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Differential Trajectories of Age-Related Changes in Components of Executive and Memory Processes

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Abstract

Several studies have demonstrated age-related declines in general executive function and memory. In this study, we examined cross-sectional and longitudinal age effects in more specific cognitive processes that constitute executive function and memory. We postulated that, whereas some components of executive and memory functions would show age differences and longitudinal declines, other specific abilities would be maintained or even improve with repeated testing. In a sample of individuals 55 years old from the Baltimore Longitudinal Study of Aging, we found longitudinal declines in inhibition, manipulation, semantic retrieval, phonological retrieval, switching, and long-term memory over a maximum of 14 years follow-up. In contrast, abstraction, capacity, chunking, discrimination, and short-term memory were maintained or even improved longitudinally, probably due in part to repeated testing. Moreover, whereas several different abilities were correlated across participants' cross-sectional performance, longitudinal changes in performance showed more heterogeneous trajectories. Finally, compared with cross-sectional performance, longitudinal trajectories showed better distinction between participants with and those without later cognitive impairment. These results show that longitudinal cognitive aging of executive and memory functions is not a uniform process but a heterogeneous one and suggest that certain executive and memory functions remain stable despite age-related declines in other component processes.

Keywords

aging; executive function; memory; longitudinal; cross-sectional

Amid a canvas of broad cognitive declines associated with aging, there is also evidence that certain cognitive abilities undergo little age-related change (Baltes, Cornelius, Spiro, Nesselrode, & Willis, 1980; Baltes & Lindenberger, 1988; Goh & Park, 2009; Hultsch, Hertzog, Dixon, & Small, 1998; Park & Goh, 2009; Park & Reuter-Lorenz, 2009; Rönnlund, Nyberg, Bäckman, & Nilsson, 2005; Schaie, 1996). Indeed, minimal age-related declines have been observed for cognitive processes involving verbal knowledge (Giambra, Arenberg, Kawas, Zonderman, & Costa, 1995; Hultsch et al., 1998; Park et al., 2002; Schaie, 1996), and when supportive information is provided or available, older adults' performance in some experimental tasks improves and may even be comparable with that of young adults in some cases (Castel, 2005, 2007; Dunlosky, Kubat-Silman, & Hertzog, 2003; Jennings, Webster, Kleykamp, & Dagenbach, 2005). Moreover, substantial variability exists in the degree to which different individuals show age-related cognitive changes, with some showing decline and others remaining relatively stable over time (de Frias, Dixon, &

Strauss, 2009; Hultsch, MacDonald, Hunter, Levy-Bencheton, & Strauss, 2000; Wilson et al., 2002). These findings suggest that cognitive decline with aging is not a uniform phenomenon and that, when considered more specifically, different cognitive abilities may be more affected by aging than others. In this study, we evaluated whether different specific cognitive abilities associated with executive function and memory undergo uniform or heterogeneous longitudinal change with aging in adults aged 55 years and older.

Two broad cognitive domains emerge across several studies that evince sensitivity to age-related effects—executive function and memory. Executive function encompasses a myriad of cognitive processes involved in mental control, including the ability to retrieve, maintain, manipulate, and inhibit information; goal switching; and the formation of concepts and strategies related to a given task. Experimental studies have documented reduced performance on executive tasks with increased age so that, compared with younger adults, older adults show less ability to inhibit irrelevant responses (Hasher, Lustig, & Zacks, 2007; Hasher & Zacks, 1988), switch task goals (Cepeda, Kramer, & de Sather, 2001; Kray & Lindenberger, 2000; Reimers & Maylor, 2005), and extract and use effective strategies when performing a cognitive task (Dunlosky et al., 2003; Naveh-Benjamin, Brav, & Levy, 2007; Verhaeghen & Marcoen, 1996). Studies using neuropsychological test batteries have also shown age-related declines in general executive functions (de Frias et al., 2009; Lamar, Resnick, & Zonderman, 2003; Lamar, Zonderman, & Resnick, 2002), such as in measures of fluid intelligence (Horn & Cattell, 1967; McArdle, Ferrer-Caja, Hamagami, & Woodcock, 2002; Raz et al., 2008; Zelinski & Stewart, 1998), capacity, manipulation, cognitive flexibility, task switching, and inhibition (Head, Kennedy, Rodrigue, & Raz, 2009; Kennedy & Raz, 2009).

Studies on memory, defined here as the ability to store and retrieve episodic information, also show age-related reduction in performance. Experimental studies have shown that older adults make more false alarms during episodic recognition (Castel & Craik, 2003; Stark, Yassa, & Stark, 2010) and tend to have poorer associative (Castel & Craik, 2003; Chalfonte & Johnson, 1996; Naveh-Benjamin, Guez, Kilb, & Reedy, 2004; Old & Naveh-Benjamin, 2008) and recollection memory (Anderson et al., 2008; Hay & Jacoby, 1999; Howard, Bessette-Symons, Zhang, & Hoyer, 2006; Prull, Dawes, Martin, Rosenberg, & Light, 2006) when compared with younger adults. Again, studies with neuropsychological batteries have also shown that older adults perform more poorly than young adults across various memory tests including measures of episodic memory over varying periods of time, such as tests on short-term and long-term memory (Giambra et al., 1995; Hultsch et al., 1998; Hultsch, Hertzog, Small, McDonald-Miszczak, & Dixon, 1992; McArdle et al., 2002; Park et al., 2002; Salthouse, 2009, 2010; Tucker-Drob, 2011).

Across these studies, executive and memory processes have typically been considered as more general domains that show age-related declines. In the present study, however, we characterize age differences and longitudinal age-related changes associated with different specific component domains that constitute executive function and memory as measured by neuropsychological tests in the Baltimore Longitudinal Study of Aging (BLSA; Shock et al., 1984). In accordance with the nonuniformity of aging described earlier and a multifaceted approach to cognitive aging (Lamar et al., 2002), we postulated that, when more specific component processes are considered that make up executive function and memory, some components will decline with age. However, other processes will manifest stability despite aging and even improve through learning from repeated testing. Thus, the focus of this study was to determine more specifically, within one study involving the same sample of participants, which aspects of executive and memory abilities show longitudinal declines and which abilities remain relatively intact with aging.

We evaluated longitudinal changes in component domains of executive function that included abstraction, chunking, switching, discrimination, inhibition, retrieval, manipulation, and capacity using measures derived from the neuropsychological test battery available within the BLSA (see Method for definitions and references). To the extent that aging results in a global reduction in executive abilities, equivalent declines would be present in the different components of executive function. If aging selectively affects specific executive abilities, however, we expected to see a more heterogeneous pattern with differential rates of decline associated with each of the components of executive function.

In tandem with executive function, we also examined longitudinal changes in memory for episodic information over shorter and longer periods of time. As such, memory was measured by tests of short- and long-term episodic memory as assessed by the neuropsychological test battery (see Method). Similar to the considerations for executive function, we evaluated whether longitudinal aging would show a uniform reduction or differential rates of decline in short- and long-term memory.

Given longitudinal changes within the domains of executive function and memory, we also examined cross-domain correlations to investigate whether longitudinal changes in component executive domains would be associated with changes in memory. It is plausible that decline in memory function may compromise the efficiency of executive processes or that changes in executive function may impair the access to and storage of information in memory (Zelinski & Stewart, 1998). To the extent that specific components of executive and memory processes are linked, we expected to see associations between longitudinal changes between the two components.

Finally, longitudinal changes in cognitive function should be particularly sensitive to individual differences so that there would be a mix of individuals who show longitudinal decline and individuals who show little change with aging. To this end, we also compared longitudinal changes in cognitive performance between participants in our sample who were subsequently diagnosed with cognitive impairment (CI participants) and those who remained clinically normal (CN participants) over the follow-up visits. We expected that there would be more differentiation between these groups when considering longitudinal compared with cross-sectional performance. Thus, CI participants should show steeper rates of longitudinal decline than CN participants across several component cognitive domains.

In summary, we expected that, as in previous literature, higher cross-sectional age would be associated with lower performance in a broad set of executive and memory abilities. With respect to longitudinal changes, however, we expected a more heterogeneous pattern so that not all cognitive abilities would show equivalent rates of decline over the follow-up visits. Note that, although our focus in this study is on executive function and memory, we also analyzed measures of visual ability, vocabulary, and processing speed to provide characterization of age-related longitudinal changes in our sample for comparison with other studies. In line with previous studies, we expected vocabulary to remain stable, whereas visual ability and processing speed decline with age (Hultsch et al., 1998; Park et al., 2002; Schaie, 1996).

Method

Participants

The present analyses were based on data from participants in the BLSA selected for a neuroimaging substudy (see Resnick et al., 2000, for more detail), allowing for future examination of the neural correlates of findings from this study. BLSA participants were recruited into the neuroimaging phase of the study on the basis of health considerations and

the amount of previous cognitive data available for each individual. This sample included 148 volunteers (87 men, 61 women; participant details are listed in Table 1). Participants' age at assessment concurrent with the first neuroimaging evaluation ranged from 56.0 to 85.9 years, and follow-up testing occurred for a maximum of 14 years for some individuals. Follow-up test sessions were separated by approximately 1 or 2 years. Participants selected into this sample were all healthy at the point of selection into the study, without neurological impairment, metastatic cancer, or severe cardiovascular disease (although treated hypertension was not exclusionary). Exclusions were minimized to allow more representative sampling in this prospective study.

Some participants within this sample developed cognitive impairment over the course of the follow-up, and data from these participants were included up to the test session before onset of the impairment. Demographic characteristics of CN and CI participants are also listed in Table 1. Inclusion into the CI group was made on the basis of a consensus diagnosis in accordance with the Diagnostic and Statistical Manual of Mental Disorders (3rd ed., rev.; *DSM-III-R*; American Psychiatric Association, 1987) criteria for dementia and the National Institute of Neurological and Communicative Disorders-Alzheimer's Disease and Related Disorders Association criteria (McKhann et al., 1984), with the use of neuropsychological diagnostic tests and clinical data (Driscoll et al., 2006). The local institutional review board approved the research protocol for this study, and informed consent was obtained at each visit from all participants.

Neuropsychological Test Battery and Component Cognitive Domains

For convenient reference, Table 2 lists and defines the component cognitive domains evaluated in this study that constituted executive function and memory, as well as several additional cognitive domains. The different cognitive domains were labeled and defined on the basis of the main cognitive processes assessed by the neuropsychological tests as conceptualized and described in previous literature (see Lezak, Howieson, & Loring, 2004, for a comprehensive review). The main aim of this study was to examine specific components of executive and memory functions. Thus, we used process-based labels to provide more direct descriptions of the cognitive domains. This approach also facilitates relating the findings in the present study to future studies involving neural correlates.

Table 3 lists the neuropsychological test outcome measures with brief descriptions and the associated cognitive domains. More detailed descriptions are available in previous publications (Lamar et al., 2003; Lamar et al., 2002). Test scores were normalized for comparability across cognitive domains so that all scores were transformed to *z* scores on the basis of the means and standard deviations of each test computed across baseline and follow-up performance. Tests for which increasing values in the original scores indexed poorer performance were reversed in sign. Subsequently, increasing values always reflect better performance in the statistical analyses. Note that, as our interest focused on evaluating whether different cognitive abilities would show uniform or heterogeneous age-related effects, we maintained the cognitive components and associated tests as distinct variables. This approach contrasts with a factor analytic-based approach such as that used in previous studies where subcomponents are grouped into common factors, constraining the ability to identify distinctive patterns of aging in specific components of executive function and memory. We formed composite scores from test measures only when the cognitive processes assessed were conceptually similar. Composite scores, where used to quantify performance in a cognitive domain, were computed as the averaged normalized scores from each of the associated outcome measures. Statistical analyses were implemented with a combination of PROC MIXED in SAS v9.2 (SAS Institute Inc., Cary, NC) and in-house scripts from Matlab Release 2010b (MathWorks Inc., Natick, MA).

As can be seen from Tables 2 and 3, nine component cognitive domains related to executive function were assessed with 13 outcome measures that were available in the neuropsychological test battery administered to this subset of BLSA participants. Abstraction refers to the ability to form conceptual associations and was scored with the Similarities test from the revised version of the Wechsler Adult Intelligence Scale (Wechsler, 1981). Capacity refers to the number of items that can be kept immediately active in mind (Baddeley, 2010) and was measured by forward digit-span performance (Wechsler, 1981).¹ Chunking was measured by the degree of semantic clustering during recall of word lists in the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987), which reflects the ability to organize information into meaningful groups (Gobet et al., 2001; for age comparisons, see Allen & Coyne, 1989; Li, Blair, & Chow, 2010). Discrimination is the ability to distinguish between relevant targets and irrelevant distractors and was measured by a composite of the d' score for recognition performance in the CVLT and the reduction in number of correctly recalled words after a distractor list is introduced in the CVLT (a second interference list is introduced between the fifth list-learning trial recall and the short-delay free recall). Inhibition is the ability to suppress task-inappropriate responses and was measured as a composite of the total number of perseverations during the category and letter verbal fluency tests (Spreeen & Benton, 1969). Manipulation is the rearrangement or reordering of item information in mind (Baddeley, 2010; see Footnote 1) and is measured as a composite of alpha span (Craik, 1990) and backward digit-span (Wechsler, 1981) performance. Phonological retrieval, measured by letter verbal fluency (Spreeen & Benton, 1969), is the ability to recall information in semantic memory associated with a phonological cue. Semantic retrieval—measured as a composite of category verbal fluency test performance (Spreeen & Benton, 1969) and performance on the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983)—involves recalling information from semantic memory based on semantic cues. Switching refers to the ability to alternately prioritize different task goals and is measured by the difference in completion time between the Trail Making Test, Part A, where participants simply draw connecting lines to incremental numbers on a test sheet, and the Trail Making Test, Part B, where participants alternate between incremental numbers and alphabetical letters (Reitan, 1992).

We measured two memory component domains (short- and long-term memory) using three neuropsychological test measures. Short-term memory is the ability to store episodic information over brief periods of time of approximately 1–10 min and was measured as a composite of short-delay free recall and total recall over five learning trials in the CVLT (Delis et al., 1987). Long-term memory refers to storage of episodic information over longer time periods of approximately 20 min or more and was measured as performance during long-delay free recall in the CVLT (with an approximately 20-min delay; Delis et al., 1987).

The neuropsychological test battery also included other measures of basic cognitive domains. Speed was measured by the Trail Making Test, Part A, and quantifies basic speed of cognitive processing (Reitan, 1992). Vocabulary captures the extent of verbal knowledge and was indexed by the Primary Mental Abilities Vocabulary test (Thurstone & Thurstone, 1962). Finally, visual processing was a composite of the Benton Visual Retention (Benton, 1974) and Card Rotations (Wilson & Vandenberg, 1978) tests, which reflect the ability to manipulate and maintain perceptual information pertaining to visual representations.

¹We note that capacity and manipulation are components of working memory (Baddeley, 2010). Nevertheless, they conceptually involve cognitive control processes, and we included them as separate executive components in this study as well to evaluate age-related longitudinal changes in these distinct processes.

Mixed-Model Analysis

Mixed-effect models accounting for the effects of cross-sectional baseline age and longitudinal follow-up intervals, as well as that of their interaction, were applied to each component cognitive domain score to test the significance of the respective predictors (Laird & Ware, 1982). These mixed-effect models also provided individual estimates of longitudinal changes associated with each cognitive domain that were subsequently used for correlating longitudinal effects across abilities.

In detail, first, to test the cross-sectional baseline age effect on performance in a cognitive domain, we applied the following mixed-effects model to each domain:

$$y_{ij} = \beta_0 + \beta_1 \text{Age}_i + \beta_2 \text{Interval}_{ij} + \beta_3 (\text{Age}_i \times \text{Interval}_{ij}) + b_{0i} + b_{1i} \text{Interval}_{ij} + \varepsilon_{ij}. \quad (1)$$

In the aforementioned model, y_{ij} is the score on the cognitive domain for the i th participant on the j th follow-up test visit. The variable age is the participant's baseline age at the first neuroimaging visit centered to 55 years of age. The variable interval is the longitudinal predictor coded as the time (in years) from baseline age (first interval is 0). β denotes fixed-effects estimates, b denotes participant-specific random-effects estimates [$b \sim N(0, D)$], where D is the covariance matrix for b], and ε is the residual error. This model captures the average effect of cross-sectional age, as well as that of the interaction between age and longitudinal interval, after accounting for participant-specific longitudinal effects. The statistical significance of β_1 in Equation 1 indicates a cross-sectional effect of age on the cognitive domain, and the significance of β_3 indicates a dependency of longitudinal change on baseline age at first assessment. Although β_2 in Equation 1 is an estimate for the longitudinal effect of interval, it is only applicable for the centered age of 55 years because of the adjustment for baseline age in Equation 1. Thus, another model is required to estimate the effect of longitudinal follow-up interval, regardless of baseline age.

To this end, we applied the following model to each domain:

$$y_{ij} = \beta_0 + \beta_1 \text{Interval}_{ij} + b_{0i} + b_{1i} \text{Interval}_{ij} + \varepsilon_{ij}. \quad (2)$$

This model captures the average effect of longitudinal change across the whole sample, accounting for participant-specific longitudinal effects, regardless of the age of the participant. The statistical significance of β_1 in Equation 2 indicates an effect of longitudinal change on the cognitive domain. Empirical Bayes estimates of slopes for each participant obtained in Equation 2 ($\beta_1 + b_{1i}$) are the individual estimates of longitudinal effects subsequently used in the correlation analysis described in the following section.

Analysis of Correlations Between Cognitive Domains

Relationships between cognitive domains for estimates of the effects of cross-sectional baseline age were examined with pairwise Pearson's correlations based on participants' first available scores on each cognitive domain. To evaluate the relationships between cognitive domains for estimates of longitudinal interval effects, we used the individual slope estimates from Equation 2 ($\beta_1 + b_{1i}$) for each domain to perform pairwise Pearson's correlations between each of the cognitive domains. Bonferroni correction for multiple comparisons (at $p < .05$) was used to compensate for the number of correlations performed.

We also compared the overall patterns of correlations between cognitive domains to the case where there were no correlations at all. For the cross-sectional and longitudinal correlation matrices, separately, we computed the root-mean-square residuals (RMRs; Jöreskog &

Sörbom, 1986) and the mean (mean R_{res}) and median (median R_{res}) residuals as indices of fit relative to a zero cross-correlation matrix (an identity matrix). Lower fit indices suggest that associations between cognitive domains were weaker.

Comparisons Between CI and CN Participants

To examine effect differences between CI and CN participants for each cognitive domain, we included another variable, group, to Equations 1 and 2 for the cross-sectional age and longitudinal interval effects, respectively. The resulting models are as follows:

$$y_{ij} = \beta_0 + \beta_1 \text{Age}_i + \beta_2 \text{Interval}_{ij} + \beta_3 \text{Group}_i + \beta_4 (\text{Age}_i \times \text{Interval}_{ij}) + \beta_5 (\text{Group}_i \times \text{Interval}_{ij}) + \beta_6 (\text{Group}_i \times \text{Age}_i) + \beta_7 (\text{Group}_i \times \text{Age}_i \times \text{Interval}_{ij}) + b_{0i} + b_{1i} \text{Interval}_{ij} + \varepsilon_{ij} \quad (3)$$

and

$$y_{ij} = \beta_0 + \beta_1 \text{Interval}_{ij} + \beta_2 \text{Group}_i + \beta_3 (\text{Group}_i \times \text{Interval}_{ij}) + b_{0i} + b_{1i} \text{Interval}_{ij} + \varepsilon_{ij}. \quad (4)$$

In the aforementioned models, group is a binary variable that indicates whether the i th participant is CN (0) or CI (1). β_6 in Equation 3 estimates the group difference between CN and CI participants in the cross-sectional age effect on a given cognitive domain. Negative values of β_6 indicate that performance was lower for CI than CN participants. Similarly, β_3 in Equation 4 estimates the difference between CN and CI participants in the longitudinal interval effect on cognitive domain performance.

Results

Cross-Sectional Age Differences and Longitudinal Interval Changes

Figure 1 shows spaghetti plots of the slopes of performance for each cognitive domain over follow-up visits and age for each participant estimated from Equation 1. Overall, it can be seen that not all cognitive domains follow the same longitudinal trajectory with aging, and a fair amount of variance in individual slopes is present for some domains. Formal statistical tests of the trends in these plots is shown in Figure 2, which depicts the magnitudes of the cross-sectional age and longitudinal interval effects, as well as that of their interactions, estimated from Equations 1 and 2. We highlight that, throughout the article, we regard cross-sectional effects as age-related *differences*, as these effects are associated with differences in performance across individuals at various base-line ages. In contrast, we regard longitudinal interval effects as age-related *changes*, as these effects are associated with temporal changes in performance within individuals as they age over time. Moreover, the mixed models were computed on normalized test scores, and both age and interval were based on unit years. Thus, the effect estimates can also be interpreted as standardized annual differences and annual changes associated with each cognitive domain for cross-sectional and longitudinal effects, respectively, and interactions between cross-sectional age and longitudinal interval can be interpreted as standardized annual change per year.

As expected, there were cross-sectional age differences in a large number of cognitive domains, including chunking, discrimination, semantic retrieval, switching, long-term memory, short-term memory, speed, vocabulary, and visual processing (see Figure 2, left panel). Across all these domains, older participants showed lower performance than younger participants. Only abstraction, capacity, inhibition, manipulation, and phonological retrieval

did not show significant cross-sectional age effects in this overall sample, and no cognitive domain showed cross-sectional improvement with age.

Critically, given this pattern of cross-sectional age differences, the changes associated with longitudinal follow-up interval evinced more heterogeneous trajectories (see Figure 2, middle panel). Of the cognitive domains that showed significant cross-sectional age-related performance reduction, semantic retrieval, switching, long-term memory, and visual processing also showed longitudinal declines with aging. This suggests that these abilities may be more sensitive to the effects of aging, despite learning from repeated testing. In contrast, chunking, discrimination, short-term memory, and vocabulary did not follow the cross-sectional age trends but either remained longitudinally stable or even improved over follow-up visits, which suggests that these abilities may be less susceptible to aging effects, that they are more able to benefit from learning, or both. In addition, although inhibition and manipulation did not show cross-sectional age effects, these abilities declined longitudinally, reflecting a sensitivity to aging but a range of performance across individuals at various ages.

Longitudinal declines in certain cognitive domains evinced a dependence on, or interaction with, participants' baseline age. Semantic retrieval, switching, and visual processing showed significant increases in the rate of longitudinal decline with greater age (see Figure 2, right panel; see also the spaghetti plots in Figure 1 for these domains). In addition, the spaghetti plots for phonological retrieval and speed in Figure 1 show a pattern of slight longitudinal improvement and then plateau, followed by longitudinal decline with increasing age, as indicated by significant interactions between cross-sectional age and longitudinal interval (see Figure 2, right panel). It is interesting that abstraction and capacity remained unaffected by cross-sectional age and were relatively stable over the longitudinal interval, which suggests that these abilities may be preserved with age.

Overall, these findings show lower performance across a broad number of executive and memory functions associated with increasing cross-sectional age. With longitudinal changes over the follow-up period in this sample, however, a more limited set of cognitive domains showed declines, with some abilities maintaining or even improving and some changes dependent on the age of the participant.

Correlations Between Domains

The correlations among cognitive domains in the cross-sectional age performance (first available score concurrent with neuroimaging assessments) and in the longitudinal interval changes (estimated slopes from Equation 2; see Method) are shown in Figure 3. In general, there are several significant positive correlations between cognitive domains when considering cross-sectional age performance. That is, at the first assessment, participants who had low performance in one test tended to have low performance in several other tests as well (overall fit indices: $RMR = .43$, mean $R_{res} = .25$, median $R_{res} = .22$) and vice versa for those who exhibited better performance. For executive domains, the following associations showed significant positive correlations: semantic retrieval with abstraction, chunking, discrimination, manipulation, and phonological retrieval; phonological retrieval with manipulation and switching; chunking with discrimination; and capacity with manipulation. Short-term and long-term memory were also positively correlated with each other, and both memory domains showed positive correlations with the executive domains abstraction, chunking, discrimination, semantic retrieval, and switching. There were no negative correlations.

When considering longitudinal changes in performance, a more heterogeneous pattern emerges again, with fewer correlations among executive domains and both positive and

negative correlations present (overall fit indices: $RMR = .01$, mean $R_{res} = .05$, median $R_{res} = .04$). Short-term and long-term memory remained positively correlated with each other as well as with the executive function chunking. In addition, short-term memory remained correlated with discrimination, and long-term memory remained correlated with semantic retrieval. Positive correlations here suggest that longitudinal declines in these abilities are associated with similar changes in the corresponding abilities. Negative correlations, however, reflect that declines in one domain were associated with improvements in the other. It is important to note that, unlike the cross-sectional age differences, longitudinal declines in cognitive performance do not appear to have a uniform relationship among most domains.

Group Differences in Cognitive Domain Performance

Figure 4 shows group differences in cross-sectional and longitudinal age effects between CN and CI participants. Note that, for group comparisons in Figure 4, the effect estimates indicate the relative group differences (Δ) in rates of annual difference and changes for cross-sectional and longitudinal effects, respectively. For the cross-sectional data, only long-term memory showed a significant group difference, so that whereas performance was lower with greater baseline age of CI participants, the lowering of performance with greater baseline age of CN participants was relatively less. For longitudinal data, however, CI participants showed significantly steeper longitudinal declines than CN participants in capacity, semantic retrieval, switching, and long-term memory. For vocabulary, note that the overall longitudinal trend across groups was improvement due to learning effects (see Figure 2, middle panel); thus, the significant longitudinal effect for CI, relative to CN, participants here represents a lack of learning over repeat testing in the CI group. Greater longitudinal declines in CI versus CN participants may indicate that cognitive decline in specific abilities was present in CI participants before the onset of the diagnosis of impairment. It is important to note that longitudinal rates of change in some abilities provided more sensitive measures of group differences than estimates of annual change based on cross-sectional age effects.

Discussion

The main finding in this study is that longitudinal trends across component cognitive domains of executive and memory function display heterogeneous trajectories, compared with cross-sectional age effects. Whereas most components of executive and memory function showed lower performance with increasing cross-sectional age, the longitudinal trends across different components consisted of declines, stability, improvements, and dependence on age. Moreover, correlations in cross-sectional performance within and between executive and memory domains showed a general positive relationship with lower performance in one domain associated with lower scores in several other domains. In contrast, correlations in longitudinal changes in performance were more heterogeneous, consisting of fewer significant correlations as well as both positive and negative correlations. Finally, comparisons between CI and CN participants revealed a significant difference in long-term memory when cross-sectional data were used to estimate annual age differences. When considering longitudinal data, which provide direct estimates of rates of change, differences between CI and CN groups were evident in capacity, semantic retrieval, switching, long-term memory, and vocabulary. In summary, these findings are consistent with greater sensitivity to heterogeneity in longitudinal data than in cross-sectional data, at least within the neuropsychological tests used over the follow-up period in this sample.

Longitudinal changes and maintenance in cognitive performance may arise from endogenous biological sources such as neural reorganization with aging and from external sources such as lifetime cognitive experiences in the environment, as well as through the

interaction of these two factors. For example, biological changes in neural processes with increasing age can render cognitive processes less efficient and result in cognitive declines (Goh & Park, 2009; Park & Goh, 2009). At the same time, even with increasing age, neural processes are still able to respond to, and benefit from, experiential cognitive learning; these learning processes may offset the effect of biological declines (Goh & Park, 2009; Park & Reuter-Lorenz, 2009). It is also plausible that, independent of the contribution of learning from experience, certain neural processes themselves remain relatively unaffected by the biological declines associated with aging. These dual biological and experiential mechanisms may operate in competition, and, to the extent that learning can compensate for biological decline in a cognitive ability, that ability is preserved. In this study, inhibition, manipulation, semantic retrieval, switching, long-term memory, and visual processing showed longitudinal declines with aging, which suggests that these abilities are particularly sensitive to age-related declines in biological processes. They also may be less sensitive to the effects of learning and experience, or the longitudinal decline may mask any learning effects. Other specific abilities remained stable or were still able to benefit from learning—namely, chunking, discrimination, short-term memory, vocabulary, and to a limited extent, phonological retrieval and basic cognitive speed. The latter two abilities improved somewhat over follow-up sessions at earlier ages, probably because of learning from repeated testing, with longitudinal decline more evident with increasing age. However, other abilities seem to be unaffected by the effects of age and aging, namely, abstraction and capacity.

Longitudinal neuroimaging studies conducted in the BLSA participants included in this study have shown selective, rather than uniform, changes in brain structure and function that also involves a fair amount of individual variability. Such findings support the notion that cognitive aging of specific abilities is a heterogeneous phenomenon with a dynamic interplay between biological aging and learning. For example, longitudinal tissue loss and cortical thinning occur at differential rates throughout the cortex, with the frontal and parietal regions declining faster than temporal and occipital regions (Resnick, Pham, Kraut, Zonderman, & Davatzikos, 2003; Thambisetty et al., 2010; see Raz et al., 2005, 2010, for non-BLSA examples). In terms of functional activity, whereas certain frontal, parietal, and temporal areas show longitudinal decreases in functional responses with aging, there are several regions within these same cortical areas that also show longitudinal stability or increases in functional responses (Beason-Held, Kraut, & Resnick, 2008a, 2008b, 2009). It has been suggested in these studies that longitudinal functional decreases may reflect reduced efficacy of neural processing with aging, whereas longitudinal functional increases may signal additional compensatory neural recruitment in response to the declining processes in other regions. Furthermore, these longitudinal changes in functional responses are task dependent, suggesting that the processes involved for specific tasks are differentially affected by aging. Finally, studies have also shown that age-related differences in brain structure and function are malleable under experiential influences such as physical exercise (Colcombe et al., 2006), environmental enrichment (Kempermann, Gast, & Gage, 2002), and group differences in cultural backgrounds (Chee, Zheng, Goh, Park, & Sutton, 2011; Goh et al., 2007). Thus, like the cognitive abilities measured in this study, age-related longitudinal changes in brain structure and function appear quite heterogeneous, evincing substantial regional and process specificity, with some brain areas more resilient to aging than others. Moreover, external experiences may modulate age-related biological effects on the brain. Subsequent studies are required to provide more direct links between the longitudinal changes in the specific executive and memory processes observed in this present study and brain structure and function.

The consistent cross-sectional and, critically, longitudinal correlations between short-term and long-term memory—as well as between these memory domains and the executive

domains chunking, discrimination (for short-term memory only), and semantic retrieval (for long-term memory only)—suggest a mechanistic link between these specific executive and episodic memory functions. In our study, chunking is measured as the degree of semantic clustering during the recall of a word list and involves the organization of words into meaningful categories. Previous studies have shown that such semantic organization of information is associated with substantially better episodic memory, and older adults benefit from such list-learning strategies (Dunlosky et al., 2003; Li et al., 2010). It is, thus, not surprising that semantic retrieval is also associated with memory function in our study, as it also involves the ability to tap into semantic organization of words, albeit for semantic rather than episodic memory. Discrimination also has an intuitive role in memory function in that the ability to represent information more distinctively is associated with more veridical retrieval and a reduced tendency to falsely endorse a novel item as an old or repeated one (Goh, Suzuki, & Park, 2010; Stark et al., 2010). It is interesting to note that longitudinal change in discrimination was more strongly related to short-term memory and that semantic retrieval was more strongly related to long-term memory. Perhaps because discrimination involves dissociating concurrent information before long-term memory storage, it has a greater effect on short-term memory. In contrast, semantic retrieval involves the ability to access semantic information from a longer time scale and, thus, has more importance for long-term memory. It is possible that part of the cross-sectional correlations between chunking, discrimination, short-term and long-term memory occurred because these measures were all derived from the CVLT. However, the correlations between chunking and discrimination and between discrimination and long-term memory were no longer significant for the longitudinal data, indicating that it is unlikely that common test effects fully account for the associations between these measures.

The negative longitudinal correlations of manipulation with capacity, semantic retrieval, and switching and of capacity with vocabulary should be interpreted with caution. It is unlikely that there is a direct inverse mechanism that operates among these abilities such that, for example, longitudinal improvement in capacity results in decline in manipulation. We note, however, that over follow-up testing, it may be easier for participants to remember the digit series for the forward digit-span task (capacity), the words used for semantic retrieval in the category verbal fluency test (semantic retrieval), and the visual path for the Trail Making Test, Parts A and B (switching), whereas rearrangement of digits and words (manipulation) may be less amenable to practice through repetition. Thus, although this is speculative, greater rates of longitudinal decline in manipulation (and less learning in vocabulary) may involve age-related biological declines that drive individuals to have a greater reliance on learning through repeated practice as a general compensatory strategy. Greater reliance on learning through repetition is then associated with improvements in capacity and relatively slower rates of decline in semantic retrieval and switching. Notwithstanding, the presence of both positive and negative correlations demonstrate the heterogeneity of longitudinal trajectories across these cognitive domains, and further studies, perhaps those that are more neural based, are again required to examine the reliability of, and the mechanisms that underlie, these correlations.

Steeper rates of decline across several cognitive processes in this small sample of CI participants relative to the CN participants is consistent with the notion that longitudinal data may be more sensitive to subsequent impairment than test scores from a single occasion (Driscoll et al., 2006). Note that data from the CI participants in our sample were restricted to assessments before the onset of impairment, suggesting that the overall performance of these participants was within normal cross-sectional range for their age. Also, in our study, the trajectory of longitudinal change across capacity, semantic retrieval, switching, long-term memory, and vocabulary was more revealing of the participants' subsequent cognitive status than the cross-sectional performance. In support of this, studies have suggested that

longitudinal declines in executive and memory functions may be antemortem indicators of declining frontal and hippocampal function associated with Alzheimer's disease (Driscoll et al., 2006; Grober et al., 2008). Indeed, in another study from the BLSA (Driscoll et al., 2009), amid age-related longitudinal volume reduction in frontal and parietal areas, participants diagnosed with cognitive impairment showed accelerated rates of longitudinal volume reductions in specific regions, including the temporal, orbitofrontal and hippocampal regions, relative to those who remained cognitively intact. Accelerated tissue loss in regions that are affected early in the development of Alzheimer's disease neuropathology provide a partial explanation of the differential effects of age on specific abilities for CI versus CN individuals. Continued follow-up studies of these individuals will further our understanding of the heterogeneity of longitudinal age changes in specific cognitive functions in individuals who remain healthy and those who develop cognitive impairment.

We note that, unlike previous studies that have found stable vocabulary ability across age (Hultsch et al., 1998; Park et al., 2002; Schaie, 1996), cross-sectional vocabulary performance in our data was lower with greater age. This most likely reflects the speeded nature of the Primary Mental Abilities Vocabulary test used in this study, which involved identifying as many synonyms as possible within 3 min (see Table 3). Indeed, cross-sectional performance for cognitive speed was lower with greater age as well. Moreover, in previous BLSA studies of vocabulary using the Wechsler Adult Intelligence Scale Vocabulary scale, performance did not decline with age (Giambra et al., 1995). We also note that the cross-sectional data in our study spanned a longer time period (30 years) than the longitudinal data (14 years), and this may have contributed to the greater number of significant cross-sectional age effects relative to longitudinal aging effects. Thus, given enough time, the longitudinal trajectories may also show broad declines across several cognitive domains. We highlight, however, that the longitudinal aging data in our study provides a complementary view on cross-sectional age differences, which sometimes may be difficult to interpret because of confounds associated with cohort differences not directly related to aging. Critically, our data show that the heterogeneous trajectories of longitudinal changes in these cognitive domains remain detectable at least within the span of 14 years in individuals aged 55 or older in this present study.

Cognitive aging studies using structural equation modeling have found that the pattern of age-related longitudinal cognitive changes typically do not provide a good fit for models that postulate one general factor or are too simplified (de Frias et al., 2009; McArdle et al., 2002; Tucker-Drob, 2011). In the present study, we also found more parsimony in a heterogeneous account of age-related longitudinal changes across specific cognitive functions than in a uniform one and, at the same time, we examined different cognitive abilities in a more specific manner. Our findings reveal specific components of executive and memory functions that are at least partially protected from aging, by means of learning or other mechanisms, in contrast to abilities that clearly decline with aging despite learning from repeat testing. Thus, although there are general changes in cognitive structure and abilities associated with aging, future studies on cognitive aging may better our understanding by evaluating more specific mechanisms. Such studies may provide insights into those processes that are spared with aging and provide compensatory resources in the face of declines in other specific cognitive functions.

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Figure 1.

Spaghetti plots showing individual estimated longitudinal slopes of performance against age for each cognitive domain. Each line represents one participant's performance over follow-up visits starting at age at first visit. Participants are sorted into those who remained clinically normal over follow-up visits (CN; black lines) and those subsequently diagnosed with cognitive impairment (CI; red lines).

Figure 2.

Cross-sectional age differences and longitudinal interval changes in performance for each cognitive domain are shown in the left and middle panels. Effects are shown as beta estimates of standardized annual differences and change obtained from Equation (Eq.) 1 and Eq. 2, respectively. The right panel shows the modulatory effect of cross-sectional age differences on longitudinal change in performance obtained from Eq. 1. Error bars show 95% confidence intervals. Yr = year.

* $p < .05$, and ** $p < .01$, both uncorrected.

Figure 3.

A matrix of cross-correlations between cognitive domains is shown as a color intensity map. Correlations for cross-sectional age estimates are in the bottom left diagonal, and those for longitudinal interval are in the top right diagonal. The threshold used for significant (nongray) correlations was $p < .05$, with Bonferroni correction.

Figure 4.

Differences between participants showing little change over follow-up visits (CN) and those subsequently diagnosed with cognitive impairment (CI) in the cross-sectional age differences and longitudinal interval changes for each cognitive domain. Effects are shown as beta estimates of relative group differences (Δ) in rates of standardized annual difference and changes obtained from Equation (Eq.) 3 and Eq. 4, respectively. Negative values indicate CI < CN. Error bars show 95% confidence intervals.

* $p < .05$, and ** $p < .01$, both uncorrected.

Table 1

Participant Details

Group	Total	CN	CI
<i>n</i>	148	123	25
Male/female	87/61	71/52	16/9
Mean age at first visit in years (and <i>SD</i>)	69.6 (7.7)	68.4 (7.5)	75.3 (6.4)
Age range in years	56.0–85.9	56.0–85.9	64–85
Mean years of follow-up (and <i>SD</i>)	8.5 (4.0)	8.9 (4.0)	6.5 (3.6)
Range of years of follow-up	1–14.2	1–14.2	1–12.8
Mean no. of follow-up sessions (and <i>SD</i>)	8.4 (3.4)	8.6 (3.4)	7.0 (3.4)
Range of no. of follow-up sessions	1–14	1–14	1–13

Note. CN = participants who remained clinically normal over follow-up, CI = participants subsequently diagnosed with cognitive impairment.

Table 2

List of Broad and Component Cognitive Domains and Definitions

Broad domain	Components	Definitions
Executive	Abstraction	Formation of conceptual associations
	Capacity	The span of items that can be actively maintained in mind at a time
	Chunking	Strategic organization of information into meaningful categories
	Discrimination	Distinguishing between targets and distractors
	Inhibition	Suppressing information or responses
	Manipulation	Reordering and rearrangement of item information in mind
	Phonological retrieval	Retrieval of information based on phonological cues
	Semantic retrieval	Retrieval of information based on semantic cues
	Switching	Alternating between different task goals
Memory	Long-term memory	Episodic memory over long periods of time
	Short-term memory	Episodic memory for a short period of time
Others	Speed	Speed of basic cognitive processes
	Vocabulary	Accumulated semantic knowledge
	Visual	Manipulating and storing visual stimuli

Table 3**Neuropsychological Test Outcome Measures and Associated Domains**

Test	Outcome measures	Domains
Alpha span	Maximum no. of list words recalled in alphabetical order with no errors	Manipulation
Benton Visual Retention	Score of visual reproduction errors	Visual
Boston Naming Test	No. of correct visual objects named	Semantic retrieval
Card Rotations	No. of correctly rotated visual shapes correctly matched	Visual
California Verbal Learning Test	Sum of words recalled across five learning trials	Short-term memory
	No. of words recalled after short delay (free recall)	Short-term memory
	No. of words recalled after long delay (free recall)	Long-term memory
	Semantic clustering ratio during word list recall	Chunking
	Change between fifth trial recall and short-delay recall after interference	Discrimination
Digit span	d' score for recognition of target words and distractors	Discrimination
	Maximum no. of digits recited in forward order with no errors	Capacity
	Maximum no. of digits recited in backward order with no errors	Manipulation
Primary Mental Ability	No. of correct word synonyms identified at 3 min	Vocabulary
Similarities	No. of correct conceptual associations between items	Abstraction
Trail Making Test, Parts A and B	Time to complete line trace of incremental number targets	Speed
	Difference between Trails A and B (alternate number and letter targets)	Switching
Verbal fluency	Total no. of words retrieved for categories (fruits, animals, vegetables)	Semantic retrieval
	Total no. of words retrieved for letters (F, A, S)	Phonological retrieval
	Total perseverations during categories retrieval	Inhibition
	Total perseverations during letters retrieval	Inhibition