Original Article

Association of Source of Memory Complaints and Increased Risk of Cognitive Impairment and Cognitive Decline: A Community-Based Study

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Abstract

Background: Memory complaint is common in the elderly. Recently, it was shown that self-report memory complaint was predictive of cognitive decline. This study aimed to investigate the predictive value of the source of memory complaints on the risk of cognitive impairment and cognitive decline in a community-based cohort.

Methods: Data on memory complaints and cognitive function were collected among 1840 Chinese participants (aged ≥55 years old) in an urban community at baseline interview and 5-year follow-up. Incident cognitive impairment was identified based on education-adjusted Mini-Mental State Examination score. Logistic regression model was used to estimate the association between the source of memory complaints and risk of cognitive impairment conversion and cognitive decline, after adjusting for covariates.

Results: A total of 1840 participants were included into this study including 1713 normal participants and 127 cognitive impairment participants in 2009. Among 1713 normal participants in 2009, 130 participants were converted to cognitive impairment after 5 years of follow-up. In 2014, 606 participants were identified as cognitive decline. Both self- and informant-reported memory complaints were associated with an increased risk of cognitive impairment (odds ratio [*OR*] = 1.60, 95% confidence interval [*CI*]: 1.04–2.48) and cognitive decline (*OR* = 1.30, 95% *CI*: 1.01–1.68). Furthermore, this association was more significant in males (*OR* = 2.10, 95% *CI*: 1.04–4.24 for cognitive impairment and *OR* = 1.87, 95% *CI*: 1.20–2.99 for cognitive decline) and in higher education level (*OR* = 1.79, 95% *CI*: 1.02–3.15 for cognitive impairment and *OR* = 1.40, 95% *CI*: 1.02–1.91 for cognitive decline).

Conclusions: Both self- and informant-reported memory complaints were associated with an increased risk of cognitive impairment conversion and cognitive decline, especially in persons with male gender and high educational background.

Key words: Cognitive Decline; Cognitive Impairment; Memory Complaints

Introduction

Memory complaints are commonly seen in community dwelling elderly persons with a prevalence of about 50%.[1] Evidence from longitudinal studies suggested that patients with memory complaints had a higher rate of progressive-to-mild cognitive impairment or Alzheimer's disease (AD).[2,3] Furthermore, current diagnostic criteria for mild cognitive impairment highlight memory complaints, reported by patient or someone close to the patient or noted by a clinician.[4,5] Although a previous study showed the efficacy of self-complaint for predicting future cognitive decline,[6] the high prevalence of self-reported memory complaint in nondemented older adults and subjectivity of self-assessment may lead to a low specificity.[7] On the other hand, evidence from a prospective blinded observational investigation suggested that informant-reported memory loss

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better predicted cognitive impairment than self-complaint.[8] Furthermore, Gifford *et al*.[9] recently found that participants of normal cognition with both self- and informant-reported complaints were at the highest risk of conversion to dementia. The cognitive complaints are an important early sign of imminent AD, especially in persons with a high level of education,[10] who played well in objective cognitive assessment because of high cognitive reserve. Therefore, measuring the predictive value of different sources of memory complaint is of importance for evaluation of future cognitive function change.

We performed a prospective population-based study on participants aged 55 years or older in an urban Chinese community, aiming to investigate the predictive value of the source of memory complaints on cognitive impairment conversion and cognitive decline.

Methods

Ethical approval

The prospective study was approved by the Ethics Committee of Ruijin Hospital affiliated to Shanghai Jiao Tong University School of Medicine. Written informed consent was obtained from all participants in this study.

Study population

This study was part of Wuliqiao (urban) Community Epidemiological Study that began in 2009.[9] In this community, a total of 3176 patients aged ≥55 years were enrolled in 2009 for cognitive complaint study.[11] After 5 years of follow-up in 2014, Mini-Mental State Examination (MMSE) was reassessed in 1840 participants (respondent rate of 57.9%). The respondent rate was low for several reasons, including too busy to complete the MMSE assessment, death, moving to other place, hearing problems, not willing to follow-up, and hospitalization. Detailed flowchart of the study is depicted in Figure 1.

Assessment of cognitive complaint

Specially trained investigators interviewed all participants face to face in 2009. Questions about memory complaints were: "Do you think that you have any problems with your memory?" for the participants and "Do you believe the subject has any problems with memory" for the spouse or the close relative who accompanied the participant for interview. The source of memory complaints was classified into three categories according to the reply to the above questions: no complaint (neither participant nor his/her spouse or relatives complain any problems with memory), self- or informant-reported memory complaint (either participant or his/her spouse or relatives complain any problems with memory), and both self- and informant-reported complaints (both participant and his/her spouse or relatives complain any problems with memory).

Assessment of cognitive function and covariant

After training, MMSE was applied by local doctors for cognitive function assessment. Participants were screened for cognitive function at baseline on May 2009 and follow-up reassessment on June 2014. Information about age, gender, and self-reported depression was obtained through questionnaire administrated by local doctors.

The diagnosis of cognitive impairment was based on MMSE scores with different cutoffs for education level: MMSE ≤17 for illiterates; MMSE ≤20 for primary school graduates (≤6 years of education); and MMSE ≤24 for junior high school graduates or above (>6 years of education).[11] The diagnosis of cognitive impairment conversion was defined as people with normal cognitive function in 2009 converting into cognitive impairment in 2014 based on education-adjusted MMSE score. The diagnosis of cognitive decline was defined as MMSE score decreased by ≥2 points during the 5-year follow-up.

Statistical analysis

All data analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). The demographic features were compared by Student's *t*-test for measurement data and Chi-square test for categorical data. Logistical regression model was used to investigate the association of the source of memory complaints with the risk of cognitive impairment conversion or cognitive decline after adjusting for covariant. A $P < 0.05$ was considered as statistical significance.

Results

A total of 1840 participants (559 males and 1281 females; mean age: 71.1 ± 10.0 years) were included into this study. Among the 1840 participants, there were 1713 normal participants and 127 cognitive impairment participants in 2009. After 5 years of follow-up, 130 normal participants were converted into cognitive impairment and 606 were with cognitive decline. Baseline demographic characteristics of all the participants in cognitive impairment conversion study are presented in Table 1, and baseline demographic characteristics of all participants in the study for cognitive decline are presented in Table 2.

For cognitive impairment conversion study, among 1713 normal participants in 2009, 130 participants were converted to cognitive impairment after 5 years of follow-up. Both self- and informant-reported memory complaints were associated with a higher risk of cognitive impairment conversion (odds ratio [*OR*] = 1.60, 95% confidence interval [*CI*]: 1.04–2.48, $P = 0.030$), after adjustment for age, gender, depression complaint, and baseline MMSE score [Table 3]. In subgroup analysis, both self- and informant-reported memory complaints conferred a high risk of cognitive impairment conversion in males (*OR* = 2.10, 95% *CI*: 1.04–4.24, $P = 0.040$) and in people with high education level (*OR* = 1.79, 95% *CI*: 1.02–3.15, $P = 0.040$; Table 3).

The similar results were found in the study of cognitive decline, in which 606 people were identified with cognitive decline after 5 years of follow-up. Both self- and informant-reported memory complaints were associated

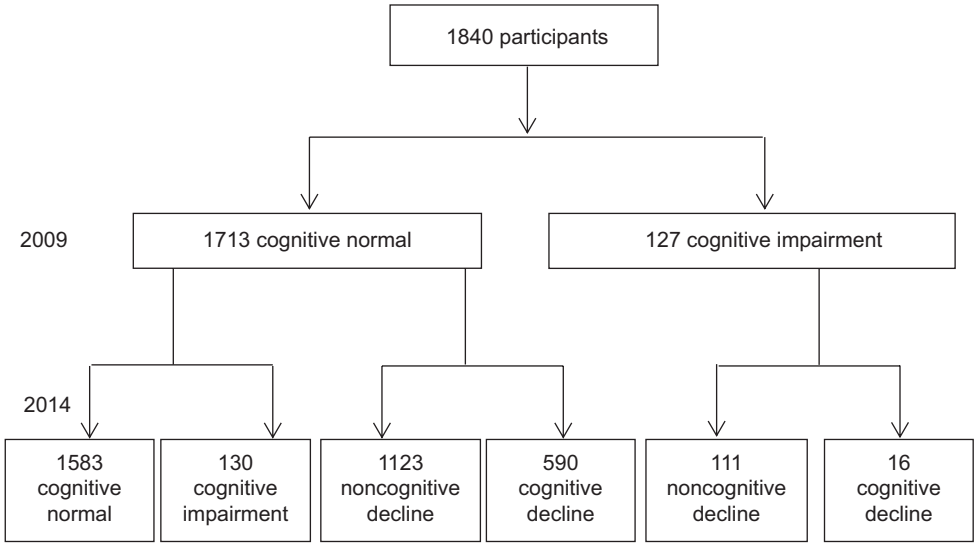

Figure 1: Flowchart of this study.

Table 1: Demographic characteristics of all participants in the study of cognitive impairment conversion ($N = 1713$)

Characteristics	Patients with cognitive impairment conversion ($n = 130$)	Participants with cognitive normal ($n = 1583$)	t or χ^2	P
Age (years), mean ± SD	76.9 ± 10.1	70.3 ± 9.6	−7.462*	<0.001
Gender, *n* (%)			2.284†	0.140
Male	47 (36.2)	472 (29.8)		
Female	83 (63.8)	1111 (70.2)		
Education level, *n* (%)			15.127†	0.001
Illiterate	32 (24.6)	211 (13.3)		
Primary school	22 (16.9)	218 (13.8)		
Junior high school or above	76 (58.5)	1154 (72.9)		
Depression, *n* (%)	4 (3.1)	36 (2.3)	0.339†	0.560
MMSE score, mean ± SD	26.52 ± 3.16	27.91 ± 2.22	4.932*	<0.001
Memory complaint, *n* (%)			8.875†	0.010
No	48 (36.9)	686 (43.3)		
Self- or informant-reported	32 (24.6)	485 (30.6)		
Self- and informant-reported	49 (37.7)	410 (26.0)		
Unable to classify	1 (0.8)	2 (0.1)		

*Student's *t*-test; †Chi-square test. MMSE: Mini-Mental State Examination; SD: Standard deviation.

Table 2: Demographic characteristics of all participants in the study of cognitive decline ($N = 1840$)

Characteristics	Cognitive decline ($n = 606$)	Noncognitive decline ($n = 1234$)	t or χ^2	P
Age (years), mean ± SD	73.2 ± 10.0	70.0 ± 9.7	−6.355*	<0.001
Gender, *n* (%)			0.052†	0.820
Male	182 (30.0)	377 (30.6)		
Female	424 (70.0)	857 (69.4)		
Depression level, *n* (%)	18 (3.0)	25 (2.0)	1.588†	0.210
Education level, *n* (%)			79.852†	<0.001
Illiterate	141 (23.3)	116 (9.4)		
Primary school	104 (17.2)	159 (12.9)		
Junior high school or above	360 (59.5)	957 (77.7)		
MMSE score, mean ± SD	27.85 ± 2.77	27.03 ± 3.18	−5.681*	<0.001
Memory complaint, *n* (%)			8.768†	0.010
No	254 (41.9)	512 (41.5)		
Self- or informant-reported	160 (26.4)	399 (32.3)		
Self- and informant-reported	190 (31.4)	322 (26.1)		
Unable to classify	2 (0.3)	1 (0.1)		

*Student's *t*-test; †Chi-square test. MMSE: Mini-Mental State Examination; SD: Standard deviation.

Table 3: Association of memory complain and cognitive impairment conversion/cognitive decline using multiple regression analysis

Items	Total	Gender, *OR* (95% *CI*)		Educational level, *OR* (95% *CI*)		
		Male	Female	Illiterate	Primary school	Junior high school or above
Cognitive impairment conversion						
No (reference)	1	1	1	1	1	1
Self- or informant-reported	0.98 (0.61–1.58)	1.10 (0.49–2.47)	0.91 (0.51–1.64)	0.77 (0.28–2.11)	0.61 (0.16–2.27)	1.15 (0.63–2.08)
Self- and informant-reported	1.60 (1.04–2.48)*,†	2.10 (1.04–4.24)*	1.36 (0.79–2.35)	1.16 (0.47–2.88)	1.31 (0.44–3.94)	1.79 (1.02–3.15)*
Cognitive decline						
No (reference)	1	1	1	1	1	1
Self- or informant-reported	0.90 (0.70–1.16)	0.98 (0.62–1.56)	0.85 (0.63–1.15)	0.53 (0.27–1.01)	1.14 (0.59–2.21)	0.98 (0.73–1.34)
Self- and informant-reported	1.30 (1.01–1.68)*,‡	1.87 (1.20–2.99)*	1.10 (0.81–1.50)	1.28 (0.68–2.39)	1.04 (0.53–2.05)	1.40 (1.02–1.91)*

*P<0.05; †Adjusted for age, gender, depression, and MMSE score in 2009; ‡Adjusted for age, gender, depression, education level, and MMSE score in 2009. MMSE: Mini-Mental State Examination; *OR*: Odds ratio; *CI*: Confidence interval.

with a higher risk of cognitive decline (*OR* = 1.30, 95% *CI*: 1.01–1.68, $P = 0.045$), after adjustment for age, gender, depression complaint, education level, and baseline MMSE score [Table 3]. In subgroup analysis, both self- and informant-reported memory complaints conferred a high risk of cognitive decline in males (*OR* = 1.87, 95% *CI*: 1.20–2.99, $P = 0.008$) and in people with high education level (*OR* = 1.40, 95% *CI*: 1.02–1.91, $P = 0.040$; Table 3).

Discussion

This study found that both self- and informant-reported complaints of cognitive impairment were associated with further cognitive impairment conversion and cognitive decline, especially for males with high educational level. These findings, combined with other studies,[6,8,10,12,13] supported that subjective memory complaints (SMCs) might be used as an appropriate measurement to predict further memory decline. The probable explanation was that subtle underlying pathological changes might be involved in memory complaint people with normal cognitive function. In line with that, kryscio *et al*.[14] reported that SMC reporters had more severe AD neuropthological burdens in an autopsy-based longitudinal study. It was found that SMCs were associated with hippocampal volumn change in another magnetic resonance imaging-based longitudinal study.

Furthermore, this study suggested that the predictive value of SMCs for cognitive change was more evident in people with high educational level, which was in consistent with the findings from van Oijen *et al*.[10] Highly educated persons usually play well on cognitive screening tests because of high cognitive reserve.[15,16] In addition, Sajjad *et al*.[17] indicated that highly educated persons were more likely to notice subtle changes in their memory than less educated, which made memory complaints an appropriate measurement to evaluate subtle cognitive impairment in highly educational elders.

Another interesting finding was that SMCs were more predictive on cognitive impairment in males than females in this community-based study. Gender differences with regard to the risk of dementia in SMCs have been reported. Pérès *et al*.[18] suggested that women with SMC were more likely to develop dementia, but other reported different result.[19,20] Although loss of the protective estrogen after menopause might make women more vulnerable to memory disorders,[21] women were twice as likely as men to suffer from depressive symptoms,[22,23] especially those in peri- or postmenopausal stage.[24-27] Therefore, it was possible that some SMCs in women were due to depressive mood and might decrease the predictive value of SMCs in women.

The strengths of this study were its population-based prospective design, its large number of participants from representative urban communities, and available data over the follow-up period. Factors that may confuse the assessment of the association between cognitive complaint and risk of cognitive impairment such as depression and objective memory function were evaluated as covariates at baseline interview.

However, some limitations still existed in this study. First, this study did not investigate informant-complaint cohort separately from self-only complaint because this study did not insist the spouse or partner who helped the participant to complete the questionnaire, which probably contributed to the limited data of informant-complaint-only cases to some degree. Second, cognitive complaint was judged by means of a single question which might lead to less well-defined SMCs. Third, MMSE scale alone is not sensitive enough to assess objective cognitive impairment, though it is commonly used in epidemiological cognitive screening. Well-designed studies with more extensive cognitive assessment are needed to overcome these problems in the future.

In conclusion, the findings of this study highlighted the predictive value of the source of cognitive complaints on progression from cognitive normal to cognitive impairment or cognitive decline, especially both self- and informant-reported memory complaints in participants with high education level and male gender. The findings might help identify community dwelling elders with those

characteristics who do well in cognitive test at baseline, but at high risk of dementia, at an early stage.

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Conflicts of interest

There are no conflicts of interest.

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记忆主诉来源与认知障碍和记忆减退的风险增加相关：来自于社区的研究

摘要

研究背景：老年人多诉记忆力减退，研究发现记忆力减退的主诉是认知功能减退的预测因素。本研究旨在探究不同来源的记忆主诉对认知障碍和认知功能减退风险的预测作用。

研究方法：本研究收集了1840名中国城市社区老年人（年龄≥55岁）基线和随访5年后的记忆主诉和记忆功能数据。用简易智能量表（MMSE）评估其认知功能。应用Logistic回归模型在调整相关因素之后分析不同来源的认知主诉与认知功能障碍和认知功能减退的关系。

研究结果：在2009年共纳入1840名社区老人，在基线1713人认知正常，另127人有认知功能障碍。随访5年后，基线认知功能正常的1713人中有130人转变为认知功能障碍。同时发现有606人认知功下降。结果显示自诉和家人诉的记忆力减退都是认知功能障碍（*OR*=1.60, 95% *CI*: 1.04–2.48）和认知功能下降（*OR*=1.30, 95% *CI*: 1.01–1.68）的危险因素。进一步分析发现在男性和教育水平较高的人群中自诉和家人诉的记忆力减退与认知功能障碍和认知功能下降的关系更大（男性：认知功障碍*OR*=2.10, 95% *CI*: 1.04–4.24;认知功能下降*OR*=1.87, 95% *CI*: 1.20–2.99；高教育水平人群：认知功障碍*OR*=1.79, 95% *CI*: 1.02–3.15;认知功能下降*OR*=1.40, 95% *CI*: 1.02–1.91）。

研究结论：自诉和家人诉的记忆力减退与认知功能障碍转归和认知功能进行性下降有关，尤其在在男性和高教育水平人群中其与认知功能障碍和下降的关系更为密切。