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Longitudinal Changes in Memory and Executive Functioning are Associated with Longitudinal Change in Instrumental Activities of Daily Living in older adults

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Abstract

Impaired everyday function is a diagnostic criterion for dementia, and a determinant of healthcare utilization and caregiver burden. Although many previous studies have demonstrated a cross-sectional relationships between cognition (particularly executive functions and memory) and everyday function in older adults, very little is known about longitudinal relationships between these domains. This study examined the association between longitudinal change in episodic memory (MEM) and executive functioning (EXEC) and change in everyday function. Participants were a cognitively heterogeneous group of 100 elderly persons including those with normal cognition, as well as those with mild cognitive impairment and dementia. They were followed for an average of five years. Random effects modeling showed that change in both MEM and EXEC were independently associated with rate of change in informant-rated instrumental activities of daily living (IADLs), even after controlling for age, education, and gender. Findings indicate that declines in MEM and EXEC over time make unique and independent contributions to declines in older adults' ability to function in daily life.

Keywords

Memory; Executive functioning; Everyday Function; dementia; Alzheimer's disease

Mild Cognitive Impairment (MCI) and dementias such as Alzheimer's disease (AD) become increasingly common with age. They are both associated with problems in everyday function that result in patient and caregiver distress, reduced quality of life, increased use of healthcare services, and nursing home placement (Hope, Keene, Gedling, Fairburn, & Jacob, 1998; Vetter et al., 1999). Given its associated burden, an improved understanding of the determinants of functional decline, including the nature of the relationship between the development of specific cognitive impairments and the development of functional impairments is paramount.

The assessment of everyday functioning in older adults typically focuses on an individual's ability to carry out activities of daily living (ADLs) because it is these activities that are critical to independent living. Basic ADLs (BADLs) include tasks such as grooming, feeding, and toileting, while instrumental ADLs (IADLs) involve complex behaviors including managing finances, handling medications, and housekeeping. BADLs are highly correlated with motor functioning and coordination (Bennett et al., 2002; Boyle, Cohen, Paul, Moser, & Gordon, 2002; Cahn & Sullivan, 1998). In contrast, declines in IADLs have been shown to be more influenced by cognitive functioning, are affected relatively early in the course of dementia (Stern, Hesdorffer, Sano, & Mayeux, 1990), and can even be present in preclinical dementia states such as mild cognitive impairment (MCI) (Griffith et al., 2003; Ritchie, Artero, & Touchon, 2001).

Previous studies have demonstrated *cross-sectional* relationships between neuropsychological performance and everyday function in older adult populations. Among these studies, the cognitive domains most consistently found to be associated with everyday function include executive functioning (Bell-McGinty, Podell, Franzen, Baird, & Williams, 2002; Cahn-Weiner, Boyle, & Malloy, 2002; Grigsby, Kaye, Baxter, Shetterly, & Hamman, 1998; Royall, Palmer, Chiodo, & Polk, 2004) and memory (Farias, Mungas, Reed, Haan, & Jagust, 2004; Goldstein, McCue, Rogers, & Nussbaum, 1992; Jefferson et al., 2008). Cross-sectional studies, however, provide limited insight into the course of decline in cognition and function, and how change in one is related to change in the other. In fact, cross-sectional research designs investigating a developmental or progressive disease process may lead to erroneous conclusions or misleading results (Kraemer, Yesavage, Taylor, & Kupfer, 2000). Evidence that two variables change in tandem using prospective longitudinal research provides increased evidence (although does not prove) that there is a causal relationship between the two. At a minimum, understanding patterns of change in these two conceptually distinct domains provides better description of the course of dementia.

To date there is very little research examining longitudinal relationships between cognition and everyday function. Those longitudinal studies available have focused on global measures of cognition rather than specific neuropsychological domains. For example, population-based longitudinal studies have shown that global measures of baseline cognitive function are associated with a faster rate of functional decline and predict the development of future disabilities in IADLs (Barberger-Gateau & Fabrigoule, 1997; Lavery et al., 2005; Royall et al., 2004; Schmeidler, Mohs, & Aryan, 1998). A few recent studies have evaluated how specific cognitive functions *measured at baseline* predict future decline in functional status, although most have been limited to examining only a single cognitive domain (Royall 2004; Lavery 2005). Our group has previously shown that executive functioning at baseline is associated with future decline in functional abilities such that the greater degree of executive dysfunction at baseline, the faster functional abilities decline over time (Cahn 2007). Others studies have suggested that cognitive domains including memory may also influence functional trajectories (Bennett et al., 2002; Dodge, Du, Saxton, & Ganguli, 2006). In summary, there seems to be emerging evidence linking cognitive performance at baseline to longitudinal functional outcomes in older adults with and without dementia. What still remains unclear is how trajectories of change in cognition relate to longitudinal trajectories of change in everyday function. That is, how does the evolution of cognitive impairment relate to the evolution of functional impairment and are there differential relationships between change in specific cognitive domains and change in everyday function? The purpose of the present study was to examine the relative contributions of longitudinal changes in memory and executive functioning to longitudinal change in everyday function in older adults. Psychometrically matched measures of cognitive functions (i.e. measures with equivalent reliability and sensitivity) were used to facilitate unambiguous interpretation of any potential differential effects. Given the results of previous cross-sectional studies, we hypothesized that longitudinal

change in executive functioning would be associated with longitudinal change in IADLs. Additionally, because several previous cross-sectional studies also suggest memory dysfunction is associated with impairments in IADLs, we also hypothesized that longitudinal decline in memory over time would make an independent contribution to declines in everyday function.

Method

Participants

Participants were part of a multicenter collaborative longitudinal study of aging, described previously (Cahn-Weiner et al., 2007; Mungas et al., 2005). All participants received a thorough clinical evaluation including neurologic examination, appropriate laboratory tests, neuropsychological testing with a standardized battery, and neuroimaging, culminating in a clinical diagnosis made at a multidisciplinary consensus case conference. Exclusion criteria included 1) neurological illness other than AD or cerebrovascular disease (CVD), 2) cortical infarction on MRI, 3) head injury with loss of consciousness lasting longer than 30 minutes, and 4) alcohol abuse within 5 years. The institutional review boards at all participating institutions approved this study, and subjects or their legal representatives gave written informed consent.

Recruitment was targeted to ensure broad variability of cognitive function in order to capture the spectrum from normal aging, through mild cognitive impairment and dementia. Participants were selected for inclusion in this study if they had at least two evaluations that included functional assessment and neuropsychological testing performed within six months of each other. In this sample diagnosis is categorized both by syndrome (normal, MCI, demented) and by etiology (dementia type). Dementia is defined according to DSM-IV criteria (American Psychological Association, 1994) that stipulate the presence of multiple cognitive deficits sufficiently severe to impair daily function. Although no strict psychometric cut-off scores are used to define cognitive impairment, cognitive impairment is identified by clinicians when a participant's performance falls approximately 1.5 standard deviations below age-matched norms and in reference to their educational and socioeconomic background. If the participant is determined to be demented, the second step of the diagnostic evaluation is to assign a dementia type. Dementia types included AD, vascular dementia (VaD) or mixed AD/vascular dementia. A diagnosis of Possible or Probable AD was based on NINCDS-ADRDA criteria (McKhann et al., 1984); a diagnosis of Probable or Possible VaD was based on California ADDTC criteria (Chui et al., 1992). The syndrome of MCI is diagnosed when there is cognitive impairment but the criteria for dementia are not met. Based on the above criterion, 100 individuals were included in the study; 45 were cognitively normal, 29 had a clinical diagnosis of MCI, and 26 had dementia (15 diagnosed with AD, 7 with VaD and 4 with a mixed AD/VaD). These diagnoses are based on the baseline evaluation. Summary data on demographic characteristics and global cognitive function (Mini Mental State Examination) are presented in Table 1. In terms of the characteristics of the informants who rated the study participants' IADLs, 48% were spouses, 28% were an adult child of the participant or a son- or daughter-in-law, 5% were other relatives of the informant, 5% were a friend of the informant, 21% served as their own informant (limited to those that were cognitively normal), and 3% had someone else as the informant.

Neuropsychological Measures

All subjects received a standardized battery of neuropsychological tests. All personnel involved in test administration were trained in administration and scoring procedures and cross-center observation and cross-scoring of test protocols were done to monitor quality of data collection. Composite scales were developed to measure episodic memory (MEM) and executive function

(EXEC). Details of scale derivation and validation have been reported previously (Mungas, Reed, & Kramer, 2003). To summarize, item response theory (IRT) analytic methods (Hambleton, Swaminathan, & Rogers, 1991) were used to create psychometrically matched scales. Within the item response theory framework, scales are matched when they demonstrate equivalent reliability over all points in the ability continuum. The MEM scale was based on the MAS Word List Learning Test (Williams, 1991), which is similar in structure to other supra-span multiple trial list-learning tests. Donor items include the immediate recall trials (trials 1 and 3), delayed free recall, and delayed cued recall trials. Donor items for the EXEC scale included WMS-R (Wechsler, 1987) Digit Span backward and Spatial Span backward total scores, the entire Initiation/Perseveration subscale of the Mattis Dementia Rating Scale, which includes items assessing abstract reasoning, (Mattis, 1973) and letter fluency (Benton & Hamsher, 1976). These measures were converted to standard scores based upon the mean and standard deviation of a group of normal controls from a larger sample of 400 from this project (Mungas et al., 2003). The scales have a mean of 100 and SD of 15 in the sample of controls, and have high reliability ($r > .90$) from about -2.0 SD below the mean of the overall development sample to 2.0 SD above the mean. These measures do not have appreciable floor or ceiling effects for participants in this sample and have linear measurement properties across a broad ability range. They are near-normally distributed, which presents advantages for statistical analyses. In previous studies MEM has been shown to be associated with hippocampal volume, and EXEC is associated with cortical volume, and the presence of subcortical lacunes and abnormal white matter hyperintensities (Carey et al., 2008; Kramer et al., 2007; Mungas et al., 2005), the latter two of which have been implicated in disruption of frontal-subcortical circuits (Chui & Willis, 1997; Cummings 1994). EXEC (and MEM) have also been shown to correlate with metabolic rate in the dorsolateral frontal cortex, while activity in temporal regions is correlated with MEM but not EXEC (Reed et al, 2004).

Activities of Daily Living Measure

Everyday function was measured using the eight items from the Blessed Roth Dementia Rating Scale (BRDRS) that assess instrumental activities of daily living (items are shown in Table 2). Each item of the scale is rated by a clinician based on caregiver report of the patient's ability to complete the task using a scale of 1 = completely unable to perform task/dependent, 0.5 = has some difficulty performing the task/needs some assistance, and 0 = performs task normally. Thus, lower scores on this instrument indicate a higher level of everyday functioning; the total score could range from 0 to 8. The BDRS has been used extensively in large scale studies as a measure of functional status because of its demonstrated correlation with postmortem biochemical and neuropathological changes (Blessed, Roth, & Tomlinson, 1968).

Data Analysis

The goal of the study was to characterize the relationship between change in MEM and EXEC with change in IADLs, after adjusting for baseline level of cognitive function. We used a growth-curve approach, fitting random-effects regression models (Laird & Ware, 1982) to test the hypothesis that the rate of change in cognition is associated with rate of change in IADL. Rather than using only the first and last IADL assessment for each person to estimate change in IADL by a difference score, these models utilized all of the available data from each subject. They enabled us to estimate the mean trajectory of IADL over time and to characterize how change in cognition modified that average trajectory. The primary outcome variable was IADL measured over time. Baseline and longitudinal (time-varying) assessments of MEM and EXEC were used as the independent variables to predict baseline and change in IADLs. The time-varying MEM and EXEC variables were coded as change since baseline. When a MEM or EXEC assessment was not available to match the IADL assessment within six months, the values from the closest MEM or EXEC assessment were used. Models used for these analyses incorporated random-effects to allow for between person variability in IADL scores

summarized by a person's tendency to be above or below the predicted average level at a given time and to decline faster or slower than average. They, therefore, also adjusted for baseline IADL levels. They also allowed for different spacing between and number of assessments across subjects. Extensions to these models, called simultaneous models, were used to estimate correlations between change in MEM or change in EXEC and change in IADLs (Beckett, Tancredi, & Wilson, 2004; Harvey, Beckett, & Mungas, 2003).

Model building began with simple models assessing the association between baseline and change in one cognitive domain with level and change in IADLs. To assess associations between change in cognition with change in IADL, a time by change in cognition interaction was included in the model. Coefficients of this interaction may be interpreted as the average annual change in IADL associated with a one unit difference in the change in cognition. Examination of the correlation between the cognitive predictors revealed only a modest association ($r = .48$ between baseline MEM and EXEC and $.44$ between change in MEM and change in EXEC) and therefore was determined to be sufficiently low to include both domains in the same model. Thus, a final joint model assessed the independent associations of change in MEM and change in EXEC with change in IADL. All models were adjusted for the possible confounding effects of age, education, and gender. Model assumptions of normality, linearity, constant variance, and bivariate normality of the random effects were examined using graphical diagnostics, including residual plots and Q-Q plots. The IADL variable was not normally distributed, so the IADL rating was shifted by one and then transformed using the natural logarithm. This transformed variable as the outcome satisfied the assumptions of the models.

Multiple imputation methods, using a Markov Chain Monte Carlo approach, were used to impute missing IADL ratings. IADL ratings were only imputed for dates at which the functional measure was attempted but not completed either due to an insufficient caregiver available to evaluate the functional ability of the subject or an incomplete questionnaire. Only 7% of the IADL ratings were imputed and 62% of those imputed were for normal subjects. We imputed 10 data sets assuming an underlying distribution of the IADL ratings centered at the baseline mean of each diagnostic group and combined the results from each of the data sets to yield final estimates of the associations. Alternative assumptions including assuming an underlying distribution centered at no functional impairments and at the baseline mean of all subjects were also considered, and results from these analyses were similar to those presented.

Results

There were 483 IADL assessments for the 100 cases, all of whom had complete neuropsychological data. The modal number of annual assessments per participant was five, and ranged from 2 to 10. The average time from the initial to last assessment was 5.3 years ($SD = 2.6$, range = 0.9-10.3). Eighty-six percent of participants had at least three assessments including the baseline visit. If we treat number of visits as a categorical variable with 3 levels (2, 3, ≥ 4), there was no significant association between diagnosis and number of visits ($p=0.3$, Fisher's exact test). 91% of normals had more than 2 visits, 90% of MCI had more than 2 visits and 73% of demented subjects had more than 2 visits. The average lag between visits did differ by diagnostic group ($F=9.5$, $p<0.001$, ANOVA), with normals seen, on average every 1.2 years ($SD=0.4$), MCI seen on average every year ($SD=0.2$) and demented subjects seen every 0.9 years ($SD=0.4$). Although these time lags were statistically different, the practical significance of these small differences seem minimal.

Baseline and rates of change in the cognitive and functional variables

Table 3 presents baseline means and average annual rate of change on the functional and cognitive measures (both the composites and donor items) by diagnostic syndrome (cognitively normal, MCI, dementia). As expected baseline MEM and EXEC differed by cognitive groups

(for overall F , p 's < .0001, all pairwise tests were also significant at $p < .05$ after adjusting for multiple comparisons) the cognitively normal group was average, the dementia group was clearly impaired, and the MCI group mean was intermediate. Thus, there was evidence of a continuum of underlying pathology and disease severity. The annual rate of change in MEM and EXEC also differed across groups (p 's = .04 and .004, respectively; pairwise comparisons reached significance after adjustment for multiple comparisons only for the normal vs. dementia comparisons) in the same pattern (normals < MCI < dementia). Interestingly the EXEC scale showed evidence of annual decline in the normal group, whereas the MEM scale did not. The MCI and dementia groups also generally showed more decline on the EXEC scale in comparison to the MEM scale.

Similar to their progressive cognitive impairment, the groups also showed progressive impairment in IADLs ($p < .001$; all pairwise comparisons also significant at $p < .05$ level after adjusting for multiple comparisons). The dementia group at baseline was rated as unable to perform over two of the eight functional abilities assessed, and the MCI group mean IADL score was intermediate to normals and the demented participants. In terms of annual rate of change in IADLs there was a significant difference between the groups ($p < .001$; MCI and demented and normals and demented were significant at $p < .05$ after adjusting for multiple comparisons). Normals at baseline showed essentially no change in everyday function over time. The MCI group gained about 0.2 points on the eight-point IADL scale per year (high scores indicate greater impairment). The dementia group gained, on average, about one point per year on the IADL scale, which roughly corresponds to becoming dependent in one more IADLs each year.

Change in cognitive associated with change in everyday function

Random effects models allowed us to investigate associations between longitudinal change in each of the cognitive variables and change in IADL ratings; however we also included terms to examine cross-sectional (baseline) relationships. First we examined the association between MEM and IADLs, independent of EXEC. In a model that included baseline MEM and MEM change (along with age, education, and gender) results showed that baseline MEM was associated with baseline IADLs ($p = 0.001$) and longitudinal change in MEM was associated with longitudinal change in IADLs ($p < 0.001$). Thus, a steeper decline in MEM over time was associated with a greater degree of functional decline. Age, education, and gender were not significantly associated with functional change.

In a separate model including baseline EXEC and change in EXEC (along with age, education, and gender), we found that baseline EXEC was associated with baseline IADLs, and change in EXEC was associated with change in IADLs (p 's < 0.001 for both). Thus again, a greater degree of decline in EXEC was associated with greater functional decline. Neither age, education nor gender were independently associated with functional change.

Finally, we examined a joint model that simultaneously included both MEM and EXEC variables (along with demographics). In this model, both baseline MEM and baseline EXEC were independently associated with baseline IADLs (p 's = < .001 and .002, respectively). Additionally, longitudinal change in both MEM and EXEC were independently associated with IADL change (p 's = 0.002 and .008, respectively), with declines in MEM and EXEC associated with greater functional decline. None of the demographic variables were associated with change in IADLs. These results are displayed in Table 4.

In order to obtain an estimate of the magnitude of the relationship between change in the cognitive variables and change in IADLs, we examined correlation coefficients between these domains. The correlation between change in MEM and change in IADLs was $-.69$ ($p < .001$) and the correlation between change in EXEC and change in IADLs was $-.72$ ($p < .001$).

Discussion

The primary purpose of this study was to examine the association between longitudinal changes in domain-specific cognitive functions with longitudinal change in IADLs. A strength of this study was that it followed older adults whose cognitive functioning was well characterized by detailed neuropsychological testing over an average of five years. Results showed that declines in both MEM and EXEC confer unique and additive effects upon everyday function. Thus, an individual who experiences a decline over time in memory would also be expected to show a concomitant decline in everyday function. Similarly, an individual who shows a decline in executive function would likely also show a decline in everyday function. Since declines in each cognitive domain have independent associations with change in everyday function, individuals who show change in both memory and executive functioning would be expected to show an even greater decline in everyday function than individuals experiencing a decline in either one of the cognitive domains alone.

Very few previous studies have examined longitudinal relationships between cognition and everyday function and so this study represents an important extension of previous cross-sectional research. As previous cross-sectional studies (i.e. (Bell-McGinty et al., 2002; Cahn-Weiner et al., 2002) have suggested, the present study further confirms that executive dysfunction has important ramifications on an individual's functional capacities. Importantly, the present study suggests that *longitudinal decline* in executive functions is associated with declines in everyday abilities. In particular, the present study suggests that change in those executive functions related to working memory, behavioral initiation and regulation, strategy generation, and abstract thinking and concept formation are associated with changes in daily function.

Perhaps somewhat more controversial, but also supported by cross-sectional studies (i.e. (Farias et al., 2004; Jefferson et al., 2008), the current study also shows that memory abilities make important contributions to a person's functional capacities. Change in memory conferred its own effect on change in IADLs and this effect remained strong even when change in executive function was jointly included in the model. Such findings help to explain other recent findings that show individuals with MCI, many of whom have cognitive deficits confined to memory, demonstrate declines in everyday functioning (Tomaszewski Farias et al., In Press).

We are aware of only one prior study that examined concurrent change in specific cognitive domains and change in everyday function in older adults. Previously Royall and colleagues (Royall, Palmer, Chiodo, & Polk, 2005) found that change in executive function, but not change in memory, was independently associated with change in functional impairment. In contrast, the current study suggests that the effect of change in memory on change in IADLs is not entirely mediated by changes in executive function. The differences in results across the two studies may, in part, be the result of differences in the measurement properties of the different scales used in each study. In the present study we used measures of memory and executive function that were specifically designed to have similar measurement properties (i.e. similar reliability and sensitivity across a broad spectrum of ability level, and linear measurement properties such that neither scale has appreciable floor or ceiling effects (Mungas et al., 2003). The use of psychometrically matched measures in the current study allows us to draw more confident conclusions about domain-specific cognitive effects on everyday function. Another potential reason for the difference in results between the current study and that of Royall and colleagues is that participants in the latter study were largely cognitively normal at baseline, whereas the sample in the present study represented greater cognitive diversity, including those with cognitive impairment and frank dementia. Thus, certain cognitive changes may be selectively important depending on baseline status: change in executive function may be more important in predicting change in normal older adults, whereas memory change likely

becomes particularly important in predicting functional decline in MCI and dementia. In some support of this hypothesis, when we repeated the primary analysis using only those with cognitive impairment (MCI or dementia) only the association between change in MEM and change in IADLs reached statistical significance. Alternatively when analysis only included the normals, change in EXEC became associated with change in IADLs, although change in MEM was still also independently associated with change in IADLs (data not shown). Additionally, we observed that the EXEC scale showed more change in the normals than the MEM scale (see Table 3) suggesting that the EXEC domain is probably more sensitive to the effects of normal aging. This finding is consistent with other literature which suggests that declines in executive functioning are associated with normal aging, and may reflect some loss in the integrity of white matter connection which are vulnerable to cerebrovascular disease (Kramer et al., 2007).

In examining the magnitude of the relationship between the two cognitive domains and everyday function we found that the overlapping variance between MEM and EXEC with IADLs ranged from 48% to 52%. Such findings suggest fairly strong relationships between these domains. In a recent review article (N Chaytor & Schmitter-Edgecombe, 2003) the authors concluded that cross-sectional relationships between neuropsychological tests and measures of everyday functioning are primarily in the moderate range, often in the 18% to 20% range (N.Chaytor, Schmitter-Edgecombe, & Burr, 2006). Thus, longitudinal relationships among cognition and everyday function may be stronger than cross-sectional relationships. Further research is need to confirm this preliminary finding but if it proves to hold true it could have important clinical relevance and suggest serial neuropsychological testing maybe particularly useful.

In the current study we specifically selected a sample with broad variability of cognition and everyday function, ranging from fully cognitively normal to moderately impaired (at baseline). The assumption is that correspondingly broad variability of brain pathology will underlie this behavioral variability. We did not focus on separate analyses for normals, MCI, and demented cases because this inherently reduces variability and decreases sample size, and ultimately does not assess the continuous effects of pathology across its full range. Further, important for longitudinal studies like the present one, separate subgroup analyses also provides limited information about how functional limitations progress from normal cognition to severely impaired (Kraemer et al., 2000).

The current study does have a number of limitations that deserve mention. A degree of caution about the generalizability of the results is warranted. The participants of this longitudinal study were as a whole, well educated and comprised of a clinical sample, primarily recruited from memory disorders clinics where AD is the predominant disease (selection bias). As such, our results may differ from studies utilizing older adults out in the community who are not actively seeking treatment.

The current study focused on two cognitive domains, memory and executive function because prior studies had identified these domains as especially important to daily function. The particular executive function scale used in this study was derived primarily, although not exclusively, from working memory and verbal fluency tests. Both verbal fluency and working memory are commonly considered measures of select aspects of executive functioning, and both have been linked to frontal lobe functions (for recent reviews see (Cabeza & Nyberg, 2000; Henry & Crawford, 2004). However, other executive functions not covered by this composite are also likely to make important contributions to everyday function. For example, measures of novel problem solving and practical judgment are likely to be particularly relevant to everyday functioning but were not included in the current study. Further research on which aspects of executive functioning are particularly important to functional abilities will be

important. Other noncognitive/behavioral variables including depression can also play an important role in everyday function but were unfortunately not available in the current study. Additionally, while the BRDRS has advantages as a measure of everyday function (it has been correlated with postmortem pathological brain changes, and it is very simple to administer and time efficient), it also has limitations because it is a fairly gross measure of everyday function. Also the use of informant-based ratings of everyday function offers both costs and benefits. Use of an informant or proxy to rate an individual's everyday functioning has been shown to be useful in differentiating individuals with dementia from healthy elders (DeBettignies, Mahurin, & Pirozzolo, 1990; Isella et al., 2006; A.F. Jorm & Jacomb, 1989; A.F. Jorm & Korten, 1988; Kemp, Brodaty, Pond, & Luscombe, 2002; Seltzer, Vasterling, Mathias, & Brennan, 2001), in predicting who will go on to show further decline (A. F. Jorm, Christensen, Jacomb, Korten, & Mackinnon, 2001), and in predicting incident dementia (Daly et al., 2000; Harwood, Hope, & Jacoby, 1997). A disadvantage of informant report is that it is subject to reporter bias.

Currently there is limited knowledge about the course and determinants of late life functional impairment, something which carries with it tremendous personal and social cost. This is the first study to show that longitudinal declines in both memory and executive functions are independently related to decline in everyday function in older adults. In conjunction with other findings, the current results provide further evidence that impairment and decline in memory and executive function play critical roles leading to functional disability in older adults.

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Table 1

Participant demographic characteristics and global cognitive status.

	Cognitively Normal (n=45)	MCI (n=29)	Dementia (n=26)
Age	73.5 (7.7)	73.0 (8.5)	74.5 (8.7)
Gender (% female)	47%	24%	31%
Education (years)	14.7 (2.9)	14.1 (3.1)	14.0 (3.5)
Ethnicity (% Caucasian)	82%	76%	88%
MMSE Score	29.0 (1.3)	28.0 (1.9)	23.8 (3.7)

Table 2**Blessed-Roth Dementia Rating Scale Instrumental Activities of Daily Living Items**

a.	Ability to find way around familiar streets
b.	Perform household tasks
c.	Cope with small sums of money
d.	Remember short lists of items
e.	Find way about indoors
f.	Interpret surroundings (e.g., to recognize whether in hospital or at home)
g.	Recall recent events (e.g., recent outings, visits of relatives)
h.	Tendency to dwell in the past

* Each item was rated as either 0 = normal performance/no difficulty, .5 = some difficulty performing task, 1 = unable to perform task

Table 3

Mean baseline cognitive and functional scores (SD in parentheses) and annual rate of change (standard deviations in parentheses) by baseline cognitive status.

Cognitive Variable	Assessment	Baseline Diagnostic Syndrome		
		Cognitively Normal (n=45)	MCI (n=29)	Dementia (n=26)
Memory (MEM)	Baseline	104.6 (15.0)	89.5 (14.4)	68.1 (16.7)
	Annual Change	0.2 (3.6)	-0.9 (5.7)	-2.5 (3.8)
	Percent Change	0.4% (3%)	-1% (6%)	-3.7% (6.2%)
Immediate Recall, Trial 1	Baseline	6.3 (1.5)	4.8 (1.8)	3.3 (1.9)
	Annual Change	0.03 (0.56)	-0.04 (0.79)	-0.5 (1.1)
	Percent Change	1.7% (10%)	4.2% (22%)	-24% (32%)
Immediate Recall, Trial 2	Baseline	8.6 (2.1)	7.0 (1.9)	5.0 (1.6)
	Annual Change	0.02 (0.58)	-0.3 (0.7)	-0.6 (1.0)
	Percent Change	1.3% (8.4%)	-4.5% (13.9%)	-16% (27%)
Immediate Recall, Trial 3	Baseline	9.7 (1.7)	7.9 (1.8)	5.8 (2.1)
	Annual Change	0.1 (0.6)	-0.3 (1.1)	-0.6 (0.8)
	Percent Change	1.5% (6.9%)	-4.7% (15.5%)	-11 % (21%)
Delayed Free Recall	Baseline	10.2 (1.9)	8.0 (3.0)	3.5 (3.6)
	Annual Change	-0.1 (0.6)	-0.3 (1.6)	-0.9 (1.5)
	Percent Change	-0.4% (6.4%)	-7.7% (21.5%)	-27% (28%)
Delayed Cued Recall	Baseline	10.4 (1.6)	9.0 (2.0)	5.8 (3.0)
	Annual Change	-0.01 (0.53)	-0.2 (0.9)	-0.4 (1.2)
	Percent Change	0.3% (5.8%)	-1.0% (10.5%)	-6.9% (24%)
Executive (EXEC)	Baseline	101.1 (12.3)	84.4 (17.4)	73.4 (14.0)
	Annual Change	-0.7 (3.9)	-1.6 (3.0)	-3.7 (3.4)
	Percent Change	-0.7% (4%)	-1.7% (3.3%)	-5.3% (5.1%)
Digit Span Backward	Baseline	6.3 (1.9)	5.0 (2.1)	5.1 (1.8)
	Annual Change	0.05 (0.09)	0.07 (0.16)	0.05 (0.19)
	Percent Change	0.9% (1.9%)	1.6% (4.0%)	1.1% (4.6%)
Visual Memory Span Backward	Baseline	6.8 (1.7)	6.3 (2.0)	5.1 (1.6)
	Annual Change	-0.1 (0.6)	-0.3 (0.6)	-0.5 (1.1)
	Percent Change	-0.8% (9.8%)	-3.4% (7.7%)	-8.8% (18%)
Initiation/Perseveration DRS	Baseline	36.0 (1.8)	32.3 (4.9)	27.4 (6.0)
	Annual Change	-0.4 (0.8)	-0.7 (1.5)	-2.5 (2.5)
	Percent Change	-1.0% (2.4%)	-1.9% (4.7%)	-10% (10%)
Letter Fluency "A"	Baseline	12.6 (4.2)	9.3 (5.2)	7.0 (3.2)
	Annual Change	-0.1 (1.2)	-0.2 (1.2)	-0.7 (1.0)
	Percent Change	-0.1% (9.9%)	3.5% (25%)	-10% (20%)
Letter Fluency "F"	Baseline	14.0 (3.9)	11.3 (5.7)	9.4 (5.0)
	Annual Change	0.2 (1.0)	-0.5 (1.3)	-0.7 (0.9)
	Percent Change	1.8% (7.4%)	-3.6% (10.8%)	-10% (13%)
Letter Fluency "S"	Baseline	15.6 (4.2)	11.9 (6.5)	9.5 (3.8)

Baseline Diagnostic Syndrome				
Cognitive Variable	Assessment	Cognitively Normal (n=45)	MCI (n=29)	Dementia (n=26)
IADL	Annual Change	-0.3 (1.4)	-0.5 (1.3)	-1.7 (1.9)
	Percent Change	-1.4% (9.0%)	-4.3% (14.3%)	-18% (19%)
	Baseline	0.28 (0.69)	0.65 (0.70)	2.6 (1.9)
	Annual Change	0.09 (0.34)	0.21 (0.33)	0.8 (0.8)

Baseline and annual change scores for the cognitive measures are in standard score points (mean = 100, SD = 15).

Baseline and annual change for the IADLs are in raw scores.

Table 4

Results of random effects modeling of baseline and longitudinal change in MEM and EXEC in association with baseline and longitudinal change in IADLs (adjusted for age, education and gender).

<i>Baseline level of log-IADL</i>			
Variable	Estimate	Standard Error	p-value
Age	0.002	0.005	0.6
Education	0.04	0.01	0.01
Male	-0.04	0.09	0.6
MEM	-0.02	0.002	<0.001
EXEC	-0.008	0.002	0.002
<i>Change in log-IADL</i>			
Variable	Estimate	Standard Error	p-value
Time	0.04	0.02	0.09
Age *time	0.001	0.001	0.29
Education*time	-0.005	0.003	0.17
Male*time	0.01	0.02	0.47
ΔMEM*time	-0.001	0.0003	0.002
ΔEXEC*time	-0.001	0.0005	0.008