



MEMENTO Imaging Study Data

In the nationwide French MEMENTO cohort study, participants were recruited in memory clinics and screened for either isolated subjective cognitive complaints (SCCs) or mild cognitive impairment (MCI; defined as test performance 1.5 SD below age, sex and education-level norms) while not demented (Clinical Dementia Rating [CDR] <1). Baseline data collection included neurological and physical examinations as well as extensive neuropsychological testing. To be included in the MEMENTO cohort, participants had to agree to undergo both brain magnetic resonance imaging (MRI) and blood sampling.

Background

The MEMENTO cohort is a clinic-based study of patients presenting with a large variety of cognitive symptoms and subjective cognitive complaints (SCCs) that will be followed over a 5-year period. Between April 2011 and June 2014, among the 2449 participants screened as meeting the inclusion criteria, 2323 patients consented to participate in the study. The recruitment took place within the French national network of university-based memory clinics (Centres de Mémoires de Ressources et de Recherche [CMRR]). Twenty-six CMRRs agreed to participate and the number of included subjects per CMRR ranged from 17 to 305.

Selection criteria:

The participants were screened for either very mild to mild cognitive impairment or isolated cognitive complaints, and they were recruited consecutively. Very mild to mild cognitive impairment was defined as

- (1) performing 1 SD worse than the subject's own age, sex and education-level group mean in one or more cognitive domains, this deviation being identified for the first time through cognitive tests performed recently (less than 6 months preceding screening phase), and
- (2) having a Clinical Dementia Rating (CDR) ≤ 0.5 and not being demented.

Exclusion criteria:

- being under guardianship
- residence in skilled nursing facility
- pregnant or breastfeeding women
- AD known as being caused by gene mutations
- history of intracranial surgery
- neurological disease such as treated epilepsy, treated Parkinson's disease, Huntington's disease, brain tumour, subdural haematoma, progressive supranuclear palsy, or history of head trauma followed by persistent neurological deficits
- stroke diagnosed in the last 3 months preceding enrolment visit
- history of stroke followed by persistent neurological deficits
- Schizophrenia history (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV], criteria)
- illiteracy (unable to count or to read)

Assessments

Baseline data collection included socio-demographic characteristics, personal and familial medical history, neurological and physical examination (including anthropometric measurements and three measures of blood pressure after 2 minutes of rest in sitting position using the Omron M6 monitor, OMRON Healthcare, Kyoto, Japan), current medication intake with detailed recording of doses as well as treatment onset date, and cognitive and non-cognitive subjective complaints.

Cognitive Assessments

Assessment Name	Assessment Description
Mini Mental State Examination (MMSE)	30-point questionnaire that is used to measure cognitive impairment. The MMSE test includes simple questions and problems in a number of areas: the time and place of the test, repeating lists of words, arithmetic such as the serial sevens, language use and comprehension, and basic motor skills.
Digit span (forward and backward)	Participants are presented with a random series of digits, and are asked to repeat them in either the order presented (forward span) or in reverse order (backwards span). The simpler forward span task requires verbal working memory and attention, while the backwards span task additionally tests cognitive control and executive function.
Free and Cued Selective Reminding Test	A memory test that controls attention and acquisition, by providing category cues in the learning process.
Delayed Matching to Sample 48 (DMS48)	Assesses both simultaneous visual matching ability and short-term visual recognition memory, for non-verbalisable patterns. The participant is shown a complex visual pattern, that is both abstract and non-verbal (the sample), followed by four similar patterns, after a brief delay. The participant must select the pattern which exactly matches the sample.
Verbal Fluency (animals and letter p)	Where participants have to produce as many words as possible from a category in a given time – in this case: animals and words beginning with letter p.
Image Naming	The participant is presented with images which they have to identify.
Praxis assessment	Praxis is defined as the ability to plan and perform skilled movements in a non-paralytic limb, based on the previously learned complex representations.
Rey-Osterrieth Complex Figure Test	Participants are asked to reproduce a complicated line drawing, first by copying it freehand (recognition), and then drawing from memory (recall).
Trail Making Test (TMT) A and B	Part A of the test requires you to connect 25 randomly placed circles in ascending numerical order. Part B also requires you to connect 24 randomly placed circles in ascending order, alternating between numbers and letters. The test is scored based on how many seconds it takes you to complete each part.
Frontal Assessment Battery (FAB)	FAB is a battery of tests, consisting of six subtests, that takes about 10 minutes and is designed as a short bedside assessment of executive function.
Neuropsychiatric Inventory–Clinician (NPI-C)	The NPI-C was revised from the original NPI and includes an additional 78 items, split domains for agitation and aggression, and an extra domain for ‘abnormal vocalization’. The most important modification of the NPI-C is the addition of clinician judgement to rate the severity of each item.

Lifestyle Assessments

Assessment Name	Assessment Description
International Physical Activity Questionnaire	This measure assesses the types of intensity of physical activity and sitting time that people do as part of their daily lives are considered to estimate total physical activity in MET min/week and time spent sitting.
Instrumental Activities in Daily Living Scale and Activities of Daily Living Scale	Assesses a person’s ability to perform tasks such as using a telephone, doing laundry, and handling finances. Measuring eight domains, it can be administered in 10 to 15 minutes.
Short Physical Performance Battery (SPPB)	A group of measures that combines the results of the gait speed, chair stand and balance tests.

Neuroimaging Procedures

MRI Procedure

As part of the inclusion criteria, participants had to agree to undergo brain MRI, and 86% of participants had a 3.0-T MRI scan (1.5 T otherwise). 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) was optional and was performed in 60% of participants.

SEQUENCE NUMBER	SEQUENCE LABELLING	SEQUENCE DURATION	ADNI MRI PROTOCOL
1	Localizer	0:10	
2	3D T1-Weighted	9:00	Yes
3	3D T2-Weighted FLAIR	4:00	Yes
4	3D T2-Weighted (GRE)	5:30	Yes
5	3D T2-Weighted TSE/FSE single-echo	1:45	
6 (Optional)	Resting-state fMRI BOLD EPI	10:00	
7 (Optional)	Diffusion-weighted imaging (DTI – DWI EPI) + B0 field map	4:30 x 2-4 1:45	

PET Procedure

PET centres participating in the MEMENTO study were equipped with systems set-up between 2003 and 2014 and consisted of 10 GE Healthcare, 6 Philips and 12 Siemens Healthcare systems, as well as 15 different models of scanners. No brain-dedicated high-resolution system or 2D tomography systems were included.

Follow-Up Evaluations

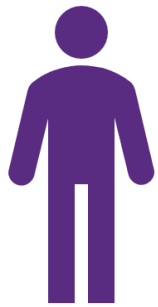
Longitudinal follow-up took place every 6 months. The table below describes the schedule of overall evaluations. During follow-up, all incident cases of dementia (DSM-IV criteria for dementia and National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer’s Disease and Related Disorders Association criteria for AD) were reviewed by an independent committee.

Schedule of evaluation in the MEMENTO cohort over 60 months of follow-up

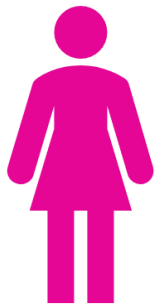
	<i>Schedules of evaluation by follow-up wave (months)</i>										
	BASE	M6	M12	M18	M24	M30	M36	M42	M48	M54	M60
Socio-demographic characteristics	■	□	■	□	■	□	■	□	■	□	■
Medical history or incident events	■	□	■	□	■	□	■	□	■	□	■
Physical, neurological exams	■	□	■	□	■	□	■	□	■	□	■
Medication	■	□	■	□	■	□	■	□	■	□	■
Clinical Dementia Rating	■	■	■	■	■	■	■	■	■	■	■
Full neuropsychological battery	■	■	■	■	■	■	■	■	■	■	■
Subjective complaints	■	■	■	■	■	■	■	■	■	■	■
Neuropsychiatric Inventory	■	■	■	■	■	■	■	■	■	■	■
Lifestyle	■	■	■	■	■	■	■	■	■	■	■
Autonomy in daily activities	■	■	■	■	■	■	■	■	■	■	■
Motricity (SPPB)	■	■	■	■	■	■	■	■	■	■	■
Quality of life (EQ-SD)	■	■	■	■	■	■	■	■	■	■	■
Blood sampling assessment	■		■		■		■		■		■
Biobank	■				■				■		
DNA sample collection	■				■				■		
RNA collection	■				■				■		
Brain structural MRI	■				■				■		
F-FDG-PET scan	☑				☑				☑		
Lumbar puncture	☑				☑				☑		

Keys: ■ At examination centre □ By phone or at examination centre ☑ Optional, at examination centre

Baseline Characteristics of the MEMENTO Cohort



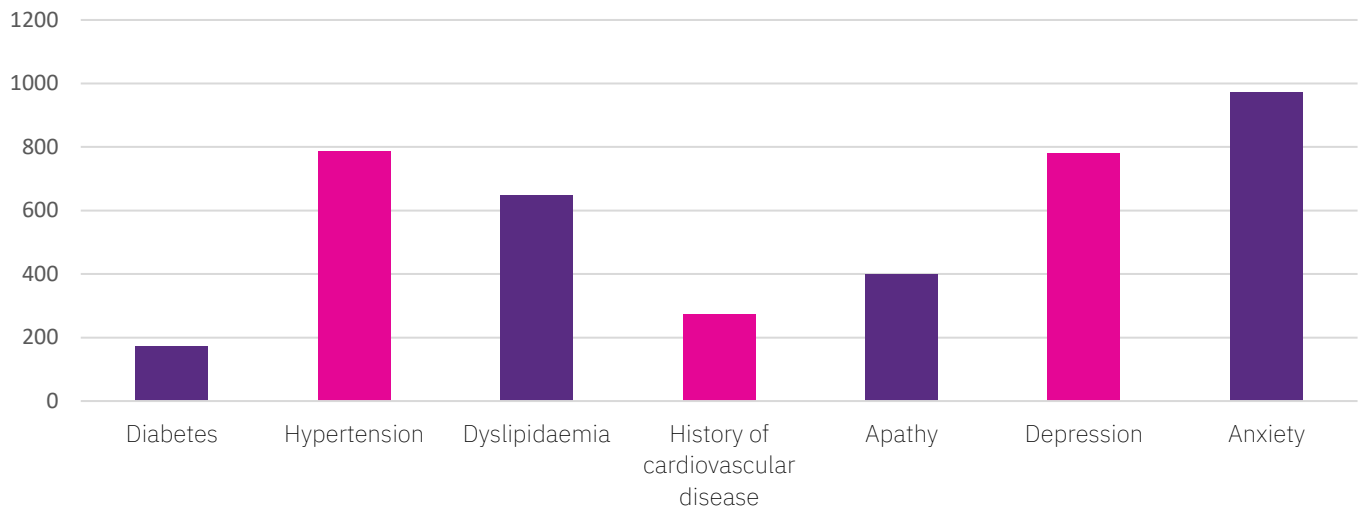
887



1436

70.9
MEAN AGE

54.8%
HIGHER EDUCATION
LEVEL



Mean Assessment Score

MMSE	27.9
Verbal Fluency, letter p	20.4
Verbal Fluency, animals	28.3
DMS48, immediate recall	44.7
Praxis	21.8
TMT A, in seconds	2.1
TMT B, in seconds	5.2
FCSRT, total immediate free recall	25.9
FCSRT, total free and cued delayed recall	14.9
Digit span	9.9
Rey Complex Figure Test, immediate copy score	32.9
Rey Complex Figure test, 3-minute copy score	15.1
FAB	16.2

Mean Image Analysis Features

Hippocampal volume, right	2.76
Hippocampal volume, left	2.66
Cortical thickness, right	2.32
Cortical thickness, left	2.33
Temporal, inferior right	1.64
Temporal, inferior left	1.62