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Subjective cognitive function and decline among older adults with psychometrically defined amnestic MCI

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SUMMARY

Objective—To examine the relationship between subjective cognitive function and subsequent cognitive decline among individuals with psychometrically defined amnestic mild cognitive impairment (MCI), and to determine whether the presence of depressive symptoms modifies this relationship.

Method—Fifty-five individuals met psychometric criteria for amnestic mild cognitive impairment (MCI). Cognitive decline was measured using the Mini-Mental State Examination (MMSE), which was administered at baseline and at follow-up two years later. Subjective cognitive function was examined using two different one-item memory complaints, as well as a scale focused on current level of cognitive function relative to past function and a scale focused on forgetting in specific everyday situations.

Results—In multiple regression analyses, the one-item complaint of change in memory at baseline predicted future cognitive decline. There was a significant interaction effect whereby this association was stronger in participants who endorsed fewer symptoms of depression.

Conclusion—Individuals showing memory deficits consistent with amnestic MCI have at least some insight regarding cognitive decline and the extent to which subjective cognitive function is useful in predicting future decline may depend on what particular questions are asked as well as presence of depressive symptoms.

Keywords

subjective cognitive function; mild cognitive impairment; depression; cognitive decline

INTRODUCTION

Several studies have found an association between memory complaints and subsequent cognitive decline or dementia (e.g. Tobiansky *et al.*, 1995; Geerlings *et al.*, 1999; Wang *et al.*, 2004). However, not all studies have replicated these findings, including one of the largest

population-based studies to date (Blazer *et al.*, 1997). Inconsistency in findings may be attributable to several factors. First, most studies have assessed subjective memory function with a single item unique to each study. Another issue is that many studies have used a mix of cognitively impaired and cognitively intact participants (Wang *et al.*, 2004). Schofield and colleagues (1997) found that memory complaints only predicted decline for individuals with objective cognitive impairment at baseline. The complex relationship between depressive symptoms and cognitive function may also influence findings. There is a strong relationship between memory complaints and depressive symptoms (Jonker *et al.*, 2000), depression is often present in individuals with objective cognitive impairment, and depression is associated with greater dementia risk (Jorm *et al.*, 2001).

The present study examines subjective cognitive function as a predictor of cognitive decline among individuals with psychometrically defined mild cognitive impairment (MCI). Not all individuals with MCI experience future cognitive and functional decline, which highlights the need for research on predictors of decline. In contrast to previous studies, this study examines subjective cognitive function measured several ways, allowing us to compare the utility of these measures for predicting cognitive decline. We hypothesized that poorer subjective cognitive function at baseline would be associated with greater future cognitive decline. We also hypothesized that poorer subjective cognitive function would be a stronger predictor of decline among individuals with fewer symptoms of depression, since poorer subjective function would be less likely to reflect depression in this group.

METHOD

Participants

The sample included participants from the longitudinal ACTIVE (Advanced Cognitive Training for Independent and Vital Elderly) study. The ACTIVE study recruited adults age 65 + who were living largely independent of formal care. Potential participants were ineligible for ACTIVE if they showed signs of dementia or significant decline in physical abilities and functional independence, as reflected in the following inclusion criteria: Age ≥ 65 years; Mini-Mental State Examination (MMSE; Folstein *et al.*, 1975) score ≥ 23 ; vision score $>20/50$; no dependence in hygiene, bathing or dressing; no diagnosis of Alzheimer's Disease; no stroke in previous 12 months; no cancer with limited life expectancy; no current chemotherapy or radiation treatment; no communication problems. The resulting sample of 2,832 individuals thus consisted of relatively healthy older adults with a mean age of 74 years at enrollment (Jobe *et al.*, 2001).

Amnesic MCI at baseline was identified using a psychometric algorithm based on cognitive composite scores (Cook *et al.*, under review). The composite memory score was derived from scores on the Hopkins Verbal Learning Test (Brandt, 1991), the Auditory Verbal Learning Test (Rey, 1941), and the paragraph recall subtest of the Rivermead Behavioural Memory Test (Wilson, 1985). Tests were standardized and composite scores were based on the average for the domain (Ball *et al.*, 2002). Participants who scored ≤ 7 th percentile on the memory composite but were not impaired on reasoning or perceptual speed composites were considered cases. This approach was generally consistent with criteria from Petersen *et al.* (1999), with the exception that subjective memory complaints were not required to identify cases (De Jager *et al.*, 2005), and functional performance data were not considered.

The criteria for inclusion in this study were classification of amnesic MCI at baseline and completion of cognitive testing at follow-up two years later. Fifty-five participants met these criteria. Overall, 3.8% of the ACTIVE sample were classified as having amnesic MCI and 52% of these cases had follow-up cognitive testing two years later. For the 55 participants, the

mean age was 76, 75% were Caucasian and 71% were women, and the mean MMSE at baseline was 26.1 (SD = 2.0).

Measures

Rate of cognitive decline was measured with the MMSE. The main independent variables were two scales of subjective cognitive function (a measure of *change in cognitive function* and a measure of *everyday forgetting*) and two items specifically assessing memory complaints (*change in memory* and *problems with memory*). These scales were administered as part of a take-home questionnaire.

Change in cognitive function used six items from the Attitude Toward Intellectual Aging scale of the Personality in Intellectual Aging Contexts (PIC) Inventory (Lachman *et al.*, 1982; items 14, 28, 34, 45, 67, 68). Shortening of this scale was done during the ACTIVE piloting phase in order to reduce subject burden. The 50% of items with the highest item-total correlations were selected. Cronbach alpha reliability coefficient was 0.81. This scale included items such as, 'The older I get, the harder it is to think clearly', and, 'I have to use a lot more mental energy for solving difficult problems'. Responses for these items ranged from 1 (strongly agree) to 6 (strongly disagree) and were summed for the overall score.

Everyday forgetting included 14 items from the General Frequency of Forgetting scale of the Memory Functioning Questionnaire (MFQ; Gilewski *et al.*, 1990; problem items g, h, i, k, l, m, o, p, r; reading-novel items c, d; reading-newspaper items b, c, d). This measure was shortened during the ACTIVE piloting phase in the same way as described above for the PIC, and resulting alpha coefficient was 0.92. Participants were asked, 'How often do these present a problem for you?' for items such as remembering phone numbers, 'things people tell you', personal dates, 'going to the store and forgetting what you wanted to buy', and 'trouble remembering what you have read'. Responses ranged from 1 (always) to 7 (never) and were summed to obtain the overall score.

Both subjective cognitive function scale scores were reversed so that higher scores reflected poorer subjective functioning. Two different memory complaint items were examined: (1) *change in memory* ('I don't remember things as well as I used to', from the PIC), with responses ranging from 1 (strongly agree) to 6 (strongly disagree), and (2) *problems with memory* ('How would you rate your memory in terms of the kinds of problems that you have?' from the MFQ), with responses ranging from 1 (major problems) to 7 (no problems). Scores for both items were reversed so that higher scores reflected greater complaints.

Age, gender, education, and depressive symptoms were the primary covariates of interest. Education was measured as total years of formal schooling. Depressive symptoms were ascertained using the Center for Epidemiologic Studies-Depression-12 Scale (CES-D; Radloff, 1977), with a 0–36 range and higher scores reflecting greater depressive symptoms.

ANALYSIS

We regressed change in MMSE performance on baseline MMSE score, subjective cognitive function, and covariates. The four subjective cognitive function measures were each entered into separate models. We standardized scores on each measure to retain comparability across scales. Because the participants were randomly assigned after the baseline assessment either to cognitive training groups (memory [$n = 15$], reasoning [$n = 12$], or speed of processing [$n = 10$]) or control group ($n = 18$) as part of the ACTIVE study, type of training was dummy-coded and controlled in all analyses. A subset of participants ($n = 18$) also received booster cognitive training, and whether they received this additional training was also controlled in the models. In addition, all models controlled for baseline MMSE, age, gender, years of education,

and depressive symptoms. To investigate whether the association between subjective function and decline was modified by depressive symptoms, an interaction term (the cross-product of depressive symptoms and the respective measure of subjective cognitive function) was included in the regression models.

RESULTS

The 55 participants were not different from the MCI cases who did not have follow-up testing in terms of baseline MMSE, depressive symptoms, age, cognitive training group, or years of education ($p > 0.05$). However, men classified as having MCI were less likely ($p < 0.05$) to return for follow-up than women.

Means, SD, and correlation coefficients for demographic characteristics and predictor variables are presented in Table 1. The four measures of subjective cognitive function were highly intercorrelated and were positively correlated with depressive symptoms. Approximately 89% of the sample reported at least 'slight' agreement for the *change in memory* item, while 51% 'strongly' agreed. For the *problems with memory* item, 67% of the sample reported at least 'minor' problems and 13% reported 'major' problems.

Results obtained from regression models estimated separately for each standardized measure of subjective cognitive function are presented in Table 2. The *change in cognitive function* measure and the one-item complaint of *change in memory* were both significant predictors of change in MMSE. Higher scores on these predictors were associated with greater cognitive decline. The model with *change in memory* as the predictor explained the greatest amount of variance in MMSE change.

There was a significant interaction for the complaint of *change in memory* and depressive symptoms. To examine this finding, we stratified the sample by level of depressive symptoms using a median split ($CES-D \leq 6$ vs $CES-D > 6$). In these *post-hoc* analyses, the association between higher score on reported *change in memory* and decline on MMSE was only significant for participants with low depressive symptoms (estimate = 1.49, standard error = 0.60, $p < 0.05$).

DISCUSSION

We found that subjective change in memory at baseline predicted subsequent cognitive decline in individuals with psychometrically defined amnesic MCI. In contrast, reported frequency of problems with memory in specific everyday situations did not predict cognitive decline. Our findings are consistent with those from Schofield *et al.* (1997), in that they also found a one-item complaint predicted decline in those with baseline cognitive impairment. However, the complaint in the Schofield *et al.* (1997) study asked about 'problems' with memory. In our study, 'problems' could have been lifelong rather than reflecting actual change in cognitive status. Another explanation for our findings regarding 'problems' vs 'change' in memory is that older adults with MCI may not perceive having problems despite awareness of memory decline.

An important finding in the current study is the interaction of depressive symptoms and complaint of change in memory for predicting decline. This finding is consistent with the possibility that among some individuals, complaining about memory may be secondary to depression rather than an indicator of cognitive decline. However, given prior findings of an association between depression and greater risk of dementia, as well as comorbidity of depression and cognitive impairment (Jorm *et al.*, 2001), the complexity of the depression-cognition relationship may have contributed to our lack of findings in individuals with depressive symptoms. The implication for clinicians charged with determining risk of decline

is that they must closely evaluate the presence of depression in individuals suspected of having amnesic MCI.

This study contributes to the existing literature by examining subjective cognitive function specifically in individuals with probable MCI. Findings from this study do not suggest that subjective measures of cognition are better than objective measures for predicting decline. We agree with the view that subjective memory loss alone is unlikely to be a useful clinical predictor of cognitive decline or dementia (St John and Montgomery, 2002). This study provides evidence that subjective measures of function may have some clinical utility when used in conjunction with neurocognitive testing. Findings also suggest that what is asked regarding memory and cognitive function may have different predictive utility. Related to this issue, a main strength of our study and a contrast to previous studies was the use of different measures of subjective cognitive function in addition to one-item memory complaints. Additionally, the predictive utility of simple measures of subjective cognitive performance may vary by depressive symptoms, with better predictive value in individuals with low levels of depressive symptoms.

This study had several limitations, including loss of participants to follow-up, use of shortened subjective cognitive function scales, and a restricted range of baseline MMSE scores for our MCI cases due to ACTIVE participation criteria. Another limitation was our classification of MCI, which was based on an algorithm rather than clinically based diagnosis. However, inclusion criteria for the ACTIVE study made it unlikely that participants classified as having MCI were actually demented or had lifelong cognitive impairment at the baseline assessment.

In conclusion, our study provides evidence that individuals with amnesic MCI have at least some insight regarding cognitive function. The extent to which subjective cognitive function may be useful in predicting decline may depend on what particular questions are asked and presence of depressive symptoms.

KEY POINTS

- Complaint of change in memory was associated with future cognitive decline in those with psychometrically defined amnesic MCI.
- Complaint of problems with memory was not associated with subsequent cognitive decline.
- The association between subjective change in memory and subsequent decline was stronger in participants with fewer depressive symptoms.

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Correlations between Demographic and Predictor Variables

Note.

b based on 6-item scale from the Personality in Intellectual Aging Contexts (PIC) Questionnaire.

^cbased on 14 items from the Memory Functioning Questionnaire (MFQ); MMSE=Mini-Mental State Examination; CES-D=Center for Epidemiologic Studies-Depression-12 Scale.

Table 2
Prediction of Change in MMSE in Multiple Regression Models for Each Measure of Subjective Cognitive Function

Predictor	Change in cognitive function (PIC)		Everyday forgetting (MFQ)		Change in memory (1-item from PIC)		Problems with memory (1-item from MFQ)	
	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
Intercept	-14.82	6.75	-15.80	7.00	-14.68*	6.47	-14.14	7.87
Predictor	1.60*	0.72	0.68	0.78	1.82**	0.55	1.28	0.82
Depressive symptoms	-0.09	0.09	-0.11	0.09	-0.04	0.08	-0.07	0.08
Predictor by depressive symptoms	-0.14	0.09	-0.03	0.08	-0.22**	0.08	-0.13	0.09
Baseline MMSE	0.35	0.20	0.37	0.21	0.32	0.19	0.38	0.23
Age	0.05	0.06	0.05	0.06	0.06	0.06	0.03	0.06
Gender	2.32**	0.86	2.51**	0.89	2.09*	0.81	2.59*	0.97
Education	0.05	0.14	0.02	0.14	0.02	0.13	-0.01	0.14
Adjusted R-square		0.12		0.04		0.22		0.04

Note.

* $p < 0.05$.

** $p < 0.01$.

Training group and booster training were also controlled. MMSE=Mini-Mental State Examination.