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A Life Course Model of Cognitive Activities, Socioeconomic Status, Education, Reading Ability, and Cognition

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Abstract

OBJECTIVES—To cross-sectionally quantify the contribution of proxy measures of cognitive reserve reflective of the lifespan, such as education, socioeconomic status (SES), reading ability, and cognitive activities, in explaining late-life cognition.

DESIGN—Prospective observational cohort study of aging.

SETTING—Retirement communities across the Chicago metropolitan area.

PARTICIPANTS—Nine hundred fifty-one older adults free of clinical dementia in the Rush Memory and Aging Project (aged 79 ± 8 , 74% female).

MEASUREMENTS—Baseline data on multiple life course factors included early-, mid-, and late-life participation in cognitive activities; early-life and adult SES; education; and reading ability (National Adult Reading Test; NART). Path analysis quantified direct and indirect standardized effects of life course factors on global cognition and five cognitive domains (episodic memory, semantic memory, working memory, visuospatial ability, perceptual speed).

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SUPPORTING INFORMATION Additional Supporting Information may be found in the online version of this article:

Table S1. Indirect Standardized Effects on Outcomes in the A Priori Models.

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RESULTS—Adjusting for age, sex, and race, education had the strongest association with global cognition, episodic memory, semantic memory, and visuospatial ability, whereas NART (followed by education) had the strongest association with working memory. Late-life cognitive activities had the strongest association with perceptual speed, followed by education.

CONCLUSIONS—These cross-sectional findings suggest that education and reading ability are the most-robust proxy measures of cognitive reserve in relation to late-life cognition. Additional research leveraging path analysis is warranted to better understand how these life course factors, reflecting the latent construct of cognitive reserve, affect abnormal cognitive aging.

Keywords

education; cognition; reading ability; cognitive reserve

Reserve is a hypothetical construct that describes the lack of correspondence between brain pathology and the clinical manifestation of such damage.^{1,2} Whereas brain reserve refers to individual differences that allow some people to cope better with neuropathology than others,^{3,4} cognitive reserve is the brain's ability to cope actively with pathological damage by efficiently engaging brain networks or implementing alternative strategies to solve cognitive demands.^{1,5,6} An extensive amount of empirical attention has been devoted to quantifying cognitive reserve to better understand how this latent variable mediates central nervous system insult or degeneration. A number of proxy measures for cognitive reserve extending throughout the lifespan have been used. These measures are hypothesized to offer some level of “protection” against neuropathological changes and include education, reading ability, socioeconomic status (SES), occupational complexity, and cognitively stimulating activities.

Perhaps the most commonly used proxy measure of cognitive reserve is education,⁷ which encompasses accumulated knowledge and skills through formal schooling. Not only is education relatively easy to quantify, but it also purportedly leads to better health through enhanced habits, skills, or resources that enable a healthier lifestyle and contribute to economic prosperity (for a review see⁸). Occupational complexity is another common proxy measure of cognitive reserve^{9–11} that offers experiences that increase one's environmental stimulation and provides enhanced opportunities for the development and compilation of skills.¹⁰ A third popular proxy measure is SES, which has been quantified for childhood¹² and adulthood.¹³ The hypothesized mechanism by which SES acts as a marker for reserve is that higher levels of SES afford economic resources and environmental enrichment, contributing to better brain health (for a review see¹⁴). Alternatively, lower SES is associated with greater risk of toxic exposures¹⁵ and poorer health status, perhaps because of substandard prenatal care or nutrition,¹⁶ all of which could compromise brain health. More recently, there has been increased interest in studying cognitively stimulating activities as a proxy measure for cognitive reserve.^{17–19} The hypothesis underlying these studies is that greater cognitive activity protects against cognitive decline, improves cognition through repetition of specific skills (making them less vulnerable to underlying neuropathological changes), and strengthens strategic cognitive skills (e.g., working memory, information processing speed) that can serve as a compensatory mechanism for cognitive changes in other areas.^{17,18} Last, reading ability (or literacy) has been used as a proxy measure of cognitive reserve^{20–22} based on the rationale that literacy may reflect native ability²³ or intelligence²⁴ and that the experience of acquiring reading abilities may enhance the brain's organization²⁵ or increase synaptic density.²³

In the cognitive aging literature, the reserve concept has been used as one theoretical framework to explain variability in the initial symptomatic expression of Alzheimer's disease (AD) and its progressive course. That is, individuals with higher cognitive reserve

(as measured according to education) appear to have greater protection against clinical symptom onset,⁷ whereas those individuals with lower cognitive reserve (as assessed according to literacy level or education) are at higher risk for clinical dementia.²⁵ Education appears to modify relations between AD neuropathology and cognitive test performance,⁷ so that higher levels of cognitive reserve may alter the clinical expression of evolving AD neuropathological burden. In essence, within the context of abnormal cognitive aging, the cognitive reserve model predicts that there will be individual differences in the amount of AD neuropathology required for the initial clinical expression and subsequent diagnosis of disease.¹

Prior work evaluating multiple proxy measures of reserve suggests that cognitive reserve is not a fixed variable but rather a combination of exposures throughout one's lifetime (for review see¹). Therefore, the proposed cross-sectional investigation aims to enhance knowledge by integrating multiple life course factors, including education; reading ability as assessed according to the National Adult Reading Test (NART);²⁶ early-life and adult SES; and early-, mid-, and late-life cognitive activities as assessed according to the Cognitive Activities Scale (CAS)²⁷ to examine relations between the latent variable construct, cognitive reserve, and late-life cognition before the onset of dementia. The theoretical framework put forth is consistent with prior studies^{7,10,17,21,25} and reviews^{1,28,29} drawing from the reserve framework and consistent with general theories of plasticity in cognitive aging.³⁰ Although some prior studies have collapsed various proxy measures of cognitive reserve to form a "reserve" composite,¹¹ the current study considered each variable individually using path analysis to better understand how the latent construct of reserve relates to late-life cognition. The implementation of path analysis in this context is valuable because it allows for the estimation of all possible linkages between multiple life course factors while considering direct and indirect effects.³¹ Thus, path analysis integrates the selection of several proxy measures of cognitive reserve by recognizing multiple interacting relationships between the variables and statistically evaluating the logical consequences of assumptions made about the nature of these associations in their relationship with late-life cognition before the onset of clinical dementia.

METHODS

Participants

The Rush Memory and Aging Project study design and selection criteria have been described elsewhere.³² The only study entry requirements were that participants agreed to annual detailed clinical evaluation and were willing to make an anatomical gift of their brain at time of death. The multi-step enrollment process included attendance at a presentation about the study, a scheduled visit with the study coordinator, and several visits that constituted the clinical evaluation (described below), all of which effectively screened out persons with known dementia at the time of enrollment.

The current sample and corresponding data were derived from a baseline visit of 1,004 participants enrolling between 2002 (when the CAS data collection was expanded to its current version) and 2008. Using procedures previously described,³² all participants underwent a uniform structured clinical assessment, including medical history, neurological examination, and neuropsychological assessment. Cognitive diagnoses were determined at study entry using a multistep process as previously reported.³³ Specifically, 11 cognitive tests were administered, and performances were adjusted for education and summarized using a computer algorithm that yielded impairment ratings. Next, a study neuropsychologist reviewed the computer summary rating; the remaining cognitive performance tests; and reports of effort, vision, and hearing and rendered a clinical judgment regarding the presence or absence of cognitive impairment. Finally, a clinician (physician or advanced practice

geriatric nurse practitioner) reviewed all available data from the evaluation that year and rendered an opinion regarding cognitive decline, cognitive impairment, and dementia. Clinical dementia (probable or highly probable dementia) required evidence of meaningful decline in cognitive function with impairment in two or more cognitive domains. People with possible dementia referred to individuals without dementia who the neuropsychologist rated as having cognitive impairment or the clinician rated as having meaningful cognitive decline. Possible dementia includes criteria for mild cognitive impairment and cognitive impairment insufficient to warrant a mild cognitive impairment diagnosis. Of the 1,004 participants consenting to study participation at baseline entry, 53 were excluded for meeting a probable or highly probable dementia diagnosis based on the comprehensive baseline entry assessment, yielding 951 eligible participants for the current study. Of the 951 participants included in the current study, 260 met criteria for possible dementia.

The Rush University Medical Center institutional review board approved the study protocol. All participants provided written informed consent before evaluation.

Neuropsychological Protocol

As previously described,²⁷ a comprehensive neuropsychological protocol was administered during a 1-hour testing session. Composite measures representing five cognitive domains (episodic memory, semantic memory, working memory, visuospatial ability, and perceptual speed) were created by converting test performances within each domain into a *z*-score and averaging the *z*-scores. A global cognition composite reflected the *z*-score averages across all protocol measures. Prior studies in this cohort have incorporated the NART into the global cognition composite and the semantic memory composite,¹⁷ but because the current study leveraged the NART as a proxy measure of cognitive reserve, it was removed from these composite scores. Protocol details, including descriptions of each domain, individual tests, and variables of interest, are outlined in Table 1.

CAS

Early-, mid-, and late-life cognitive activities were measured using the CAS, a structured questionnaire assessing the frequency of participation in specific cognitive activities.¹⁸ All CAS items were scored on a scale from 1 to 5, with higher values reflecting more-frequent activity (1 = least frequent and 5 = most frequent). As previously described, composite measures for childhood, young adult, and mid- and late-life cognitive activities were calculated by averaging the item scores in each life period. The average of childhood and young adult scores was used to form an early-life measure. A description of items contained in the early-, mid-, and late-life categories is provided below:

Early-life cognitive activities include three items assessing childhood activities at age 6, including playing games, having someone in the home read to the participant, and having someone in the home tell stories to the participant, and eight items assessing childhood activities at ages 12 and 18, including the amount of time the participant spent reading daily, writing letters, playing games, performing homework, and visiting a library, along with the frequency with which the participant read newspapers, magazines, and books.

Midlife cognitive activities include nine items assessing activities at age 40, including the amount of time the participant spent reading daily and the frequency with which the participant visited a museum; attended a concert, play, or musical; visited the library; read newspapers, magazines, and books; wrote letters; and played games.

Late-life cognitive activities include nine items assessing current cognitive activities (captured at study entry) and comprised the same items as the midlife cognitive activities detailed above.¹⁸

Education—Education was quantified at baseline entry with possible ranges from 0 (e.g., immigrants with no formal education) to 30, which allows for the quantification of multiple advanced degrees.

Socioeconomic Status—Early-life SES was based on several components, including parental education (mean years of schooling completed by the participant's mother and father), paternal occupation (the father's principal occupation coded according to perceived prestige),³⁴ total number of children in the family, and community-level SES.³⁵ The estimate of adult SES used in the Rush Memory and Aging Project includes education, occupation, baseline (study entry) household income, and household income at age 40,¹⁸ but for the purpose of the current study, education was removed, because it was being considered separately as a proxy measure of cognitive reserve in the statistical plan below.

Statistical Analysis

Before analyses, responses to each CAS item were averaged to yield composite measures of early- (childhood and young adult CAS items), mid- (aged 40), and late-life activity (current), as previously described.¹⁷ Because the effects of education were to be examined separately, the adult SES score available in the Rush Memory and Aging Project dataset was recalculated without education (as mentioned above). Similarly, to isolate the effects of reading ability as assessed according to the NART, semantic memory and global cognition composites were recomputed excluding the NART scores. Finally, to remove the effects of age, sex, and race from the cognitive tests, residuals were used by regressing each cognitive score on age, sex, and race (dichotomized into white or not white) as outcomes. All variables were standardized to z-scores, with a mean of 0 and a standard deviation of 1.

Path analysis was used to decompose associations between proxy measures of cognitive reserve across the lifespan and cognition by quantifying the total direct and indirect standardized effects of the life course factors (reading ability as assessed according to the NART; education; early-life and adult SES; and early-, mid-, and late-life cognitive activities as assessed according to the CAS) on global cognition and five specific cognitive domains (episodic memory, semantic memory, working memory, visuospatial ability, and perceptual speed). First, an a priori model for global cognition and its five domains was constructed using a classical path analysis approach,³⁶ such that the variables of interest were arranged in such a manner that the upstream variables would affect variation in the downstream variables but not vice versa (Figure 1A). Specifically, late-life variables were not allowed to affect variation in childhood or midlife variables, and midlife variables were not allowed to affect variation in childhood variables. Standardized path loadings and the standardized total direct and indirect effects were calculated. Next, an empirically driven model was formed that was allowed to deviate from the original hypothesis. Plausible paths in the a priori model for global cognition were added and deleted to obtain conventional levels of acceptable fit by adding or deleting the path with the largest modification index. The revised model was then fit for each of the five domains (episodic memory, semantic memory, working memory, visuospatial ability, and perceptual speed). Fit was assessed using the Comparative Fit Index, the Tucker-Lewis Index, and the root mean square error of approximation.

In secondary analyses, whether the loadings for participants with possible dementia ($n = 260$) differed from those of the participants with no cognitive impairment ($n = 691$) was

assessed. For each outcome, a multiple group version of the a priori model was fit, with the loadings constrained to be the same for both subgroups. Chi-square tested whether allowing any of the loadings to differ between the groups significantly improved model fit. If so, the largest difference was accepted into the model, and the process was repeated until no significant differences remained. For all analyses, maximum likelihood parameter estimation techniques were employed that used all available data on each person under missing-at-random assumptions (as opposed to a complete case analysis), making imputation of missing data unnecessary. Significance was set a priori as $P < .05$. All data were analyzed using Stata version 11 (Stata Corp., College Station, TX) and Mplus version 5.2 (Muthén & Muthén, Los Angeles, CA).

RESULTS

Participant Characteristics

Participant characteristics are provided in Table 2 for the entire sample and broken down into cognitively normal and possible dementia subgroups. The entire sample had a mean age of 79 (range 54–100), mean education of 14 years (range 0–28 years), 74% of participants were women, and 90% were white. CAS scores for the entire sample ranged from 1.3 to 4.5 (3.1 ± 0.6).

Path Analysis—A Priori Models

Most paths in the a priori models (Figure 1A) were significant as hypothesized (Table 3). The direct effects of late-life CAS, adult SES, and education on each particular domain varied (as an example, see Figure 1B). The direct effect of late-life CAS on working memory; the direct effect of adult SES on episodic memory, visuospatial ability, and global cognition; and the direct effect of education on perceptual speed were all nonsignificant in their respective models. One advantage of path modeling is that the total effect of a variable can be calculated, and the total effect of education was highly significant in all models (Table 3). In addition to education, NART had strong independent effects and was the strongest correlate of working memory. Of the CAS scores across the lifespan, late-life CAS had the strongest effect and early-life CAS the weakest effect. Late-life CAS was the strongest correlate of perceptual speed and was second only to education on semantic memory, but as noted above, late-life CAS had little association with working memory. Early-life SES was stronger than adult SES in all models. For complete model results, loadings for the indirect paths are available as an online supplement.

Path Analysis—Revised Models

Next the a priori model was revised using empirically driven modifications to the global cognition model. The data suggested removing the paths from early-life SES to midlife and late-life CAS. Three paths were added: early-life CAS to late-life CAS, midlife CAS to the NART, and adult SES to the NART. As would be expected in a data-driven model, standardized total effects were generally higher, but the differences for early-life CAS and early-life SES were notably stronger than in the a priori model (Table 4). Some paths that were significant in the global model were not important for particular domains, and these differences mirrored the a priori models.

Finally, whether any of the path loadings in the a priori model differed according to cognitive status (possible dementia vs no cognitive impairment) was assessed. In the global cognition model, the only path loading in which the two groups were statistically different was the path from education to NART ($\chi^2 = 4.8$, $P = .03$), although this difference was of small magnitude (a loading of 0.40 in the possible dementia group and 0.35 in the no cognitive impairment group). For the five specific cognitive domains, the two groups were

again statistically different for the path from education to NART, with magnitudes of difference comparable with those seen in the global cognition model. The only additional between-group difference that emerged was the direct path from education to visuospatial ability ($\chi^2 = 9.9$, $P = .002$ with a loading of 0.35 for the possible dementia group and 0.22 for the no cognitive impairment group).

DISCUSSION

In this study of a community-dwelling cohort of adults without dementia, multiple life course dimensions of cognitive reserve were cross-sectionally related to late-life cognition. Using path analysis, comprehensive models that integrate a combination of lifetime exposures were created to better understand complex relations between proxy measures of cognitive reserve and late-life cognition before the onset of dementia. The life course factor that was most prominently and strongly associated with late-life cognition was education, which primarily related to global cognition, episodic memory, semantic memory, and visuospatial ability. Reading ability, as assessed according to the NART, was most strongly associated with working memory and secondarily associated with episodic memory and global cognition. Thus, some combination of education and NART strongly influenced several cognitive domains (global cognition, episodic memory, working memory) statistically. The major exception to this pattern was that perceptual speed was most strongly associated with late-life cognitive activities (but secondarily with years of education).

A large volume of prior research has suggested that lower levels of education are strongly associated with greater risk for late-life cognitive decline³⁷ and incident dementia,^{2,38} and recent meta-analytic findings suggest that this association is probably causal.³⁹ Acknowledging that the findings of the current study are cross-sectional and cannot speak to causality, the theoretical explanation accounting for the association between lower education and risk of cognitive decline is that a higher education level delays the clinical expression of underlying neuropathological changes associated with dementia,⁷ because higher levels of education are associated with enhanced habits, skills, and resources that enable a healthier lifestyle and better health status.⁸ Furthermore, education level has been related to markers of brain reserve, such as enlarged intracranial volume⁴⁰ and head size in older adults without dementia.⁴¹ Thus, the findings augment the existing volume of literature by suggesting that, when multiple life course factors are considered in a path model, late-life cognition is still most strongly associated with education before the onset of dementia.

The second major finding from the current study is that NART performance was most strongly associated with working memory performance but also secondarily to episodic memory and global cognition. The NART is often used as an estimate of premorbid intellectual ability or reading ability.⁴² Its utility as a proxy measure for cognitive reserve is largely based on the fact that the NART reflects an accumulation of experience, because one must have come in contact with test items before testing to recognize their irregular sound-to-spelling correspondence. It has been suggested that measures of reading ability may more accurately reflect native ability than years of education because one's literacy level can be enhanced throughout the lifespan.²³ Prior path analysis results assessing latent constructs associated with NART performance in mid-life have supported the idea that the NART reflects an accumulation of experience, because several variables, including childhood cognition, educational attainment, and adult occupation, all contribute independently to NART performance.²² Thus, taken together with past results, the cross-sectional findings of the current study suggest that higher levels of reading ability protect individuals against cognitive impairment in later life, particularly working memory, episodic memory, and global cognition (and perhaps the expression of AD pathology), to a greater extent than many other life course factors of cognitive reserve in early and midlife.

Another primary finding from the current study was that late-life cognitive activities (rather than education or NART performance) were most strongly associated with perceptual speed (including inhibition and information processing speed measures) and secondarily associated with semantic memory (including lexical retrieval measures). Prior work suggests that more-frequent cognitive activity in later life reduces the risk of AD.^{17,18,43} A number of factors may account for the observation that, in the absence of dementia, more late-life cognitive activities are related to better performance on perceptual speed and semantic memory tests. Greater cognitive activity may protect against cognitive decline, improve cognition through the repetition of specific skills, or strengthen strategic cognitive skills that act as a compensatory mechanism for cognitive changes in other domains,^{17,18} all of which may delay the clinical expression of underlying neuropathological changes associated with dementia.⁴⁴ Furthermore, high levels of cognitive activity may create or reflect an enriched environment, leading to greater brain reserve, such as greater synaptic density,^{44,45} blood flow,⁴⁶ or hippocampal neurogenesis.^{47,48} It is certainly plausible that high-functioning older adults may naturally lead more intellectually rich lives. Alternatively, although the CAS was developed with the intention of including cognitive activities with minimal reliance on physical demands,⁴⁹ the possibility cannot be excluded that motor demands confound the association between late-life cognitive activities and the perceptual speed index (which includes two cognitive measures with a motor component). Additional research is warranted to better understand the association between late-life cognitive activities and cognitive decline.

Secondary analyses assessed the accuracy of the a priori model. The empirically driven model indicated that the theoretically driven a priori model underestimated the importance of early-life SES and early-life cognitive activities. Secondary analyses also assessed how cognitive status affected the primary results. When path loadings were allowed to differ according to cognitive status (no cognitive impairment vs possible dementia), findings were only slightly attenuated on one path, such that, across all models, there was a modest difference in magnitude between groups for the path from education to NART (i.e., the magnitude for the direct effect was slightly larger for the possible dementia group). The only additional between-group difference observed was that education was modestly stronger in its association with visuospatial ability for the possible dementia group than for the no cognitive impairment group. In general, the effects on the outcomes did not change, and the modest differences observed were only for magnitude of the associations; therefore, it was concluded that the models did not differ substantively according to cognitive status, which the modest cognitive impairment associated with the possible dementia categorization within this cohort may explain.

Overall, the current findings suggest that education and NART performance are the most-robust cross-sectional proxy measures of cognitive reserve across the lifespan when related to late-life cognitive function. Collectively, the present findings complement the extensive literature on cognitive reserve and risk for cognitive decline in several ways. First, the current analytical approach simultaneously integrates multiple proxy measures of cognitive reserve across the lifespan. Second, multiple cognitive domains, versus just a global measure, were considered to test whether life course factors of cognitive reserve relate differently to specific aspects of cognition. Third, the statistical approach (path analysis) allowed for assessment of direct and indirect effects of multiple life course factors on late-life cognition. Finally, the current data are based on an aging cohort free of clinical dementia, extending prior work focused on incident dementia or AD as an outcome. These findings have important implications for prevention strategies for cognitive decline, because cognitive screening of individuals with lower education levels and poorer reading abilities before the onset of cognitive complaints or impairment could aid in the detection of subtle and early signs of abnormal cognitive aging.

This study has a number of strengths, including the large community-based cohort and detailed and structured assessment of cognitive status and lifetime cognitive activity that offers a unique opportunity to examine links between life course factors of cognitive reserve and late-life cognition, although a few caveats temper the present findings. First, the cohort was predominantly white, well-educated, and was geographically constrained, which may limit the generalizability of the findings. Replication in more-diverse populations is required. Second, age, education, cultural background, and cognitive status may inherently confound the assessment of life course factors, such as self-reported cognitive activities, in later life. For instance, cognitively healthy older adults may engage in or report engaging in more cognitive activities, whereas those with evolving cognitive difficulties (in the absence of dementia) may engage in or report engaging in fewer cognitive activities. The retrospective nature by which cognitive activity is reported is a third limitation. Fourth, another investigative team with a different theoretical framework and latent measures of cognitive reserve could easily have made different decisions on the ordering of variables in the path analysis, yielding different models and potentially different results. It is for this reason that extensive coefficient data were included, so that others can replicate or modify the models in future studies. Fifth, the analyses are cross-sectional, so the generalizability of the findings is limited and cannot speak to whether the various proxy measures of cognitive reserve over the life course causally affect the cognitive variables of interest or are associated with cognitive decline over time or incident dementia. Finally, inherent to path analysis, the specific variables selected for inclusion in the models limit the models, and the observed effects (or lack of effects) may be due to variables not considered. Replication of the findings is required, and future studies should implement path analysis to better understand complex relationships between multiple life course factors and incident dementia and AD neuropathology.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Illustration of select path models. (A) Basic a priori model for all cognitive outcomes. (B) Path model of relationships between life course factors and global cognition. CAS = Cognitive Activities Scale; NART = National Adult Reading Test; SES = socioeconomic status.

Table 1**Neuropsychological Protocol Description**

Factor and Neuropsychological Test	Dependent Variable of Interest	Test Description
Episodic memory		
WMS-R Logical Memory—Story A	Immediate and delayed recall	Assesses immediate and 30-minute delayed free recall of a paragraph story. Raw scores reflect number of items recalled.
East Boston Story	Immediate and delayed recall	Assesses immediate and 15-minute delayed recall of a short story. Raw scores reflect number of items recalled.
Word List Learning	Memory, recall, and recognition	Assesses immediate recall of 12 unrelated words over four trials, followed by free recall after an interference condition with a 30-minute delayed free recall and recognition trial. Raw scores reflect number of items recalled.
Semantic memory		
Boston Naming Test—15 item	Total correct	Assesses confrontation naming and lexical retrieval abilities. Raw scores reflect number of correctly identified items.
Verbal Fluency	Total correct	Assesses rapid word generation. Raw scores reflect the number of words generated across three different 60 second trials.
Working memory		
WMS-R Digit Span	Forward and backward total correct	Assesses auditory attention. Raw scores reflect number of correctly recalled digits.
Digit Ordering	Total correct	Assesses auditory attention. Raw scores reflect number of correctly repeated series.
Visuospatial Ability		
Judgment of Line Orientation—15 item	Total correct	Assesses ability to estimate spatial relationships between line segments. Raw scores reflect correct number of spatial matches across 30 items.
Raven's Progressive Matrices—16 item	Total correct	Assesses nonverbal abstract reasoning using a multiple-choice visual pattern-completion task. Raw scores reflect the number of correctly completed patterns.
Perceptual speed		
Symbol Digit Modalities Test	Total correct	Assesses complex scanning and visual tracking. Raw scores reflect the number of correctly matched number–symbol pairs.
Number Comparison	Total correct	Assesses complex scanning and visual tracking. Scores reflect the number of correct responses minus the number of incorrect responses.
Stroop Color-Word Interference	Total correct	Assesses inhibition involving suppression of an automatic response (word reading) in favor of a novel response (color naming). Raw scores reflect total completion time.

Note: In prior Rush Memory and Aging Project–related studies, the global cognition and semantic memory index has included the National Adult Reading Test, but it was removed for the current analyses.

WMS-R=Wechsler Memory Scale, Revised.

Table 2**Participant Characteristics**

Characteristic	Total Sample N=951	Cognitively Normal n=691	Possible Dementia n=260
Age, mean $\pm$ SD	79 $\pm$ 8	78 $\pm$ 8	82 $\pm$ 8 [*]
Female, %	74	77	68 [*]
White, %	90	91	88
Education, years, mean $\pm$ SD	14 $\pm$ 3	14 $\pm$ 3	14 $\pm$ 3
Cognitive Activities Scale score, mean $\pm$ SD [†]			
Total	3.1 $\pm$ 0.6	3.1 $\pm$ 0.6	3.0 $\pm$ 0.6 [*]
Early life	3.0 $\pm$ 0.7	3.0 $\pm$ 0.7	2.9 $\pm$ 0.7 [*]
Midlife	3.2 $\pm$ 0.7	3.0 $\pm$ 0.7	2.9 $\pm$ 0.7 [*]
Late life	3.1 $\pm$ 0.7	3.2 $\pm$ 0.6	3.1 $\pm$ 0.7 [*]
SES, mean $\pm$ SD [‡]			
Early life	0.0 $\pm$ 0.7	0.0 $\pm$ 0.7	-0.1 $\pm$ 0.7
Maternal education	9.6 $\pm$ 4.0	9.7 $\pm$ 4.0	9.6 $\pm$ 3.9
Paternal education	9.5 $\pm$ 4.5	9.5 $\pm$ 4.5	9.3 $\pm$ 4.4
Adult [§]	0.0 $\pm$ 0.8	0.0 $\pm$ 1.0	-0.1 $\pm$ 1.0 [*]
Occupational prestige (range 13–81), mean $\pm$ SD	40 $\pm$ 13	41 $\pm$ 13	40 $\pm$ 13
Household income, \$, %			
At age 40			
<20,000	41	40	43
20,000–34,999	37	36	40
35,000	22	24	17
At study entry			
<20,000	27	25	32
20,000–34,999	29	30	25
35,000	44	44	43
Mini-Mental State Examination score, mean $\pm$ SD	28 $\pm$ 2	28 $\pm$ 2	26 $\pm$ 3 [*]
National Adult Reading Test score, mean $\pm$ SD	12 $\pm$ 3	12 $\pm$ 3	11 $\pm$ 4 [*]

SD=standard deviation.

^{*} Possible dementia subgroup statistically differed from cognitively normal group, $P < .05$.[†] A composite of seven common activities rated on a 5-point scale, with higher scores indicating more-frequent activity.²²[‡] A composite z-score based on parental education, paternal occupation, number of children in the family, and community level socioeconomic status (SES) with higher z-scores indicating higher SES. Only parental education is reported in the table.[§] A composite z-score based on years of education, occupation, baseline household income, and household income at age 40. For the purpose of the current study, education was removed from this formula.^{||} Assessed by presenting 10 income categories and asking the participant to report the letter that corresponds to their income category. For ease of presentation, these values have been condensed into three categories here.

Table 3

Total Standardized Effects (Direct+Indirect) in the A Priori Models

Life Course Factor	Global Cognition *	Episodic Memory	Semantic Memory *	Working Memory	Visuospatial Ability	Perceptual Speed
Total effects on outcome						
Early-life CAS	0.061 [†]	0.036 [†]	0.069 [†]	0.021 [†]	0.034 [†]	0.086 [†]
Midlife CAS	0.099 [†]	0.063 [†]	0.111 [†]	0.025	0.054 [†]	0.143 [†]
Late-life CAS	0.224 [†]	0.143 [†]	0.252 [†]	0.057	0.122 [†]	0.325 [†]
Early-life SES	0.209 [†]	0.126 [†]	0.186 [†]	0.163 [†]	0.182 [†]	0.180 [†]
Adult SES	0.128 [†]	0.034	0.165 [†]	0.136 [†]	0.081 [†]	0.153 [†]
Education	0.353 [†]	0.232 [†]	0.279 [†]	0.285 [†]	0.338 [†]	0.257 [†]
NART	0.309 [†]	0.202 [†]	0.187 [†]	0.341 [†]	0.163 [†]	0.250 [†]
Direct effects on outcome						
Late-life CAS	0.224 [†]	0.143 [†]	0.252 [†]	0.057	0.122 [†]	0.325 [†]
Adult SES	0.062	-0.009	0.114 [†]	0.080 [†]	0.046	0.085 [†]
Education	0.138 [†]	0.111 [†]	0.085 [†]	0.094 [†]	0.217 [†]	0.029
NART	0.309 [†]	0.202 [†]	0.187 [†]	0.341 [†]	0.163 [†]	0.250 [†]

Outcomes are adjusted for age, sex, and race.

Total effects are the sum of direct and indirect effects in the model, expressed in standardized effect size units (i.e., the perstandard deviation difference in the outcome per standard deviation difference in the predictor). Total and direct effects are conditional effects, meaning that they are estimates that reflect the simultaneous adjustment for the effects of other predictors in the model. When total effects and direct effects are the same, the factor was not mediated by any other in explaining variability in the outcome.

CAS = Cognitive Activities Scale; SES = socioeconomic status.

* Semantic memory and global cognition differ from previous Rush Memory and Aging Project-related publications because the National Adult Reading Test (NART) was excluded in the current study.

[†] $P < .05$.

Table 4

Total Standardized Effects (Direct+Indirect) in the Revised Models

Life Course Factor	Global Cognition*	Episodic Memory	Semantic Memory*	Working Memory	Visuospatial Ability	Perceptual Speed
Early-life CAS	0.118 [†]	0.073 [†]	0.127 [†]	0.057 [†]	0.064 [†]	0.152 [†]
Midlife CAS	0.129 [†]	0.084 [†]	0.159 [†]	0.074 [†]	0.070 [†]	0.157 [†]
Late-life CAS	0.227 [†]	0.145 [†]	0.185 [†]	0.059	0.123 [†]	0.328 [†]
Early-life SES	0.255 [†]	0.156 [†]	0.322 [†]	0.215 [†]	0.206 [†]	0.215 [†]
Adult SES	0.107 [†]	0.020	0.130 [†]	0.113 [†]	0.070	0.135 [†]
Education	0.305 [†]	0.201 [†]	0.320 [†]	0.242 [†]	0.313 [†]	0.211 [†]
NART	0.308 [†]	0.203 [†]	0.589 [†]	0.340 [†]	0.163 [†]	0.246 [†]

Outcomes are adjusted for age, sex, and race.

Total effects are the sum of direct and indirect effects in the model, expressed in standardized effect size units (i.e., the per standard deviation difference in the outcome per standard deviation difference in the predictor). Total, direct, and indirect effects are conditional effects, meaning that they are estimates that reflect the simultaneous adjustment for the effects of other predictors in the model. When total effects and direct effects are the same, the factor was not mediated by any other in explaining variability in the outcome.

CAS = Cognitive Activities Scale; SES = socioeconomic status.

* Semantic memory and global cognition differ from previous Rush Memory and Aging Project-related publications because the National Adult Reading Test (NART) was excluded in the current study.

[†] $p < .05$.