

# Shanghai Cohort Study on Mild Cognitive Impairment: Study Design and Baseline Characteristics

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## Abstract

**Objective:** Establish cohort of patients with mild cognitive impairment (MCI) in order to identify the risk factors and validation of neuropsychological tests for early detection of Alzheimer disease.

**Methods:** Four hundred participants with MCI were enrolled in at Huashan Hospital in Shanghai, China. All patients will be followed once annually for 3years. The primary endpoint is the time of conversion from diagnosis of MCI to Alzheimer disease (AD).

**Results:** of the 400 subjects, 170 (42.5%) were male, and the average mean age and education was 68.7 (Standard Deviation, SD: 8.2, 45- 90 years old) and 12 years (SD: 3.1), respectively. At baseline age, education and being single influenced MMSE, ADAS-cog13 and most domains of cognition.

**Conclusions:** Baseline characteristics of the Shanghai MCI cohort study indicate the participants were younger, less educated and had a moderate gender ratio compared to other studies conducted so far and represent the target population. 3 years later when the cohort will be finished some risk factors Associated with the conversion will be validated and some novel factors will be identified.

**Keywords:** Alzheimer disease; Mild cognitive impairment; Cohort study; Design; Baseline characteristics

## Introduction

Alzheimer's disease (AD) is a progressive, neurodegenerative disease characterized by loss of memory and other cognitive function. Currently, there is no effective treatment. Although the cause of the disease is still unknown, basic research indicates that Beta amyloid accumulation is a crucial early player in disease pathogenesis, ultimately leading to the onset of dementia [1]. Amyloid precursor protein (APP) cleaving enzyme 1 (BACE1), the enzyme that initiates A $\beta$  production by cleaving the extracellular domain of APP or antibody to clear beta amyloid, has been the target of drug development for decades. Unfortunately, the several inhibitors of BACE1 and immunotherapy used to lower cerebral A $\beta$  concentrations and treat Alzheimer disease that have been tested in human clinical trials failed to show effectiveness, and many questions remain about the safety of these drugs [2]. 99% of Alzheimer drug trials in the past decade have failed [3], and there is an 'urgent' need to improve therapies.

Recent clinical research, histopathology and amyloid imaging results suggest that amyloid deposition might begin more than a decade before the appearance of cognitive deficits and diagnosis of Alzheimer disease [4,5]. Targeting the production of beta amyloid at the prodromal stage in order to prevent the onset of dementia may be an important strategy for conquering the disease. However, the MCI based on current diagnostic criteria showed MCI is heterogeneity. That MCI progresses to Alzheimer disease at a rate of roughly 10–15% per year depending on the clinical diagnosis of MCI [6]. It remains uncertain how to identify the right subjects in such a preventive approach. Individual risk estimation based on amyloid imaging (PiB) remains difficult because many normal control individuals have a brain amyloid increased the risk of cognition decline. Predictors with high sensitivity and specificity for the early detection of Alzheimer disease are always of interest for research. Zhou's analysis using ADNI data indicated the combination of neuropsychological tests of clinical rating scale and ADAS-cog can

predict the conversion rate of 92.7% (95%CI: 82.4-100.00), which is better than single cerebrospinal fluid Abeta42 or MRI findings [7].

The objectives of the Shanghai cohort study on mild cognitive impairment for the early detection of Alzheimer disease were to explore the factors associated with the conversion from MCI to AD, to identify any special characteristics of the factors in Chinese people and to confirm the findings in ADNI for the global development of drug clinical trial. We conducted an MCI cohort at Huashan Hospital in Shanghai based on routine clinical practice. Here, we report the design and baseline characteristics of the subjects enrolled.

## Material and Methods

### Study design

The study is a prospective cohort study that included 400 subjects with MCI and a follow-up once annually for three years. The objectives are to identify individuals with MCI who convert to AD and to explore factors associated with the conversion. The observation time point is every 12 months and phone interview on 6<sup>th</sup>, 18<sup>th</sup> month. The primary endpoint was the time from diagnosis to the conversion from MCI to Probable AD Dementia. The secondary endpoints are the time to conversion from MCI to "Possible AD Dementia" or "Probable AD

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Dementia”, time to Conversion from MCI to “All-cause Dementia”, Overall survival, Changes in Neuropsychological examinations and Changes in MRI from baseline to the end of follow-up. The planned research duration was from Jan 2012 to Dec. 2016. The study is also registered in clinicaltrials.gov as NCT01552265.

## Subjects

**Inclusion/exclusion criteria:** MCI was diagnosed according to NIA criteria [8]. The inclusion criteria used are as follows: 1. Cognitive concern reflecting a change in cognition reported by the patient, informant or clinician; 2. Mini-Mental State Examination (MMSE) scores between 18-30 (inclusive); 3. Clinical Dementia Rating (CDR) = 0.5; Memory Box score of at least 0.5; 4. Essentially preserved the activities of daily living based on the Alzheimer’s Disease Cooperative Study - Activities of Daily Living (ADCS-ADL); 5. Does not meet criteria for dementia [9]; 6. Willing to and able to undergo all test procedures, including neuroimaging, and agreed to longitudinal follow up; 7. Written informed consent for participating in this study was obtained. Exclusion criteria: 1. Obvious vascular causes of cognitive decline; 2. Traumatic causes of cognitive decline; 3. Medical causes of cognitive decline (e.g. use of psychoactive medications, alcohol abuse and some types of disease including depression and epilepsy); 4. History of other diseases or unstable conditions which could lead to difficulty in complying with the protocol.

**Enrollment:** From February 2012 to June 2014, a total of 400 participants with mild cognitive impairment patients were enrolled in Huashan Hospital located at Fudan University in Shanghai, China. All participants underwent detailed informed consent procedures and provided written consent in accordance with the procedures approved by the institutional review boards on Jan. 12<sup>th</sup>, 2012 at Huashan Hospital and Dec. 9<sup>th</sup>, 2011 at Translational Research Informatics Center (TRI).

## Study procedure

**Clinical examination:** The procedure of screening and diagnosis is presented in the follow-chart. At the memory clinic in Huashan Hospital, first the patients are interviewed by neurologist at memory clinic of extensive clinical examination and brief neuropsychological tests and then recommended to neuropsychological tests, blood laboratory and 3D MRI according to the results of first interview. Medical history, and family history. Information pertaining to the activities of daily living was gathered via clinical interviews of the patient and caregiver. Information of degree of education total education years, marital status, medical history (hypertension, diabetes, stroke, myocardial infarction, head injury, general anesthesia, depression), smoking and drinking status were collected. Type, frequency and period of physical activities was gathered via interview of the patient and caregivers. Neurological system and general physical examinations were performed although the data were not input in the database.

**Neuropsychological assessment:** Participants underwent comprehensive cognitive examination during the baseline and follow-up visits. The neuropsychological assessments included the MMSE, Rey auditory-verbal learning test (RAVLT), logical memory (LM) subtest of the Wechsler memory scale (WMS), Stroop color-word conflict test (SCWT), Rey-Osterrieth complex figure test (CFT), verbal fluency test (VFT), trail-making tests A and B (TMTA and TMTB), symbol digit modalities test (SDMT), clock drawing test (CDT), Boston naming test (BNT), clinical dementia rating (CDR) and ADAS-cog13. RAVLT included 5 sub-tests—RAVLT1, RAVLT2, RAVLT3, RAVLT4, and RAVLT5. The LM test included the assessment of immediate recall (LM I) and delayed recall (LM II) of a short story, for which the cut-offs were 7

and 5 for the diagnosis of dementia, respectively. The Stroop color-word conflict test included the 6 sub-tests of Atime, Acorrect, Btime, Bcorrect, Ctime and Ccorrect. The CFT had 2 components which are CFT-copy and CFT-delayed, respectively. VFT included the assessment of the correct number of animals (VFT1) and vegetables (VFT2) identified within 1 min. The results of TMTA and TMTB indicate the mean time taken to complete parts A and B. All neuropsychological tests have been validated for use and have a cut-off point for dementia according to the age group in the Chinese population [10]. Neuropsychiatric Inventory (NPI) and Center for epidemiological survey depression scale (CESD-C) were used to evaluate general psychiatric behavior and status of depression, respectively. The score of 13 items in ADAS-cog (ADAS-cog13) and sum of six boxes of CDR (CDR-sob) were used in analysis.

**Diagnostic consensus conference:** The primary endpoint is the time from diagnosis to the conversion of AD. The secondary endpoints are Time to Conversion from MCI to “Possible AD Dementia” or “Probable AD Dementia”

Time to Conversion from MCI to “All-cause Dementia”, overall survival, changes in Neuropsychological examinations and Changes in MRI. At baseline after all examinations, a consensus diagnosis and enrollment was made by two experts, then the subject was registered. During follow-up the data collected were reviewed and diagnosis was made by an international committee that includes 3 experts from China and Japan. Diagnostic consensus conferences were held at Huashan Hospital monthly to assess potential clinical core enrollees for cognitive diagnoses. These meetings were designed to ensure that enrollees meet the criteria for MCI diagnostic criteria and increase inter-rater reliability among clinicians, a neuropsychologist, behavioral neurologist, and study support personnel.

The Diagnosis of dementia and AD are according to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders fourth edition) and McKhann’s criteria [9], respectively. If the test of delayed recall of the Wechsler Memory Scale and logical memory showed evidence of memory impairment, the subject was classified as amnesic MCI (aMCI). There are two sub-types of aMCI, single-domain (s-aMCI) and multiple-domain (m-aMCI), based on the number of domains impaired.

**Laboratory measures/ imaging:** Laboratory tests include chemical panel tests, complete blood count and Lipid Profile. MRI neuroimaging was collected via standard manualized procedures to ensure uniform collection. All patients had Siemens MRI scan to collect the Whole brain volume, hippocampus volume (R, L), temporal lobe volume (R, L), entorhinal cortex volume (R, L) are calculated. GE 1.5T • 14.0M4 TwinSpeed 8Ch, • 14.0M4 TwinSpeed 8Ch Phantom. GE 3.0T • 3T 14.0M4 TwinSpeed 8Ch • 3T 14.0M4 TwinSpeed 8Ch Phantom.

**Data entry and data center:** Cognitive and clinical data was reviewed by the psychometrist and study nurse and verified at the clinical consensus meeting. All data was input at Huashan Hospital via a web-based CRF with a data center at the Translational Research Informatics Center in Kobe, Japan. Source data verification (SDV) of the baseline data was conducted to ensure the research quality.

## Analysis

The sample size is 400. The calculation was based on the conversion rate of about 12% per year based on prior data in the Huashan hospital (unpublished data). From the experience in the Huashan hospital, a total of 400 subjects may be enrolled during 2 years. If 400 subjects are enrolled for this study, a width of 95% confidence interval for the

conversion rate is 9.8% ( $\pm$  4.9%) at a maximum unless the conversion rate equals to 0 or 100%.)

Distribution of the test scores were assessed by the mean and standard deviation (SD) for the sample as a whole.

A composite Z score of the five cognitive domains was calculated to evaluate the factors associated with cognition. The five domains were memory (RAVLT5, RAVLT1-4, LMI &II, CFT- delayed recall), spatial processing (CFT-copy and CDT), language (AFT animal, BNT), attention (SDMT, TMT-A), and executive function (SCWT-C-time, SCWT-C-right, TMT-B).

Z score = (sample value-sample mean)/standard deviation. The z scores of the tests in each domain mentioned above were averaged to obtain a z score for all domains. T-test exact tests were used to determine the differences in demographic factors and measure each neuropsychological domain and global cognition. The higher score indicated good performance in AVLT, CFT-copy and delayed, CDT, AFT, SDMT and BNT; bad in TMT and SCWT. All analyses were conducted using SAS (9.0 SAS Corp.)

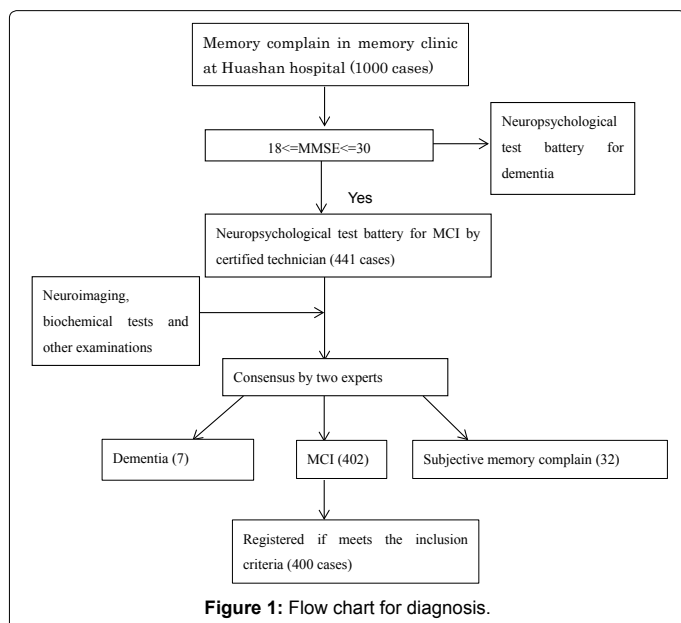
T-tests or ANOVA were used to assess the relationship between baseline demographic factors associated with cognition. Multiple linear regression models fit with the independent effects on each domain, and the three comprehensive tests MMSE, CDR-sob and ADAS-cog13. Factors which showed significant by univariate analysis were determined into multiple stage. Analyses were conducted in SAS version 9.3 (SAS Institute Inc, Cary, North Carolina).

## Results

441 patients in the memory clinic in Huashan Hospital in Shanghai were screened, and 400 diagnosed with MCI were enrolled from February 2012 to June 2014. Figure 1 shows the flow chart of screening and diagnosis.

### Cohort demographics and distribution of neuropsychological features

Tables 1-3 provide the demographic and neuropsychological



features of the total cohort, respectively. Of the 400 subjects, 170 (42.5%) were male, and the average mean age was 68.7 (SD 8.2, ranged from 45 to 90 years old). The average education level was 12 years (SD: 3.1), and 5.3%, 27.8%, 32% and 365, respectively, graduated from elementary school, junior high school, senior high school and university or higher. The top three medical history diseases were hypertension (41.8%), diabetes (13.5%) and general anesthesia (10.5%). Average education was 12 years (SD: 3.1). Almost 80% never smoked or drank alcohol.

The average scores of MMSE, CDR-sob and ADAS-cog were 26.5 (SD: 1.9), 1.6 (SD: 1.1) and 20.1 (SD: 6.3), respectively.

The distribution of age crossed with education in the whole cohort of 400 cases divided into the three age groups of  $\leq$  65, 65~74 and  $\geq$  74 years old was 116 (29.2%), 187 (47.0%) and 23.9%, respectively. Subjects with senior high school or higher education numbered 127 (31.9%) and 144 (36.2%). In the subjects educated above university level, 40% of those were aged over 75 years greatly exceeded by more than 11% those aged less than 65 years.

### The association of demographic factors and medical history with cognition

Language was influenced factors of sex, education and living alone; memory by age and living alone; visuospatial by education;

Characteristics	N. (%) or mean (SD)
Female	230 (57.5)
Age (years)	68.7 (8.2)
Education	12.0 (3.1)
Elementary school	17 (4.3)
Junior high school	110 (27.6)
Senior high school	127 (31.9)
University and above	144 (36.2)
Hypertension	167 (41.8)
Diabetes	54 (13.5)
Stroke	14 (3.5)
Myocardial infarction	2 (0.5)
Head injury	15 (3.8)
General anesthesia	42 (10.5)
Depression	7 (1.8)
BMI	22.9 (3.1)
Family history of AD	56 (14.0)
Smoking status	
Never	320 (80.0)
Former	54 (13.5)
Current	26 (6.5)
Drinking status	
Never	318 (79.5)
Former	39 (9.8)
Current	43 (10.8)
Marital status	
single	43 (10.7)
married	357 (89.3)
Live alone	21 (5.3)
ApoE4	
0	268 (68.2)
1	99 (25.2)
2	26 (6.6)

**Table 1: Baseline characteristics.**

Item	N	Mean (SD)	Median
MMSE	400	26.5 (1.9)	30
CDR-sob	400	1.6 (1.1)	1.5
Logical memory I-C*	399	4.9 (2.8)*	5.0
Logical memory II-C*	399	3.4 (2.7)*	3.0
AVLT-long-term delayed recall*	400	2.0 (2.0)	2.0
AVLT-recognition*	400	17.5 (3.7)*	18.0
AVLT-Total N1~ N5*	400	15.8 (6.8)	15.0
CESD-C	400	8.8 (10.9)	5.0
ADAS-cog13	400	20.1 (6.3)	68.0
Category fluency test-C : animals	400	13.8 (3.8)	14.0
Category fluency test-C : cities	400	12.1 (3.9)	12.0
Boston naming test	400	20.1 (4.7)	21.0
Clock Drawing Test*	400	21.2 (5.3)	22.0
Trail Making Test -A (Sec)	398	87.3 (42.0)	76.0
Trail Making Test- B (Sec)	394	234.7 (101.9)	222.5
Symbol Digit Modalities Test	398	27.8 (10.8)	28.0
Rey-Osterrieth CFT-C - Copy	400	32.3 (4.5)	33.5
Rey-Osterrieth CFT-C -Delayed Recall	398	10.0 (6.8)	9.0
Stroop-C color-word (Sec)	393	97.9 (33.6)	92.0
Stroop-C color-word (number)	399	40.0 (9.6)	43.0
NPI	224	5.1 (7.9)	1.0
NPI of caregiver distress	224	1.2 (2.8)	0.0
ADCS-ADL: Total Score	400	67.6 (5.9)	68.0
Brain Ventricle Volume (mm <sup>3</sup> )	262	37234.56	32736.45
Left-Hippocampus (mm <sup>3</sup> )	262	3392.21	3389.3
Right-Hippocampus (mm <sup>3</sup> )	262	3624.89	3651.5
lh_entorhinal_volume (mm <sup>3</sup> )	262	1508.76	1529
rh_entorhinal_volume (mm <sup>3</sup> )	262	1422.78	1383.5
Left-Temporal Lobe (mm <sup>3</sup> )	262	45656.30	45930.5
Right-Temporal Lobe (mm <sup>3</sup> )	262	46217.69	46069.5
Whole Brain Volume (mm <sup>3</sup> )	262	1027436.14	1022962

\* modified in the Shanghai cohort.

**Table 2:** Distribution of neuropsychological tests and brain volume at baseline.

	Age group			Total
	≤65	65-74	≥75	
Education				
Elementary school	12 (3.0)	4 (1.0)	1 (0.3)	17 (4.3)
Junior high school	56 (14.1)	39 (9.8)	15 (3.8)	110 (27.6)
Senior high school	32 (8.0)	71 (17.8)	24 (6.0)	127 (31.9)
University	16 (4.0)	73 (18.3)	55 (13.8)	144 (36.2)
Total	116 (29.2)	187 (47.0)	95 (23.9)	398 (100.0)

**Table 3:** Distribution of age and education.

attention by sex and education; executive function by age and sex. No one factor involved in the study, such as sex, age and education, was associated with CDR-sob. MMSE was influenced by education and living alone more than 5 years; ADAS-cog 13 by age and marital status (Table 4).

### Multivariable models

Based on the results of the univariate analysis, five factors were included in the multiple linear regression models. In Table 5 the results show that age and education influenced MMSE and most of the domains of cognition. In addition, being single was associated with poor performance in ADAS-cog13 and executive function and as well as poor attention and executive function in males; CDR-sob was not influenced by any of the factors included in the study used in multiple models.

### Discussion

There have been several large studies on mild cognitive impairment launched around the world to explore the risk factors and establish early diagnosis criteria. Compared to the five studies [9] showed in the appendix, the four hundred subjects enrolled in the Shanghai MCI cohort study were younger with an average age of 68.7 (SD: 8.2) and moderately female (57.5%), and there were fewer subjects with higher education (36.2%).

To know the extent of and identify the impairment is always the goal of such MCI cohort studies. Therefore, the neuropsychological tests used to identify the level and severity of impairment, which can differ substantially depending on the stage of cognitive impairment, are important. In our study, we used the MMSE, CDR, ADAS-cog13, AVLT, LM, CDT, TMT and AFT tests. These tests are often used to evaluate the domains of cognition. We also selected the CWT-C and CFT tests to measure executive function and spatial processing.

Longitudinally, the aim of the Shanghai MCI cohort study is to better characterize patients with MCI for additional clinical research studies with the objective of analyzing promising biomarkers for the early diagnosis of AD and validation of some findings of neuropsychological tests and MRI findings in ADNI as a foundation for clinical trials. Although many of the long term goals of this study are to identify the right population of MCI cases who convert to AD and the right time for intervention, use of a study design that is not population-based can limit the generalizability of certain results to the wider population. For example, the study enrolled participants with varying levels of disease severity, which restricts our ability to track the natural history of cognitive impairment in MCI from the time of disease onset. However, the large sample size at an early stage of cognitive impairment will undoubtedly allow us to describe the cognitive impairment trajectory for people with varying levels of cognitive impairment. Lack of beta amyloid imaging and cerebrospinal fluid data is one limitation, instead we focus on the neuropsychological tests.

The subjects in the Shanghai cohort study performed worse on the CDT, BNT, TMTA and B tests than that in ADNI. Lower average education is one of the reasons for such poor performance based on the fact our study showed that education, while associated with some domains of cognition, has no impact on CDR-sob or ADAS-cog13. In terms of the risk factors associated with cognition, we found that education influenced the three domains of language, attention and spatial processing. Memory, executive function and spatial processing are affected by one of either education or sex, respectively. It is well known that most neuropsychological tests are influenced by age and education [11-13]. These two factors were not found to be associated with the CDR-sob score, so this test can be used generally in any population without consideration for the impact of age or education. It is known that higher education decreases the risk of dementia. However, poor performance in some single neuropsychological tests, one domain, such as episodic memory [14-16], or in a combination of several tests predict conversion from MCI to AD and future decline of MCI [17,18]. Whether or not the influenced domains in our study predict incidence of dementia better than others is a challenge that remains for future research.

Females are consistently associated with higher levels of dementia than males. In our study, female subjects accounted for 57.7% of all subjects, and they performed worse than males in the domains of language and executive function. Whether or not differences in sex in the domains of cognitive impairment indicate future differences in the

Factors	N	MMSE	Cognition Mean (SD)			Memory	Spatial	Language	Attention	Executive
			CDR-sob	ADAS-cog						
Age										
< 65	116	26.65 (1.76)	1.53 (1.00)	18.36 (5.92)*	0.16 (0.81)*	0.05 (0.74)	-0.04 (0.79)	-0.04 (0.45)	-0.15 (0.52)*	
65-75	188	26.52 (1.87)	1.55 (1.02)	20.56 (6.33)	-0.01 (0.78)	0.05 (0.78)	0.03 (0.77)	-0.00 (0.45)	0.06 (0.53)	
≥ 75	96	26.45 (1.98)	1.81 (1.18)	21.41 (6.25)	-0.17 (0.70)	-0.17 (0.91)	-0.01 (0.83)	0.05 (0.48)	0.04 (0.53)	
Sex										
Male	170	26.55 (1.9)	1.62 (1.10)	20.55 (5.78)	-0.02 (0.74)	0.05 (0.87)	0.19 (0.81)*	-0.06 (0.41)*	0.08 (0.62)*	
Female	230	26.53 (1.84)	1.60 (1.03)	19.81 (6.63)	0.01 (0.81)	-0.03 (0.76)	-0.14 (0.75)	0.05 (0.49)	-0.07 (0.46)	
Education										
< Elementary	17	25.88 (1.69)*	1.59 (0.91)	21.35 (9.31)	0.09 (0.79)	-0.53 (0.83)*	-0.72 (0.76)*	-0.12 (0.63)*	0.09 (0.41)	
Junior	111	26.47 (1.84)	1.64 (1.14)	19.86 (5.37)	-0.07 (0.80)	-0.16 (0.81)	-0.25 (0.70)	-0.13 (0.42)	-0.11 (0.53)	
Senior	128	26.16 (1.78)	1.63 (0.99)	19.58 (6.03)	-0.03 (0.78)	0.07 (0.59)	0.03 (0.74)	0.01 (0.45)	0.04 (0.48)	
University	144	27.01 (1.88)	1.56 (1.08)	20.68 (6.74)	0.07 (0.75)	0.12 (0.92)	0.25 (0.80)	0.10 (0.45)	0.02 (0.59)	
Live alone										
No	377	26.53 (1.87)	1.61 (1.05)	20.10 (6.18)	-0.01 (0.77)	0.00 (0.80)	-0.02 (0.79)*	-0.01 (0.45)	-0.01 (0.54)	
yes	21	26.81 (1.63)	1.36 (1.11)	20.90 (8.34)	0.13 (0.81)	0.01 (0.90)	0.35 (0.65)	0.11 (0.54)	0.02 (0.51)	
Years living alone										
< 5	10	27.7 (0.95)*	1.05 (0.76)	18.40 (7.26)	0.59 (0.58)*	0.17 (0.80)	0.38 (0.86)	0.16 (0.59)	-0.11 (0.49)	
≥ 5	11	26.0 (1.73)	1.64 (1.32)	23.18 (8.93)	-0.29 (0.79)	-0.15 (1.00)	0.33 (0.43)	0.07 (0.52)	0.15 (0.53)	
Marital status										
Single	43	26.28 (1.62)	1.62 (1.15)	22.09 (8.18)*	0.06 (0.85)	-0.21 (0.96)	-0.12 (0.84)	0.07 (0.55)	0.14 (0.61)	
Married	357	26.57 (1.89)	1.61 (1.05)	19.89 (5.99)	-0.01 (0.77)	0.03 (0.79)	0.02 (0.78)	-0.01 (0.45)	-0.02 (0.53)	

\* p < 0.05

Table 4: Demographic factors associated with cognition by univariate analysis.

Factors	Covariate	Coefficient	SE	P
MMSE	Age	-0.025	0.012	0.045
	Gender	0.107	0.192	0.578
	Education (year)	0.107	0.032	0.001
	Live alone	0.813	0.536	0.130
	marriage	0.579	0.389	0.138
CDR-sob	Age	0.011	0.007	0.093
	Gender	0.009	0.110	0.937
	Education (year)	-0.008	0.019	0.686
	Live alone	-0.476	0.308	0.123
	marriage	-0.198	0.223	0.376
ADAScog13	Age	0.148	0.042	0.0004
	Gender	-0.746	0.650	0.252
	Education (year)	-0.069	0.109	0.530
	Live alone	-2.123	1.813	0.242
	marriage	-0.286	1.317	0.030
memory	Age	-0.020	0.005	0.0001
	Gender	0.018	0.080	0.823
	Education (year)	0.029	0.014	0.03
	Live alone	0.130	0.224	0.564
	marriage	-0.072	0.163	0.661
visuospatial	Age	-0.023	0.005	0.001
	Gender	-0.028	0.082	0.734
	Education (year)	0.064	0.014	0.001
	Live alone	0.317	0.229	0.169
	marriage	0.292	0.166	0.080
language	Age	-0.017	0.005	0.0007
	Gender	-0.243	0.077	0.002
	Education (year)	0.080	0.213	0.0004
	Live alone	0.759	0.213	0.0004
	marriage	0.363	0.155	0.020
attention	Age	-0.002	0.003	0.494
	Gender	0.159	0.046	0.0007
	Education (year)	0.038	0.008	<0.001
	Live alone	0.035	0.130	0.785
	marriage	-0.048	0.094	0.615
executive	Age	0.009	0.003	0.011
	Gender	-0.152	0.055	0.006
	Education (year)	-0.002	0.009	0.838
	Live alone	-0.205	0.154	0.185
	marriage	-0.259	0.112	0.021

Table 5: Multiple linear regression models of the associations of factors with cognition.

conversion from MCI to AD will be better answered after the follow-up of the cohort.

Compared with single subjects, married subjects performed better at ADAS-cog13 and spatial processing but performed worse at executive function. Our results differed from the Brenowitz [19] study in that compared with married participants, risk of MCI was significantly lower in widowed participants but not for divorced/separated or never-married participants. Compared to living with a spouse/partner, risk of MCI was significantly higher for subjects living with others but not for subjects living alone [20]. Although this was a clinic-based cohort and thus may not represent the community at large, it is worth noting that such factors affect some domains of cognition. Further research is needed to clarify if such factors increase the risk of MCI and/or dementia.

The Shanghai MCI cohort study is a clinically and cognitively well-characterized cohort of patients with MCI. To date, the enrolled cohort has provided baseline, cross sectional data that enhances the understanding of the extent of cognitive impairment present in MCI and progression from MCI to AD, as well as a foundation for longitudinal examination of the relationship between cognition and neuro-imaging biomarkers. Age and education influenced MMSE, ADAS-cog13 and most domains of cognition. Several social demographical factors such as living alone and being single were associated with some domains of cognition. CDR is not influenced by such factors.

## Conclusion

Baseline characteristics of the Shanghai MCI cohort study indicate a younger, lower educated and moderate gender ratio compared to other studies and represent the target population. 3 years later when the cohort will be finished some risk factors associated the conversion will be validated and some novel factors will be identified. Although the limitation in design, however the results of neuropsychological tests may provide important contribution to the future multiple-nation prevention clinical trial design for Alzheimer's disease.

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