomarkers for Alzheimer’s disease

Samples
- Blood (mandatory and includes serum, plasma, DNA, RNA) and CSF (optional)

Biobank Key Facts
- Sampling at baseline, 2 and 4 year follow-up
  - Baseline samples obtained for 2 283 participants
  - 2- and 4-year follow-up samples ongoing
- For blood sampling at each wave: 28 aliquots stored
**TECHNICAL MODALITIES & SPECIFICATIONS**

**ORGANIZATION**

- **Centralized storage** in a **principal and a mirror biobanks**
  - Principal storage at the Genomic Analysis Lab, (LAG, Pasteur Institute, Lille)
  - Mirror storage at ICM (Brain & Spine Institute, Paris)
- **LAG** is responsible for organizing transport from local biobanks to centralized biobank as part of its assignments in contract
- Biological samples are identified using a **bar code system**

**SPECIFICATIONS**

- The first sampling has been performed in **July 2011**
- **Sampling frequency**: **every 2 years**
- **Responsible** for the biobank: **Bordeaux University Hospital**
- The **database associated to each sample** includes information on:
  - Collection, transport & storage conditions
  - Date of birth
  - Gender of participant
- Biobank is being constituting according to standardized protocol for sampling, **Standard Operating Procedure** for ensuring the homogenization in terms of treatment and storage quality and **high standards with quality checking procedures**
- Biological samples are available for collaborations through a research project application, according to the modalities specified in the MEMENTO data **access charter**
A financial estimation of the MEMENTO biological samples is not yet available but is underway.

BIOLOGICAL SAMPLE COLLECTION & ACCESS

The collected samples are used for the validation of disease diagnosis.

The biological sample analysis-derived data are accessible to the scientific community, according to the charter rules.

Industrial research team proposing a project are invited to identify the laboratory able to perform sample analyses and find the specific funding for biological measurements.

A charter specifying biobank access modalities is available since 2013 and describes the MEMENTO general principles and path to follow for data and biospecimen access, ancillary project and publication submission.

The biobank is opened to a large scientific community (academic and industrial), without any restriction regarding the nature of the biospecimens and in accordance with the charter terms.

Industrials wishing to access to the MEMENTO biobank have to submit a research project to the Steering and the Scientific Committees for review.

Transfer of biological samples to public or to private/industrial teams is possible upon granted access and after following specific rules of the charter.

Biological samples may be shareable with a foreign company under conditions depending on the purpose, the analysis,…..
RESEARCH COLLABORATION OPPORTUNITIES

**Translational research**

- Identification and validation of new biomarkers or combination of biomarkers for the early diagnosis of Alzheimer’s disease and associated disorders
- Identification of prognosis factors for transition from isolated cognitive complaints to mild cognitive impairment to dementia
- Validation of surrogate markers of Alzheimer’s disease for future clinical trials
- Validation of preclinical and pre-dementia stages of Alzheimer’s disease

**Clinical development**

- Definition phenotypes of patients at high risk of clinical dementia that should be the target of future clinical trials
- Structuration of clinical research in the field of Alzheimer’s disease
- Platform for clinical research

**Outcomes research**

- Better characterization of etiologies of dementia
- Pharmaco-economic studies cost/benefit of new biomarkers for Alzheimer’s disease and associated disorders
- Provide data to health authorities on the added value of biomarkers for care and treatment of patients
- Assess the impact of early diagnosis of Alzheimer’s disease and associated disorders on the patient and its family

**BIBLIOGRAPHY**

**Translational research**

- Chêne G, Translational epidemiology: are we ready for a population perspective in our research? Harvard School of Public Health, Department of Society, Human Development and Health Seminar Series, Boston, USA, 09/2012.

**Methodological development**


**Outcomes research**

- Godin O et al., Antihypertensive treatment and change in blood pressure are associated with the progression of white matter lesion volumes: the Three-City (3C)-Dijon Magnetic Resonance Imaging Study. Circulation 2011;123(3):266-73.