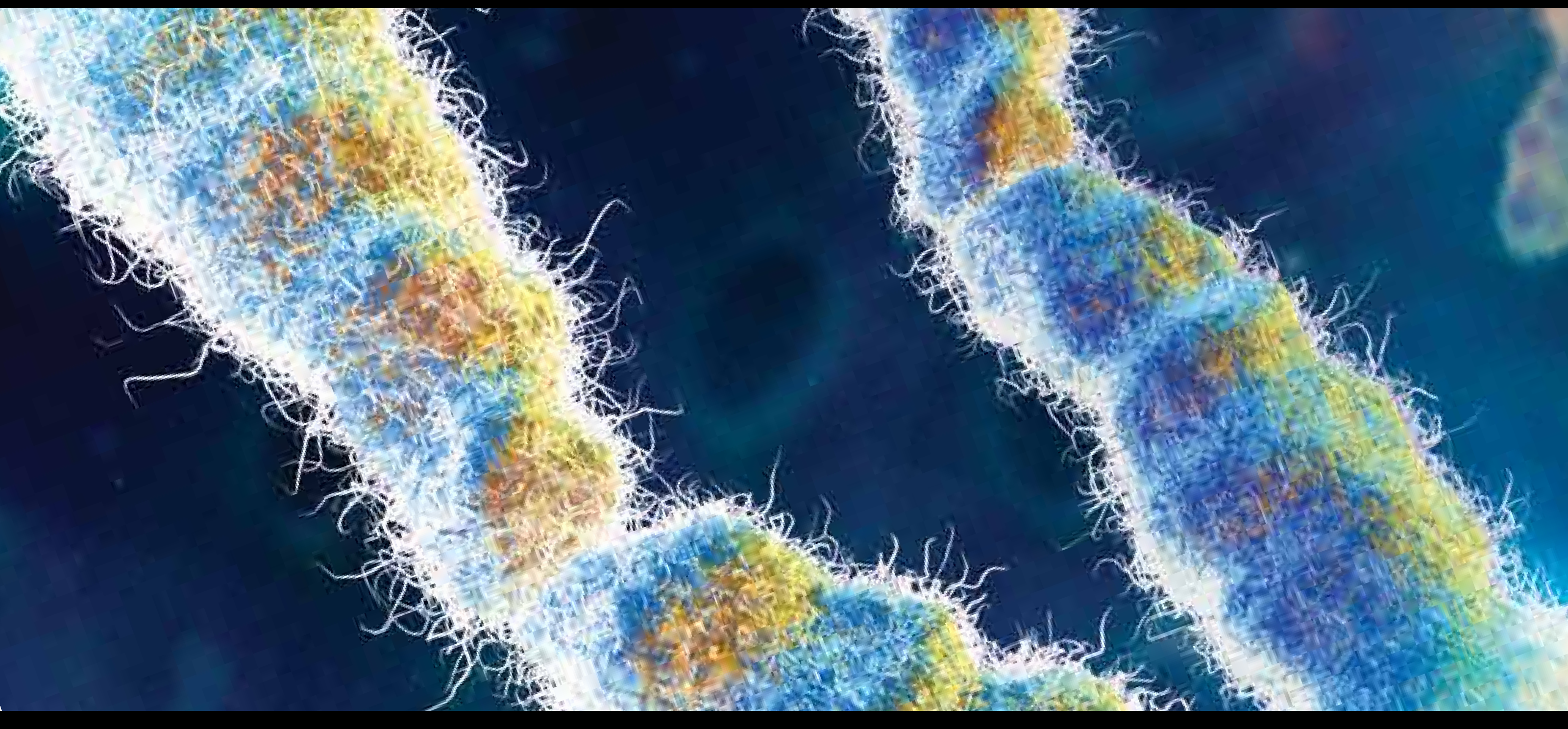
Journal of Aging Research

# Lifestyle Factors and Cognitive Ageing: Variation across Ability and Lifestyle Domains

Guest Editors: Alan J. Gow, Allison A. M. Bielak, and Denis Gerstorf



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# Editorial Board

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*Editorial*

# Lifestyle Factors and Cognitive Ageing: Variation across Ability and Lifestyle Domains

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Cognitive abilities change with age. However, as there are marked individual differences in the timing and trajectory of these changes [1, 2], it is a research priority to discover factors that contribute to these differences. Lifestyle factors, particularly those which are malleable across the life course, may be highly informative for the development of interventions to reduce or delay age-related cognitive decline. Factors of interest, to name only a few, include aspects of social, leisure, and physical activity; personality; social networks, support and relationships; and health behaviours [3]. The purpose of this special issue was to bring together research that addresses the associations between cognition in older adulthood and these various factors, thereby allowing overarching themes, trends, and conclusions to emerge.

Efforts to identify lifestyle factors that are associated with cognitive ageing are challenged by a number of methodological issues. For example, conclusions are often limited by short periods of follow-up or an assessment of a narrow range of cognitive abilities. In addition, lifestyle factors are often considered in isolation, which, although convenient, may not accurately reflect the way in which individuals actually experience these factors. Approaching the issue from a multivariate perspective might allow the identification of which factors have a more prominent association with cognition over and above other influences. Another concern is the difficulty of distinguishing between alternative explanations for a given lifestyle factor's association with cognitive ability: does the lifestyle factor lead to differential preservation, that is, does it actually predict subsequent differential cognitive change? Alternatively, is the association the result of preserved differentiation, where the factor is associated with individual differences in baseline performance and with the maintenance of these differences over time, but not with further differential change [4–6]?

Each of the papers in this special issue describes an attempt to tackle one or more of the unknowns about associations between lifestyle factors and cognition, including the consideration of neurological factors underlying some of the observed effects. Although no single study can address all pertinent issues, those included often combined a long period of follow-up in old age with a diverse assessment of cognitive abilities. One set of studies sampled a wide range of lifestyle factors simultaneously so as to compare their effects with one another, and another suite of papers considered a range of lifestyle factors across distinct samples. A number of the papers approached the differential preservation/preserved differentiation conundrum by considering lifestyle effects on both cognitive ability level and cognitive change across time. The papers in this special issue are broadly arranged into four themes:

(i) mental health and health behaviours,
(ii) social activity and networks,
(iii) cognitive engagement, and
(iv) neurological factors.

The previously mentioned issues are spread throughout these four themes, highlighting that researchers are cognizant of the need to address these critical issues across lifestyle domains. We first summarize each of the papers within these domains before providing an overall conclusion from this suite of papers.

*Mental Health and Health Behaviours.* Firstly, E. L. Mortensen et al. examined whether hostility and depression shape developmental trajectories of cognitive abilities across adulthood. Under the premise that these personality factors are linked with various aspects of stress, the authors applied growth curve modelling to cognitive data obtained from a sample tested every ten years over a period of 30 years. After adjusting for sociodemographic variables and a wide range of lifestyle factors (e.g., blood pressure, smoking, physical activity, and obesity, as well as blood samples of serum cholesterol, triglycerides, and insulin), results revealed that depressive traits and hostility were indeed associated with cognitive ability level, but there was no prediction of differential change.

In D. Cadar et al., the authors investigated the unique and combined effects of various health behaviours measured in midlife—smoking, physical activity, and nutrition—on later cognitive ability. Dietary choices and physical activity were independently associated with cognitive change, particularly in the memory and perceptual speed domains.

Though M. Lindwall et al. considered only one of these same health behaviours—physical activity—they addressed the associations using a coordinated analytical approach across four distinct longitudinal samples (two further papers from this group focusing on alternative lifestyle factors appear later in this special issue). Accounting for expected age-related declines, changes in physical activity were associated with concomitant changes in reasoning and fluency.

*Social Activity and Networks.* Three papers in this special issue consider associations between social lifestyle factors and cognitive ageing. In the first, L. C. Giles et al. examined whether a particular aspect of an individual's social network was linked to cognitive ageing in old and very old age. Of the different types of social networks assessed—children and other family, friends, and confidant—it was particularly the effect of an individual's network of friends (number, personal contact, and phone contact) that was beneficial for maintaining episodic memory across the 15-year follow-up.

C. L. Brown et al. also focused on associations between social activity and cognition, and represents the second paper using a coordinated analysis of four longitudinal samples. Across studies and multiple cognitive domains (reasoning, memory, fluency, and semantic knowledge), the authors consistently observed associations with level for most of the abilities assessed, but there was little evidence that social activities predicted differential cognitive change.

Finally in this section, S. M. Sisco and M. Marsiske took a broader view of lifestyle influences on cognition by examining whether neighbourhood-level socioeconomic position was associated with cognitive ability, and whether this association was stronger for certain abilities than for others. The authors reported that vocabulary was the only domain uniquely affected by neighbourhood factors, suggesting social acculturation effects of one's environment. However, they also acknowledged possible alternative interpretations, including selection effects and the lingering influence of the socioeconomic position of one's childhood neighbourhood.

*Cognitive Engagement.* The next group of studies examined the effect of cognitive engagement, stimulation, or activity. Firstly, J. M. Parisi et al. investigated cross-sectional associations between education and a range of cognitive abilities (reading ability, processing speed, and memory), while considering the potential mediating role of a variety of lifestyle factors, including intellectual, social, physical, creative, and passive activities. Although strong inferences cannot be drawn from cross-sectional mediation models, both separate and conjoint analyses revealed intellectual activities as the strongest mediator between education and cognition.

S. von Stumm took a different perspective on the activity-cognition issue by comparing how activity engagement and its link with cognition might differ from that between the predisposition to engage in these activities (investment trait) and cognition. Interestingly, the predisposition to engage in activity, but not cognitive activity itself, was related to baseline cognition, though neither factor mediated the association between age and cognitive ability.

In the last of the papers combining the results from four samples, M. B. Mitchell et al. reported associations between cognitive activity and cognitive ability across a number of domains. Though there were significant baseline associations, there was no evidence of baseline activity predicting subsequent cognitive change. However, associations between changes in activity and changes in cognitive ability were apparent, once again highlighting the challenges of examining temporal precedence, even with longitudinal data.

*Neurological Factors.* The remaining two papers moved beyond describing associations between lifestyle factors and cognitive ageing to trying to elucidate potential neurological factors shaping such linkages. In B. D. James et al., associations between social engagement and structural parameters from MR brain imaging were examined. Higher social engagement was associated with larger total brain and grey matter volumes, though not white matter volume. Such findings are interesting, particularly because lifestyle factors are proposed as cognitively protective. It is important to describe and better understand the actual physical effects such lifestyle factors might have on the ageing brain.

Similarly, T. D. Verstynen et al. used structural MR imaging to test whether cardiorespiratory fitness was associated with cognitive flexibility and attentional control. The results suggested that cardiorespiratory fitness predicted cognitive flexibility via larger greater grey matter volume in the dorsal striatum.

*Conclusions.* The papers included in this special issue considered a number of lifestyle factors which have been proposed as cognitively protective. Indeed, the results of some papers are in accordance with that proposal, but not all. Rather, what might be more informative for our understanding about this complex relationship is what generalities appeared across the suite of papers, at the same time as acknowledging persistent differences by cognitive domain and lifestyle factor.

The simultaneous examination of lifestyle effects on both cognitive ability level and longitudinal cognitive change in many of the papers suggests that concurrent associations of a factor with cognitive ability do not necessarily generalize to significant associations with cognitive change. The repeated demonstration of this phenomenon across multiple areas (social networks, physical, social, and cognitive activity, depression, diet, and smoking) is relevant to the debate between preserved differentiation versus differential preservation. If a factor is not associated with differential cognitive change, is the factor still relevant to the eventual goal of promoting healthy cognitive ageing? These findings can have implications for those interested in translating such observational findings into interventions aimed at reducing or delaying age-related cognitive decline. Where there are few associations with cognitive change, then interventions may be less likely to succeed. However, associations between lifestyle factors and cognitive ability level might suggest the potential to increase cognitive ability *level* across the lifespan via lifestyle-based interventions. An increase in level of cognitive ability would still be of benefit because (everything else being equal) it would increase the time before reaching some defined threshold for impairment.

At the same time as noting commonalities, we would be remiss to ignore the persistent variation that seems to exist throughout this special issue. The results of the present studies varied extensively by the investigated lifestyle factor, including activity domain, and the cognitive domain considered. It may be that the associations between each lifestyle and cognitive domain are unique and subject to variation, or it may be that they are in fact similar along various threads or facets that we simply have not yet identified. Regardless, there are clearly many additional questions to be investigated. To aid in this search, we suggest that studies of cognitive ageing include a diverse assessment of cognitive ability across a number of domains. Such detailed assessments are often lacking from studies in this literature, and those utilising a single broad, often basic screening measure (such as the Mini-Mental State Examination [7]) are not uncommon. Other approaches worthy of greater usage would be the combining of disparate studies in coordinated analyses, as demonstrated by several papers in this special issue, potentially allowing constructive replication of the effects investigated [8]. Analyses which also involve the simultaneous consideration of multiple lifestyle factors might more realistically examine the ways in which individuals participate in a range of somewhat interrelated behaviours, and how these combinations are associated with cognitive ability in older adulthood.

The search for malleable determinants of cognitive ageing is important, even more so with the trend towards increasingly older populations. The individual variation observed in cognitive ageing trajectories is a tantalising hint that factors which influence this do exist, though the identification of these likely small effects has been difficult. In closing, we note that one of the next steps the field could substantially benefit from would be to move from examining between-person associations to a thorough investigation of within-person associations [9]. To do so, however, studies with more frequent and more closely spaced multi-domain measurements are needed. It is only then that we can examine whether and how lifestyle factors and cognitive ageing indeed go hand in hand at the individual (rather than the population) level.

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*Research Article*

# Dynamic Associations of Change in Physical Activity and Change in Cognitive Function: Coordinated Analyses of Four Longitudinal Studies

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The present study used a coordinated analyses approach to examine the association of physical activity and cognitive change in four longitudinal studies. A series of multilevel growth models with physical activity included both as a fixed (between-person) and time-varying (within-person) predictor of four domains of cognitive function (reasoning, memory, fluency, and semantic knowledge) was used. Baseline physical activity predicted fluency, reasoning and memory in two studies. However, there was a consistent pattern of positive relationships between time-specific changes in physical activity and time-specific changes in cognition, controlling for expected linear trajectories over time, across all four studies. This pattern was most evident for the domains of reasoning and fluency.

## 1. Introduction

Previous research has clearly demonstrated that cognitive change in old age does not occur in a homogenous manner for all individuals [1–3]. A number of predictors of cognitive change in old age have been identified, such as education, hypertension, objective indices of health and cardiovascular disease, and apolipoprotein E [4]. Regular engagement in different types of activities may also influence cognitive change. More specifically, according to the "use it or lose it" hypothesis [5], regular engagement in different activities may buffer age-related decline in cognitive functioning. A number of studies have found that general lifestyle activity engagement (often operationalized as the combination of intellectual, social, and physical activities) is associated with cognitive change [6–8] and that decline in activity in older age is associated with decline in cognitive functioning.

In addition to general activity, other studies have specifically targeted the association of physical activity with cognitive change. Indeed, a growing body of the literature highlights the potential benefits of physical activity on the structure and function of the brain [9, 10]. The first line of evidence for the relationship between physical activity and cognition comes from a number of cross-sectional studies demonstrating that physically active older adults have higher cognitive performance and functioning compared with less active older adults [11, 12].

However, the evidence derived from these cross-sectional studies is limited, as it is not. possible to draw conclusions in terms of more complex associations of change. Stronger evidence may be found in longitudinal studies. Longitudinal studies may be viewed as the second line of evidence, offering valuable information on the relationship between physical activity and cognition across time. Several prospective, longitudinal studies provide evidence for the association of physical activity with cognitive functioning [13–20]. These studies have generally shown that higher physical activity at baseline is associated with less decline in cognitive functioning over time, offering support for the notion that regular physical activity may buffer against future cognitive decline. However, results from these longitudinal studies are inconclusive [4] and several critical questions remain [21].

The longitudinal studies described above may test two different classes of hypotheses regarding the relationship of lifestyle variables, such as physical activity and cognitive change [6]. The first type of hypothesis stipulates that the level of physical activity is related to subsequent cognitive change. The majority of the abovementioned studies have targeted this first class of hypothesis, examining a stable change hypothesis by looking at how physical activity at baseline predicts change in cognitive functioning. The second class of hypothesis instead examines the relationship between concomitant change in activity and change in cognition. In contrast to the baseline effect of activity, this hypothesis deals with the concept of intraindividual change and associations among intraindividual rates of change, providing a more dynamic perspective. For example, positive changes (increases) in physical activity across time may be hypothesized to contribute to a less negative change (less decline) in cognitive functioning, whereas a negative change in activity (decreased activity) would be expected to be related to faster cognitive decline with age.

Mackinnon and colleagues [7] used a latent growth curve modeling approach to examine how change in overall activity (defined as a composite of physical activity, rest, interest and hobby related, and planned activities), rather than physical activity, was related to change in health and cognitive performance. They found substantial correlations between rates of change in activity and cognitive and health measures, and it was concluded that decline in mental and physical activity in older age is paralleled by decline in cognitive functioning and health. However, decline in cognitive functioning was still evident for participants who were stable in their level of activity across time, suggesting that maintenance of activity may not be enough to protect from cognitive decline.

Unfortunately, few previous studies have actually targeted the hypothesis of whether there are associations among rates of individual change in physical activity and cognitive functioning in long-term observational studies of aging individuals. Van Gelder and colleagues [17] found that men who decreased their physical activity duration or intensity also demonstrated a stronger decline in overall cognition (measured by the Mini Mental State Examination) compared with men who maintained their activity duration and intensity. However, several limitations should be noted in this study. First, only change in one global measure of cognitive functioning was used, rather than several different measures that may capture more diverse and complex relationships of cognitive ability with activity change. Moreover, in the study, change in physical activity was categorized in terms of quality (change/no change) rather than quantity (how much change). Finally, the analyses were based on between-group comparisons and therefore did not target relationships of within-person changes in physical activity and cognition.

Bielak and colleagues [22], however, used random effects models to examine how level and change in physical activity were related to level (within-person mean) and inconsistency (within person standard deviation across trials) of cognitive speed at baseline and change in level and inconsistency. Although physical activity at baseline was related to mean cognitive speed in some tasks, there were no associations between change in physical activity and change in cognitive speed. Moreover, a recent study [23] using bivariate dual-change-score models to analyze data from the Victoria Longitudinal Study found that changes in physical activity influenced changes in verbal speed and episodic memory. However, they also found that changes in cognition influenced changes in activity, thus supporting a dual-coupling model or a reciprocal relationship between physical activity change and change in cognition.

Although previous longitudinal studies have resulted in increased understanding of how physical activity at one point (baseline) may predict future cognitive performance, or change in cognitive performance, they have generally not helped us understand the more complex and dynamic characteristics of the longitudinal relationship between physical activity and cognition. Relevant questions remain unanswered. For example, is there an association between within-person change in physical activity and within-person changes in cognitive functioning when taking into account the change in cognition due to time? Or, put differently, do persons demonstrate lower cognitive scores (relative to their *within-person* trajectory over time) on occasions when they also report less physical activity? Relative to a cross-sectional analysis that compares individuals to other similar aged individuals, the answers to these questions afford relevant insight into the more complex and dynamic patterns of associations between changes in physical activity and cognitive functioning within individuals across time. Another question that has not been properly addressed by previous longitudinal studies is if physical activity, or change in activity, has similar effects across different cognitive domains and/or tests. From previous experimental work using randomized controlled trial designs, there is support for the notion that physical activity training has the strongest effect on executive control processes and working memory, supporting the "selective-improvement hypothesis" [24]. However, as the majority of previous longitudinal studies of the relations between physical activity and cognition have included a single measure of cognition (often MMSE) rather than different tests and domains, the theoretically, as well as practically, important question of whether changes in physical activity may relate more strongly to changes in some cognitive domains relative to others remains unresolved.

An essential step for the sound cumulative development of this body of knowledge is the reproduction and extension of research findings across independent longitudinal studies that focus on observed within-person change [25]. Although most previous longitudinal studies have found that physical activity is protective against age-related cognitive decline, the findings are disparate and far from clear [21]. Moreover, previous studies have typically used data from one population (e.g., adults ranged from 55–94 in age) and one design (e.g., 3 waves of measurements over a 6-year period), leaving the generalization of the results highly contingent on sample specific-characteristics. Differences between studies in terms of sample, design, measures, and analytical approach make it difficult to compare results across studies and to derive more general conclusions of the meaning of these results. Therefore, there is a clear need for more coordinated integrative data analyses that use data from different samples with different measures, but examine these data with the same research question and the same analytic approach [25]. Using a coordinated analysis approach for cross-study comparisons and synthesis of independent results has the potential to bring new relevant information to the field of cognitive change and physical activity [26].

The purpose of the present study is to investigate the longitudinal associations of physical activity with four domains of cognition (i.e., reasoning (executive function), episodic memory, fluency, and semantic knowledge) in older adults using a coordinated approach with data from four independent longitudinal studies: Long Beach Longitudinal Study (LBLS), the Seattle Longitudinal Study (SLS), the Victoria Longitudinal Study (VLS), and the Origins of Variance in the Oldest-Old: Octogenarian Twins Study (OCTO-Twin). More specifically, the following research questions were examined:

(i) Is physical activity at baseline associated with cognition at baseline?

(ii) Is baseline physical activity associated with the rate of change in cognition?

(iii) Are occasion-specific changes in physical activity associated with occasion-specific changes in cognition, controlling for change in cognition due to time alone?

## 2. Methods

*2.1. Design and General Analytical Framework.* This research, initiated as a partnership between the Advanced Psychometric Methods Workshop series (Mungas et al., NIA conference grant) and the Integrative Analysis of Longitudinal Studies on Aging (IALSA) network [25, 26], brought workshop participants together with researchers from four IALSA member studies. These studies were specifically selected based on their collection of cognitive, physical, and social activity data along with a range of cognitive functioning measures over multiple occasions held in common across the four studies. While the activity and cognitive functioning variables are not always identical, the subsets of variables in each study were chosen based on the rationale that they tapped similar domains at the construct level (e.g., fluid reasoning (Gf), crystallized knowledge (Gc), short-term memory (Gsm,) and long-term storage and retrieval (Glr; category fluency) [27]. In some cases the measures are the same, but more often they differ, providing opportunities for both strict and conceptual replication.

*2.2. OCTO-Twin (Origins of Variance of the Oldest-Old) Sample (Sweden).* The OCTO-Twin study is comprised of the oldest-cohort of the Swedish Twin Registry aged 80 and older at the time of first examination. Beginning in 1991–93, the longitudinal design included a maximum of five measurement occasions at 2-year intervals. Individuals with a dementia diagnosis at baseline ($n = 98$) were excluded from the initial sample of 702 participants. The remaining 604 individuals were included in analyses. Approximately 20% of the sample was lost to follow up at each wave (10% per year), but most of this attrition was due to death. Descriptive statistics are provided in Table 1.

*2.3. OCTO-Twin Materials and Procedures*

*2.3.1. OCTO-Twin Cognitive Ability Measures. Reasoning* was assessed using Block Design [28]. In this task, participants were presented with red and white blocks and instructed to reproduce the design shown on a card using these blocks within a predetermined time limit. *Fluency* was not assessed in the OCTO-Twin Study. *Memory* was assessed using immediate recall of the Prose Recall test, in which participants were presented with a brief, 100-word story that had a humorous element [29]. Amount of information recalled was coded in a manner similar to the scoring of story units in the Wechsler Memory Scale Logical Memory test [30]. *Semantic knowledge* was assessed using the Swedish version of the Information Task, in which participants provided responses to factual knowledge questions [31]. Raw scores were transformed into T-scores with a mean of 50

Table 1: OCTO-Twin participant characteristics.

| Measure | Year of testing | | | | |
|---|---|---|---|---|---|
| | Baseline ($N = 574$) | Year 2 ($N = 471$) | Year 4 ($N = 363$) | Year 6 ($N = 275$) | Year 8 ($N = 201$) |
| | M (SD) | M (SD) | M (SD) | M (SD) | M (SD) |
| Retention from previous testing (%) | | 82.0 | 77.1 | 75.8 | 73.1 |
| Age | 83.3 (3.0) | 85.2 (2.8) | 86.9 (2.5) | 88.8 (2.5) | 90.7 (2.4) |
| Education | 7.3 (2.4) | 7.3 (2.3) | 7.3 (2.3) | 7.2 (2.1) | 7.2 (2.2) |
| Sex, female ($n$ (%)) | 371 (65) | 346 (65) | 236 (65) | 196 (71) | 148 (74) |
| Reasoning | 11.5 (7.1) | 11.4 (7.2) | 11.3 (7.1) | 10.8 (7.2) | 10.0 (7.3) |
| Memory | 9.6 (4.0) | 9.4 (4.3) | 9.2 (4.4) | 9.2 (4.7) | 8.9 (4.5) |
| Semantic knowledge | 28.1 (11.2) | 28.6 (11.2) | 27.5 (12.4) | 26.7 (13.0) | 26.1 (11.4) |
| Physical activity | 0.7 (0.7) | 0.9 (0.7) | 0.8 (0.7) | 0.7 (0.7) | 0.6 (0.6) |
| Physical activity change[a] | | 0.1 (0.7) | −0.0 (0.8) | −0.1 (0.8) | −0.3 (0.9) |

M: mean, SD: standard deviation. The scoring ranges for each measure with a defined upper limit are as follows: reasoning: 0–42; memory: 0–16; semantic knowledge: 0–44; physical activity: 0–2. [a]Physical activity change represents change from baseline.

and standard deviation of 10 to facilitate comparisons across measures.

*2.3.2. OCTO-Twin Physical Activity Measure.* Respondents were asked, at each of the five waves, the following: *"Are you presently doing or have you previously done anything special to train your body or keep your body fit?"* The possible responses were "no" (0), "yes, to some extent" (1), or "yes, to a great extent" (2). Hence, a scale from 0 to 2 was used. The participants gave one reply for their present physical activity status and one in regards to their previous status. Only the answer for the present status was used in the analyses. Physical activity change scores were computed by subtracting baseline activity from each follow-up activity measure.

*2.4. Long Beach Longitudinal Study Sample (California, USA).* The LBLS was initiated in 1978 when participants were recruited from the Family Health Plan Health Maintenance Organization (HMO), mainly including residents of Long Beach and Orange County. This first panel included 583 individuals aged 28–36 or 55–87. The ethnic composition of the older group (98% Caucasian) was similar to the 65+ population for the area based on the 1970 census. Panel 2, initiated in 1992, included 633 individuals from the same HMO (64 were excluded due to frank dementia or serious sensory or neurological problems).

In order to include the same measures as those in the Seattle Longitudinal Study, LBLS Panel 1 ($n = 106$) and Panel 2 ($n = 631$) data from 1994 to 2003, excluding participants younger than age 55 in 1994 ($n = 541$), were used in the current analysis. During this period, data were collected at 3-year intervals. Attrition was approximately 50% over each interval or 17% per year. Dementia incidence is not known. Descriptive information for the sample is presented in Table 2.

*2.5. LBLS Materials and Procedures*

*2.5.1. LBLS Cognitive Ability Measures.* *Reasoning* was based on a composite score of the Letter and Number Series tests from the Schaie-Thurstone Adult Mental Abilities Test (STAMAT; [32]. In this task, participants viewed a series of letters (e.g., a b c c b a d e f f) and were asked to identify the next letter in the series from alternate choices by extracting the rule that governed the series. Responses were made by choosing the correct alternative from an array of possible alternatives. Participants were given six minutes to complete as many of the 30 items as possible. *Fluency* was assessed using Word Fluency, in which participants wrote down as many words as possible that begin with the letter "s" during a five-minute period according to predetermined rules. These rules included no proper names and no addition of endings to words that the participant had already provided (e.g., "sit," "sitting," and "sits"). *Memory* was measured using immediate written recall of a 20-item noun list that participants had studied for 3.5 minutes. *Semantic knowledge* was assessed using the STAMAT Recognition Vocabulary test. Participants were provided with 50 target words and asked to select the synonym from four choice alternatives. Performance was based on total correct responses provided in a five-minute period.

*2.5.2. LBLS Physical Activity Measure.* The physical activity measure was based on selected questions from the Life Complexity Scale. A composite score was created by summing the number of physical activities (e.g., walking, outdoor hobbies, etc.) that included one or more hours of these activities per week. The range of possible scores was from 0 to 4. Activity change variables were computed by subtracting the activity measure in 1994 from activity in 1994, 1997, 2000, and 2003. This resulted in difference scores that were referent to the baseline testing in 1994.

*2.6. Seattle Longitudinal Study Sample (Washington, USA).* The SLS is a long-running longitudinal study initiated by K. Warner Schaie, who first recruited members of a local Health Maintenance Organization in 1956. Current analyses used up to four waves of SLS data from 1984–2005, which include an expanded set of measures that also overlapped with the Long Beach Study. Only participants 55 years and

Table 2: LBLS participant characteristics.

| Measure | Year of testing | | | |
|---|---|---|---|---|
| | Baseline ($N = 541$) | Year 3 ($N = 275$) | Year 6 ($N = 140$) | Year 9 ($N = 94$) |
| | M (SD) | M (SD) | M (SD) | M (SD) |
| Retention from previous testing (%) | | 50.8 | 50.9 | 67.1 |
| Age | 73.6 (9.0) | 75.1 (8.5) | 75.1 (8.0) | 75.9 (7.1) |
| Education | 13.8 (3.0) | 13.9 (2.9) | 14.3 (2.7) | 14.2 (2.7) |
| Sex, female (*n* (%)) | 258 (51) | 137 (50) | 71 (51) | 45 (48) |
| Reasoning | 22.5 (11.7) | 24.1 (11.4) | 25.4 (11.5) | 25.3 (10.7) |
| Fluency | 32.7 (11.4) | 33.7 (11.2) | 33.6 (12.9) | 34.5 (11.8) |
| Memory | 11.4 (4.0) | 11.7 (4.3) | 11.5 (4.5) | 11.2 (4.8) |
| Semantic knowledge | 38.7 (10.1) | 39.6 (9.6) | 40.6 (8.8) | 39.7 (9.9) |
| Physical activity | 1.7 (1.0) | 1.6 (1.1) | 1.5 (1.0) | 1.6 (0.9) |
| Physical activity change | 0.0 (0.0) | −0.2 (1.0) | −0.4 (1.0) | −0.4 (1.1) |

M: mean, SD: standard deviation. The scoring ranges for each measure with a defined upper limit are as follows: education: 0−20, reasoning: 0−30, memory: 0−20, vocabulary: 0−36, physical activity: 0−4.

older at baseline were included in the analysis. Baseline was defined as each participant's first study visit, and time was measured in all analyses as years in study (coded as 0, 7, 14, and 21). Attrition during these 7-year intervals was approximately 50% or 7% per year. Dementia prevalence and incidence are not known. See Table 3 for SLS participant characteristics over the four waves of data analyzed here.

*2.7. SLS Materials and Procedures*

*2.7.1. SLS Cognitive Measures.* *Reasoning* was assessed with the Word Series test from the Schaie-Thurstone Adult Mental Abilities Test (STAMAT; [32]). In this task, participants were provided with a printed word series that was ordered according to an inherent rule. The participant's task was to select, from multiple-choice options, the next word in the series consistent with that rule. Total score was based on number of correct responses to the 30 trials completed in 6 minutes. As in LBLS, *Fluency* was indexed by performance on the Word Fluency Test from the Primary Mental Abilities test [33] and *Memory* by the verbal list-learning task. *Semantic knowledge* was assessed with the test of Advanced Vocabulary from the Educational Testing Service (ETS), in which participants identified synonyms for printed words from five choices [34]. The total score was derived from the number of correct responses provided within 4 minutes to the 36-itemtest.

*2.7.2. SLS Physical Activity Measure.* The methodology described in the LBLS method portion of this paper was used in order to generate roughly equivalent indices of physical activity. Following this methodology, a composite physical activity measure was created by summing dichotomized test responses from a modified version of the Life Complexity Scale [3], resulting in a four-item physical activity composite (playing sports, walking, fitness, and outdoor hobbies). *Activity change* was computed by subtracting baseline activity from each follow-up activity measure.

*2.8. Victoria Longitudinal Study Sample (British Columbia, Canada).* The Victoria Longitudinal Study began in 1986–87 with a sample of 484 community residing volunteers. Using a longitudinal sequential design, second and third independent samples began in 1992-93 ($n = 530$) and 2001-2002 ($n = 550$) [35]. Each sample is tested at three-year intervals. To date, Sample 1 has been tested on seven occasions (over 18 years), Sample 2 on five (over 12 years), and Sample 3 on two occasions (over 6 years). Participants in all three samples were recruited between the ages of 55 and 85 years.

Data from seven waves of Sample 1 and five waves of Sample 2 were included in the current investigation. Characteristics of the subsample analyzed here are provided in Table 4. Approximately 20% of the sample was lost to follow up at each wave, or 10% per year. Dementia prevalence and incidence are not known.

*2.9. VLS Materials and Procedures*

*2.9.1. VLS Cognitive Ability Measures.* *Reasoning* was indexed by Letter Series [33]. In this task, participants were presented with a series of letters and asked to identify the next letter in the sequence based on the rule that governed the sequence. *Fluency* was measured by performance on a Similarities task [34], in which participants were presented with target words and asked to write as many words as possible with the same or nearly the same meaning during a 6-minute period. *Memory* was indexed based on free recall of a 30-item noun list comprised of five semantic categories. Participants were given two minutes to study the words and then five minutes to recall them [35]. *Semantic knowledge* was assessed using a 54-item recognition vocabulary test adapted from the ETS Kit of Factor Referenced Tests [34].

*2.9.2. VLS Physical Activity Measure.* The physical activity measure was derived from a subset of four items from the VLS- Activity Lifestyle Questionnaire (VLS-ALQ; [6]). These items indexed the physical activities of gardening, jogging,

Table 3: SLS participant characteristics.

| Measure | Year of testing<br>Baseline (N = 1658)<br>M (SD) | Year 7 (N = 940)<br>M (SD) | Year 14 (N = 447)<br>M (SD) | Year 21 (N = 181)<br>M (SD) |
|---|---|---|---|---|
| Retention from previous testing (%) | | 56.7 | 47.6 | 40.5 |
| Age | 67.1 (8.2) | 73.0 (7.3) | 78.9 (6.4) | 81.9 (4.9) |
| Education | 14.6 (2.9) | 14.7 (2.8) | 14.8 (2.7) | 14.8 (2.8) |
| Sex, female (*n* (%)) | 862 (52) | 507 (54) | 257 (57) | 108 (60) |
| Reasoning | 15.6 (5.8) | 15.2 (5.6) | 14.3 (5.5) | 14.0 (5.3) |
| Fluency | 38.5 (12.8) | 37.5 (13.1) | 36.7 (12.7) | 38.8 (14.5) |
| Memory | 12.5 (4.0) | 12.0 (4.1) | 11.5 (4.2) | 11.7 (3.9) |
| Semantic knowledge | 25.0 (6.7) | 25.3 (6.6) | 25.8 (6.2) | 25.8 (5.9) |
| Physical activity | 1.0 (1.1) | 1.8 (1.1) | 1.7 (1.0) | 1.6 (0.9) |
| Physical activity Change | — | −0.1 (1.1) | −0.2 (1.1) | −0.0 (1.1) |

M: mean, SD: standard deviation. The scoring ranges for each measure with a defined upper limit are as follows: education: 0–20, reasoning: 0–30, memory: 0–20, vocabulary: 0–36, physical activity: 0–4.

Table 4: VLS participant characteristics.

| Measure | Year of testing<br>Baseline (N = 977)<br>M (SD) | Year 3 (N = 723)<br>M (SD) | Year 6 (N = 571)<br>M (SD) | Year 9 (N = 412)<br>M (SD) | Year 12 (N = 282)<br>M (SD) | Year 15 (N = 91)<br>M (SD) | Year 18 (N = 52)<br>M (SD) |
|---|---|---|---|---|---|---|---|
| Retention from Previous testing (%)[a] | — | 74 | 79 | 72 | 68 | 75 | 57 |
| Age | 68.6 (6.7) | 71.3 (6.6) | 73.7 (6.4) | 76.5 (5.9) | 79.3 (5.2) | 82.2 (4.6) | 85.1 (3.6) |
| Years of education at baseline | 14.9 (3.3) | 15.4 (3.2) | 15.6 (3.1) | 15.8 (3.1) | 15.9 (3.1) | 15.2 (3.1) | 14.8 (2.8) |
| Sex, female (*n* (%)) | 614 (63) | 450 (62) | 348 (61) | 252 (61) | 177 (63) | 60 (66) | 35 (67) |
| Reasoning[b] | 11.2 (4.5) | 11.7 (4.2) | 10.4 (4.7) | 10.4 (4.6) | 9.9 (4.6) | 7.5 (4.7) | 6.5 (4.2) |
| Fluency | 17.7 (4.3) | 17.9 (4.4) | 17.8 (4.4) | 17.2 (4.8) | 16.3 (4.9) | 14.7 (5.8) | 13.8 (5.4) |
| Memory[c] | 13.7 (5.9) | 14.6 (6.0) | 14.7 (6.2) | 14.9 (6.4) | 11.8 (5.5) | 13.0 (6.3) | — |
| Semantic knowledge | 43.7 (7.4) | 44.7 (6.2) | 44.3 (6.0) | 44.2 (5.8) | 43.5 (5.7) | 42.7 (7.1) | 42.6 (6.6) |
| Physical activity | 15.4 (5.1) | 15.4 (5.1) | 15.0 (4.9) | 14.8 (5.2) | 13.4 (5.1) | 14.0 (5.2) | 12.3 (5.0) |
| Physical activity change | 0.0 (0.0) | –0.1 (4.0) | –0.8 (4.2) | –1.3 (4.6) | –2.8 (4.8) | –2.7 (5.0) | –4.4 (5.2) |

M: mean, SD: standard deviation. The scoring range for each measure with a defined upper limit are as follows: Reasoning 0–20, Fluency 0-maximum number of words produced in 6 minutes, Memory 0–30, Vocabulary 0–54. Physical Activity 0–36. The physical activity change scores are on a normal metric with means of approximately 0 and SD of approximately 0.8.
[a]The 1986 cohort was followed for up to 18 years, the 1993 cohort for up to 12.
[b]The reasoning measure was not given until year 6 for the 1986 cohort.
[c]The memory measure was not given in year 18.

sailing, and tennis. For each item, participants indicated the frequency of engagement in that activity over the past two years on a scale from 0 to 9 (i.e., *never, less than once a year, about once a year, 2 or 3 times a year, about once a month, 2 or 3 times a month, about once a week, 2 or 3 times a week, and daily)*.

*2.10. Analytic Approach.* In order to examine the effects of physical activity on cognition, a series of multilevel models was fit with time varying covariates [36] using multilevel mixed-effects regression in Stata (StataCorp, 2011), the restricted maximum likelihood estimator (REML), and an unstructured covariance matrix. Separate models were fit for each of the four cognitive measures (reasoning, fluency (except OCTO-Twin), memory, and semantic knowledge) and for each of the four studies. In order to improve ease of interpretation of our results, age, education, and activity measures were mean centered to the baseline mean of each measure in the sample so that the intercept and linear slope terms could be interpreted as the expected value for an individual at the mean age, education, and respective activity level at baseline. The reference category for sex was male. OCTO-Twin participants were modeled as nested within their twin pair and in VLS we controlled for enrolment cohort.

Our goal was to build a common model for comparisons across all outcomes for the four longitudinal studies. This common model was not necessarily the optimal model for each of the 16 cognition-physical activity combinations. An initial 19-term model included all ten two-way interactions that included activity, change in activity or time, and three 3-way interactions of time and activity with age, sex, or education. However, several terms were not significant for most of the studies and outcomes and so were trimmed to facilitate model interpretation. First, the 3-way interactions were eliminated, then the interactions with change in activity. Last, the baseline activity by sex interaction was dropped. This resulted in a final model that included 12 terms summarized in Table 5 for separate cognitive constructs of reasoning, memory, semantic knowledge, and fluency. Our significance criterion of $P < 0.05$ shaped the "familywise" alpha rate within each study, however our focus was on the repetition of results across studies, which we used to minimize the potential impact of chance associations. We did not implement formal meta-analytic techniques as they require identical measures and a larger number of studies.

## 3. Results

*3.1. Baseline Covariates and Longitudinal Relationships.* Between-person age differences are seen at the first occasion of measurement for all memory, reasoning, and fluency tests, with older adults performing less well. Semantic knowledge results are less consistent, with older adults performing less well in LBLS and OCTO-Twin, but better in VLS. At baseline, individuals with more years of education had higher cognitive performance. LBLS and SLS women scored higher than men of the same age on all measures, except for semantic knowledge. OCTO-Twin and VLS women had higher memory scores than did the men. OCTO-Twin women had lower scores on semantic knowledge.

For the reference individuals (men with sample average baseline age and years of education), within-person declines were seen over time in all cognitive abilities and all samples except SLS (the youngest), where the relationship, as in LBLS and VLS, depended on age. Older individuals declined faster on all VLS, SLS, and LBLS measures except LBLS immediate memory. No clear pattern was identified in regards to differential decline related to sex or education.

*3.2. Physical Activity.* Higher physical activity at baseline was associated with higher scores on reasoning and memory in OCTO-Twin and VLS and fluency in SLS. The association between physical activity score at baseline and cognitive score did not differ by age. However, there was some indication that the relation between physical activity and cognition differed by education. For semantic knowledge in LBLS and SLS the association with physical activity at baseline was stronger for people with less education. In terms of associations with cognitive decline, higher physical activity score at baseline was related only to less decline on fluency in VLS and SLS.

However, we found a consistent pattern of positive relationships between time-specific changes in physical activity and time-specific changes in cognition beyond those expected by the estimated linear trajectories in the four studies. This pattern was most evident for the domains of reasoning and fluency. More specifically, after controlling for the trend in cognitive functioning over time, time-specific changes in physical activity change were related to cognitive fluctuations in the following cognitive domains: (a) reasoning in all four studies; (b) fluency in two (VLS and SLS) of three studies; (c) memory in two studies (OCTO-Twin and VLS); (d) semantic knowledge in one study (OCTO-Twin).

## 4. Discussion

Using data from four longitudinal studies of aging, the present study examined the relationship between physical activity and cognitive functioning at three different levels: (a) cross-sectionally; (b) longitudinally using physical activity as predictor of cognitive change; (c) longitudinally using change in physical activity as a time-varying covariate to predict change in cognition, adjusting for the normative development (effect of time) in cognition. On the cross-sectional level, higher physical activity at baseline was associated primarily with higher scores on reasoning and fluency, generally supporting previous studies demonstrating that physically active older adults have higher cognitive performance and functioning compared with less active older adults [11, 12]. Although relevant, these well-known and well-documented findings contribute little to a deeper understanding of the likely very complex relationship between activity and cognition.

The second level of analysis addressed more theoretically relevant and interesting longitudinal associations and the question of whether physical activity at baseline is associated with cognitive change. From a broader perspective, this research question is also linked to the "use it or lose it" hypothesis [5, 21], generally proposing that physical activity may buffer against future cognitive decline. A number of prospective studies have found support for this notion [13–20], offering preliminary support for the longitudinally beneficial and buffering effect of physical activity on cognitive decline. A general limitation in many of these previous prospective studies, however, is that they have examined the association between physical activity and a broad global measure of cognition (typically MMSE), thereby proving an incomplete picture of the potentially diverse longitudinal associations between different cognitive domains and physical activity. As a consequence, these previous studies generally have not answered the theoretically and practically relevant question "what cognitive domains most benefit from physical activity?" [21].

In the present study four different domains were examined, representing a broader spectrum of cognitive abilities,

Table 5: Mixed effects model summaries across four studies with baseline physical activity and activity change predicting four cognitive outcomes.

| | OCTO-Twin | | | LBLS | | | SLS | | | VLS | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* |
| Reasoning | | | | | | | | | | | | |
| Intercept | 10.66 | 0.56 | <.001 | 21.53 | 0.56 | <.001 | 37.88 | 1.02 | <.001 | 9.53 | 0.59 | <.001 |
| Age | –0.37 | 0.12 | 0.002 | –0.62 | 0.05 | <.001 | –0.35 | 0.01 | <.001 | –0.25 | 0.02 | <.001 |
| Sex | 0.90 | 0.68 | 0.186 | 2.12 | 0.81 | 0.009 | 1.67 | 0.24 | <.001 | –0.01 | 0.31 | 0.969 |
| Education | 0.57 | 0.13 | <.001 | 1.30 | 0.14 | <.001 | 0.52 | 0.04 | <.001 | 0.33 | 0.05 | <.001 |
| Activity | 1.19 | 0.40 | 0.003 | –0.50 | 0.40 | 0.209 | –0.57 | 0.89 | 0.519 | 0.01 | 0.03 | 0.827 |
| Age × activity | 0.06 | 0.14 | 0.699 | 0.03 | 0.04 | 0.502 | 0.01 | 0.01 | 0.398 | 0.00 | 0.00 | 0.587 |
| Education × activity | –0.09 | 0.13 | 0.479 | –0.12 | 0.14 | 0.372 | 0.00 | 0.04 | 0.983 | 0.00 | 0.01 | 0.840 |
| Time | –0.51 | 0.09 | <.001 | –0.46 | 0.09 | <.001 | 0.15 | 0.10 | 0.141 | –0.24 | 0.03 | <.001 |
| Age × time | –0.02 | 0.02 | 0.296 | –0.02 | 0.01 | 0.001 | –0.01 | 0.00 | <.001 | –0.01 | 0.00 | <.001 |
| Sex × time | 0.13 | 0.10 | 0.206 | 0.09 | 0.11 | 0.445 | 0.02 | 0.03 | 0.318 | 0.00 | 0.03 | 0.968 |
| Education × time | 0.02 | 0.02 | 0.258 | –0.06 | 0.02 | 0.007 | –0.01 | 0.00 | 0.090 | –0.01 | 0.00 | 0.065 |
| Activity × time | 0.06 | 0.07 | 0.354 | 0.04 | 0.06 | 0.506 | 0.01 | 0.01 | 0.183 | 0.00 | 0.00 | 0.332 |
| Activity change | 0.85 | 0.21 | <.001 | 0.54 | 0.24 | 0.028 | 0.18 | 0.09 | 0.045 | 0.05 | 0.02 | 0.013 |
| Fluency | | | | | | | | | | | | |
| Intercept | | | | 31.19 | 0.62 | <.001 | 58.66 | 2.55 | <.001 | 11.73 | 0.56 | <.001 |
| Age | | | | –0.25 | 0.05 | <.001 | –0.34 | 0.04 | <.001 | –0.10 | 0.03 | <.001 |
| Sex | | | | 4.25 | 0.90 | <.001 | 3.54 | 0.59 | <.001 | 0.46 | 0.36 | 0.200 |
| Education | | | | 1.04 | 0.16 | <.001 | 1.29 | 0.11 | <.001 | 0.64 | 0.05 | <.001 |
| Activity | | | | 0.45 | 0.45 | 0.314 | 4.45 | 22.4 | 0.047 | –0.06 | 0.03 | 0.098 |
| Age × activity | | | | 0.07 | 0.05 | 0.159 | –0.06 | 0.03 | 0.070 | 0.00 | 0.00 | 0.952 |
| Education × activity | | | | –0.29 | 0.15 | 0.059 | –0.02 | 0.09 | 0.844 | –0.01 | 0.01 | 0.159 |
| Time | | | | –0.27 | 0.11 | 0.013 | 0.78 | 0.23 | 0.001 | –0.13 | 0.03 | <.001 |
| Age × Time | | | | –0.03 | 0.01 | 0.001 | –0.02 | 0.00 | <.001 | –0.01 | 0.00 | 0.002 |
| Sex × Time | | | | –0.22 | 0.15 | 0.132 | 0.13 | 0.05 | 0.007 | 0.07 | 0.04 | 0.070 |
| Education × Time | | | | 0.00 | 0.03 | 0.983 | –0.01 | 0.01 | 0.106 | 0.00 | 0.01 | 0.950 |
| Activity × Time | | | | 0.03 | 0.08 | 0.680 | 0.05 | 0.02 | 0.048 | 0.01 | 0.00 | 0.045 |
| Activity Change | | | | 0.05 | 0.35 | 0.894 | 0.41 | 0.20 | 0.043 | 0/07 | 0.03 | 0.003 |
| Memory | | | | | | | | | | | | |
| Intercept | 8.59 | 0.31 | <.001 | 10.78 | 0.20 | <.001 | 23.50 | 0.74 | <.001 | 17.36 | 0.42 | <.001 |
| Age | –0.22 | 0.06 | <.001 | –0.19 | 0.02 | <.001 | –0.18 | 0.01 | <.001 | –0.19 | 0.02 | <.001 |
| Sex | 1.14 | 0.38 | <.002 | 1.55 | 0.30 | <.001 | 1.65 | 0.17 | <.001 | 1.65 | 0.27 | <.001 |
| Education | 0.39 | 0.07 | <.001 | 0.29 | 0.05 | <.001 | 0.32 | 0.03 | <.001 | 0.32 | 0.04 | <.001 |
| Activity | 0.48 | 0.22 | 0.003 | 0.15 | 0.15 | 0.312 | –0.17 | 0.65 | 0.789 | 0.05 | 0.03 | 0.042 |
| Age × Activity | –0.09 | 0.08 | 0.232 | 0.00 | 0.02 | 0.817 | 0.00 | 0.01 | 0.671 | 0.00 | 0.00 | 0.223 |
| Education × Activity | 0.02 | 0.07 | 0.837 | –0.05 | 0.05 | 0.346 | –0.03 | 0.03 | 0.215 | 0.00 | 0.01 | 0.607 |
| Time | –0.32 | 0.07 | 0.001 | –0.17 | 0.05 | 0.001 | 0.33 | 0.08 | <.001 | –0.27 | 0.03 | <.001 |
| Age × Time | –0.01 | 0.01 | 0.700 | 0.00 | 0.00 | 0.578 | –0.01 | 0.00 | <.001 | –0.01 | 0.00 | <.001 |
| Sex × Time | 0.08 | 0.08 | 0.319 | –0.04 | 0.07 | 0.601 | 0.03 | 0.02 | 0.077 | –0.02 | 0.03 | 0.469 |
| Education × Time | 0.01 | 0.02 | 0.972 | 0.01 | 0.01 | 0.379 | 0.00 | 0.00 | 0.449 | –0.01 | 0.00 | 0.232 |
| Activity × Time | –0.02 | 0.05 | 0.660 | –0.02 | 0.04 | 0.531 | 0.02 | 0.01 | 0.078 | 0.00 | 0.00 | 0.202 |
| Activity Change | 0.44 | 0.15 | 0.004 | –0.08 | 0.15 | 0.593 | 0.08 | 0.08 | 0.309 | 0.06 | 0.02 | 0.001 |
| Semantic knowledge | | | | | | | | | | | | |
| Intercept | 30.21 | 0.85 | <.001 | 38.36 | 0.56 | <.001 | 23.41 | 1.29 | <.001 | 43.86 | 0.71 | <.001 |
| Age | –0.60 | 0.17 | <.001 | –0.26 | 0.05 | <.001 | 0.01 | 0.02 | 0.531 | 0.08 | 0.03 | 0.013 |
| Sex | –3.88 | 1.04 | <.001 | 1.47 | 0.81 | 0.069 | 0.56 | 0.30 | 0.069 | 0.02 | 0.47 | 0.971 |
| Education | 1.60 | 0.21 | <.001 | 1.11 | 0.14 | <.001 | 1.11 | 0.05 | <.001 | 0.77 | 0.07 | <.001 |
| Activity | 0.85 | 0.57 | 0.134 | –0.54 | 0.40 | 0.174 | 1.61 | 1.14 | –0.160 | –0.02 | 0.04 | 0.716 |
| Age × Activity | 0.02 | 0.20 | 0.914 | –0.02 | 0.04 | 0.672 | –0.02 | 0.02 | 0.174 | 0.01 | 0.01 | 0.331 |
| Education × Activity | –0.22 | 0.21 | 0.307 | –0.31 | 0.14 | 0.023 | –0.11 | 0.05 | 0.020 | –0.01 | 0.01 | 0.588 |
| Time | –0.93 | 0.12 | <.001 | –0.44 | 0.09 | <.001 | 0.45 | 0.08 | <.001 | –0.14 | 0.03 | <.001 |

Table 5: Continued.

| | OCTO-Twin | | | LBLS | | | SLS | | | VLS | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* |
| Age × Time | –0.05 | 0.03 | 0.056 | –0.04 | 0.01 | <.001 | –0.01 | 0.00 | <.001 | –0.01 | 0.00 | <.001 |
| Sex × Time | 0.27 | 0.14 | 0.054 | 0.08 | 0.12 | 0.486 | 0.07 | 0.02 | <.001 | 0.01 | 0.04 | 0.736 |
| Education × Time | 0.03 | 0.03 | 0.279 | –0.03 | 0.02 | 0.134 | 0.00 | 0.00 | 0.792 | –0.01 | 0.01 | 0.152 |
| Activity × Time | –0.02 | 0.09 | 0.804 | 0.10 | 0.07 | 0.147 | 0.01 | 0.01 | 0.087 | 0.00 | 0.00 | 0.319 |
| Activity Change | 1.06 | 0.26 | <.001 | –0.04 | 0.25 | 0.881 | 0.11 | 0.08 | 0.148 | 0.02 | 0.02 | 0.258 |

Values represent model coefficients and their standard error. Across all studies, time was measured in years since baseline visit, and activity change was entered as a time-varying covariate. All other variables represent baseline measurements alone, in interaction with one another, or in interaction with time.

ranging from the more crystallized knowledge-based domain of semantic knowledge to more fluid or process-based factors of reasoning, fluency, and memory. Higher baseline physical activity was associated with less fluency decline in two of three studies. Thus, the preliminary answer to the question what cognitive domain benefits most from physical activity, based on the results of the present study, is fluency, which is one of the more process-based/fluid domains. However, it should be mentioned that for most cognitive domains across the four studies, we did not find support for the protective effect of baseline levels of physical activity on cognitive decline.

Aside from the more stationary change relationships typically investigated in previous studies (how level of physical activity at baseline relates to change in cognition), we also targeted more dynamic associations between changes in physical activity and changes in cognitive functioning by using change in physical activity from baseline as a time-varying covariate in longitudinal multilevel models. The time-varying covariate model used in this study examined occasion-specific intraindividual relations between physical activity and cognition, after controlling for individual rates of change over time. Such time-specific associations between fluctuations in activity and cognition have rarely been examined and may be highly relevant to understanding how to prescribe exercise and how to design and implement interventions including physical activity to optimize effects on cognition [37]. As associations of change and time-specific fluctuations are of key importance in the analyses and interpretation of intervention studies, the results of studies like the present one may offer new relevant information both from a scientific as well as from an applied perspective.

The results from these analyses were surprisingly consistent across studies and domains. Variation in physical activity was associated with variation in reasoning in all four studies and in fluency in two of three studies. Hence, although evidence for the association of between-person differences in baseline physical activity with subsequent cognitive change was generally weak across domains, aside from fluency, support for the notion that change in physical activity covaries with fluctuations in cognition is much more robust across studies. These results are inline with previous work [16], indicating that physical activity may specifically moderate the decline in cognitive domains that is typically associated with aging. Moreover, from a broader perspective, the stronger associations across time of physical activity with more fluid cognition may be linked to the hypothesis that exercise and aerobic fitness training results in selective improvement in executive control processes and working memory [24]. Although the cognitive tests used in the present study to measure reasoning and fluency were derived from a psychometric tradition of psychological testing and do not map well onto more recent conceptualizations of executive processing, they do share some of these features, being a more fluid measure of cognition.

An obvious limitation of the current study is the observational nature of the longitudinal designs, making inferences in terms of cause and effect irresolvable. The notion that decline in cognition leads to decline in physical activity is equal in validity to the interpretation that a decline in physical activity leads to a decline in cognition, that the relationship is reciprocal, or that both are a result of some third variable. Recent studies provide evidence for not only the reciprocal relationship across time between physical activity and mental health in older adults [38], but also for the reciprocal relationship between physical activity and cognition [23].

Another limitation is the problem associated with using different tests in different studies to tap the same cognitive domains. As noted earlier, the studies were selected because they shared similar measures of activity and cognition. Moreover, single cognitive tests are always imperfect markers of a cognitive domain. Therefore, a general feature of the integrated analytical approach in the present study, where data and tests from four different studies are used to answer the same research question, is the risk of heterogeneity in terms of how well the different tests indicate the higher order construct they should measure. As a result, when patterns of results are not consistent across studies, additional questions, testable in future research, are raised with respect to the source of these differences. It is, for example, interesting to note that for OCTO-Twin, in which physical activity was operationalized as the extent to which persons saw themselves as purposefully “keeping their body fit,” baseline activity was associated with cognitive functions more consistently than were the physical activity measures in the other studies. The apparent importance of physical activity, however, may also be due to the more advanced age of this sample. In situations where the studies with identical measures agree with each other, but not the remaining studies, for example, where neither SLS nor LBLS shows associations between memory performance and either baseline or change in activity, but OCTO-Twin and VLS do, we may draw conclusions that something about the measurement is important. In contrast, LBLS and SLS fluency results do not agree, suggesting instead that some detail relevant to the sampling, retest interval, or other study characteristic may be relevant.

On the other hand, when patterns of results do show consistency across studies that have used different measures to tap the same underlying construct, such as the association of change in activity with change in reasoning and fluency, these differences become a major strength, as the reliability of the conclusions drawn is considerably strengthened compared with traditional analysis of a single dataset.

Moreover, in contrast with the more specific measurement of cognition, the physical activity variables used in the current analyses were broad and self-reported and did not differentiate aerobic from strength or resistance training. Combining objective measures of physical activity with more specific multi-item, self-report instruments would likely provide future studies with a more robust base for the analysis of the association of change in activity with change in cognition.

The dynamic associations between physical activity and cognitive functioning underscore the broader question of associations between biological and cognitive aging [39]. Also, the effect of intraindividual change in physical activity on cognitive functioning (adjusting for the trend in cognition) raises the question of what drives, or causes, these relationships across time? These dynamic associations with the more fluid cognitive domains may be mediated, or explained, by a number of factors [40], such as physical resources (sleep, energy/fatigue, appetite, pain, or drug/medication use), disease states (hypertension, diabetes, and CVD), and mental resources (chronic stress, depression, and self-efficacy). More specifically, a number of physiological mediators, such as aerobic fitness, hormones, lipid profiles, cerebral blood flow, blood pressure, neurotransmitters, and neurotrophins have all been identified as potential mediators in physical activity-cognition relationships [41]. Although intuitively appealing and quite frequently investigated, the hypothesis of physical activity leading to improved cognition via increased aerobic fitness (the cardiovascular fitness hypothesis) is not, however, supported by meta-analyses [24, 42]. Thus, although single mediation models are theoretically attractive, and may fit data to some extent, the more complete pathways explaining why physical activity and cognition seem to change together more likely include multiple mediators and complex micromediational chains [41], that also may vary in strength and validity across individuals and groups. Nevertheless, increasing knowledge about what precise mechanisms are active ingredients in the effects of physical activity on cognition constitutes a vital step towards the development of appropriate physical activity intervention designs to test these specific models of mediation and the effects of physical activity and exercise on cognition in experimentally controlled trials.

The major strength of the present study is the ability to elucidate consistent patterns of complex associations across time through coordinated analyses of data from four longitudinal studies. Contrary to previous research based on analyses of single samples, which are limited by the specific characteristics of the sample and data, we instead used a coordinated and integrated analytical approach and framework [25, 26] to examine the same research question in data from four longitudinal studies, thereby making the conclusions less vulnerable to study specific characteristics. As such, the present study is unique (in particular considering the choice of analytical approach) and may pave the way for similar collaborative projects where the same research question and analytical approaches are used to answer relevant questions simultaneously across different studies linked to the association of lifestyle, physical activity, and cognitive functioning.

The four studies included afford considerable heterogeneity in terms of age (ranging from mean age of 67 in SLS to 83 in OCTO-Twin), number of available waves of measurement (four in SLS and LBLS to seven in VLS), years of followup (8 years in OCTO-Twin to 21 years in SLS), years between measurements (every 2 years in OCTO-Twin to every 7 year in SLS), and cultural background (Scandinavia to North-America). Yet, as discussed above, a surprisingly clear pattern emerged across studies in the relation of change in activity to fluctuations in cognition. Thus, in terms of capacity to identify patterns of associations from a larger and broader perspective and to be able to generalize results and conclusions, the present study brings reproduced evidence to the field as well as to practitioners working with health related behavior, lifestyle, and cognition in elderly. Based on the results in the present study, the main message is that change in activity, and not only previous or current level of activity, seems to matter and may play a significant role in the pursuit of maintaining benign nondecreasing trajectories of cognition along the path of cognitive aging.

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*Research Article*

# Cognitively Stimulating Activities: Effects on Cognition across Four Studies with up to 21 Years of Longitudinal Data

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Engagement in cognitively stimulating activities has been considered to maintain or strengthen cognitive skills, thereby minimizing age-related cognitive decline. While the idea that there may be a modifiable behavior that could lower risk for cognitive decline is appealing and potentially empowering for older adults, research findings have not consistently supported the beneficial effects of engaging in cognitively stimulating tasks. Using observational studies of naturalistic cognitive activities, we report a series of mixed effects models that include baseline and change in cognitive activity predicting cognitive outcomes over up to 21 years in four longitudinal studies of aging. Consistent evidence was found for cross-sectional relationships between level of cognitive activity and cognitive test performance. Baseline activity at an earlier age did not, however, predict rate of decline later in life, thus not supporting the concept that engaging in cognitive activity at an earlier point in time increases one's ability to mitigate future age-related cognitive decline. In contrast, change in activity was associated with relative change in cognitive performance. Results therefore suggest that change in cognitive activity from one's previous level has at least a transitory association with cognitive performance measured at the same point in time.

## 1. Introduction

With the rising proportion of older adults and increases in life expectancy [1], there has been increased interest in maintaining and promoting cognitive health in later life. Although declines in some domains of cognition are part of the natural course of aging [2, 3], sufficient evidence from prospective and observational studies indicates that the trajectories and outcomes of cognitive decline may be mitigated by participating in cognitively stimulating activities [4, 5]. Recent reviews of cognitive interventions suggest some potential benefits that may improve functioning in healthy older adults or slow decline in individuals with mild cognitive impairment (MCI) and those already affected with dementia [6–9]. Results from a meta-analysis of randomized controlled trials in healthy aging revealed a strong positive effect on cognition at immediate, medium-, and long-term followup after cognitive training [10]. Compelling results from large longitudinal studies have also shown that engagement in everyday cognitive activities predicts preserved cognition [11, 12] and decreases in incident Alzheimer's disease [13]. It is therefore not surprising that the market for "brain fitness" technologies, currently valued at $300 million, is projected to swell exponentially within this decade [14].

A facet of this research that is relatively understudied involves examining the degree to which discrete types of everyday cognitive activity relate to change in specific cognitive domains over time. Most of the aforementioned trials incorporated training in multiple cognitive abilities and accordingly found support for cognitive training in general, but some reviews report less promising results for domain-specific training. Memory is frequently the targeted cognitive domain in many interventions, with training involving efforts to improve recall of newly learned information, including skills training, imagery, and mnemonic strategy use; however, meta-analyses reveal minimal efficacy for memory-focused techniques [15]. Investigations of the effectiveness of training in other cognitive abilities such as executive functions [16] and working memory [17] suggest that these have farther-reaching effects on cognitive function, but results are regarded as preliminary. Formal interventions employing cognitive skills training are rarely conducted outside of clinical trials, leaving observational studies as a valuable resource for evaluating potential benefits of everyday cognitive activities. Observational studies typically include self-report inventories of activities commonly regarded as cognitively stimulating, such as solving puzzles, listening to the radio, or reading books. While such studies are not experimental by design, they contribute a significant addition to the literature by assessing changes in accessible, everyday cognitive activities as these relate to change in cognitive abilities in a naturalistic setting.

Despite the promising body of work that has accumulated in recent years, definitive conclusions regarding the benefits of cognitive activity are precluded by several methodological concerns [11, 18]. Limitations include the inadequacy of activity assessments, psychometric variability of cognitive outcome measures, conceptual differences in the expected relationships between activities and specific cognitive domains, and insufficient assessment of moderating variables such as level of education and sex. While a study in which all these limitations are fully addressed has yet to be conducted, existing data from several longitudinal studies can be leveraged to disentangle some of these effects. In this paper, we intend to demonstrate that a coordinated analysis of four large longitudinal studies of aging can elucidate the benefits of changes in cognitive activity over time to performance trajectories in specific cognitive domains.

Thus, the purpose of this study was to examine the effects of self-reported everyday cognitive activities and changes in these activities on changes in four domains of cognition (reasoning, fluency, memory, and semantic knowledge) in longitudinal models that incorporate data from the Origins of Variance in the Oldest-Old: Octogenarian Twins Study (Octo-Twin), the Long Beach Longitudinal Study (LBLS), the Seattle Longitudinal Study (SLS), and the Victoria Longitudinal Study (VLS). This investigation was part of a larger coordinated effort to examine the effects of lifestyle activities on cognitive function across multiple large-scale longitudinal studies of aging that formed the basis of a meeting of the Advanced Psychometrics Methods in Cognitive Aging Workshop. The aim of this workshop was to use a common analytic protocol across studies from the Integrative Analysis of Longitudinal Studies on Aging (IALSA [19]) network.

These studies were specifically selected based on their collection of cognitive, physical, and social activity data along with a range of cognitive functioning measures over multiple occasions. While the cognitive activity and cognitive function variables are not always identical, the subsets of variables in each study were chosen based on the rationale that they tapped similar domains at the construct level; specifically, we chose measures thought to tap fluid reasoning (Gf, i.e., verbal reasoning, block design, and verbal fluency measures), short-term memory (Gsm, i.e., immediate recall of a verbally presented story or word list), and crystallized knowledge (Gc, i.e., measures of vocabulary and acquired knowledge [20]). In some cases the measures are the same, but more often they differ, precluding statistical combination of indicators and outcomes between studies. However, we argue that concurrently analyzing the data with the same method provides opportunities for both strict and conceptual replication within the same study—an approach that to our knowledge has not been attempted previously. Thus, our goal was to build and implement a common model to each dataset to enable comparisons across all outcomes for the four longitudinal studies. The two primary hypotheses we tested were whether (1) cognitive activity at baseline would predict the trajectory of cognitive function over time and (2) change in cognitive activity would predict change in cognitive function over time.

## 2. Method

*2.1. Multistudy Analysis Overview.* We report a series of mixed effects models that included baseline and change in cognitive activity predicting cognitive function over up to 21 years of time in four large-scale longitudinal studies of older adults. Three of the four studies included in this analysis (LBLS, SLS, and VLS) specifically aimed to study healthy aging and only recruited community-dwelling older adults who were presumed to be cognitively normal at baseline. The fourth study, Octo-Twin, also included a largely cognitively normal sample of older adults, but those who did have dementia diagnoses at baseline ($n$ = 98) were excluded from the present analysis. In order to model roughly equivalent cognitive outcomes across the four study samples in this coordinated effort, analyses included selected measures of reasoning, fluency, episodic memory, and semantic knowledge from the larger battery of tests included within each longitudinal study sample. In the Octo-Twin study, there was no fluency measure available, and we thus present only three of the four cognitive outcomes. These cognitive tasks were selected to represent a range of cognitive abilities from basic to more complex functions. Study sample characteristics and demographic, cognitive function, and cognitive activity measures are described below (Tables 1–4).

*2.2. Origins of Variance in the Oldest-Old (Octo-Twin) Sample (Sweden).* The Octo-Twin study is based on the oldest cohort of the Swedish Twin Registry and includes 702 participants aged 80 years and older at the time of the first examination. All individuals with a dementia diagnosis at baseline were excluded from the analyses ($n$ = 98). The total sample included 604 participants, of whom 572 had cognitive measures. The longitudinal design for survivors included a maximum of five measurement times at two-year intervals beginning in 1991–1993. The average rate of attrition from one test interval to the next was 20% (10% per year), primarily due to death. Table 1 provides a summary of participant characteristics for the Octo-Twin participants included in this study.

### *2.3. Octo-Twin Materials and Procedure*

*2.3.1. Octo-Twin Cognitive Ability Measures. Reasoning* was assessed using block design [21], in which participants are presented with red and white blocks and instructed to assemble the blocks to reproduce a design portrayed on a card within a predetermined time limit. As previously mentioned, the Octo-Twin study did not have a measure of fluency so this cognitive domain was not analyzed and compared with fluency results from the three other longitudinal studies. *Memory* was assessed using the Prose Recall test in which participants were asked for immediate free recall of a brief (100 word) story that had a humorous point [22]. Responses were coded for the amount of information recalled in a manner similar to the scoring of story units in the Wechsler Memory Scale Logical Memory test [23]. *Semantic knowledge* was assessed using the Swedish version of the WAIS Information Task [24], which requires participants to provide answers to questions assessing acquired knowledge of facts [25].

*2.3.2. Octo-Twin Cognitive Activity Measure.* The cognitive activity measure was based on self-report of engagement in six cognitively stimulating activities including playing games (e.g., chess and bridge), completing crossword puzzles, reading literature, writing, conducting genealogical research, or any other documentation, studies, or other mentally demanding activity (e.g., handicraft), each rated dichotomously as "no" (0) or "yes" (1). Participants were also asked if they "train their memory or keep their mind active" rated as "no" (0), "yes, to a certain degree" (1), or "yes, definitely" (2). A composite score for cognitive activity was created by summing responses across items (range = 0–8). Change in cognitive activity was computed by subtracting the cognitive activity score at baseline from all subsequent activity scores.

*2.4. Long Beach Longitudinal Study Sample (California, USA).* The LBLS was started in 1978 in Long Beach, California, with participants recruited from the Family Health Plan Health Maintenance Organization (HMO) who were primarily from Long Beach and Orange Counties. Panel 1 included 583 individuals aged 28–36 or 55–87. The ethnic composition of the older group (98% Caucasian) was similar to the 65+ population for the area based on the 1970 census. Panel 2, initiated in 1992, included 633 contacted from the same HMO (64 were excluded due to frank dementia, serious sensory, or neurological problems). In order to include the same measures as those in the Seattle Longitudinal Study, LBLS Panel 1 ($n$ = 106) and Panel 2 ($n$ = 631) data from 1994 to 2003 were used in the current analysis. During this period, data were collected at 3-year intervals. Only visits occurring at age of 55 or older were included in this study (baseline $n$ = 561). Dementia incidence is not known.

Demographic information and descriptive statistics for the sample are presented in Table 2. The table displays the number of participants at each test occasion that completed the four cognitive measures and the retention rates for those measures from one testing to the next (top line). Collapsed across measures and testing, the average retention rate from one testing to the next was 55.8% or 17% per year. Age and education increased from the first to the fourth test occasions, suggesting that the sample became more selective over time. Similar patterns of selection were observed for the cognitive measures of reasoning, memory, fluency, and semantic knowledge.

### *2.5. LBLS Materials and Procedure*

*2.5.1. LBLS Cognitive Ability Measures. Reasoning* was indexed as a composite score of the Schaie-Thurstone Adult Mental Abilities Test (STAMAT [26]) Letter and Word Series tests. In Letter Series, participants viewed a series of letters (e.g., a b c c b a d e f f) and were asked to discover the rule that governs the series by identifying the letter from an array of four possible responses that should come next in the series. Participants were to complete as many of the 30 items as possible within six minutes. Word Series was a parallel test to Letter Series but the letters were replaced

Table 1: Octo-Twin participant characteristics.

| Measure | Year of testing Baseline ($n$ = 572) | Year 2 ($n$ = 470) | Year 4 ($n$ = 361) | Year 6 ($n$ = 274) | Year 8 ($n$ = 194) |
|---|---|---|---|---|---|
| Retention from previous testing (%) | | 82.2 | 76.8 | 75.9 | 70.8 |
| Age [M (SD)] | 83.3 (3.0) | 85.2 (2.8) | 86.9 (2.5) | 88.8 (2.5) | 90.7 (2.4) |
| Education [M (SD)] | 7.2 (2.4) | 7.3 (2.4) | 7.3 (2.3) | 7.2 (2.1) | 7.2 (2.3) |
| Sex, female [$n$ (%)] | 369 (65) | 304 (65) | 235 (65) | 195 (71) | 144 (74) |
| Reasoning [M (SD)] | 11.5 (7.1) | 11.4 (7.2) | 11.4 (7.1) | 10.8 (7.2) | 10.3 (7.3) |
| Memory [M (SD)] | 9.6 (4.0) | 9.4 (4.2) | 9.2 (4.4) | 9.2 (4.7) | 9.0 (4.4) |
| Semantic knowledge [M (SD)] | 28.1 (11.1) | 28.6 (11.2) | 27.5 (12.4) | 26.7 (13.0) | 26.2 (11.4) |
| Cognitive activity [M (SD)] | 2.1 (1.7) | 1.7 (1.6) | 1.3 (1.4) | 1.2 (1.4) | 1.1 (1.3) |
| Activity change [M (SD)] | — | −0.3 (1.3) | −0.6 (1.3) | −0.8 (1.5) | −1.1 (1.6) |

M: mean; SD: standard deviation. The theoretical ranges for each measure with a defined upper limit are as follows: reasoning = 0–42, Memory = 0–16, semantic knowledge = 0–44, and cognitive activity = 0–8.

Table 2: LBLS participant characteristics.

| Measure | Year of testing Baseline ($n$ = 561) | Year 3 ($n$ = 292) | Year 6 ($n$ = 144) | Year 9 ($n$ = 101) |
|---|---|---|---|---|
| Retention from previous testing (%) | | 52.0 | 49.3 | 70.1 |
| Age [M (SD)] | 73.7 (9.2) | 75.4 (8.7) | 75.1 (8.0) | 76.1 (7.1) |
| Education [M (SD)] | 13.7 (3.0) | 13.9 (2.8) | 14.2 (2.7) | 14.2 (2.7) |
| Sex, female [$n$ (%)] | 285 (51) | 146 (50) | 70 (49) | 51 (51) |
| Reasoning [M (SD)] | 22.3 (11.7) | 23.9 (11.5) | 25.4 (11.6) | 25.2 (11.1) |
| Fluency [M (SD)] | 32.4 (11.6) | 33.7 (11.1) | 33.3 (13.3) | 34.4 (11.7) |
| Memory [M (SD)] | 11.4 (4.0) | 11.6 (4.3) | 11.6 (4.5) | 11.2 (4.6) |
| Semantic knowledge [M (SD)] | 38.5 (10.3) | 39.5 (9.6) | 40.7 (9.0) | 39.7 (9.8) |
| Cognitive activity [M (SD)] | 2.5 (1.3) | 2.8 (1.4) | 2.7 (1.3) | 2.6 (1.3) |
| Activity change [M (SD)] | — | 0.2 (1.3) | 0.2 (1.4) | −0.2 (1.3) |

M: mean; SD: standard deviation. The theoretical ranges for each measure with a defined upper limit are as follows: education = 0–20, reasoning = 0–30, memory = 0–20, semantic knowledge = 0–36, and cognitive activity = 0–6.

Table 3: SLS participant characteristics.

| Measure | Year of testing Baseline ($n$ = 1649) | Year 7 ($n$ = 939) | Year 14 ($n$ = 445) | Year 21 ($n$ = 178) |
|---|---|---|---|---|
| Retention from previous testing (%) | | 56.4 | 47.7 | 40.8 |
| Age [M (SD)] | 67.1 (8.2) | 72.9 (7.3) | 77.9 (6.4) | 81.8 (4.9) |
| Education [M (SD)] | 14.6 (2.9) | 14.7 (2.8) | 14.8 (2.7) | 14.8 (2.8) |
| Sex, female [$n$ (%)] | 859 (52) | 502 (54) | 255 (57) | 108 (60) |
| Reasoning [M (SD)] | 15.6 (5.8) | 15.2 (5.6) | 14.3 (5.5) | 14.0 (5.3) |
| Fluency [M (SD)] | 38.6 (12.8) | 37.5 (13.1) | 36.7 (12.7) | 38.8 (14.5) |
| Memory [M (SD)] | 12.5 (4.0) | 12.0 (4.1) | 11.5 (4.2) | 11.6 (4.0) |
| Semantic knowledge [M (SD)] | 25.0 (6.7) | 25.3 (6.6) | 25.8 (6.2) | 25.8 (5.9) |
| Cognitive activity [M (SD)] | 2.4 (1.2) | 2.5 (1.2) | 2.5 (1.2) | 2.3 (1.2) |
| Activity change [M (SD)] | — | −0.1 (1.1) | −0.2 (1.1) | −0.5 (1.3) |

M: mean; SD: standard deviation. The theoretical ranges for each measure with a defined upper limit are as follows: education = 0–20, reasoning = 0–30, memory = 0–20, semantic knowledge = 0–36, and cognitive activity = 0–5.

Table 4: VLS participant characteristics.

| Measure | Year of testing | | | | | | |
|---|---|---|---|---|---|---|---|
| | Baseline ($n$ = 1011) | Year 3 ($n$ = 733) | Year 6 ($n$ = 579) | Year 9 ($n$ = 417) | Year 12 ($n$ = 286) | Year 15 ($n$ = 91) | Year 18 ($n$ = 52) |
| Retention from previous testing (%)[a] | — | 73 | 79 | 72 | 69 | 72 | 57 |
| Age [M (SD)] | 68.8 (6.8) | 71.4 (6.7) | 73.7 (6.5) | 76.6 (6.0) | 79.3 (5.2) | 82.2 (4.6) | 85.1 (3.6) |
| Years of education at baseline [M (SD)] | 14.9 (3.3) | 15.4 (3.2) | 15.7 (3.1) | 15.8 (3.1) | 15.8 (3.1) | 15.2 (3.1) | 14.8 (2.8) |
| Sex, female [$n$ (%)] | 642 (63.5) | 459 (62.6) | 353 (61.0) | 256 (61.4) | 177 (61.9) | 60 (65.9) | 35 (67.3) |
| Reasoning [M (SD)][b] | 11.1 (4.6) | 11.6 (4.2) | 10.3 (4.7) | 10.3 (4.6) | 9.9 (4.6) | 7.5 (4.7) | 6.5 (4.2) |
| Fluency [M (SD)] | 17.5 (4.4) | 17.9 (4.4) | 17.7 (4.4) | 17.2 (4.8) | 16.3 (4.9) | 14.7 (5.8) | 13.8 (5.4) |
| Memory [M (SD)][c] | 13.7 (5.9) | 14.6 (6.0) | 14.7 (6.1) | 14.8 (6.4) | 11.8 (5.5) | 13.0 (6.3) | — |
| Semantic knowledge [M (SD)] | 43.6 (7.5) | 44.6 (6.3) | 44.3 (6.0) | 44.2 (5.9) | 43.6 (5.7) | 42.7 (7.1) | 42.6 (6.6) |
| Cognitive activity [M (SD)] | | | | | | | |
| Communication | 0.1 (0.8) | 0.1 (0.8) | 0.0 (0.8) | −0.1 (0.8) | −0.2 (0.8) | −0.4 (0.8) | −0.4 (0.7) |
| Computation | 0.1 (0.8) | 0.0 (0.8) | 0.0 (0.8) | 0.0 (0.8) | −0.1 (0.8) | −0.3 (0.7) | −0.5 (0.7) |
| Conundrums | 0.0 (0.8) | 0.0 (0.8) | 0.0 (0.8) | 0.0 (0.8) | 0.0 (0.8) | −0.2 (0.9) | −0.2 (0.8) |
| Activity change [M (SD)] | | | | | | | |
| Communication | — | 0.0 (0.5) | −0.2 (0.6) | −0.3 (0.6) | −0.4 (0.6) | −0.5 (0.6) | −0.6 (0.5) |
| Computation | — | −0.1 (0.6) | −0.2 (0.6) | −0.3 (0.6) | −0.4 (0.7) | −0.4 (0.7) | −0.5 (0.8) |
| Conundrums | — | 0.0 (0.6) | −0.1 (0.6) | −0.1 (0.7) | −0.2 (0.6) | −0.3 (0.8) | −0.4 (0.7) |

M: mean; SD: standard deviation. The theoretical ranges for each measure with a defined upper limit are as follows: reasoning 0–20, memory 0–30, and semantic knowledge 0–54. The cognitive activity scores are on a normal metric with means of approximately 0 and SD of approximately 0.8.
[a]The 1986 cohort was followed for up to 18 years and the 1993 cohort for up to 12.
[b]The reasoning measure was not given until year 6 for the 1986 cohort.
[c]The memory measure was not given in year 18.

with months (e.g., January) and days of the week (e.g., Monday). *Fluency* was measured using Word Fluency, in which participants were instructed to write down as many words as possible in five minutes that begin with a specified letter "s." Participants were instructed that they could not use proper nouns or create words by changing endings of other listed words (e.g., if the letter was "w" and you already said "want," you should not also say "wants," "wanting," or "wanted"). *Memory* was measured using immediate written recall of a list of 20 concrete high-frequency nouns studied for 3.5 minutes. *Semantic knowledge* was assessed using the STAMAT Recognition Vocabulary test. Participants were given a word and asked to circle a synonym of that word from four possible alternatives. The test included 50 items completed within a 5 minute time limit.

*2.5.2. LBLS Cognitive Activity Measure.* The cognitive activity measure was derived from a modified version of the Life Complexity Scale (LCS), originally developed for the Seattle Longitudinal Study [27]. The modified scale consisted of six items from the LCS: educational activities, leisure reading, playing musical instruments, writing letters, playing games, and cultural activities. Participants were asked to record the number of "hours per week on average" they spent doing each activity. Due to extreme variability in reported hours observed within and between items, responses were dichotomized for the present analysis with those who reported no time spent on a given activity coded as 0 and those who reported one or more hours of activity coded as 1. Items were summed to create a composite measure of cognitive activity (range = 0–6). Change in cognitive activity was computed by subtracting the cognitive activity score at baseline from all subsequent activity scores.

*2.6. Seattle Longitudinal Study Sample (Washington, USA).* The SLS was initiated in 1956 in Seattle, Washington, and includes eight samples recruited from a local HMO at seven-year intervals and followed longitudinally every seven years (total $n$ across all study samples = 4,854). The current analysis includes data from participants in the study from 1984 to 2005 (total $n$ across 1984–2005 study samples = 2,040) and includes longitudinal data for up to four testing occasions. This subset of the larger study was selected due to changes in measures used over the course of the entire study in order to have equivalent measures of cognition and activity at each time point and with the LBLS. Only visits occurring at age 55 or older were included in our analyses, yielding a total of 1,649 participants at baseline. Baseline was defined as each participant's first study visit, and time was measured in all analyses as years in study (coded as 0, 7, 14, and 21). Attrition during these 7-year intervals was approximately 50%, or about 7% per year. Dementia prevalence and incidence are not known. See Table 3 for SLS participant characteristics over the four waves of data analyzed here.

*2.7. SLS Materials and Procedure*

*2.7.1. SLS Cognitive Measures.* *Reasoning* was assessed with the Word Series test from the Schaie-Thurstone Adult Mental

Abilities Test (STAMAT [26]), in which participants were provided with a printed word series and instructed to choose the next word in the series in multiple-choice format by identifying the rule that governed a series. The test consisted of 30 items, and total score was based on number of correct responses completed in 6 minutes. *Fluency* was assessed with the Word Fluency test from the Primary Mental Abilities test [28], in which participants were asked to write down words beginning with the letter "s" following a rule set (do not use proper nouns and do not use different conjugations of the same word). Total score was based on number of correct responses generated in 5 minutes. *Memory* was assessed with a task in which participants were asked to study a list of 20 printed words for 3.5 minutes and provide immediate written recall of the items. *Semantic knowledge* was assessed with the Educational Testing Service (ETS) test of Advanced Vocabulary, in which participants were asked to identify synonyms for printed words from 5 choices [29]. Total score was based on number of correctly identified synonyms out of 36 test items completed within 4 minutes.

*2.7.2. SLS Cognitive Activity Measure.* The cognitive activity measure was derived by summing dichotomized test responses to five cognitive activity items (reading, educational activities, music, writing, and cultural activities) from a modified version of the Life Complexity Scale [27]. Cognitive activity change was computed by subtracting baseline activity from each follow-up activity measure.

*2.8. Victoria Longitudinal Study Sample (British Columbia, Canada).* The VLS was begun in the 1986 in Victoria, British Columbia, and consists of three cohorts started in 1986, 1992, and 2001, respectively, followed longitudinally at 3-year intervals. Longitudinal data used in this study were from Samples 1 (baseline $n = 484$) and 2 (baseline $n = 530$). For this investigation, data from seven waves of Sample 1 and five waves of Sample 2 were included in analyses. Approximately 25% of the sample was lost to follow up at each wave or 8% per year. Dementia prevalence and incidence are not known. Relevant demographic information regarding the study sample is provided in Table 4.

### *2.9. VLS Materials and Procedure*

*2.9.1. VLS Cognitive Ability Measures. Reasoning* was indexed by Letter Series [30] in which participants were presented with a series of letters and asked to identify the next letter in the sequence that was consistent with the sequence rule. *Fluency* was measured by performance on a similarities task [30]. In this timed task, participants were presented with target words and asked to write as many words as possible with the same or nearly the same meaning within 6 minutes. *Memory* was indexed using a 30-item noun list learning task comprised of five semantic categories. Participants studied the word list for 2 minutes followed by a 5-minute free recall task [30]. *Semantic knowledge* was assessed using a 54-item recognition vocabulary test. This task was adapted from the ETS Kit of Factor Referenced Tests [29].

*2.9.2. VLS Cognitive Activity Measure.* The cognitive activity measure included a subset of items from the VLS Activity Lifestyle Questionnaire [3]. The 27 items comprising the Novel Information Processing scale were selected due to the cognitively stimulating nature of the activities. For each item, participants indicated the frequency of engagement in that activity over the past two years on a scale from 0 to 9 (i.e., *never, less than once a year, about once a year, 2 or 3 times a year, about once a month, 2 or 3 times a month, about once a week, 2 or 3 times a week,* and *daily)*. Individual item distributions were reviewed, and 11 of the 27 original items with little to no variability were eliminated. The remaining items were a priori hypothesized to fall into three general types of activities: those involving what we termed "Communication," "Computations," or "Conundrums." Confirmatory factor analysis using Mplus version 6.0 [31] was conducted to test a three-factor model including six items indexing Communication (enrolling in college courses, giving a talk, attending lectures, studying a second language, writing, and writing letters specifically), five items indexing Computation (balancing a check book, performing mathematical calculations, working on taxes, engaging in business activity, and using a calculator), and five items indexing Conundrums (engaging in crosswords, chess/checkers, knowledge games, word games/scrabble, and jigsaw puzzles). Fit criteria were the comparative fit index (CFI) and the root mean squared error of approximation (RMSEA), where criteria for excellent fit include CFI > 0.95 and RMSEA < 0.05 [32]. Allowing for within-factor residual correlations, the model demonstrated acceptable fit (CFI = 0.95, RMSEA = 0.04). The factor scores generated by this analysis were then used as the primary predictor variables in three separate mixed effects models.

*2.10. General Analytic Approach.* The current analysis was conducted as part of a larger effort to examine the effects of lifestyle activities on cognitive function using the same analytic approach across studies from the Integrative Analysis of Longitudinal Studies on Aging (IALSA) network [19], and models were selected in part to maintain consistency across lifestyle activities. Across all four studies, we examined common demographic covariates including age (in years), years of formal education, and sex (coded as 0 = male, 1 = female). Age and education were mean centered to their respective study's baseline mean value. In order to maximize use of all available data, we defined baseline as the first study visit for each participant with available cognitive activity data. We analyzed the data with mixed effects modeling using Stata software, version 12 (StataCorp, 2011) and restricted maximum likelihood (REML) estimation, random slopes and intercepts, and an unstructured covariance matrix. In the Octo-Twin study, participants were nested within their twin pair. In the VLS, we controlled for enrolment cohort. Model assumptions were verified by examining residuals computed using predicted values that included the random effects. Separate models were fit for each of the four cognitive measures. We defined the criterion for significance as $P < 0.05$. While we recognize that this criterion may be viewed as liberal, given the large number of comparisons across all statistical models in our analysis, we assert that this approach is warranted in this study as we are representing results from four independent longitudinal studies following similar statistical procedures for each. Thus, the emphasis in this paper is replication of the pattern of results across the studies. In this way, the "strictness" of the evaluation of the effects comes from noting whether a particular effect is replicated across the different samples. The "familywise" alpha rate is that which occurs within each study, not across all of them together.

## 3. Results

An initial 19-term model included the following terms: (1) baseline age, (2) sex, (3) education, (4) baseline activity, (5) baseline activity × age, (6) baseline activity × sex, (7) baseline activity × education, (8) individually defined time since baseline, (9) time × baseline age, (10) time × sex, (11) time × education, (12) time × baseline activity, (13) time × baseline activity × baseline age, (14) time × baseline activity × sex, (15) time × baseline activity × education, (16) change in activity from baseline (activity change), (17) activity change × baseline age, (18) activity change × sex, and (19) activity change × education. This full model was evaluated in each study data set independently, and terms that were not significant in any of the four studies were dropped in order to present a parsimonious set of results that retained the fullest set of parameters found in any study. This process eliminated 7 of the 19 terms, including all 3-way interactions, and four of the 2-way interactions, including the interactions between activity change and age, sex, or education, as well as the interaction between baseline activity level and sex. This resulted in a final model that included 12 terms summarized in Table 5. As a proper meta-analytic summary would require identical measures across a larger number of studies, we rely on straightforward comparison of the conclusions derived from each study.

*3.1. Baseline Covariates and Cross-Sectional Relationships.* There was a significant relationship between self-reported cognitive activity at baseline and baseline performance on tests of cognitive abilities across all measures and studies but the LBLS, which did not find this relationship in the reasoning and memory models. Overall, these findings suggest that participants who were more cognitively active at baseline tended to have better cognitive performance. One of the studies (VLS) included three distinct measures of cognitive activity—those involving Communication (e.g., writing), Computations (e.g., managing finances), and Conundrums (e.g., completing crossword puzzles)—enabling us to determine if specific cognitive activities were differentially related to the cognitive outcomes. While all three types of cognitive activities showed significant cross-sectional relationships with cognitive outcomes (all $P < 0.001$), the strongest relationships with cognitive function were found for Conundrums, followed by Computation and Communication.

Older age was associated with lower baseline performance across all studies on measures of reasoning, fluency, and memory. In contrast, the relationship between age and baseline performance on semantic knowledge measures was inconsistent, with LBLS and Octo-Twin results suggesting lower performance in older age, SLS showing no age differences, and VLS suggesting that older age was associated with better performance. Baseline associations between sex and cognitive performance showed a consistent relationship across studies for all memory outcomes, with women consistently performing higher than similar aged men. SLS and LBLS women additionally performed higher than men on reasoning and fluency measures. Across other cognitive outcomes, baseline associations between performance and sex were less consistent, with VLS women performing better on fluency in the Computations model and Octo-Twin women performing lower than men on semantic knowledge. Higher education was consistently associated with higher baseline cognitive performance across all studies and cognitive outcomes.

Two baseline covariate interaction terms were retained in the final model, and both showed inconsistent relationships across studies and outcome measures: the age by baseline cognitive activity interaction term was significant in the VLS memory models and the Conundrums/semantic knowledge model. There was a similarly significant interaction between baseline age and activity level in the LBLS reasoning model ($P < 0.05$). The education by baseline cognitive activity interaction term in the VLS Communication models for reasoning, fluency, and semantic knowledge was significant, suggesting that those with lower education had a higher association between baseline activity and cognitive test performance. The VLS Computation and Octo-Twin models for semantic knowledge also showed this relationship.

*3.2. Longitudinal Relationships.* Across all studies and cognitive outcomes, there was, with one exception (VLS computation with reasoning), no evidence for baseline level of cognitive activity predicting change in cognitive outcomes over time. There was, however, a consistent positive relationship between change in cognitive activity from baseline and within person variability in cognitive outcomes across nearly all cognitive outcomes in all four studies. Specifically, after accounting for the expected linear within person trajectories, variation in cognitive activity was significantly related to variation in performance on all measures in all studies except reasoning and fluency in LBLS and reasoning and memory, in the case of Conundrums only, in VLS.

Within-person declines were seen over time across all studies and all cognitive outcomes except LBLS fluency. Older participants declined faster compared to younger participants on all VLS, SLS, and LBLS cognitive outcome measures except LBLS memory. Evidence for differential decline in older participants was not seen in Octo-Twin, which has a much narrower age range. Women declined less than men on fluency measures in the SLS and VLS Computations models and on semantic knowledge measures in the SLS and Octo-Twin study. Level of education was

Table 5: Mixed effects model summaries across four studies with baseline cognitive activity and activity change predicting four cognitive outcomes.

| Reasoning | Octo-Twin | | | LBLS | | | SLS | | | VLS Communication | | | VLS Computation | | | VLS Conundrums | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* |
| Intercept | 11.17 | 0.64 | <0.001 | 20.98 | 0.58 | <0.001 | 14.83 | 0.18 | <0.001 | 9.60 | 0.58 | <0.001 | 9.06 | 0.56 | <0.001 | 9.64 | 0.57 | <0.001 |
| Age | −0.32 | 0.10 | 0.002 | −0.60 | 0.05 | <0.001 | −0.35 | 0.01 | <0.001 | −0.25 | 0.02 | <0.001 | −0.22 | 0.02 | <0.001 | −0.24 | 0.02 | <0.001 |
| Sex | 0.10 | 0.59 | 0.862 | 2.58 | 0.82 | 0.002 | 1.40 | 0.24 | <0.001 | −0.12 | 0.31 | 0.700 | 0.42 | 0.31 | 0.170 | −0.19 | −0.19 | 0.300 |
| Education | 0.39 | 0.14 | 0.015 | 1.24 | 0.15 | <0.001 | 0.48 | 0.05 | <0.001 | 0.29 | 0.05 | <0.001 | 0.25 | 0.05 | <0.001 | 0.32 | 0.05 | <0.001 |
| Activity | 1.46 | 0.18 | <0.001 | 0.02 | 0.33 | 0.956 | 0.34 | 0.11 | 0.001 | 0.45 | 0.20 | 0.024 | 1.24 | 0.19 | <0.001 | 0.94 | 0.19 | <0.001 |
| Age × activity | 0.05 | 0.06 | 0.389 | 0.09 | 0.04 | 0.020 | 0.01 | 0.01 | 0.286 | 0.00 | 0.02 | 0.876 | 0.04 | 0.02 | 0.078 | 0.02 | 0.02 | 0.447 |
| Education × activity | −0.05 | 0.06 | 0.453 | 0.04 | 0.10 | 0.702 | −0.05 | 0.03 | 0.168 | −0.12 | 0.05 | 0.020 | 0.00 | 0.05 | 0.923 | 0.05 | 0.05 | 0.404 |
| Time | −0.45 | 0.09 | <0.001 | −0.50 | 0.08 | <0.001 | −0.25 | 0.02 | <0.001 | −0.24 | 0.03 | <0.001 | −0.25 | 0.03 | <0.001 | −0.25 | 0.03 | <0.001 |
| Age × time | −0.02 | 0.02 | 0.274 | −0.03 | 0.01 | 0.000 | −0.01 | 0.00 | <0.001 | −0.01 | 0.00 | <0.001 | −0.01 | 0.00 | <0.001 | −0.01 | 0.00 | <0.001 |
| Sex × time | 0.09 | 0.10 | 0.367 | 0.07 | 0.11 | 0.536 | 0.01 | 0.02 | 0.545 | 0.02 | 0.03 | 0.598 | 0.04 | 0.03 | 0.232 | 0.01 | 0.03 | 0.643 |
| Education × time | 0.03 | 0.02 | 0.224 | −0.06 | 0.02 | 0.008 | −0.01 | 0.00 | 0.092 | −0.01 | 0.01 | 0.091 | −0.01 | 0.00 | 0.061 | −0.01 | 0.00 | 0.138 |
| Activity × time | 0.02 | 0.03 | 0.595 | 0.05 | 0.05 | 0.337 | 0.01 | 0.01 | 0.173 | 0.03 | 0.02 | 0.145 | 0.05 | 0.02 | 0.025 | −0.01 | 0.02 | 0.692 |
| Activity change | 0.41 | 0.13 | 0.002 | 0.28 | 0.20 | 0.164 | 0.24 | 0.09 | 0.006 | 0.38 | 0.14 | 0.005 | 0.49 | 0.13 | <0.001 | 0.23 | 0.12 | 0.059 |

| Fluency | — | | | LBLS | | | SLS | | | VLS Communication | | | VLS Computation | | | VLS Conundrums | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* |
| Intercept | | | | 30.94 | 0.66 | <0.001 | 36.46 | 0.46 | <0.001 | 11.68 | 0.53 | <0.001 | 11.28 | 0.55 | <0.001 | 11.73 | 0.53 | <0.001 |
| Age | | | | −0.31 | 0.05 | <0.001 | −0.34 | 0.04 | <0.001 | −0.08 | 0.02 | 0.001 | −0.08 | 0.02 | 0.002 | −0.07 | 0.02 | 0.006 |
| Sex | | | | 3.42 | 0.93 | <0.001 | 2.88 | 0.61 | <0.001 | 0.63 | 0.34 | 0.065 | 1.02 | 0.36 | 0.005 | 0.54 | 0.34 | 0.115 |
| Education | | | | 0.88 | 0.17 | <0.001 | 1.17 | 0.11 | <0.001 | 0.47 | 0.05 | <0.001 | 0.58 | 0.05 | <0.001 | 0.60 | 0.05 | <0.001 |
| Activity | | | | 1.14 | 0.37 | 0.002 | 1.03 | 0.27 | 0.001 | 1.80 | 0.22 | <0.001 | 0.81 | 0.22 | <0.001 | 1.68 | 0.21 | <0.001 |
| Age × activity | | | | 0.07 | 0.04 | 0.121 | 0.00 | 0.03 | 0.900 | 0.01 | 0.03 | 0.709 | 0.04 | 0.03 | 0.112 | 0.04 | 0.03 | 0.094 |
| Education × activity | | | | 0.05 | 0.11 | 0.651 | 0.00 | 0.08 | 0.995 | −0.12 | 0.06 | 0.042 | −0.04 | 0.05 | 0.489 | 0.03 | 0.06 | 0.659 |
| Time | | | | −0.22 | 0.11 | 0.052 | −0.42 | 0.04 | <0.001 | −0.11 | 0.03 | <0.001 | −0.13 | 0.03 | <0.001 | −0.13 | 0.03 | <0.001 |
| Age × time | | | | −0.02 | 0.01 | 0.015 | −0.02 | 0.00 | <0.001 | −0.01 | 0.00 | 0.001 | −0.01 | 0.00 | 0.001 | −0.01 | 0.00 | 0.001 |
| Sex × time | | | | −0.17 | 0.15 | 0.252 | 0.11 | 0.05 | 0.025 | 0.07 | 0.04 | 0.058 | 0.08 | 0.04 | 0.050 | 0.07 | 0.04 | 0.078 |
| Education × time | | | | 0.01 | 0.03 | 0.778 | −0.01 | 0.01 | 0.105 | 0.00 | 0.01 | 0.823 | 0.00 | 0.01 | 0.955 | 0.00 | 0.01 | 0.954 |
| Activity × time | | | | −0.06 | 0.07 | 0.350 | 0.02 | 0.02 | 0.324 | 0.00 | 0.03 | 0.868 | 0.02 | 0.03 | 0.448 | 0.01 | 0.03 | 0.793 |
| Activity change | | | | 0.49 | 0.30 | 0.097 | 0.50 | 0.20 | 0.012 | 0.76 | 0.18 | <0.001 | 0.68 | 0.18 | <0.001 | 0.48 | 0.16 | 0.003 |

| Memory | Octo-Twin | | | LBLS | | | SLS | | | VLS Communication | | | VLS Computation | | | VLS Conundrums | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* |
| Intercept | 8.84 | 0.29 | <0.001 | 10.73 | 0.21 | <0.001 | 11.68 | 0.13 | <0.001 | 17.37 | 0.41 | <0.001 | 17.06 | 0.40 | <0.001 | 17.51 | 0.41 | <0.001 |
| Age | −0.18 | 0.06 | 0.001 | −0.20 | 0.02 | <0.001 | −0.18 | 0.01 | <0.001 | −0.19 | 0.02 | <0.001 | −0.17 | 0.02 | <0.001 | −0.18 | 0.02 | <0.001 |
| Sex | 0.91 | 0.99 | 0.006 | 1.41 | 0.30 | <0.001 | 1.40 | 0.18 | <0.001 | 1.58 | 0.26 | <0.001 | 2.13 | 0.27 | <0.001 | 1.50 | 0.26 | <0.001 |
| Education | 0.35 | 0.07 | <0.001 | 0.25 | 0.05 | <0.001 | 0.26 | 0.03 | <0.001 | 0.23 | 0.04 | <0.001 | 0.25 | 0.04 | <0.001 | 0.30 | 0.04 | <0.001 |
| Activity | 0.59 | 0.10 | <0.001 | 0.17 | 0.12 | 0.142 | 0.41 | 0.08 | <0.001 | 0.96 | 0.17 | <0.001 | 1.17 | 0.16 | <0.001 | 0.85 | 0.16 | <0.001 |
| Age × activity | −0.01 | 0.04 | 0.930 | 0.00 | 0.01 | 0.776 | 0.00 | 0.01 | 0.901 | 0.07 | 0.02 | <0.001 | 0.06 | 0.02 | 0.002 | 0.06 | 0.02 | 0.002 |
| Education × activity | −0.02 | 0.04 | 0.663 | 0.04 | 0.04 | 0.247 | 0.00 | 0.02 | 0.948 | −0.07 | 0.04 | 0.127 | −0.02 | 0.04 | 0.658 | −0.04 | 0.05 | 0.345 |
| Time | −0.27 | 0.07 | <0.001 | −0.17 | 0.05 | 0.001 | −0.17 | 0.01 | <0.001 | −0.26 | 0.03 | <0.001 | −0.26 | 0.03 | <0.001 | −0.28 | 0.03 | <0.001 |
| Age × time | 0.00 | 0.02 | 0.947 | 0.00 | 0.00 | 0.627 | −0.01 | 0.00 | <0.001 | −0.01 | 0.00 | <0.001 | −0.01 | 0.00 | <0.001 | −0.01 | 0.00 | <0.001 |
| Sex × time | 0.06 | 0.08 | 0.465 | −0.03 | 0.07 | 0.705 | 0.03 | 0.02 | 0.112 | −0.01 | 0.03 | 0.783 | −0.01 | 0.03 | 0.736 | −0.01 | 0.03 | 0.660 |
| Education × time | 0.00 | 0.02 | 0.932 | 0.01 | 0.01 | 0.691 | 0.00 | 0.00 | 0.549 | 0.00 | 0.01 | 0.349 | 0.00 | 0.00 | 0.349 | −0.01 | 0.00 | 0.246 |
| Activity × time | 0.03 | 0.02 | 0.231 | 0.04 | 0.03 | 0.216 | 0.00 | 0.01 | 0.827 | 0.01 | 0.02 | 0.708 | 0.00 | 0.02 | 0.923 | 0.03 | 0.02 | 0.164 |
| Activity change | 0.35 | 0.09 | <0.001 | 0.25 | 0.12 | 0.039 | 0.25 | 0.07 | 0.001 | 0.71 | 0.13 | <0.001 | 0.78 | 0.12 | <0.001 | 0.18 | 0.12 | 0.126 |

Table 5: Continued.

| Semantic knowledge | Octo-Twin | | | LBLS | | | SLS | | | VLS | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Communication | | | Computation | | | Conundrums | | |
| | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* |
| Intercept | 31.60 | 0.69 | <0.001 | 37.89 | 0.59 | <0.001 | 24.54 | 0.23 | <0.001 | 44.23 | 0.68 | <0.001 | 43.66 | 0.68 | <0.001 | 44.07 | 0.69 | <0.001 |
| Age | −0.40 | 0.14 | 0.004 | −0.29 | 0.05 | <0.001 | 0.01 | 0.02 | 0.501 | 0.09 | 0.03 | 0.004 | 0.11 | 0.03 | <0.001 | 0.09 | 0.03 | 0.004 |
| Sex | −5.17 | 0.85 | <0.001 | 1.60 | 0.84 | 0.056 | 0.12 | 0.31 | 0.688 | −0.07 | 0.44 | 0.865 | 0.68 | 0.46 | 0.137 | −0.18 | 0.45 | 0.687 |
| Education | 1.60 | 0.20 | <0.001 | 0.95 | 0.15 | <0.001 | 0.99 | 0.06 | <0.001 | 0.58 | 0.07 | <0.001 | 0.65 | 0.07 | <0.001 | 0.72 | 0.07 | <0.001 |
| Activity | 2.21 | 0.25 | <0.001 | 0.75 | 0.34 | 0.026 | 0.81 | 0.14 | <0.001 | 1.97 | 0.28 | <0.001 | 1.77 | 0.28 | <0.001 | 1.37 | 0.27 | <0.001 |
| Age × activity | 0.03 | 0.09 | 0.737 | 0.05 | 0.04 | 0.199 | 0.02 | 0.02 | 0.277 | 0.05 | 0.03 | 0.113 | 0.06 | 0.03 | 0.074 | 0.07 | 0.03 | 0.039 |
| Education × activity | −0.23 | 0.10 | 0.014 | −0.05 | 0.10 | 0.647 | −0.05 | 0.04 | 0.206 | −0.33 | 0.07 | <0.001 | −0.28 | 0.07 | <0.001 | −0.09 | 0.08 | 0.242 |
| Time | −0.92 | 0.12 | <0.001 | −0.40 | 0.09 | <0.001 | −0.11 | 0.01 | <0.001 | | 0.03 | <0.001 | −0.14 | 0.03 | <0.001 | −0.16 | 0.03 | <0.001 |
| Age × time | −0.05 | 0.03 | 0.064 | −0.03 | 0.01 | <0.001 | −0.01 | 0.00 | <0.001 | −0.01 | 0.00 | <0.001 | −0.01 | 0.00 | <0.001 | −0.01 | 0.00 | <0.001 |
| Sex × time | 0.30 | 0.14 | 0.036 | 0.05 | 0.12 | 0.678 | 0.06 | 0.02 | 0.001 | 0.03 | 0.04 | 0.379 | 0.02 | 0.04 | 0.533 | 0.03 | 0.04 | 0.439 |
| Education × time | 0.04 | 0.03 | 0.155 | −0.03 | 0.02 | 0.185 | 0.00 | 0.00 | 0.447 | 0.00 | 0.01 | 0.510 | 0.00 | 0.01 | 0.725 | 0.00 | 0.01 | 0.453 |
| Activity × time | −0.02 | 0.04 | 0.571 | 0.03 | 0.05 | 0.627 | 0.01 | 0.01 | 0.069 | 0.02 | 0.02 | 0.442 | −0.01 | 0.02 | 0.773 | 0.01 | 0.02 | 0.524 |
| Activity change | 0.47 | 0.17 | 0.005 | 0.44 | 0.20 | 0.027 | 0.26 | 0.07 | <0.001 | 0.49 | 0.15 | 0.001 | 0.53 | 0.14 | <0.001 | 0.49 | 0.13 | <0.001 |

Values represent model coefficients and their standard error. Across all studies, time was measured in years since baseline visit, and activity change was entered as a time-varying covariate. All other variables represent baseline measurements alone, in interaction with one another or in interaction with time.

not a significant predictor of rate of cognitive decline in all but one study (LBLS) and one outcome measure (reasoning, coefficient = −0.06, $P < 0.01$).

## 4. Discussion

Our results provide compelling evidence across four longitudinal studies that changes in everyday cognitive activity level tracks with variation in multiple aspects of cognitive function. In three of the four studies (Octo-Twin, SLS, and VLS), participants reported engaging in fewer cognitive activities over time. In the fourth study (LBLS), participants endorsed a slight increase in average number of cognitive activities over time, which was likely due to differential retention of higher functioning individuals. While the overall trend was for participants to report slightly less cognitive activity at each follow-up visit in all but the LBLS sample, there was actually considerable variability in activity change scores, with some participants in each study reporting increased cognitive activity at follow-up visits relative to their baseline levels.

These results suggest that there is an increased risk of cognitive decline for individuals whose engagement in cognitive activities decreases over time relative to their baseline levels, and, conversely, the results suggest that increases in cognitive activity from baseline are associated with better than expected cognitive performance. Cognitive activity change appeared to most consistently track with variation in semantic knowledge, as the activity change term was significant in all six models. Strong evidence of activity change tracking with fluctuations in memory and fluency was also indicated, as five of six models had significant activity change terms in the memory models and in four of the five fluency models. Activity change was significantly related to variation in reasoning in four of the six models, making the models with reasoning outcomes the least consistent relative to models with the other cognitive outcomes. That two of the four inconsistent findings occurred in LBLS, which had the most similarity with SLS, in terms of both measures and sampling, suggests that some other factor, such as attrition, may be responsible for these differences. It is interesting to note, however, that the standard deviation of reported activity level did not differ from that of SLS. The lack of association with reasoning and memory for one of the three VLS activity variables (Conundrums) could be due to chance, although this finding may also suggest that changes in level of engagement on tasks involving problem solving are less related to changes in reasoning and memory function than they are to changes in fluency and semantic knowledge.

Across studies, with the exception of VLS Computation with reasoning, there were no significant relationships between baseline cognitive activity and change in cognition over time, suggesting that level of cognitive activity at an earlier point in time is not related to subsequent cognitive decline. Thus, these results do not demonstrate that level of engagement in cognitively stimulating activities earlier in older adulthood can somehow increase one's cognitive reserve or ability to maintain cognitive function in spite of age-related brain changes [33]. Nonetheless, our results do have important clinical implications in that they suggest that individuals who exhibit changes from a previous level of cognitive activity can be expected to have associated fluctuations in cognitive performance, or vice versa.

In terms of cross-sectional relationships, all studies provide evidence for activity/cognition relationships, and the VLS results allow us to conclude that level of engagement in cognitive activities involving what we termed "Conundrums" (e.g., playing chess, completing crossword puzzles) are most strongly and consistently related to concurrent function across cognitive domains, but evidence for relationships between engagement in activities involving Computations (e.g., balancing a check book) and Communication (e.g., writing letters) was also demonstrated. Thus, while the data do not provide particularly compelling evidence that engagement in one type of cognitively stimulating activity is preferable, activities involving novel information processing appear to be most related to concurrent cognitive function, a finding that is consistent with the extant literature [34].

The lack of evidence for cognitive activity level at baseline predicting cognitive decline over time in some respects may be interpreted as discouraging, as it implies that older adults who more frequently engage in cognitive activities may not be influencing the trajectory of their cognitive function in the coming years. However, across all studies, change in level of cognitive activity from baseline generally followed a normal distribution, with considerable portions of each sample reporting an increase in level of cognitive activity from baseline levels. The positive association between cognitive activity change and the cognitive outcomes across studies thus suggests that individuals who increase their cognitive activities may be effectively reducing age-related cognitive decline.

Our results demonstrate that older age is associated with faster decline, which supports the overall validity of our approach and suggests that we are detecting relevant change. The finding that education was not predictive of rate of cognitive decline with one exception (the LBLS reasoning model) suggests that education is not protective or predictive of a faster decline in normal aging. These multistudy results build upon findings from a recent paper using data from one of the studies (VLS) included in the current paper [35], in which the authors conclude that the relationship between education and cognitive performance is merely a cross-sectional relationship between level of education and cognitive function, and that longitudinal models that covary for baseline cognitive function are in effect creating a statistical artifact that is seen as an effect of education on rate of decline [34]. However, it is important to note that all studies included in the current analysis were designed to characterize normal cognitive aging, and results are not directly comparable to studies examining the effect of education level or cognitive reserve on the incidence and rate of decline in Alzheimer's disease [33].

The current study has many strengths, including the large sample sizes and multinational representation in our study samples, which improves the generalizability of the findings. In addition, the inclusion of four separate studies with unique sample characteristics, methodologies for recruitment, different methods for measuring cognitive activity and cognitive function, and differing frequency and length of followup, all serve to minimize the likelihood that these findings are spurious. When results across such a coordinated analysis are inconsistent, any one of these differences between studies could be responsible for discrepancies and reflect a limitation of the design. For example, the inconsistencies in the relationships between baseline covariates and their interactions (e.g., sex and age with baseline activity level) highlight a weakness of our study design. Inconsistencies could also be attributable to the heterogeneity in the activity measures used across the four longitudinal studies, as the scales included different items with different response ratings, yielding restricted ranges of responses on some measures. It is also possible that the inconsistencies are due to differences in the cognitive outcomes used in the different studies, or any number of other differences in the methodologies across studies. However, it is important to note that when the model results demonstrate consistent patterns across studies despite variations in methodology, the heterogeneity of measures and sampling methods becomes a major strength of the multi-study approach, as there is improvement in the reliability of conclusions that can be drawn from the results, relative to the typical single-study design.

Perhaps the most obvious limitation inherent in the observational design of all studies included in this investigation is that conclusions implying causality cannot be inferred from these results. Specifically, while an increase in cognitive activity from baseline was associated with better than expected cognitive performance, and, conversely, activity decrease was associated with worse than expected performance, it is not possible to conclude that change in activity level was the cause for change in rate of cognitive decline. An alternative explanation is that decreases in level of cognitive activity from baseline levels observed in this study result from deteriorating cognitive functions rather than cause it. Put simply, this study design does not answer whether completing crossword puzzles reduces one's risk of cognitive decline or if cognitive decline reduces the likelihood that one will complete crossword puzzles. In addition, this study does not address the protective effects of cognitive activity for incident dementia or Alzheimer's disease. While there is a large body of the literature examining the beneficial effects of cognitive activity in reducing dementia risk (e.g., [36]), the studies included in the current investigation were based on normal cognitive aging, and individuals with dementia diagnoses were excluded from the present analysis.

What these results impart, however, is that regardless of the causal mechanisms underlying these changes, the associations between cognitive activity and cognitive outcomes in this study are in directions that are intuitively and scientifically consistent with prior literature. This fact, coupled with the large-scale naturalistic, observational design of this study, lends credence to the burgeoning literature that directly examines the causal effect of cognitive activity on cognitive outcomes. Extension of this work in populations at great risk for dementia, or with individuals already diagnosed with neurodegenerative diseases, remains a worthwhile goal.

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*Research Article*

# Association of Social Engagement with Brain Volumes Assessed by Structural MRI

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We tested the hypothesis that social engagement is associated with larger brain volumes in a cohort study of 348 older male former lead manufacturing workers ($n = 305$) and population-based controls ($n = 43$), age 48 to 82. Social engagement was measured using a summary scale derived from confirmatory factor analysis. The volumes of 20 regions of interest (ROIs), including total brain, total gray matter (GM), total white matter (WM), each of the four lobar GM and WM, and 9 smaller structures were derived from T1-weighted structural magnetic resonance images. Linear regression models adjusted for age, education, race/ethnicity, intracranial volume, hypertension, diabetes, and control (versus lead worker) status. Higher social engagement was associated with larger total brain and GM volumes, specifically temporal and occipital GM, but was not associated with WM volumes except for corpus callosum. A voxel-wise analysis supported an association in temporal lobe GM. Using longitudinal data to discern temporal relations, change in ROI volumes over five years showed null associations with current social engagement. Findings are consistent with the hypothesis that social engagement preserves brain tissue, and not consistent with the alternate hypothesis that persons with smaller or shrinking volumes become less socially engaged, though this scenario cannot be ruled out.

## 1. Introduction

Social engagement, the performance of meaningful social roles for either leisure or productive activity, has been shown to be associated with better cognitive function and lowered rates of cognitive decline and dementia in older adults [1–4]. Yet many questions remain regarding how social engagement can potentially get "under the skull" to preserve cognitive abilities. Inconsistencies in measurement across studies is frequent with a number of overlapping constructs such as social activity [1, 5], social networks [6, 7], and social support [8] linked to cognitive outcomes; each has been theorized to affect the brain through separate mechanisms. Yet the neurological mechanisms that could lead to preservation of cognitive function remain unclear and perhaps the largest obstacle is a lack of research to directly explore the biological effects of social engagement on the brain. A popular hypothesis is that social engagement helps to build a brain reserve capacity that allows the brain to tolerate neuropathologic damage due to aging or disease without deterioration of cognitive abilities [9, 10]. In a case of "use it or lose it," remaining socially engaged as one ages may build this brain reserve through neuroplastic changes in the brain such as attenuated neuronal loss, or increased synaptic count [11–13] or the growth of new neurons [14]—all of which could be reflected in an increase or attenuated shrinking of brain volume. In the context of aging, larger brain volumes are associated with better cognitive function [15, 16], and preservation of cognitive function in the face of neuropathology [17]. Demonstrating a link between social engagement and larger brain volumes would provide support for the brain reserve hypothesis and our understanding of the neurological mechanisms at play.

We examined the relationship between social engagement and brain volumes using two complementary methods, a region-of-interest (ROI) analysis to investigate recognized anatomical brain regions, and voxel-based morphometry (VBM) to explore unbiased associations across the entire brain. Utilizing available longitudinal MRI data, we were also able to evaluate whether change in ROI volumes over five years prior to assessment of social engagement was associated with current level of social engagement in order to better discern temporal relations. We hypothesized that more socially engaged persons have larger brain volumes, especially for GM, which was found to evidence larger age-related declines in volume compared to WM in this population [18].

## 2. Methods

*2.1. Study Population and Design.* We used data from a study of lead exposure and cognitive function in former employees of a chemical manufacturing plant in the eastern United States and population-based controls with no history of occupational lead exposure [19]. The controls were selected from the same geographical residential as the former lead workers resided in using random selection from a telephone database and frequency-matched to lead workers for age, education, and race [20]. We used data from the third phase of this study when assessment of social engagement and a second MRI were obtained from study participants; an initial baseline structural MRI was acquired in phase 2, on average 5 years earlier. Detailed methods for study design and recruitment in phases 1 (1994–1997; 703 former lead workers and 130 controls, mean age 56 years) [20, 21] and 2 (2001–2003; 589 of 979 former lead workers and 67 of 131 controls completed MRI; mean age 56 at enrollment) [22] are described elsewhere. During phase 3 (2005–2008), 396 participants returned for an additional study visit. All phases of the study were reviewed and approved by the Johns Hopkins Bloomberg School of Public Health Committee on Human Research and written informed consent was obtained from all participants.

During phase 3, participants who completed the first MRI in phase 2 (589 former lead workers and 67 controls) were invited for a second MRI; 317 (54%) former lead workers and 45 (67%) controls completed a second MRI. Thus, two MRIs were obtained from 362 participants, representing 91% of the 396 participants who returned for phase 3 of the study. Nine of these had poor quality scans, leaving 353 participants with useable MRIs. Participants with phase 3 MRIs were on average younger than participants with no MRI or only a phase 2 MRI [18]. Five participants had missing data on social engagement; our final analysis included 348 participants.

*2.2. Structural Magnetic Resonance Imaging Acquisition.* A 3 T General Electric scanner was utilized for the phase 3 MRI. T1-weighted images were acquired using spoiled gradient recalled acquisition (SPGR) in steady state sequence (repetition time (TR) = 21 ms, echo time (TE) = 8 ms, field of view (FOV) = 24 cm, flip angle = 30° one excitation, voxel size = 0.9375 mm by 0.9375 mm by 1.5 mm, field of view 24 cm, matrix size $256 \times 256$). Methods for phase 2 MRI have been previously published [22].

*2.3. Image Analysis.* Quantitative analysis of MR volumes was completed using previously published methods [23]. First, extracranial tissue and brainstem structures were stripped. A validated specialized image analysis method was employed to segment the images into GM and WM. The CLASSIC algorithm [24] employs a 4-dimensional segmentation framework in which the first and second scans are considered jointly to minimize discrepancies between the two segmentations. The segmented images provide quantitative volumetric measures of total GM, WM, and brain (GM plus WM) matter.

To obtain volumes of predefined ROIs, regional analysis was performed via computerized template matching techniques previously reported and validated [22, 25]. In brief, a computerized image analysis algorithm based on pattern matching was used to warp a reference digital brain atlas to each participant's MRI. The resulting 20 nonmutually exclusive ROIs included the volumes of total brain, total GM, total WM, major lobar subdivisions, and a number of smaller structures.

For the voxel-wise approach, regional analysis of volumes examined in normalized space (RAVENS) was used to yield brain maps for analysis of local volumetric differences not constrained by *a priori* anatomic definitions [23]. This method can provide confirmatory evidence of associations in predefined regions or provide additional insights into areas of the brain linked to social engagement that are not apparent from using the ROI approach. Using previously published methods [25], segmented images were transformed into a standard coordinate space using an elastic deformation algorithm. This procedure yields tissue density maps for GM and WM whose values are direct measurements of local tissue volumes. Associations of predictor variables with GM and WM volumes could then be examined on a voxel-by-voxel basis, not constrained by arbitrary anatomical boundaries, thereby revealing spatial patterns of such associations.

*2.4. Social Engagement.* Social engagement was measured for the first time in phase 3 of this study (i.e., at the time of the second MRI). The measure of social engagement came from the enacted function profile (EFP), a 20-item scale designed to measure multiple domains of enacted functional performance in older adults based on pre-existing theory regarding the measurement of actual functional performance (rather than theoretical functional capacity) in daily life [26]. The EFP asks respondents how often they have engaged in a number of common daily activities over the past week or month. To test our measurement theory and to correct for random measurement error, we used confirmatory factor analysis to examine the conditional independence of four domains of enacted function (social engagement, community involvement, self-care, and productive activities) and to derive factor scores to represent our theorized latent constructs. For the analysis, a factor-based score based on the 8 social engagement items was generated using MPLUS version 5. The social engagement items and scale details are included in the appendix.

*2.5. Statistical Analysis*

*2.5.1. ROI-Based Approach.* We first evaluated whether higher social engagement was associated with larger volumes of predefined anatomical ROIs (dependent variable) in a cross-sectional analysis of phase 3 data. Associations between social engagement and brain volumes were examined using linear ordinary least squares regression modeling, with a separate model for each ROI. Because tibia lead is associated with smaller brain volumes [22], but was only available for lead workers, we first evaluated whether tibia lead level altered the association of interest or if it was appropriate to include both lead workers and controls in our main analyses without adjusting for lead. Tibia lead was not associated with social engagement and there was no evidence that the association of social engagement and brain volumes differed by control status or by tibia lead level, so we combined former lead workers and controls in all subsequent analyses.

All models were adjusted for intracranial volume, handedness, and control status (versus former lead workers). Demographic and health factors that could confound the relationship between social engagement and brain volume included age (centered), race/ethnicity (all minorities versus whites), education (five categories, with high school plus trade school as the reference group), cardiovascular disease risk factors known to be associated with brain pathology (hypertension and diabetes), and tibia lead level (measured in lead workers only). Effect modification by age, education, race/ethnicity, cardiovascular risk factors, and control status was evaluated using models with cross-product terms. To facilitate comparisons across ROIs, standardized regression coefficients are presented. Model diagnostics were performed to examine model fit and influential points. Because the 20 ROIs are not independent, we did not adjust for multiple comparisons in this analysis choosing instead to report standard errors and unadjusted tests of associations. Analyses were performed with SAS 9.1 statistical software.

*2.5.2. ROI-Based Analysis to Address Temporality.* To discern temporal relations, we performed secondary analyses using the available longitudinal data from the first and second MRI. We modeled social engagement (measured at the time of the second MRI) as the *outcome variable* regressed upon the change in ROI volumes from first to second MRI (to address whether change in brain volumes over five years is associated with social engagement at the end of the interval). Standardized regression coefficients are presented. Strength of association and model fit for these models were compared to our main models.

*2.5.3. Voxel-Wise Approach.* We next used voxel-based analysis to identify areas of GM and WM associated with social engagement. At each voxel we conducted linear regression of the voxel volume versus social engagement controlling for the aforementioned covariates. From the regression output we obtained a $t$-statistic for each voxel. We identified 3-dimensional clusters of 100 or more contiguous voxels exceeding the statistical threshold $t > 3.11$ (corresponding to an uncorrected $P$ value $<0.001$). To address multiplicity, we conducted a permutation test to assess the statistical significance of each cluster with respect to the permutation distribution of the largest cluster of suprathreshold $t$-statistics. More specifically, for 250 repetitions, we permuted the brain images (e.g., voxel volumes) across subjects, keeping the covariate data fixed. Then for each permuted dataset, we performed the same analysis as was done on the original dataset, identifying the largest cluster of contiguous voxels exceeding $t > 3.11$. We finally obtained a $P$ value for each cluster by calculating the proportion of repetitions for which the size of the cluster in question was greater than or equal to the largest cluster of the permuted data. This voxel-wise analysis was conducted separately for the gray and white matter maps.

## 3. Results

*3.1. Descriptive Summary of Study Participants.* Study participants were 48 to 82 years of age (mean (S.D.) = 65.2 (7.9)); the majority were white/non-Hispanic, had a high school education plus trade school, were hypertensive, and not diabetic (Table 1). The oldest individuals and the most educated were more socially engaged. Younger participants, white non-Hispanic persons, and those without hypertension or diabetes had larger brain volumes. There was a complex pattern of association between brain volumes and levels of education, as persons with a graduate degree had brain volumes similar to those with less than high school education; both groups had smaller total brain volumes compared with the high school plus trade school reference group. Participants in both the lowest and highest education groups were an average of 3.5 years older than participants in the middle categories. Former lead workers were less socially engaged than population-based controls but had larger brain volumes on average.

*3.2. Associations of Social Engagement with Brain Volumes*

*3.2.1. ROI-Based Method.* Inferences did not significantly differ for base models and fully adjusted models, so only fully adjusted models are presented. Higher social engagement was significantly associated with larger total brain volume and total GM volume, as well as larger temporal and occipital GM lobar volumes (Table 2), but not with total or lobar WM ROIs. Among the other ROIs evaluated, social engagement was only significantly associated with corpus callosum volume. There was no evidence of effect modification by age, education, race/ethnicity, or cardiovascular risk factors on relations of social engagement with ROI volumes.

*3.2.2. Analysis to Discern Temporal Relationships.* We evaluated whether changes in ROI volumes from the first to second MRI were associated with social engagement at the time of the second MRI. Information on changes in brain volumes

Table 1: Descriptive statistics.

| | $N$ | (%) | Social Engagement (Range −0.79, 1.09) | (SD) | Total brain volume (Range 880.6, 1449.3) | (SD) |
|---|---|---|---|---|---|---|
| All | 348 | (100%) | 0.01 | (0.33) | 1137.4 | (100.4) |
| Age | | | | | | |
| 48–59 | 82 | (23.6%) | −0.07 | (0.35) | 1187.5 | (94.6) |
| 60–64 | 92 | (26.4%) | 0.04 | (0.32) | 1161.3 | (90.6) |
| 65–69 | 84 | (24.1%) | 0.02 | (0.29) | 1123.9 | (81.8) |
| 70–82 | 90 | (25.9%) | 0.07 | (0.33) | 1079.7 | (100.4) |
| | | | $P = 0.028$ | | $P < 0.001$ | |
| Race/ethnicity | | | | | | |
| White/Non-Hispanic | 315 | (90.5%) | 0.02 | (0.32) | 1141.6 | (99.9) |
| All other | 33 | (9.6%) | −0.05 | (0.40) | 1097.1 | (97.9) |
| | | | $P = 0.25$ | | $P = 0.015$ | |
| Educational attainment | | | | | | |
| <High school | 25 | (7.2%) | −0.05 | (0.41) | 1083.1 | (74.7) |
| High school | 90 | (25.9%) | −0.05 | (0.32) | 1139.8 | (97.4) |
| High school + trade school | 167 | (48.0%) | 0.03 | (0.30) | 1135.8 | (101.6) |
| College degree | 56 | (16.1%) | 0.04 | (0.34) | 1171.6 | (92.2) |
| Graduate degree | 10 | (2.9%) | 0.28 | (0.41) | 1086.1 | (137.9) |
| | | | $P = 0.018$ | | $P = 0.002$ | |
| Hypertension | | | | | | |
| Yes | 180 | (51.7%) | 0.01 | (0.32) | 1116.6 | (97.5) |
| No | 168 | (48.3%) | 0.01 | (0.33) | 1159.6 | (99.0) |
| | | | $P = 0.97$ | | $P < 0.001$ | |
| Diabetes | | | | | | |
| Yes | 54 | (15.5%) | −0.01 | (0.29) | 1098.8 | (90.5) |
| No | 294 | (84.5%) | 0.02 | (0.34) | 1144.4 | (100.7) |
| | | | $P = 0.59$ | | $P = 0.002$ | |
| Control status | | | | | | |
| Population-based control | 43 | (12.4%) | 0.12 | (0.29) | 1103.5 | (100.5) |
| Former lead worker | 305 | (87.6%) | 0.00 | (0.33) | 1142.1 | (99.6) |
| | | | $P = 0.018$ | | $P = 0.018$ | |

All $P$-values from analysis of variance (ANOVA) tests.

in this cohort has been previously reported [18]. Changes in brain volumes over five years were not associated with social engagement at the end of the interval, except for temporal WM ($P = 0.034$) (Table 3).

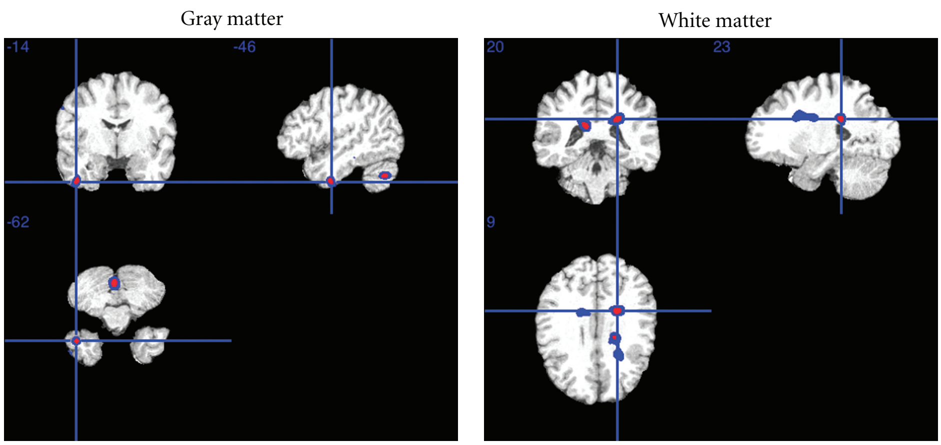
*3.2.3. Voxel-Based Method.* Clusters of voxels were identified in both GM and WM where social engagement was associated with larger voxel volume after adjustment for the aforementioned covariates (Table 4, Figure 1). There were twelve GM clusters of 100 or more voxels exceeding a statistical threshold of $t = 3.11$ ($P < 0.001$). The largest GM cluster was 4581 voxels (peak $t = 4.23$, $P < 0.0001$) and the second largest was 2501 voxels (peak $t = 4.23$, $P < 0.0001$). The permutation test-based $P$ values for the largest two clusters were 0.05 and 0.14, respectively. Although social engagement was not associated with total or lobar WM ROIs, the VBM analysis identified six suprathreshold WM clusters of more than 100 contiguous voxels. The largest two WM clusters consisted of 3221 voxels (peak $t = 3.95$, $P < 0.001$) and 2592 voxels (peak $t = 4.06$, $P < 0.0001$), respectively. These clusters were localized to the interior regions near the cerebral fissure. Applying the cluster-based permutation test, the $P$ value for the largest cluster was 0.10.

As the VBM analysis was not constrained by anatomical regions, there were a number of similarities as well as differences. Significant GM clusters were observed in the temporal lobe (Figure 1), the region found to have the strongest association with social engagement in the ROI analysis, but a number of clusters were observed in regions not identified by the ROI analysis, including clusters in the parietal lobe and cerebellum. Furthermore, there were no

Table 2: Adjusted associations between social engagement (independent variable) and ROI volumes (dependent variables).

| ROI | Mean volume (cc) | Social engagement standardized coefficient | $P$ value |
|---|---|---|---|
| **Total brain volume** | **1137.96** | **0.037** | **0.011** |
| **Total gray matter (GM)** | **534.14** | **0.072** | **0.007** |
| Total white matter (WM) | 603.82 | 0.001 | 0.975 |
| Gray matter lobes | | | |
| Frontal GM | 134.85 | 0.037 | 0.273 |
| **Temporal GM** | **96.58** | **0.083** | **0.009** |
| Parietal GM | 65.40 | 0.068 | 0.081 |
| **Occipital GM** | **45.56** | **0.076** | **0.048** |
| White matter lobes | | | |
| Frontal WM | 201.47 | 0.008 | 0.761 |
| Temporal WM | 119.03 | 0.021 | 0.501 |
| Parietal WM | 106.08 | 0.026 | 0.456 |
| Occipital WM | 58.22 | 0.007 | 0.869 |
| Smaller structures | | | |
| Cerebellum | 119.63 | −0.013 | 0.763 |
| Medial structures | 80.63 | 0.047 | 0.135 |
| Cingulate gyrus | 21.02 | 0.045 | 0.269 |
| Insula | 13.94 | 0.008 | 0.865 |
| **Corpus callosum** | **11.89** | **0.127** | **0.004** |
| Internal capsule | 9.85 | 0.026 | 0.520 |
| Hippocampus | 7.42 | −0.004 | 0.923 |
| Amygdala | 2.43 | 0.037 | 0.453 |
| Entorhinal cortex | 2.37 | −0.016 | 0.756 |

From models adjusted for age, education, intracranial volume, race/ethnicity, hypertension, diabetes, handedness, and control status.
Bold: $P \leq 0.05$.




(a) Gray matter (b) White matter

Figure 1: The highlighted zones indicate regions in which higher social activity was associated with larger brain volumes from voxel-based morphometry analysis. Only clusters of 100+ voxels shown. See Table 4 for cluster-specific statistics.

significant associations with lobar WM volumes in the ROI analysis, but large significant clusters were observed in WM in the VBM analysis. These were in the corpus callosum, which aligns with the ROI analysis.

## 4. Discussion

These findings provide some of the first published evidence that higher social engagement is associated with larger brain volumes as assessed by structural MRI using ROI- and voxel-based methods. In contrast, change in brain volumes over the five-year-period was not associated with social engagement. Therefore, these findings are consistent with the hypothesis that social engagement preserves brain tissue, and provide some evidence against the alternate hypothesis that persons with smaller or shrinking volumes become less socially engaged, although we cannot rule out the possibility that changes in social engagement over a longer period than five

Table 3: Adjusted associations between change in ROI volumes (independent variable) and social engagement (dependent variable).

| ROI | ΔROI standardized coefficient[1] | *P* value |
|---|---|---|
| Total brain volume | 0.023 | 0.713 |
| Total gray matter (GM) | 0.062 | 0.299 |
| Total white matter (WM) | −0.039 | 0.494 |
| Gray matter lobes | | |
| Frontal GM | 0.032 | 0.599 |
| Temporal GM | 0.112 | 0.055 |
| Parietal GM | 0.092 | 0.133 |
| Occipital GM | −0.011 | 0.849 |
| White matter lobes | | |
| Frontal WM | 0.010 | 0.851 |
| **Temporal WM** | **−0.115** | **0.034** |
| Parietal WM | −0.035 | 0.526 |
| Occipital WM | 0.046 | 0.416 |
| Other structures (GM and WM) | | |
| Cerebellum | 0.022 | 0.695 |
| Medial structures | 0.005 | 0.937 |
| Cingulate gyrus | −0.023 | 0.696 |
| Insula | −0.014 | 0.803 |
| Corpus callosum | −0.019 | 0.730 |
| Internal capsule | 0.067 | 0.244 |
| Hippocampus | 0.005 | 0.934 |
| Amygdala | 0.050 | 0.368 |
| Entorhinal cortex | 0.027 | 0.633 |

From models adjusted for age, education, intracranial volume, race/ethnicity, hypertension, diabetes, handedness, and control status.
[1]Social engagement at time of 2nd MRI was the dependent variable.
Bold: $P \leq 0.05$.

years may be associated with later volumes. The primary associations were with temporal and occipital lobar GM volumes, and likely as a result of this, with total GM and total brain volumes. There were no associations with lobar WM volumes. The findings support the brain reserve hypothesis by providing evidence that social engagement is associated with larger brain volumes in specific regions, which may in turn help to preserve cognitive function at older ages.

There are a number of proposed biological mechanisms by which social engagement could affect cognitive function through changes in brain volume, especially in GM, the site of the neuronal cell bodies and a variety of connections between neural and glial tissues. Total brain volume loss [27], GM loss [28], neuronal shrinkage [29], and synaptic loss [30] are common consequences of aging. Neuronal and synaptic loss, as well as accelerated gross atrophy, are well-documented pathophysiologic correlates of early Alzheimer's disease [31]. Brain areas with larger volumes may be able to tolerate more loss caused by aging or disease before exhibiting declines in cognitive function because of a higher number of remaining healthy neurons and synapses [32]. Social engagement may lead to larger brain volumes through a decrease in neuronal death or shrinkage, neurogenesis in certain areas of the brain [12], increased dendritic spine growth or axonal rearrangement [33]. Other lines of research provide support for a link between social engagement and larger brain volumes, including associations between social engagement and other aspects of brain pathology or function and demonstrated neuroplastic increases in volume due to human behavior such as activity and learning. Furthermore, experiments with animals placed in enriched environments with increased opportunity for learning, activity, and interaction with other animals have demonstrated neurogenesis, synaptogensis, and reduced neuronal loss [11, 13, 34–36].

The localization of the social engagement-volume relationship should be interpreted with caution, but some initial conjectures can be made. The association with social engagement was strongest in GM in the right temporal lobe. Facial and verbal recognition, long-term memory, and personality features reside in the temporal lobe [37]. Loss of GM in this area occurs during aging [28]. GM was not significantly associated with social engagement in the frontal lobe, which displays the most loss during brain aging [38]. Furthermore, no significant associations were found for the hippocampus, a structure important to memory and cognition and vulnerable to aging [39], though some studies have shown preservation of hippocampal volumes with aging [40]. Research on enriched environments in animal models have found evidence of neurogenesis in the hippocampus, [14] and a study in humans showed larger hippocampi in socially engaged persons [41]. However, the hippocampus is a small structure and it is likely measured with less accuracy due to greater proportional error. The only WM structure found to be significantly associated with social engagement in the ROI-based analysis was the corpus callosum. There is some evidence that hemispheric asymmetry is a marker of reserve [42], and it is hypothesized that larger corpus callosum volume (which facilitates communication across hemispheres) may compensate for psychomotor slowing in later life [43]. Moreover, it is possible that preservation of lobar GM volumes could also preserve inter-hemispheric connections between those areas resulting in a larger corpus callosum.

Strengths of this study include the relatively large number of subjects with MRIs, the robustness of brain imaging analysis, the use of a rigorous measure of social engagement, the availability of longitudinal data, and the ability to control for important confounders. Conducting analyses using both ROIs and VBM gave us two separate but complimentary ways to examine the association between social engagement and tissue volume in specific areas of the brain [15]. The ROI analysis was informed by recognized anatomical structures while the VBM analysis did not rely on *a priori* structural boundaries but rather examined the entire brain in an unbiased region-by-region basis.

One important limitation was the lack of a baseline social engagement measure, preventing us from examining the association between social engagement and change in brain structure or the association of change in social engagement with later brain structure. Another limitation is the unique nature of this cohort, which includes persons with past

Table 4: Cluster statistics from voxel-wise analysis.

| $X$ | $Y$ | $Z$ | Maximum $t$-statistic | Unadjusted $P$ value | Cluster size | Cluster $P$ value |
|---|---|---|---|---|---|---|
| Gray matter | | | | | | |
| −42 | 50 | −54 | 4.23 | 0.00002 | 4581 | 0.05 |
| −3 | 51 | −66 | 4.23 | 0.00001 | 2501 | 0.14 |
| −65 | −17 | 21 | 3.97 | 0.00004 | 1278 | 0.34 |
| 64 | 4 | 15 | 3.78 | 0.00009 | 1029 | 0.43 |
| −46 | −14 | −63 | 4.16 | 0.00002 | 908 | 0.48 |
| −56 | −32 | −64 | 4.08 | 0.00003 | 892 | 0.49 |
| −65 | 17 | −14 | 3.86 | 0.00007 | 511 | 0.68 |
| −57 | 66 | −25 | 3.9 | 0.00006 | 315 | 0.74 |
| 57 | 1 | −46 | 3.73 | 0.00011 | 272 | 0.76 |
| 17 | 71 | −31 | 3.54 | 0.00023 | 227 | 0.79 |
| 30 | −37 | 32 | 3.47 | 0.00029 | 162 | 0.82 |
| −50 | 14 | −39 | 3.26 | 0.00062 | 119 | 0.82 |
| White matter | | | | | | |
| 24 | −21 | 12 | 3.95 | 0.00005 | 3221 | 0.10 |
| −14 | 18 | 3 | 4.06 | 0.00003 | 2592 | 0.14 |
| 23 | 20 | 9 | 4.12 | 0.00002 | 1904 | 0.23 |
| 13 | −47 | −15 | 3.45 | 0.00031 | 797 | 0.44 |
| 35 | 45 | −21 | 3.46 | 0.00030 | 198 | 0.77 |
| 27 | 41 | −6 | 3.33 | 0.00048 | 102 | 0.83 |

Displays cluster centroid ($x$-, $y$-, and $z$- MNI coordinates), maximum $t$-statistic within the cluster, $P$ value (unadjusted) of the maximum $t$-statistic, cluster size in number of contiguous voxels, and permutation test-based cluster $P$ value. The cluster $P$-value compares the size of each suprathreshold cluster to the permutation distribution of the largest cluster, thereby accounting for multiple comparisons. Only results from clusters of 100+ voxels shown.

Table 5: Social engagement assessment.

| Item: in the last week/month have you... | Response scale | Mean (std dev) |
|---|---|---|
| (i) been in touch with friends or relatives by phone or by letters? | W | 2.6 (1.2) |
| (ii) gotten your hair [MEN cut WOMEN done] or dressed up to go out at least once? | M | 2.5 (1.3) |
| (iii) done any unpaid volunteer work or community service? | M | 0.9 (1.5) |
| (iv) been out to have lunch or dinner with someone? | M | 2.8 (1.4) |
| (v) been to a meeting at a club, senior center, or organization in which you are active other than religious institution? | M | 0.8 (1.2) |
| (vi) been out socially with friends or relatives, for example, to see a show, a party or holiday celebration, or some other social event? | M | 1.2 (1.1) |
| (vii) gone shopping for food, clothes, or something else you needed? | M | 2.8 (1.2) |
| (viii) done any indoor or outdoor recreational activity like bowling, working out, fishing, hiking, boating, swimming, golfing? | M | 1.8 (2.0) |

occupational lead exposure. Although we found no evidence that associations differed after control for lead dose or in comparing former lead workers to controls, the findings may not be generalizable to the general older adult population. The cohort is also racially and occupationally homogenous, and all male. Thus, we have no information on social engagement and the older female brain or differences across race/ethnic groups. However, homogeneity in occupation and socioeconomic status in this cohort may increase internal validity by lessening concerns of confounding by other factors linked to brain reserve and correlated with social engagement. Some potential confounders we were not able to adjust for include genes, IQ, stress response, personality, history of head injury, and MCI or prodromal dementia, all of which could be associated with both social engagement and brain structure. Finally, a limitation that could in part relate to the observed lack of an association between social engagement and WM is that we did remove white matter lesions from volumetric measures prior to analysis.

For more than a decade, recommendations have been made for older adults to stay socially engaged to keep their brains healthy based on evidence from epidemiologic studies of cognition and dementia. These studies have not addressed the “black box” regarding how social engagement may be related to the neuroanatomical substrate. Ours is an example, in a community-dwelling older adult population, of this

Table 6: The 8 social engagement items form one factor, of four, in the 20-item enacted function profile. Measurement properties of the enacted function profile follow.

| | |
|---|---|
| Chi-square test of model fit | |
| Value | 68.437 |
| Degrees of freedom | 46 |
| *P* value | 0.018 |
| CFI/TLI | |
| Comparative fit index (CFI) | 0.950 |
| Tucker-lewis fit index (TLI) | 0.946 |
| RMSEA (Root mean square error of approximation) | |
| Estimate | 0.035 |
| WRMR (Weighted root mean square residual) | |
| Value | 0.676 |

necessary piece to the puzzle of why socially engaged persons are more cognitively intact at advanced ages.

## Appendix

See Tables 5 and 6.

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*Research Article*

# Social Activity and Cognitive Functioning Over Time: A Coordinated Analysis of Four Longitudinal Studies

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Social activity is typically viewed as part of an engaged lifestyle that may help mitigate the deleterious effects of advanced age on cognitive function. As such, social activity has been examined in relation to cognitive abilities later in life. However, longitudinal evidence for this hypothesis thus far remains inconclusive. The current study sought to clarify the relationship between social activity and cognitive function over time using a coordinated data analysis approach across four longitudinal studies. A series of multilevel growth models with social activity included as a covariate is presented. Four domains of cognitive function were assessed: reasoning, memory, fluency, and semantic knowledge. Results suggest that baseline social activity is related to some, but not all, cognitive functions. Baseline social activity levels failed to predict rate of decline in most cognitive abilities. Changes in social activity were not consistently associated with cognitive functioning. Our findings do not provide consistent evidence that changes in social activity correspond to immediate benefits in cognitive functioning, except perhaps for verbal fluency.

## 1. Introduction

Cognitive decline in older adulthood remains an area of great concern as the population ages. Some changes in cognitive function, such as decreased processing speed, are considered normative aspects of the aging process [1]. However, the impact of even mild cognitive impairment on functional capacity highlights the importance of maintaining cognitive function for as long as possible [2]. Substantial evidence suggests that lifestyle factors and cognitive function in older adulthood are related [3]. Sometimes summarized by the adage "use it or lose it," current evidence suggests that leading an active lifestyle "using it" may buffer the effects of age-related cognitive decline "losing it" [3–5]. The mechanisms by which an active and engaged lifestyle may be related to better or preserved cognitive function in older adulthood remain to be fully elucidated. However, the cognitive reserve hypothesis predicts that some individuals are better able to withstand the physiological insults to the brain without measurable cognitive deficits because they had greater capacity to begin with [6]. Individuals may be able to actively increase their "reserve" through engaging in cognitively stimulating activities [3].

Social activities are considered part of what constitutes an active and engaged lifestyle, alongside cognitive and physical activities [3, 4, 7–9]. However, the evidence for a relationship between social activity participation and cognitive function is mixed. Some studies have found a relationship between social activities and cognitive function [10], while others have failed to do so [11]. In an intervention study, older adults living in residential care with normal cognitive function, after participation in daily short duration social and physical activity sessions, performed better cognitively than they had during their baseline assessment. However, the study design confounded physical and social activity [12]. Conversely, Aartsen et al. [11] found no relationship between social activities and cognitive function six years later using a cross-lagged regression approach that attempted to elucidate the strongest causal pathway. Similarly, Green et al. [13] did not find support for the hypothesis that social contact is protective against later cognitive decline.

The inconclusiveness of results has been acknowledged previously and suggested to relate to differences in statistical techniques [4, 8]. However, among studies that have used similar analytical methods, such as logistic regression, results are still mixed (e.g., [14–17]). Research examining whether social engagement can predict cognitive function and change in cognitive function over time, using growth modeling techniques, has also lacked a consistent finding. James and colleagues [10] found that social activity at baseline was associated with a higher baseline level of global cognitive function and lower rate of decline. Ertel et al. [18] found that baseline social integration was associated with a slower rate of memory decline, but not baseline memory performance. In a study of Danish twins, McGue and Christensen [19] found that social activity at baseline was related to level of cognitive function but not to change in cognitive function over time. They also found that, within monozygotic same-sex twin pairs, there was no evidence that the more socially active twin was less likely to experience cognitive decline than the less active cotwin. Overall, these studies demonstrate that many questions remain about the relationship between social activity and cognitive function [4, 7].

It is not clear whether it is a lifetime of social engagement (the effects of social activity accrued over time) that is protective, or if changes in social activity are related to cognitive function. Small and colleagues [20] examined the relationship between changes in social activity and changes in cognitive function and found stronger evidence for changes in cognitive function predicting changes in social activity than the reverse. Other studies have included only baseline social activity as predictor. Yet, social relations have been found to change qualitatively as people age [21]. Changes in social activity at any point in time may correlate with changes in cognitive functioning after controlling for its overall trend.

The current paper builds on previous work by exploring whether including social activity as a variable that changes over time can clarify the relationship between social activity and cognitive function in older adulthood. Using multilevel growth modeling with social activity as a time-varying covariate allows an examination of the relations between time-specific changes in cognition and social activity. This allows for a detailed test of whether the impact of social activity on cognitive function is accrued over time or whether changing social activity levels might relatively quickly impact cognitive function. Examining the temporal relationship between social engagement and cognitive function is needed to inform theories of possible mechanisms.

The current analysis examines the relationship between social activity, change in social activity, and four domains of cognition including: reasoning, memory, fluency, and semantic knowledge in four different populations. The same models are tested with data from four different longitudinal studies: the Long Beach Longitudinal Study (LBLS), the Seattle Longitudinal Study (SLS), the Victoria Longitudinal Study (VLS), and the Origins of Variance in the Oldest-Old: Octogenarian Twins Study (OCTO-Twin). This addresses the possibility that differing analytical methods may produce differing results and provides the opportunity for immediate replication and direct comparison of results. The diversity of the samples, two American, one Canadian, and one Swedish, increases the generalizability of the results and decreases the possibility that findings might be due to the particular features of one country or community.

## 2. Method

This research, initiated as a partnership between the Advanced Psychometric Methods Workshop series (Mungas et al., NIA conference grant) and the Integrative Analysis of Longitudinal Studies on Aging (IALSA) network [22], brought workshop participants together with researchers from four IALSA member studies. These studies were specifically selected based on their collection of cognitive, physical, and social activity data along with a range of cognitive functioning measures over multiple occasions held in common across the four studies. While the activity and cognitive functioning variables are not always identical, the subsets of variables in each study were chosen based on the rationale that they tapped similar domains at the construct level (e.g., Fluid Reasoning (Gf), Crystallized Knowledge (Gc), Short-term Memory (Gsm), and Long-term Storage and Retrieval (Glr; e.g., category fluency)) [23]. In some cases the measures are the same, but more often they differ, providing opportunities for both strict and conceptual replication. An exception to this is the OCTO-Twin dataset, for which a fluency measure was not available.

*2.1. Origins of Variance in the Oldest-Old (OCTO-Twin) Participants (Sweden).* The OCTO-Twin study is based on the oldest cohort of the Swedish Twin Registry and includes 702 participants aged 80 years and older at the time of the first assessment. Beginning in 1991–1993, the longitudinal design included a maximum of five measurement occasions at 2-year intervals. All individuals with a dementia diagnosis at baseline were excluded from the analyses ($n = 98$). The total sample includes 604 individuals, of whom 524 had the social activity measure and at least one of the cognitive measures. Approximately 20% of the sample was lost to followup at each wave (10% per year), but most of this attrition was due to death. The ratios for gender, education, socioeconomic status, marital status, and housing of the OCTO-Twin sample correspond to population statistics for this age range of the Swedish population [24]. Demographic information for the sample appears in Table 1.

*2.1.1. OCTO-Twin Measures and Procedure*

*OCTO-Twin Cognitive Measures. Reasoning* was assessed using Koh's Block Design Test [25]. In this task, participants are presented with red and white blocks and several patterns on cards and asked to construct the design on the card with the blocks. *Memory* was assessed using the Prose Recall test in which participants are asked for immediate free recall of a brief (100 words) story that has a humorous point [26]. Responses are coded for the amount of information recalled in a manner similar to the Wechsler Memory Scale [27]. *Semantic knowledge* was assessed using the Swedish version of the Information Task [28], which includes questions of general knowledge.

*OCTO-Twin Social Activity.* Participants were asked at each wave: "*How many people do you see?*" The possible response was: "none" (0); "1-2" (1); "3–5" (2); "6–10" (3), or "11 or more" (4).

*2.2. Long Beach Longitudinal Study Participants (CA, USA).* The LBLS was initiated in 1978 when participants were recruited from the Family Health Plan Health Maintenance Organization (HMO), including mainly residents of Long Beach and Orange County. This first panel included 583 individuals aged 28–36 or 55–87. The ethnic composition of the older group (98% Caucasian) was similar to the 65+ population for the area based on the 1970 census. Panel 2, initiated in 1992, included 633 individuals contacted from the same HMO (64 were excluded due to frank dementia or serious sensory or neurological problems).

In order to include the same measures as those in the Seattle Longitudinal Study, LBLS Panel 1 ($n = 106$) and Panel 2 ($n = 631$) data from 1994 to 2003 were used in the current analysis, excluding individuals younger than age 55 in 1994 (baseline $n = 565$). During this period, data were collected at 3-year intervals. Attrition was approximately 50% over each interval, or 17% per year. Dementia incidence is not known. Descriptive information for the sample is presented in Table 2. Additional information on the LBLS design, measures, and participants can be found elsewhere [29, 30].

*2.2.1. LBLS Measures and Procedure*

*LBLS Cognitive Measures. Reasoning* was assessed using a composite score of the Schaie-Thurstone Adult Mental Abilities Test (STAMAT; Schaie, [31]) Letter and Number Series tests. In Letter Series, participants view a series of letters (e.g., a b c c b a d e f f) and are asked to discover the rule that governs the series by identifying the letter that should come next in the series. Participants were to complete as many of the 30 items as possible within six minutes. Word Series was a parallel test to Letter Series but the letters were replaced with months (e.g., January) and days of the week (e.g., Monday). *Memory* involved immediate written recall of a list of 20 concrete high-frequency nouns studied for 3.5 minutes. *Fluency* was assessed by a word fluency task where participants were instructed to write down as many words as possible in five minutes that begin with the letter "s." Participants were instructed that they could not use proper nouns or create words by changing endings of other listed words (e.g., if the letter was "w" and you already said "want," you should not also say "wants," "wanting," or "wanted"). *Semantic knowledge* consisted of the STAMAT Recognition Vocabulary test. Participants were given a word and asked to circle a synonym of that word from four possible alternatives. The test included 50 items that were to be completed in five minutes.

*LBLS Social Activity Measure.* A measure of social activity was derived from a modified version of the Life Complexity Scale that was originally developed for the Seattle Longitudinal Study [32]. Participants were asked to record the number of "hours per week on average" they spent doing various activities (e.g., "going to parties"). The LBLS version of the scale included 34 specific activities, 7 of which were considered social. In the current study, these activity measures were dichotomized in order to distinguish those who reported no activity (coded as 0) from those who reported one or more hours of activity per week (coded as 1). This was done because the range of scores varied greatly within and between measures, and because some scores were highly deviant (skewed) from expected values (e.g., reporting more than 100 hours of reading per week).

The social activity variable was created by selecting questions from the Life Complexity Scale that fit the social activity construct. That is, a composite score was formed by summing up the number of social activity items that were endorsed as having one or more hours of activity per week. The measure consisted of seven questions including: phone conversations, voluntary activities, going to parties, going to dances, playing cards, visiting others, and attending church. The range of possible scores was 0 to 7. A social activity change variable was computed by subtracting the social activity measure in 1994 from social activity in 1994, 1997, 2000, and 2003. This resulted in a difference score that references the baseline testing in 1994.

Table 1: OCTO-twin participant characteristics.

| Measure | Year of testing<br>Baseline ($n$ = 524)<br>M (SD) | Year 2 ($n$ = 424)<br>M (SD) | Year 4 ($n$ = 326)<br>M (SD) | Year 6 ($n$ = 245)<br>M (SD) | Year 8 ($n$ = 175)<br>M (SD) |
|---|---|---|---|---|---|
| Retention from previous testing (%) | | 82.9 | 76.7 | 76.2 | 72.8 |
| Age | 83.2 (2.9) | 85.2 (2.8) | 86.9 (2.5) | 88.8 (2.5) | 90.7 (2.4) |
| Education | 7.2 (2.3) | 7.3 (2.4) | 7.3 (2.3) | 7.2 (2.1) | 7.2 (2.3) |
| Sex, female [$n$ (%)] | 365 (66) | 299 (65) | 233 (66) | 193 (72) | 146 (74) |
| Reasoning | 11.6 (7.1) | 11.6 (7.1) | 11.5 (7.0) | 10.2 (7.3) | 10.2 (7.3) |
| Memory | 9.6 (4.0) | 9.5 (4.2) | 9.5 (4.2) | 9.1 (4.4) | 9.1 (4.4) |
| Semantic knowledge | 28.2 (11.1) | 28.8 (11.1) | 28.8 (11.1) | 26.1 (11.4) | 26.1 (11.4) |
| Social activity | 3.0 (1.0) | 3.0 (1.0) | 3.1 (0.9) | 2.8 (1.0) | 2.8 (0.9) |
| Social activity change | — | −0.1 (1.0) | −0.0 (1.1) | −0.2 (1.1) | −0.4 (1.2) |

M: mean, SD: standard deviation. The range for each measure with a defined upper limit is as follows: reasoning = 0–42, memory = 0–16, semantic knowledge = 0–44, and social activity = 0–4. Higher scores represent higher activity.

Table 2: LBLS participant characteristics.

| Measure | Year of testing<br>Baseline ($n$ = 565)<br>M (SD) | Year 3 ($n$ = 300)<br>M (SD) | Year 6 ($n$ = 143)<br>M (SD) | Year 9 ($n$ = 102)<br>M (SD) |
|---|---|---|---|---|
| Retention from previous testing (%) | | 53 | 48 | 71 |
| Age | 73.8 (9.1) | 75.5 (8.7) | 75.29 (8.01) | 76.4 (7.2) |
| Education | 13.7 (3.0) | 13.9 (2.8) | 14.2 (2.70) | 14.1 (2.7) |
| Sex, female [$n$ (%)] | 278 (49) | 148 (49) | 74 (52) | 50 (49) |
| Reasoning | 22.1 (11.7) | 23.7 (11.5) | 25.2 (11.63) | 25.0 (11.1) |
| Fluency | 32.3 (11.7) | 33.5 (11.1) | 33.3 (13.29) | 34.3 (11.7) |
| Memory | 11.4 (4.0) | 11.5 (4.2) | 11.6 (4.52) | 11.1 (4.7) |
| Semantic knowledge | 38.4 (10.2) | 39.3 (9.8) | 40.8 (8.95) | 39.4 (9.9) |
| Social activity | 3.3 (1.5) | 3.5 (1.6) | 3.5 (1.4) | 3.5 (1.5) |
| Social activity change | — | 0.0 (1.4) | 0.1 (1.5) | −0.0 (1.4) |

M: mean, SD: standard deviation. The range for each measure with a defined upper limit is as follows: education = 0–20, reasoning = 0–30, memory = 0–20, semantic knowledge = 0–36, and social activity = 0–7.

*2.3. Seattle Longitudinal Study Participants (WA, USA).* The SLS is a very long-running longitudinal study initiated by Schaie, who first recruited members of a local Health Maintenance Organization in 1956 [33]. Current analyses used up to four waves of SLS data from 1984 to 2005, which include an expanded set of measures that also overlap with the LBLS. Only participants of 55 years and older at baseline were included in the analysis. Baseline was defined as each participant's first study visit, and time was measured in all analyses as years in study (coded as 0, 7, 14, and 21). Attrition during these 7-year intervals was approximately 50%, or 7% per year. Dementia prevalence and incidence are not known. See Table 3 for SLS participant characteristics over the four waves of data analyzed here.

### *2.3.1. SLS Measures and Procedure*

*SLS Cognitive Measures.* In order to model roughly equivalent cognitive outcomes across the four studies included in this coordinated effort, our analysis included measures of reasoning, fluency, memory, and semantic knowledge from a larger battery of tests. *Reasoning* was assessed with the Word Series test from the Schaie-Thurstone Adult Mental Abilities Test (STAMAT [31]), in which participants were asked to determine a rule that governs a series of words (months or days of the week) by identifying what word should come next in a given series. Participants were provided with a printed word series and instructed to choose the next word in the series in multiple-choice format. The test consists of 30 items and total score is based on number of correct responses completed in 6 minutes. As in LBLS, *Fluency* was assessed with the word fluency test from the Primary Mental Abilities test [34]. *Memory* was assessed with a task in which participants were asked to study a list of 20 printed words for 3.5 minutes and provide immediate written recall of the items. *Semantic knowledge* was assessed with the Educational Testing Service (ETS) test of Advanced Vocabulary, in which participants were asked to identify synonyms for printed words from 5 choices [35]. Total score was based on number of correctly identified synonyms out of 36 test items completed within 4 minutes.

*SLS Social Activity Measure.* We followed the methodology described in the LBLS method portion of this paper in

Table 3: SLS participant characteristics.

| Measure | Year of testing | | | |
|---|---|---|---|---|
| | Baseline ($n$ = 1657) | Year 7 ($n$ = 940) | Year 14 ($n$ = 446) | Year 21 ($n$ = 181) |
| | M (SD) | M (SD) | M (SD) | M (SD) |
| Retention from previous testing (%) | | 57 | 47 | 41 |
| Age | 67.1 (8.2) | 73.0 (7.23) | 78.0 (6.4) | 81.9 (4.9) |
| Education | 14.6 (2.9) | 14.7 (2.8) | 14.8 (2.7) | 14.8 (2.8) |
| Sex, female [$n$ (%)] | 861 (52) | 507 (54) | 256 (57) | 108 (60) |
| Reasoning | 15.6 (5.8) | 15.2 (5.6) | 14.3 (5.5) | 14.0 (5.25) |
| Fluency | 38.5 (12.8) | 37.5 (13.1) | 36.7 (12.7) | 38.8 (14.5) |
| Memory | 12.5 (4.0) | 12.0 (4.1) | 11.5 (4.1) | 11.6 (4.0) |
| Semantic knowledge | 25.0 (6.7) | 25.3 (6.6) | 25.8 (6.2) | 25.9 (5.9) |
| Social activity | 3.5 (1.6) | 3.5 (1.6) | 3.5 (1.6) | 3.3 (1.6) |
| Social activity change | — | −0.1 (1.5) | −0.2 (1.6) | −0.4 (1.7) |

M: mean, SD: standard deviation. The range for each measure with a defined upper limit is as follows: education = 0–20, reasoning = 0–30, memory = 0–20, semantic knowledge = 0–36, and social activity = 0–7.

order to generate a roughly equivalent index of social activity (see LBLS section for a detailed description). Following this methodology, we created a composite activity measure by summing dichotomized responses from a modified version of the Life Complexity Scale [32] creating a seven-item social activity composite (volunteering, playing cards, phone conversations, visiting others, attending church, dancing, and partying). *Social activity change* was computed by subtracting baseline activity from each follow-up activity measure.

*2.4. Victoria Longitudinal Study Participants (Victoria BC, Canada).* The Victoria Longitudinal Study began in 1986-1987 with a sample of 484 community residing volunteers and three-year retest intervals. Using a longitudinal sequential design, second and third independent samples began in 1992-1993 ($n$ = 530) and 2001-2002 ($n$ = 550) [36]. Each sample is tested at three-year intervals. To date, Sample 1 has been tested on seven occasions (over 18 years), Sample 2 on five (over 12 years), and Sample 3 on two occasions (over 6 years). Participants in all three samples were recruited between the ages of 55 and 85 years.

Data from seven waves of Sample 1 and five waves of Sample 2 were included in the current investigation. Characteristics of the subsample analyzed here are provided in Table 4. Approximately 25% of the sample was lost to followup at each wave, or 8% per year. Dementia prevalence and incidence are not known. Further detail on the VLS design, measures, and participants can be found elsewhere [36].

*2.4.1. VLS Materials and Procedure*

*VLS Cognitive Ability Measures. Fluency* was measured by performance on a Similarities task [35]. In this timed task, participants were presented with target words and asked to write as many words as possible with the same or nearly the same meaning within six minutes. *Memory* was indexed using a 30 item, noun list learning task comprised of five semantic categories. Participants studied the word list for two minutes followed by a five minute free recall task [37]. *Reasoning* was indexed by Letter Series [35] in which participants were presented with a series of letters and asked to identify the next letter in the sequence that was consistent with the sequence rule. Participants were given six minutes to complete the task. *Semantic knowledge* was assessed using a 54-item recognition vocabulary test. This task was adapted from the ETS Kit of Factor Referenced Tests [35].

*VLS Social Activity/Lifestyle Measure.* The social activity/lifestyle measure used in the presented investigation included a subset of items from the VLS Activity Lifestyle Questionnaire. Individual item distributions were reviewed and a small number of poorly distributed items were eliminated. Seven items were selected due to their social nature (Eat at restaurants, visit friend/relative, give dinner party, attend church, meetings of service organizations, meetings of clubs, and do volunteer work). For each item, participants indicated the frequency of engagement in that activity over the past two years on a scale from 0 to 9 (i.e., *never, less than once a year, about once a year, 2 or 3 times a year, about once a month, 2 or 3 times a month, about once a week, 2 or 3 times a week, daily*).

*2.5. General Analytic Approach.* The current analysis was conducted as part of a larger effort to examine the effects of lifestyle activities on cognitive function using the same analytic approach across studies from the Integrative Analysis of Longitudinal Studies on Aging (IALSA) network [22]. Thus, final models were selected in part to maintain consistency across lifestyle activities.

In order to improve ease of interpretation of our results, age, education, and social activity measures were mean centered for each study. The means for baseline age, education, and social activity were subtracted from their baseline values for each individual. This centered the covariates so that the intercept and linear slope terms would be interpreted as the expected value for an individual at the mean age and with the

Table 4: VLS participant characteristics.

| Measure | Year of testing | | | | | | |
|---|---|---|---|---|---|---|---|
| | Baseline ($n$ = 977) | Year 3 ($n$ = 723) | Year 6 ($n$ = 571) | Year 9 ($n$ = 411) | Year 12 ($n$ = 275) | Year 15 ($n$ = 91) | Year 18 ($n$ = 52) |
| | M (SD) | M (SD) | M (SD) | M (SD) | M (SD) | M (SD) | M (SD) |
| Retention from previous testing (%)[a] | — | 74 | 79 | 72 | 67 | 79 | 57 |
| Age | 68.6 (6.7) | 71.3 (6.6) | 73.7 (6.4) | 76.5 (5.9) | 79.3 (5.2) | 82.2 (4.6) | 85.1 (3.6) |
| Years of education at baseline | 14.9 (3.3) | 15.4 (3.2) | 15.6 (3.1) | 15.9 (3.1) | 15.8 (3.1) | 15.2 (3.1) | 14.8 (2.8) |
| Sex, female [$n$ (%)] | 614 (62.8) | 450 (62.2) | 346 (60.6) | 251 (61.1) | 170 (61.8) | 60 (65.9) | 35 (67.3) |
| Reasoning[b] | 11.2 (4.7) | 11.7 (4.2) | 10.3 (4.7) | 10.3 (4.6) | 9.9 (4.6) | 7.5 (4.7) | 6.5 (4.2) |
| Fluency | 17.7 (4.3) | 17.9 (4.4) | 17.7 (4.5) | 17.2 (4.8) | 16.3 (4.9) | 14.7 (5.8) | 13.8 (5.4) |
| Memory[c] | 13.7 (5.9) | 14.7 (6.0) | 14.7 (6.1) | 14.9 (6.4) | 11.7 (5.4) | 13.0 (6.3) | — |
| Semantic knowledge | 43.7 (7.4) | 44.7 (6.2) | 44.3 (6.0) | 44.2 (5.8) | 43.5 (5.7) | 42.7 (7.1) | 42.6 (6.6) |
| Social activity | 23.0 (6.9) | 23.2 (7.2) | 22.8 (7.3) | 22.5 (7.2) | 21.2 (7.1) | 22.8 (7.7) | 21.1 (7.2) |
| Social activity change | — | −0.1 (5.4) | −0.3 (6.0) | −0.9 (6.4) | −2.5 (6.9) | −3.5 (7.5) | −5.3 (8.1) |

M: mean, SD: standard deviation. The range for each measure with a defined upper limit is as follows: reasoning = 0–20, Memory = 0−30, and Semantic knowledge 0−54.

[a]The 1986 cohort was followed for up to 18 years, the 1993 cohort for up to 12.

[b]The reasoning measure was not given until year 6 for the 1986 cohort.

[c]The memory measure was not given in year 18.

mean level of education for the study. The reference category for sex was male.

In order to examine the effects of social activity on cognition, a series of multilevel models was fit with social activity as a baseline and a time varying covariate [38], with time specified as time since baseline, using multilevel mixed-effects regression in StataCorp [39], the restricted maximum likelihood estimator (REML), and an unstructured covariance matrix. In the OCTO-Twin study, participants were nested within their twin pair. In the VLS, we controlled for enrolment cohort. Model assumptions were verified by examining the residuals. Separate models were fit for each of the four cognitive measures (reasoning, fluency, memory, and semantic knowledge) resulting in four reported models for each study. While the “familywise” alpha rate within each individual study may be somewhat liberal, given our use of $P < .05$ as significance criterion, our focus on repetition of findings across studies imposes a strict limit to any reliance on chance findings. Formal meta-analytic methods, which would require identical measures and a larger number of studies, were not used. Instead we relied on comparison of the conclusions derived from each study.

An initial 19-term model included the following terms: (1) baseline age, (2) sex, (3) education, (4) baseline social activity, (5) baseline social activity × age, (6) baseline social activity × sex, (7) baseline social activity × education, (8) individually defined time since baseline, (9) time × baseline age, (10) time × sex, (11) time × education, (12) time × baseline social activity, (13) time × baseline social activity × baseline age, (14) time × baseline social activity × sex, (15) time × baseline social activity × education, (16) change in social activity from baseline (activity change), (17) social activity change × baseline age, (18) social activity change × sex, and (19) social activity change × education. However, several terms were not significant for most of the studies and outcomes and so were trimmed to facilitate model interpretation. This process eliminated 7 of the 19 terms, first the 3-way interactions were eliminated, then the interactions with change in social activity. Last, the baseline social activity by sex interaction was dropped. This resulted in a 12-term final model, presented in Table 5 for separate cognitive constructs of reasoning, memory, semantic knowledge, and fluency.

## 3. Results

Significant between person age differences were seen at the first occasion of measurement for all memory, reasoning, and fluency tests, with older adults performing less well than their younger counterparts (all $P < .01$). Semantic knowledge results were less consistent, with SLS showing no age differences, $b = 0.02$, $P = .35$, LBLS and OCTO-Twin suggesting the older individuals score worse, $b = -0.28$, $P < .01$, and $b = -0.55$, $P < .01$, respectively, and VLS finding that older individuals performed slightly better, $b = 0.08$, $P = .02$.

At baseline, individuals with more years of education had significantly higher cognitive performance on all tasks, across all studies (all $P < .01$). Women at the mean baseline age had higher memory scores than did same aged men across all studies (all $P < .01$). LBLS and SLS women scored higher than men on all measures (reasoning: $P = .02$ and $P < .01$; fluency: both $P < .01$), except for LBLS semantic knowledge ($P = .13$, SLS $P = .02$). OCTO-Twin women had significantly lower Information scores, considered semantic knowledge, at baseline than OCTO-Twin men ($b = -4.20$, $P < .01$).

Significant within person declines were seen over time in study in all cognitive abilities and all studies (all $P$s $< .01$). A significant time ∗ age interaction indicated that within each sample, those who were older at baseline declined

Table 5: Mixed model results of four longitudinal studies.

| | OCTO-Twin | | | LBLS | | | SLS | | | VLS | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* |
| Reasoning | | | | | | | | | | | | |
| Intercept | 10.89 | 0.55 | <.01 | 21.43 | 0.53 | <.01 | 14.65 | 0.17 | <.01 | 9.52 | 0.59 | <.01 |
| Age | −0.33 | 0.12 | .01 | −0.62 | 0.04 | <.01 | −0.35 | 0.01 | <.01 | −0.26 | 0.02 | <.01 |
| Female | 0.68 | 0.67 | .31 | 1.86 | 0.77 | .02 | 1.57 | 0.24 | <.01 | −0.15 | 0.31 | .62 |
| Education | 0.56 | 0.13 | <.01 | 1.30 | 0.13 | <.01 | 0.52 | 0.04 | <.01 | 0.32 | 0.05 | <.01 |
| Social activity | 1.01 | 0.28 | <.01 | 0.08 | 0.25 | .74 | 0.11 | 0.08 | .14 | 0.05 | 0.02 | .03 |
| Age × social activity | −0.02 | 0.11 | .83 | 0.08 | 0.03 | <.01 | 0.01 | 0.01 | .15 | 0.00 | 0.00 | .40 |
| Education × social activity | 0.04 | 0.11 | .71 | −0.04 | 0.08 | .67 | −0.03 | 0.03 | .26 | −0.01 | 0.01 | .69 |
| Slope | −0.44 | 0.08 | <.01 | −0.50 | 0.08 | <.01 | −0.25 | 0.02 | <.01 | −0.25 | 0.03 | <.01 |
| Age | −0.02 | 0.02 | .28 | −0.03 | 0.01 | <.01 | −0.01 | 0.00 | <.01 | −0.01 | 0.00 | <.01 |
| Female | 0.08 | 0.09 | .42 | 0.08 | 0.11 | .48 | 0.01 | 0.02 | .51 | 0.01 | 0.03 | .76 |
| Education | 0.01 | 0.02 | .56 | −0.05 | 0.02 | <.01 | −0.01 | 0.00 | .11 | −0.01 | 0.00 | .08 |
| Social activity | 0.06 | 0.05 | .24 | 0.04 | 0.04 | .30 | 0.02 | 0.01 | .02 | 0.00 | 0.00 | .44 |
| Social activity change | 0.65 | 0.15 | <.01 | 0.04 | 0.17 | .83 | 0.13 | 0.06 | .04 | 0.03 | 0.00 | .02 |
| Fluency | | | | | | | | | | | | |
| Intercept | | | | 31.01 | 0.61 | <.01 | 36.11 | 0.44 | <.01 | 11.5 | 0.56 | <.01 |
| Age | | | | −0.30 | 0.05 | <.01 | −0.34 | 0.04 | <.01 | −0.10 | 0.03 | <.01 |
| Female | | | | 3.39 | 0.88 | <.01 | 3.36 | 0.60 | <.01 | 0.51 | 0.36 | .16 |
| Education | | | | 1.05 | 0.15 | <.01 | 1.31 | 0.11 | <.01 | 0.63 | 0.05 | <.01 |
| Social activity | | | | 0.99 | 0.29 | <.01 | 0.24 | 0.19 | .20 | 0.04 | 0.03 | .12 |
| Age × social activity | | | | 0.03 | 0.03 | .40 | 0.00 | 0.02 | .89 | −0.01 | 0.01 | .29 |
| Education × social activity | | | | −0.11 | 0.10 | .24 | 0.04 | 0.07 | .59 | −0.01 | 0.01 | .07 |
| Slope | | | | −0.24 | 0.11 | .02 | −0.43 | 0.04 | <.01 | −0.12 | 0.03 | <.01 |
| Age | | | | −0.03 | 0.01 | <.01 | −0.02 | 0.00 | <.01 | −0.01 | 0.01 | <.01 |
| Female | | | | −0.20 | 0.15 | .18 | 0.11 | 0.05 | .02 | 0.06 | 0.04 | .16 |
| Education | | | | −0.01 | 0.03 | .65 | −0.01 | 0.01 | .15 | −0.01 | 0.01 | .74 |
| Social activity | | | | 0.07 | 0.05 | .15 | 0.02 | 0.02 | .26 | 0.01 | 0.01 | .83 |
| Social activity change | | | | 0.73 | 0.25 | <.01 | 0.18 | 0.15 | .21 | 0.06 | 0.02 | <.01 |
| Memory | | | | | | | | | | | | |
| Intercept | 8.70 | 0.32 | <.01 | 10.80 | 0.20 | <.01 | 11.56 | 0.13 | <.01 | 17.28 | 0.41 | <.01 |
| Age | −0.20 | 0.06 | <.01 | −0.19 | 0.02 | <.01 | −0.18 | 0.01 | <.01 | −0.19 | 0.02 | <.01 |
| Female | 0.99 | 0.39 | .01 | 1.50 | 0.28 | <.01 | 1.59 | 0.17 | <.01 | 1.45 | 0.27 | <.01 |
| Education | 0.34 | 0.07 | <.01 | 0.29 | 0.05 | <.01 | 0.32 | 0.03 | <.01 | 0.31 | 0.04 | <.01 |
| Social activity | 0.34 | 0.07 | <.01 | 0.00 | 0.09 | .98 | 0.14 | 0.06 | .01 | 0.06 | 0.02 | <.01 |
| Age × social activity | −0.09 | 0.06 | .10 | 0.01 | 0.0 | .61 | 0.00 | 0.01 | .51 | −0.01 | 0.01 | .95 |
| Education × social activity | 0.01 | 0.06 | .91 | −0.02 | 0.03 | .57 | −0.02 | 0.02 | .18 | −0.01 | 0.01 | .19 |
| Slope | −0.26 | 0.07 | <.01 | −0.18 | 0.05 | <.01 | −0.17 | 0.01 | <.01 | −0.27 | 0.03 | <.01 |
| Age | 0.00 | 0.02 | .97 | 0.00 | 0.01 | .46 | −0.01 | 0.00 | <.01 | −0.01 | 0.01 | <.01 |
| Female | 0.05 | 0.08 | .55 | −0.03 | 0.07 | .64 | 0.02 | 0.02 | .15 | −0.02 | 0.03 | .56 |
| Education | −0.01 | 0.02 | .73 | 0.01 | 0.01 | .40 | 0.00 | 0.00 | .58 | −0.01 | 0.01 | .15 |
| Social activity | 0.07 | 0.04 | .07 | 0.03 | 0.02 | .15 | 0.01 | 0.01 | .37 | 0.01 | 0.01 | .25 |
| Social activity change | 0.47 | 0.11 | <.01 | 0.11 | 0.10 | .30 | 0.12 | 0.06 | .03 | 0.06 | 0.01 | <.01 |
| Semantic knowledge | | | | | | | | | | | | |
| Intercept | 30.49 | 0.86 | <.01 | 38.19 | 0.54 | <.01 | 24.08 | 0.22 | <.01 | 43.77 | 0.71 | <.01 |
| Age | −0.55 | 0.17 | <.01 | −0.28 | 0.04 | <.01 | 0.02 | 0.02 | .35 | 0.08 | 0.03 | .02 |
| Female | −4.20 | 1.05 | <.01 | 1.19 | 0.78 | .13 | 0.70 | 0.30 | .02 | −0.01 | 0.46 | .99 |
| Education | 1.43 | 0.19 | <.01 | 1.03 | 0.14 | <.01 | 1.12 | 0.05 | <.01 | 0.77 | 0.07 | <.01 |
| Social activity | 0.87 | 0.40 | .03 | 0.10 | 0.25 | .70 | −0.22 | 0.10 | .02 | 0.02 | 0.03 | .63 |
| Age × social activity | −0.10 | 0.15 | .47 | 0.08 | 0.03 | <.01 | −0.01 | 0.01 | .61 | 0.01 | 0.01 | .77 |
| Education × social activity | 0.03 | 0.17 | .84 | −0.06 | 0.09 | .50 | −0.05 | 0.03 | .15 | 0.01 | 0.01 | .61 |

Table 5: Continued.

| | OCTO-Twin | | | LBLS | | | SLS | | | VLS | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* | *b* | SE | *P* |
| Slope | −0.85 | 0.11 | <.01 | −0.46 | 0.08 | <.01 | −0.12 | 0.01 | <.01 | −0.16 | 0.03 | <.01 |
| Age | −0.05 | 0.02 | .03 | −0.04 | 0.01 | <.01 | −0.01 | 0.00 | <.01 | −0.01 | 0.01 | <.01 |
| Female | 0.19 | 0.13 | .15 | 0.12 | 0.12 | .30 | 0.06 | 0.02 | <.01 | 0.03 | 0.04 | .42 |
| Education | 0.03 | 0.03 | .29 | −0.02 | 0.02 | .32 | 0.00 | 0.00 | .78 | −0.01 | 0.01 | .18 |
| Social activity | 0.11 | 0.07 | .12 | 0.01 | 0.04 | .95 | 0.01 | 0.01 | .01 | −0.01 | 0.01 | .40 |
| Social activity change | 0.86 | 0.19 | <.01 | 0.17 | 0.17 | .33 | 0.08 | 0.06 | .13 | −0.01 | 0.01 | .93 |

Values represent model coefficients and their standard error. Across all studies, time was measured in years since baseline visit and activity change was entered as a time-varying covariate. All other variables represent baseline measurements alone, in interaction with one another, or in interaction with time.

significantly faster than the younger participants on all VLS, SLS, and LBLS measures except LBLS immediate memory. Except for the Information test, evidence for differential decline in older individuals was not seen in OCTO-Twin, which has a much narrower age range.

Women showed less decline than men in the SLS data only, and only for the fluency and semantic knowledge measures. Evidence for differential decline related to education was seen only for the LBLS reasoning measure.

Higher social activity levels at baseline, for individuals of average age and education, were associated with higher scores on reasoning within the VLS and OCTO-Twin studies, $b = 0.05$, $P = .03$, and $b = 1.01$, $P < .01$, respectively. The most consistent finding was that individuals with higher social activity levels at baseline also had higher memory scores. This was true for the SLS, VLS, and OCTO-Twin studies, $b = 0.14$, $P = .01$, $b = 0.06$, $P < .01$, $b = 0.34$, $P < .01$, respectively. Baseline social activity was also positively related to fluency in the LBLS (though the same measure was not significant in SLS sample). Social activity at baseline and semantic knowledge was positively related in the OCTO-Twin sample (operationalized as information; $b = 0.87$, $P = .03$), but negatively related in the SLS sample (operationalized as vocabulary; $b = -0.22$, $P = .02$). The OCTO-Twin sample was the only one where all cognitive measures considered had a positive association with baseline social activity levels.

The Baseline Age ∗ Social Activity interaction terms were significant and positive for LBLS reasoning ($b = 0.08$, $P < .01$) and semantic knowledge ($b = 0.08$, $P < .01$), indicating a stronger effect of social activity for older participants than for younger participants. However, the interaction of age and social activity was not significant for any other studies or cognitive measures ($Ps > .05$). The interaction between education and social activity at baseline was not significantly associated with any cognitive measure within any of the samples.

In terms of within person age changes, social activity at baseline was significantly related to the slope of semantic knowledge for SLS participants such that higher social activity at baseline was associated with less semantic knowledge decline ($P = .01$). There were no other significant relationships between social activity at baseline and rate of change for any cognitive measure within any of the samples (all $P > .05$).

In examining associations with change in social activity as a time-varying covariate in each of the models, several significant relationships were found. A reported increase in social activity was positively associated with performance on the fluency measures in all studies except SLS (LBLS $P < .01$, VLS $P < .01$, SLS $P = .21$), such that individuals who increased their level of social activity from their own baseline level exhibited higher occasion-specific fluency performance relative to their expected linear trajectory over time. In VLS and SLS, a significant relationship was also found between change in social activity and the reasoning (VLS $P = .02$, SLS $P = .04$) and memory (VLS $P < .01$, SLS $P = .03$) measure, indicating that participants who increased their social activity level also scored higher relative to their expected trajectory on the reasoning or memory measure. Changes in social activity were related to all cognitive measures in the OCTO-Twin study (all $P < .05$), such that OCTO-Twin participants who increased their social activity level from baseline had higher occasion-specific cognitive scores relative to their own linear trajectory in all domains tested.

## 4. Discussion

Comparing results of the same statistical model across four longitudinal studies of aging, we observed relatively few consistent associations between social activity and cognitive functioning. Looking at within person change in social activity and the four cognitive measures, the most consistent finding was an association with fluency in two of the three studies measuring it, after adjusting for linear effects of time and other covariates. Change in social activity was associated with memory performance in only half of the four studies (SLS and VLS). In only one study, OCTO-Twin, change in social activity was significantly related to performance in all three of the cognitive domains considered (fluency measure not available). The OCTO-Twin sample was the oldest and had the narrowest range of ages. Social activity in the OCTO-Twin study was defined by the number of people with whom participants had contact, whereas the other studies included a range of activities with a social component. Given that within person decreases in performance were seen across all cognitive measures in all studies, the positive relationships generally represent attenuated decline, rather than improvement in cognitive performance.

The use of within person change in social activity as a time-varying predictor of cognitive function is somewhat unique. However, in another study examining the temporal relations of social activity change and cognitive function, Small and colleagues [20] found significant coupling of social activity change and three cognitive domains: semantic decision speed (similar to our fluency measure), episodic memory, and semantic memory. They, however, found greater support for models where cognitive measures predicted changes in social activity levels, than the reverse.

There was little evidence that initial levels of social activity were related to within person rate of decline in cognitive function. Although higher initial levels of social activity were associated with less decline on the SLS semantic knowledge measure, this was not evident in any other samples. SLS has the widest interval between measurements and so correspondingly greater attrition between waves (though a similar yearly rate), but this does not suggest an obvious reason for the difference. The findings from the other studies are consistent with McGue and Christensen [19], who found that social activity at the first assessment was related to initial level of cognitive function but not change in cognitive function. However, other groups have found that social activity levels are associated with both baseline cognitive function and a reduced rate of decline over time [10]. Contrary to our findings, but similarly examining specific cognitive domains, Ertel et al. [18] found that social integration was related to a slower rate of memory decline. We did not include a composite measure of general cognitive function, but our results, and the results of others who have examined specific facets of cognition, suggest that it is important to examine cognitive domains separately.

Several between person differences were found. Specifically, individuals with higher initial levels of social activity performed better on the memory measures in three of the four samples. Interestingly, the sample that did not show the effect was the LBLS, which used the same measure as the SLS study. This suggests the discrepancy is not a function of different memory measures being used, or how social activity was characterized in the study. It is perhaps related to differences in samples, although both were similar in average years of education and were American, although from different regions. It is possible that how well a measure captures social activity varies by community. This, and the accessibility of the activities, may influence the association with cognitive function. However, such differences would not likely be specific to memory performance. The mean age of LBLS participants was about six years older and the first wave of LBLS assessment included in the present study was conducted ten years later than the first assessment of the SLS. The age differences are not an obvious explanation, because the mean age of LBLS participants is only slightly older than SLS and VLS participants and is nearly ten years younger than OCTO-Twin participants. The LBLS is the only study for which the majority of participants are not female, though this difference is slim (49% female in the LBLS versus 52% in SLS at baseline). It is possible another factor, such as attrition, is playing a role. The LBLS does have the highest yearly rate of attrition (17% versus 10%, 7%, and 8%), although the loss at each measurement wave is similar to that of SLS. It is unclear how this would affect the association between baseline social activity and memory performance; however, particularly considering that the mean social activity and memory measure scores for the LBLS and SLS were similar. It would be interesting in future work to consider general health and its age gradient in each of the studies. The lack of obvious reasons for discrepant findings, however, supports the importance of considering the reproducibility of results in coordinated, rather than pooled, analyses.

Social integration has been posited to influence general health through multiple pathways that may overlap with those influencing cognition [40]. Unfortunately, our findings do not strongly suggest that increased engagement in social activities confers immediate benefit in terms of cognitive function. Nor do they suggest that social participation reduces risk of cognitive decline in any domain apart from fluency. The cognitive reserve hypothesis suggests that, over time, “reserve” can be built up through stimulating activities and that individuals with high reserve can withstand more physiological deterioration before cognitive decline is observable [6]. That social participation does not reduce the risk of cognitive decline in a broad range of measures suggests that it is not conferring “reserve.”

One possible mechanism through which social engagement and cognitive function are related may be the cognitively stimulating nature of social activities [20]. The cognitive training literature has found that training in specific tasks (e.g., memory tasks) does not necessarily transfer to other cognitive domains [3]. This may be similarly true of social activity participation, whereby a relationship is only seen in cognitive domains that are being challenged by the social activity. Social interactions do typically involve verbal communication, and thus fluency, likely specifically verbal fluency, may be the cognitive domain most similar to our participants’ social activities.

Discrepancies in which activities are considered social may contribute to the lack of consistent association between social activity and cognitive function. For example, some activities (e.g., card games) may generally be more cognitively demanding than others (e.g., visits from family members), or primarily tax different cognitive skills, but this is likely to differ across individuals and situations. Although plausible, further research would need to confirm the validity of such hypothesis. In the context of physical health, others [40] have suggested that different social factors (e.g., social influence, social engagement, and social support) may act primarily through different behavioral, psychological, and physiological pathways. Similarly, cognitive function may be differentially influenced depending on the particular combination of social factors and pathways. In this way, how social activity is conceptualized and measured may be related to the mechanistic pathway and thus differentially related to various domains of cognitive function. These effects may have contributed to the discrepancies between OCTO-Twin and the other three studies in the current analysis, as OCTO-Twin focused on frequency of contact with people as the social activity measure, whereas the other three encompassed a variety of activities. However, the lack of consistency between the two studies employing the same measures suggests that conceptualization of social activity does not fully explain the findings. A clue to the source of inconsistency across LBLS and SLS may be the very small average change in the LBLS social activities measure, though its variance is comparable to those of SLS and OCTO-Twin. The association between cognition and social activity in LBLS in particular also seems to vary by age more than in the other studies.

A considerable strength of our analysis is the replication of the models across four longitudinal studies from geographically separate regions. This limits the possibility of spurious findings taking on undue importance and provides an opportunity to examine consistencies and inconsistencies between sample groups.

In terms of potential methodological limitations, Hertzog et al. ([41] for slope covariances; [42] for variance components) suggest that the power to detect correlated change is extremely low. However, analysis of longitudinal studies on aging, including those used in the current paper, has consistently reported statistically significant variances and covariances in rates of change in cognitive outcomes ([43–54], for summary see [55]). In addition, the tests used by Hertzog et al. are based on significance tests for variance components whereas change was evaluated in our paper by examining fixed effects which will generally have greater power [56]. Lending support to the argument that analyses in the current paper were adequately powered are the findings of significant associations between the identical set of cognitive outcomes in these same studies and physical and cognitive activities [57, 58].

Another limitation to our analysis is that while the study samples were restricted to initially healthy older adults, efforts were not made to exclude individuals who developed dementia over the course of the study periods (dementia diagnosis was available only in the OCTO-Twin study). We cannot assume that any protective effects of social activity on cognitive function would be equivalent across healthy and dementing older adults. Including individuals whose cognitive decline may have been driven by the dementia process may impact the associations between social activity and cognitive function over time in nondementing individuals, and this may also contribute to inconsistencies in the literature.

Finally, it is difficult to rule out the possibility that individuals decrease their social activities because their declining cognitive abilities make it more difficult for them to maintain social ties. The difficulty of determining the directionality of the relationship has been well acknowledged in the literature and it is similarly difficult to determine causal pathways in the current analysis [4, 5, 10]. Some attempts have been made to determine the most likely direction of the relationship, but the evidence is limited [20]. The longitudinal nature of the studies considered here, and allowing social activity to vary across time, have narrowed the temporal distance between the social activity and cognitive performance, at least partially disentangling whether the relationship is primarily based on historical activity levels or whether the two tracks over time.

Across four studies in three countries, baseline social activity levels failed to predict rate of decline in most cognitive abilities, and changes in social activity were not consistently associated with within person fluctuations in cognitive functioning. Our findings leave little support for the hypothesis that changes in social activity correspond to immediate benefits in cognitive functioning, except perhaps for fluency.

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*Research Article*

# The Role of Lifestyle Behaviors on 20-Year Cognitive Decline

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This study examined the association between smoking, physical activity and dietary choice at 36 and 43 years, and change in these lifestyle behaviors between these ages, and decline in verbal memory and visual search speed between 43 and 60–64 years in 1018 participants from MRC National Survey of Health and Development (NSHD, the British 1946 birth cohort). ANCOVA models were adjusted for sex, social class of origin, childhood cognition, educational attainment, adult social class, and depression; then the lifestyle behaviors were additionally mutually adjusted. Results showed that healthy dietary choice and physical activity were associated, respectively, with slower memory and visual search speed decline over 20 years, with evidence that increasing physical activity was important. Adopting positive health behaviors from early midlife may be beneficial in reducing the rate of cognitive decline and ultimately reducing the risk of dementia.

## 1. Introduction

With an increase in the ageing population, the number of older people affected by cognitive decline and dementia is continually rising, causing a major public health impact on individuals and governments around the world [1]. Despite major progress in understanding the neurobiology of cognitive impairment and dementia, there are still no clear determinants and complete causal models available for explaining risks for this condition [2]. Substantial evidence suggests that certain lifestyle behaviors (particularly smoking, sedentary lifestyle, and poor dietary choices) predict faster cognitive decline [3–5], and higher risk of dementia [6, 7], while physical, mental and social leisure activities are found to be protective [8, 9]. A study of London civil servants [10] highlights that the number and duration of unhealthy behaviors are associated with subsequent cognitive function in later life. Similar findings from the Suwon Longitudinal Aging Study (SLAS) showed that a combination of multiple positive lifestyle behaviors (such as nonsmoking, vegetable consumption, and social activity) was associated with higher cognitive ability [11]. However, since these behaviors tend to cluster [12, 13], the extent to which apparent effects of one behavior are attributable to (i.e., confounded by) another is uncertain.

In addition, relatively little is known about the longitudinal effects of these behaviors on cognitive decline; yet associations among multiple health behaviors place the emphasis on longitudinal studies, since patterns of behaviors tend to develop over decades, with implications for targeted interventions to change the aggregate public health risk [14]. The life course approach to age-related diseases [15, 16] provides an important opportunity to identify the nature and timing of different environmental contributions to neuronal damage and the risk of dementia across life [17]. The present study therefore focuses on behavioral risk in early midlife, at a stage of the life course when people are still more likely to have control over modifiable risk and protective factors for cognitive decline than in later life.

Although clinically significant cognitive decline and the onset of dementia occur in older age (65+ years), it is important to take in consideration early signs of cognitive decline that appear in midlife. This is because conditions such as dementia develop slowly and silently over the preceding decades [18–20]. Neuroimaging also show pathological changes in midlife before the clinical signs of the disease appear [21, 22]. Consistent with this, subtle cognitive decline begins as least as early as the 5th decade [23, 24].

Risk and protective factors for health can exert their most critical influences at different ages [25]. This is acknowledged by the life course approach and the hypothesis that positive lifestyle behaviors such as nonsmoking, being physically active, and choosing healthier diets may protect cognitive functioning and slow cognitive decline in later life. Fratiglioni et al. identified key periods for potential risk and protective factors [25]. Early life seems to be most critical for the development of cognitive reserve (learning and education) [26], when distal adverse influences (such as poor childhood social circumstances) contribute to the risk of adult disease or later life risk of dementia. Lifestyle behaviors, including those that influence cardiovascular and metabolic risk, become more influential in midlife, although some, such as diet and physical activity, track back into childhood [27, 28], whereas mental and physical activity patterns may continue to moderate these risks into later life [29, 30].

The fact that the lifestyle behaviors are modifiable implies that encouraging a healthy lifestyle may prevent or ameliorate cognitive decline and underlying cerebrovascular and cardiovascular risk factors [31]. Such interventions should take into account the relative beneficial effect of each independent behavior as well as their combined and cumulative effect.

*1.1. Present Study.* The aim of the current study was to examine the role of individual and combined lifestyle behaviors (smoking, physical activity, and dietary choice) on a 20-year interval of cognitive decline. We used measures of memory and psychomotor speed over this interval, which are sensitive to decline associated with ageing and neurodegeneration. The repeated measures of lifestyle behaviors at 36 and 43 years were used as predictors of cognitive change from 43 to 60–64 years. In addition to the independent and combined effects of these behaviors, we also examined the cumulative effects of these behaviors across early midlife and the changes in these behaviors from one age to another.

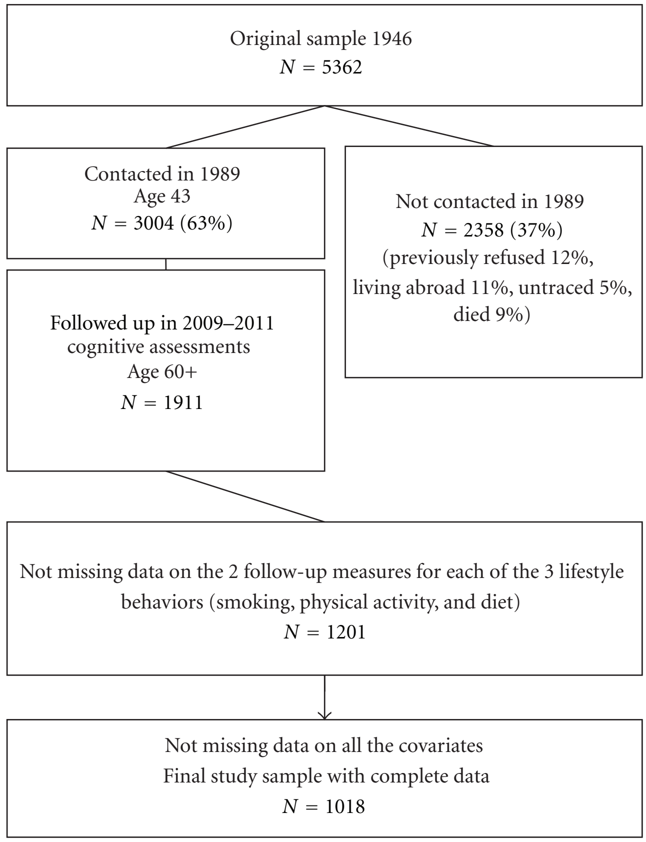


Figure 1: Flow chart of lifestyle behaviors, cognitive functioning and covariates data follow up (considered since baseline cognition-at age 43) in the Medical Research Council National Survey of Health and Development.

## 2. Methods

*2.1. Study Members.* The Medical Research Council National Survey of Health and Development (NSHD) originally consisted of a socially stratified sample of 5362 children born within marriage in one week in March 1946 in England, Scotland, and Wales [32, 33]. This cohort has been followed up prospectively 23 times, from birth onwards. In 1989, when study members were aged 43 years, 3262 were successfully contacted, of whom 3004 have completed both cognitive tests. Of these, 1911 had successfully completed the most recent cognitive assessment, conducted between 2006 and 2011 when survey members were aged 60 to 64 years (henceforth 60+ years). This data collection began with a postal questionnaire sent to the target 3163 sample [33]. This was followed by an invitation to an assessment by trained nurses at one of six clinical research facilities (based in Cardiff, Birmingham, Edinburgh, London (at UCL and St Thomas' hospitals), and Manchester), or, if preferred, at a home visit. This was supplemented by a further questionnaire sent to those who agreed to a clinic or home visit. These questionnaires, along with additional questions asked by the nurses, updated information on general health, household composition, family structure, socioeconomic status, daily function, life events, and lifestyle. Contact was not attempted for 2198 (718 deaths, 567 living abroad, 594 prior refusals, and 320 permanently lost). From the current respondents, a total of 1,018 study members had nonmissing data for all variables incorporated in these analyses (see Figure 1).

*2.2. Ethical Approval.* The study protocol received ethical approval from the Greater Manchester Local Research Ethics Committee for the five English sites; from Scotland Research Ethics Committee for the data collection taking place in Edinburgh. Written informed consent was obtained from the study member at each stage of data collection.

*2.3. Cognitive Function.* Cognitive functioning was measured at 43 and 60+ years using two tests: verbal memory and speed and concentration. The verbal memory test consisted of a 15-item word learning task devised by the NSHD research team. Each word was shown for two seconds. When all 15 words were shown, the study member was asked to write down as many of these as possible, in any order. The total number of words correctly recalled over three identical trials was summed to provide an overall score for short-term verbal memory (maximum score = 45). This was followed by a letter search test (see below), after which an uncued delayed free recall trial was administered.

Speed and concentration were assessed with a letter search task in which participants were required to cross out the letters P and W, randomly embedded within a page of other letters, as quickly as possible within 1 minute. At age 43 years the total number of letters to be searched was 450, and at age 60+ years it was 600. Scores were computed as total number of letters searched.

*2.4. Lifestyle Behaviors.* Data on lifestyle behaviors were extracted from questionnaires, interview-based prospective information, and diet diaries completed in early midlife (36 and 43 years).

*2.5. Smoking.* Interview-based prospective information on cigarette smoking frequency was obtained at age 36 and 43 years. Smoking frequency was categorized at each age as 0 (nonsmoker), 1 to 20 (light smoker), or more than 20 cigarettes per day (heavy smokers).

A midlife smoking score was derived by assigning those classified as nonsmokers a value of 0, those as light smokers a value of 1, and those as heavy smokers a value of 2 at each age (36 and 43 years) and then summing the values for the 2 ages whereby an individual with a midlife smoking score of 0 was categorized as nonsmoker, an individual with a midlife smoking score of 1 to 3 was categorized as moderate smoker, and the remaining individuals were categorized as heavy smokers (sum equal 4).

A score for change in smoking behavior was also derived by assigning those classified as nonsmokers at each age a value of 0; those reporting an increase in smoking a score of 1; those who reported a decrease in smoking a score of 2; those who were constantly moderate or heavy smokers across early midlife a score of 3.

*2.6. Physical Activity.* Physical activity levels were ascertained at ages 36 and 43 years during interviews at the study participants' home. Questions about physical activity at age 36 years were based on the Minnesota leisure time physical activity questionnaire [27, 34]. The questions addressed engagement in sports and recreational activities in the previous month, utilizing a checklist of 27 different leisure time activities. At age 43 years, participation in any sports, vigorous leisure activities, or exercise was reported, although this was based on answers to an open-ended question, rather than the above checklist. However, the monthly frequency of these activities was also reported, enabling a similar categorization to the 36 year measure. At each age, participants were categorized as inactive (reported no participation); moderately active (participated in relevant activities 1–4 times in the previous month at age 36 years, and per month at age 43 years); or most active (participated in relevant activities five or more times in the previous month at age 36 years and per month at age 43 years) [35].

A total physical activity score was derived by assigning those classified as inactive a value of 0, those as moderately active a value of 1, and those as most active a value of 2 at each age (36 and 43 years) and then summing the values for the two ages. This was categorized as inactive (score 0), moderately active (score 1 to 3), and most active (score 4).

A score for change in physical activity behavior, was derived in a similar fashion as for smoking, by assigning those classified as inactive at each age a value of 0; those reporting an increase in activity a score of 1; those who reported a decrease in their physical activity levels a score of 2; those whose physical activity levels were moderate or most active at both ages a score of 3.

*2.7. Dietary Choice.* Dietary intake was assessed by a five-day diary [36] at both 36 and 43 years. All food and drinks consumed both at and away from home were recorded in the diaries, including brand names of food products, food preparation methods, and recipes used. Participants were asked to record the amount eaten in household measures, with guidance notes and photography provided in the diary to assist in estimating portion size [37]. From this information, an overall score representing level of healthy food choice was derived, by summing scores for four separate criteria: (1) consumption of breakfast (a score of 0 representing no consumption to 1 some days and 2 all days); (2) type of milk (from 0 whole only to 3 skim milk only); (3) type of bread (from 0 white only to 4 wholemeal only); (4) number of daily portions of fruit and vegetables (from 0 to maximum 5 portions per day); a dietary reference score representing the percentage of energy from fat, carbohydrates, and protein (scores from 1-highest to 5-lowest percentages less than 30% energy). The total score was subject to a median split (median = 10 at age 36 years and median = 11 at age 43 years; minimum score 0 and maximum 19) to represent low versus high (energy dense/nutrient poor versus healthier) dietary choice. The range of dietary scores varied from a minimum of 5 to a maximum of 19; $M = 10.22$, SD = 1.84 at age 36; $M = 11.42$, SD = 2.27 at age 43).

A midlife dietary choice score was also derived by assigning those classified as making poorer choices for their diet a value of 0 and those making healthier choices a value of 1 at each age (36 and 43 years) and then summing up the values for the 2 ages. Midlife dietary choice was categorized as making poorer (low) choices at both ages (score 0) and making healthier dietary choices (high) at least at one age (score 1 or 2).

A score for change in diet was also derived. Those classified as choosing a low-quality diet at each age were assigned a value of 0; those reporting an increase from a low-quality to a high-quality diet a score of 1; those who changed to a lower-quality diet a score of 2; those who constantly maintain a high-quality diet were assigned a score of 3.

*2.8. Covariates.* Based on previous findings, the following variables were treated as potential confounders: sex; father social class; childhood cognitive ability; educational attainment; midlife household occupational social class and depression [14, 38–40].

*2.9. Occupational Social Class of Origin.* *Occupational social class of origin* was represented by father's social class when participants were aged 11 years, or if this was unknown, at age 4 or 15 years. This was classified as professional managerial intermediate, skilled nonmanual, skilled manual, semi-skilled manual, or unskilled, according to the UK Registrar General's Classification of Occupations [41].

*2.10. Prior Cognitive Ability.* Childhood cognitive ability at age eight years was represented as the sum of four tests of verbal and nonverbal ability devised by the National Foundation for Educational Research [42]. These tests were (1) reading comprehension (selecting appropriate words to complete 35 sentences); (2) word reading (ability to read and pronounce 50 words); (3) vocabulary (ability to explain the meaning of 50 words); (4) picture intelligence, consisting of a 60-item nonverbal reasoning test.

*2.11. Educational Attainment.* The highest educational qualification achieved by age 26 years was dichotomized into those with advanced ("A level", taken during the final year of secondary/high school) or higher (university or equivalent) qualifications, versus those below this level.

*2.12. Occupational Social Class.* Household midlife occupational social class was used at each time of the health behavior (36 or 43 years), or the latest age for longitudinal behavioral measures (see below). This was coded according to the Registrar General (as for social class of origin).

*2.13. Depression and Anxiety Symptoms.* Frequency and severity of common symptoms of depression and anxiety were assessed by the Psychiatric Symptom Frequency scale (PSF) [43] at age 43 years, and with the 28-item General Health Questionnaire (GHQ) [44] at age 60+.

*2.14. Statistical Analyses.* Multivariable ANCOVA models were used to test associations between smoking, physical activity, and diet at each age, entered as categorical variables and cognitive decline, used as continuous variables. First, we tested the association between each lifestyle behavior at 36 and 43 years and change in both cognitive outcomes (verbal memory and letter search speed); then we used the cumulative behavior scores for both these ages; finally we tested associations between change in behaviors between these ages and change in the cognitive outcomes between ages 43 and 60+ years. In order to reduce the effect of regression to the mean and because of the difference in size of the letter search matrix at ages 43 and 60+ years, we used conditional models of change by adjusting cognitive scores at age 60+ years for their corresponding score at 43 years [23]. Positive coefficients represent a slower rate of decline, and negative coefficients represented a faster rate of decline. Model 1 adjusted raw associations for sex (since there was no evidence of sex x lifestyle behavior interactions on the outcomes), social class of origin, prior cognitive ability at age 8 years, educational attainment, occupational class, and symptoms of anxiety and depression. Model 2 included these covariates but additionally tested the specificity of lifestyle behaviors by mutually adjusting each for the other behaviors. For cumulative effects, model 2 was further adjusted for the cumulative scores of the additional behaviour; for change in behaviour from 36 to 43, model 2 was mutually adjusted for the change in other lifestyle behaviours. All analyses were based on the sample with complete data on cognitive tests at the 2 time points, lifestyle behaviors at the 2 time points, and all the selected covariates.

## 3. Results

*3.1. Sample Description and Missing Data.* Participants with missing scores on memory and visual search at age 43 were more likely to be men, to have less than advanced educational attainment, to be in a manual occupation in midlife, and to have lower cognitive capability scores at age 8 years (all $P < 0.001$). A similar pattern was observed for those without cognitive scores at age 60+. Those with missing scores on memory at age 43 had a marginally higher total anxiety and depression score at the same age than those who underwent memory testing ($P = 0.058$). Those who did not complete data on lifestyle behaviors at both 36 and 43 years had lower cognitive scores for both verbal memory ($P < 0.001$) and visual search ($P = 0.076$; $P = 0.010$) at age 43 and 60+, were more likely to belong to a manual occupation of social class of origin ($P < 0.001$), and had less than advanced levels of educational attainment by age 26 years ($P < 0.001$).

Participants included in the current analysis were mostly nonsmokers at either 36 (76.6%) or 43 years (80.1%) and at least moderately active at ages 36 (68.1%), although less so at 43 years (53.2%), but had a similar quality of diet at both 36 and 43 years (55.4% and 51.1%, respectively, were in the lower median split).

Table 1 shows means for the total verbal memory and visual search speed scores at age 60+, by the three lifestyle behaviors (at 36 and 43 years, and the cumulative and change scores for these ages), by sex, father's social class, educational attainment, and midlife social class and depression of the 1018 participants. All three lifestyle behaviors (smoking, physical activity, and diet) at age 36, 43 years, as cumulative scores or change in behavior were strongly associated with verbal memory at age 60+. The effect was monotonic, with those who did not smoke or decreased their level of smoking; those who were most physically active or increased their level of activity or had a healthier or improved diet, having better memory scores at age 60+. For visual search speed at age 60+ the general trend was for slower function with heavy and increased smoking across early midlife; a positive association for high and increased physical activity; a positive association for consistently high and increased diet quality.

*3.2. Association between Lifestyle Behaviors and Memory Decline.* Table 2 shows results for the ANCOVAs for each health behavior (at 36 and 43 years, the cumulative and change scores for these ages) and memory decline from 43 to 60+ years. Trends can be observed for associations

Table 1: Characteristics and mean scores for memory and search speed at age 60+ years, by lifestyle behaviour profiles and dichotomous covariates.

| Variable | $N$ | Memory at age 60+ years | $P$ | Search speed at age 60+ years | $P$ |
|---|---|---|---|---|---|
| Smoking at age: | | | | | |
| 36 years | | | | | |
| Non-smoker | 780 | 25.00 (5.88) | <0.001 | 273.47 (73.13) | 0.002 |
| 1–20 c/day | 200 | 24.18 (6.37) | | 266.7 (69.88) | |
| 20+ cig/day | 38 | 21.23 (7.33) | | 233.26 (59.33) | |
| 43 years | | | | | |
| Non-smoker | 816 | 25.05 (5.95) | <0.001 | 274.45 (72.55) | 0.001 |
| 1–20 c/day | 159 | 23.99 (6.05) | | 258.60 (68.67) | |
| 20+ cig/day | 43 | 20.72 (7.05) | | 242.83 (73.49) | |
| Midlife score | | | | | |
| Non-smoker | 744 | 25.05 (5.90) | <0.001 | 274.51 (73.69) | <0.001 |
| Moderate smoker | 252 | 24.07 (6.30) | | 263.48 (67.50) | |
| Heavy smoker | 22 | 20.18 (7.25) | | 221.81 (59.74) | |
| Change in smoking | | | | | |
| Non-smoker | 744 | 25.05 (5.90) | 0.005 | 274.51 (73.69) | 0.011 |
| Increase | 55 | 22.89 (5.91) | | 254.63 (65.05) | |
| Decrease | 79 | 24.77 (6.51) | | 272.29 (60.10) | |
| Constant med/heavy | 140 | 23.52 (6.60) | | 255.44 (72.33) | |
| Physical activity at age: | | | | | |
| 36 years | | | | | |
| Inactive | 324 | 23.82 (5.83) | <0.001 | 264.87 (72.81) | 0.138 |
| Moderate active | 275 | 24.61 (5.98) | | 270.04 (68.14) | |
| Most active | 419 | 25.44 (6.24) | | 275.49 (74.58) | |
| 43 years | | | | | |
| Inactive | 475 | 23.85 (6.13) | <0.001 | 263.83 (69.38) | <0.001 |
| Moderate active | 251 | 25.15 (6.05) | | 267.10 (69.13) | |
| Most active | 292 | 25.69 (5.84) | | 284.76 (78.01) | |
| Midlife score | | | | | |
| Inactive | 221 | 23.37 (6.01) | <0.001 | 259.08 (74.61) | 0.003 |
| Moderate active | 608 | 24.81 (5.98) | | 270.87 (68.78) | |
| Most active | 189 | 25.90 (6.20) | | 283.43 (79.00) | |
| Change in physical activity: | | | | | |
| Inactive | 221 | 23.37 (6.01) | <0.001 | 259.08 (74.61) | 0.003 |
| Increase | 164 | 25.03 (5.35) | | 282.39 (74.40) | |
| Decrease | 354 | 24.61 (6.30) | | 266.84 (66.91) | |
| Constant active | 279 | 25.68 (6.08) | | 277.72 (74.71) | |
| Diet at age: | | | | | |
| 36 years | | | | | |
| Low quality | 564 | 24.01 (6.19) | <0.001 | 267.26 (69.12) | 0.096 |
| High quality | 454 | 25.55 (5.84) | | 274.85 (76.14) | |
| 43 years | | | | | |
| Low quality | 521 | 23.72 (6.13) | <0.001 | 267.24 (69.30) | 0.124 |
| High quality | 497 | 25.72 (5.86) | | 274.21 (75.41) | |
| Midlife score | | | | | |
| Low quality | 234 | 22.51 (5.90) | <0.001 | 260.02 (67.96) | 0.010 |
| High quality | 784 | 25.34 (5.99) | | 273.81 (73.41) | |
| Change in diet: | | | | | |
| Constant low quality | 234 | 22.55 (5.90) | <0.001 | 260.02 (67.96) | 0.022 |
| Increase | 330 | 25.06 (6.18) | | 272.39 (69.57) | |
| Decrease | 94 | 23.98 (5.44) | | 263.80 (71.44) | |
| Constant high | 360 | 25.96 (5.88) | | 277.73 (77.16) | |

Table 1: Continued.

| Variable | $N$ | Memory at age 60+ years | $P$ | Search speed at age 60+ years | $P$ |
|---|---|---|---|---|---|
| Sex: | | | | | |
| Male | 490 | 23.72 (5.94) | <0.001 | 265.36 (71.84) | 0.024 |
| Female | 528 | 25.61 (6.07) | | 275.54 (72.63) | |
| Father social class | | | | | |
| Non-manual | 507 | 26.28 (5.90) | <0.001 | 278.69 (75.64) | <0.001 |
| Manual | 511 | 23.12 (5.84) | | 262.66 (68.16) | |
| Education: | | | | | |
| <advanced | 567 | 22.77 (5.66) | <0.001 | 263.03 (70.09) | <0.001 |
| ≥advanced | 451 | 27.12 (5.71) | | 280.21 (74.17) | |
| Midlife social class at age: | | | | | |
| 36 years | | | | | |
| Non-manual | 617 | 26.24 (5.79) | <0.001 | 280.36 (71.29) | <0.001 |
| Manual | 401 | 22.33 (5.75) | | 255.69 (71.62) | |
| 43 years | | | | | |
| Non-manual | 696 | 26.08 (5.79) | <0.001 | 276.31 (71.73) | <0.001 |
| Manual | 322 | 21.72 (5.60) | | 258.38 (72.42) | |
| Depression at age: | | | | | |
| 43 years | | | | | |
| No symptoms | 966 | 24.80 (6.05) | 0.036 | 271.08 (72.92) | 0.403 |
| Depressive symptoms | 52 | 22.98 (6.47) | | 262.46 (61.78) | |
| 60+ years | | | | | |
| No symptoms | 805 | 24.85 (6.09) | 0.194 | 270.03 (73.61) | 0.531 |
| Depressive symptoms | 171 | 24.19 (5.74) | | 273.87 (69.23) | |

between heavy smoking at age 43 and for increase in smoking consumption and faster memory decline at all stages of model adjustment, but these trends were not significant at the $\alpha = 0.05$ level. Directions of associations between physical activity and memory decline were inconsistent across the various categories of this behavior, but none were significant. On the other hand a consistently healthy dietary choice at 36 and 43 years was associated with slower memory decline, although none of the dietary change categories were associated with this outcome.

*3.3. Association between Lifestyle Behaviors and Visual Search Speed Decline.* Table 3 shows results for the ANCOVAs for each health behavior (at 36 and 43 years, and the cumulative and change scores for these ages) and decline in visual search speed from 43 to 60+ years. Heavy smoking at 43 years was associated with faster decline in search speed compared to nonsmokers after adjustment for the covariates in Model 1, but not at 36 years or at both these ages (the latter an effect of reduced statistic power) and not at 43 years after mutual adjustment for the other health behaviors. Nor were there associations between change in smoking and this outcome. On the other hand high physical activity at 43 years was associated with slower search speed decline, after full adjustment. This was also the case for those most active at both 36 and 43 years and for those who increased their level of activity between these ages. There were no associations at the $\alpha = 0.05$ level between any measure of dietary choice and rate of search speed decline.

## 4. Discussion

The principal aim of this study was to test associations between lifestyle behaviors in early midlife and cognitive decline over 20 years. Key findings were that a consistently healthy dietary choice was associated with slower memory decline, and that consistently high or increasing physical activity from early midlife to midlife was associated with slower visual search speed decline, independently of each other lifestyle behavior and of social class of origin, childhood cognition, educational attainment, adult social class, and symptoms of anxiety and depression. Smoking was not associated with either cognitive outcome. It should be noted that the current findings for dietary choice and physical activity were not always consistent at different ages across midlife, compared to effects of the cumulative scores and change in behavior between the 2 time points. It will be important to seek replication elsewhere before these findings can be treated as authoritative.

*4.1. Strengths and Limitations.* Strengths of this study include use of a nationally representative sample; availability of a wide range of prospectively-obtained potential confounders, including childhood cognition to rule out selection by prior ability; a detailed assessment of lifestyle behaviors in midlife, including 5-day diet diaries; estimation of cumulative and change effects with two measures of health behaviors; availability of cognitive outcomes that are age and morbidity sensitive [45, 46]; a 20-year interval for capturing decline in

Table 2: Regression coefficients (95% confidence intervals) representing rate of decline in verbal memory from 43 to 60+ years per level increase in each health behavior at 36 and 43 years and per cumulative and change in health behavior scores.

| | *N* (%) | Verbal memory decline 43 to 60+ (95% CI) Model 1 | Model 2 |
|---|---|---|---|
| Smoking at age: | | | |
| 36 y | | | |
| Non-smoking | 780 (76.6) | 0.00 | 0.00 |
| 1–20 c/day | 200 (19.6) | −0.16 (−0.85, 0.53) | −0.12 (−0.81, 0.57) |
| 20+ cig/day | 38 (3.7) | −0.22 (−1.67, 1.22) | −0.17 (−1.62, 1.28) |
| *P* value | | 0.610 | 0.701 |
| 43 y | | | |
| Non-smoking | 816 (80.1) | 0.00 | 0.00 |
| 1–20 c/day | 159 (15.6) | −0.08 (−0.83, 0.67) | −0.07 (−0.83, 0.69) |
| 20+ cig/day | 43 (4.2) | −1.38 (−2.75, −0.01) | −1.24 (−2.61, 0.11) |
| *P* value | | 0.124 | 0.165 |
| Midlife score: | | | |
| Non-smoker | 744 (73.0) | 0.00 | 0.00 |
| Moderate smoker | 252 (24.7) | −0.20 (−0.83, 0.43) | −0.12 (−0.76, 0.51) |
| Heavy smokers | 22 (2.1) | −0.22 (−2.10, 1.66) | −0.01 (−1.90, 1.87) |
| *P* value | | 0.535 | 0.750 |
| Change in smoking: | | | |
| Non-smoker | 744 (73.0) | 0.00 | 0.00 |
| Increase | 55 (5.4) | −1.11 (−2.32, 0.09) | −1.00 (−2.21, 0.21) |
| Decrease | 79 (7.7) | 0.10 (−0.91, 1.12) | 0.09 (−0.92, 1.11) |
| Constant med/heavy | 140 (13.7) | −0.03 (−0.83, 0.77) | 0.04 (−0.78, 0.86) |
| *P* value | | 0.363 | 0.473 |
| Physical activity at age: | | | |
| 36 y | | | |
| Inactive | 324 (31.8) | 0.00 | 0.00 |
| Moderately active | 275 (27.0) | −0.06 (−0.76, 0.64) | −0.07 (−0.78, 0.63) |
| Most active | 419 (41.1) | 0.21 (−0.42, 0.86) | 0.17 (−0.47, 0.82) |
| *P* value | | 0.484 | 0.571 |
| 43 y | | | |
| Inactive | 475 (46.6) | 0.00 | 0.00 |
| Moderately active | 251 (24.6) | 0.06 (−0.61, 0.75) | 0.02 (−0.65, 0.71) |
| Most active | 292 (28.6) | −0.06 (−0.72, 0.59) | −0.12 (−0.79, 0.54) |
| *P* value | | 0.878 | 0.731 |
| Midlife score: | | | |
| Inactive | 221 (21.7) | 0.00 | 0.00 |
| Moderate | 608 (59.7) | −0.13 (−0.82, 0.54) | −0.23 (−0.91, 0.45) |
| Most active | 189 (18.5) | −0.16 (−1.05, 0.71) | −0.31 (−1.20, 0.56) |
| *P* value | | 0.697 | 0.472 |
| Change in activity: | | | |
| Inactive | 221 (21.7) | 0.00 | 0.00 |
| Increase | 164 (16.1) | −0.35 (−1.25, 0.54) | −0.47 (−1.37, 0.43) |
| Decrease | 354 (34.7) | −0.10 (−0.84, 0.63) | −0.18 (−0.92, 0.55) |
| Constant mod/active | 279 (27.4) | −0.06 (−0.87, 0.73) | −0.17 (−0.98, 0.63) |
| *P* value | | 0.871 | 0.768 |
| Diet at age: | | | |
| 36 y | | | |
| Low-quality diet | 564 (55.4) | 0.00 | 0.00 |
| High-quality diet | 454 (44.6) | 0.38 (−0.17, 0.93) | 0.35 (−0.20, 0.91) |
| *P* value | | 0.176 | 0.212 |
| 43 y | | | |
| Low-quality diet | 521 (51.1) | 0.00 | 0.00 |
| High-quality diet | 497 (48.8) | 0.20 (−0.34, 0.75) | 0.17 (−0.38, 0.73) |
| *P* value | | 0.468 | 0.549 |

Table 2: Continued.

| | $N$ (%) | Verbal memory decline 43 to 60+ (95% CI) Model 1 | Model 2 |
|---|---|---|---|
| Midlife score: | | | |
| Low-quality diet | 234 (22.9) | 0.00 | 0.00 |
| High-quality diet | 784 (77.0) | 0.71 (0.04, 1.38) | 0.70 (0.02, 1.38) |
| $P$ value | | 0.037 | 0.043 |
| Change in diet: | | | |
| Low-quality | 234 (22.9) | 0.00 | 0.00 |
| Increase in quality | 330 (32.4) | 0.65 (−0.08, 1.40) | 0.65 (−0.10, 1.41) |
| Decrease in quality | 94 (9.2) | 0.95 (−0.09, 2.00) | 0.91 (−0.14, 1.97) |
| Constant high-quality | 360 (35.3) | 0.78 (0.02, 1.53) | 0.76 (0.00, 1.54) |
| $P$ value | | 0.146 | 0.180 |

Model 1: model adjusted for sex, childhood social class, childhood cognition at age 8, SEP (own occupation and education), and depression.
Model 2: model 1 plus other lifestyle behaviors.

these measures upto an age when decline may begin to have functional consequences. In addition, while there are many reports examining associations with single lifestyle behaviors [47–49], very little work has focused on the combined influence of these behaviors on cognitive functioning [10, 11] and none at all to our knowledge on cognitive decline. Furthermore, we believe that the long interval between repeat administrations of the cognitive tests would have minimized potential practice effects.

We should also highlight a number of limitations. First, there was a disproportional loss of those who were less advantaged, in terms of lower childhood cognitive ability, education, and SES, although we have no reason to suspect that this affected the pattern of results observed. Second, all information on lifestyle behaviors was dependent on self-report and was not validated by independent measures, for example, cotinine in the case of smoking. Third, there is the possibility of regression to the mean effect when analyzing cognitive ability data over a long period of time, for example, one may assume that some of those who had high cognitive ability score at age 43 may have lower scores at age 63 years and vice versa. We have tried to reduce this effect by using the conditional model of change [50].

In regard to previous findings in NSHD, the inverse association between physical activity and memory decline from 43 to 53 years reported by Richards et al. [51] was not seen here for 20-year decline. This may be because the previous study had additional specificity through adjusting for non-physical spare-time activities, which would have been too cumbersome in the context of multiple lifestyle behaviors in the present study, or because of the longer period of cognitive change. The associations between physical activity and slower decline in visual search speed and between healthy dietary choice and memory are new findings and were not previously tested in this cohort; in the former case physical activity was not investigated in relation to search speed in the previous study; in the latter case midlife cognition has not previously been studied in relation to diet in this cohort. On the other hand the associations between heavy smoking at age 43 and faster memory decline previously reported between ages 43 and 53 years [40] were not replicated here with the 20-year period of cognitive change from 43 to 60+. The loss of the cumulative midlife heavy smoking-memory decline association may be due low statistical power resulting from the relatively high odds of morbidity and premature mortality in this subgroup (135 study members smoking more than 20 cigarettes per day at age 43 were represented in the previous study, compared to 22 in the present study).

In relation to other cohorts, Sabia et al. found an effect of sex on the association between smoking and cognitive decline in a study of London civil servants. Their results showed that men who smoked showed faster decline than nonsmoking men over a 10-year period, after adjusting for the effects of heart disease, stroke, and lung function on mental abilities, while for women there were no differences in cognitive scores over the same time period. This could be related to a lower number of female participants in contrast to males in the Whitehall II study [52]. In relation to physical activity, leisure-time physical activity at least twice a week in midlife was associated with reduced risk of memory decline in the Cardiovascular Risk Factors, Aging and Incidence of Dementia (CAIDE) study after adjustment for age, sex, education, follow-up time, locomotor disorders, APOE genotype, vascular disorders, smoking, and alcohol consumption [53]. Similarly, in The Mayo Clinic Study of Aging, moderate exercise in midlife or late life was associated with reduced odds of Mild Cognitive Impairment (MCI) [54]. In contrast, results from the Chicago Health and Aging Project reported that physical activity conducted within 2 weeks of the date of baseline cognitive assessment was not associated with risk of cognitive decline in an older population [55].

Our finding that maintained healthy dietary choice was associated with a slower rate of memory decline is consistent with the results of a recent systematic review, which highlighted that a diet high in saturated fat represents an increased risk of cognitive decline and subsequent dementia [6]. The emphasis on identifying specific nutrients associated with cognitive ability in later life, such as antioxidants (vitamin C, E, carotenoids, and polyphenols), minerals, and dietary lipids (total, trans, and saturated mono-and

Table 3: Regression coefficients (95% confidence intervals) representing rate of decline in visual search from 43 to 60+ years per level increase in each health behavior at 36 and 43 years and per cumulative and change in health behavior scores.

| | *N* (%) | Visual search decline 43 to 60+ (95% CI) | |
|---|---|---|---|
| | | Model 1 | Model 2 |
| Smoking at age: | | | |
| 36 y | | | |
| Non-smoking | 780 (76.6) | 0.00 | 0.00 |
| 1–20 c/day | 200 (19.6) | −1.90 (−11.77, 7.96) | −1.79 (−11.68, 8.09) |
| 20+ cig/day | 38 (3.7) | −18.70 (−39.27, 1.86) | −19.44 (−40.05, 1.17) |
| *P* value | | 0.156 | 0.148 |
| 43 y | | | |
| Non-smoking | 816 (80.1) | 0.00 | 0.00 |
| 1–20 c/day | 159 (15.6) | −4.19 (−14.92, 6.53) | −2.73 (−13.55, 8.08) |
| 20+ cig/day | 43 (4.2) | −19.54 (−38.97, −0.12) | −18.52 (−38.00, 0.94) |
| *P* value | | 0.060 | 0.103 |
| Midlife score: | | | |
| Non-smoker | 744 (73.0) | 0.00 | 0.00 |
| Moderate smoker | 252 (24.7) | −4.85 (−13.93, 4.21) | −4.82 (−13.93, 4.28) |
| Heavy smokers | 22 (2.1) | −24.80 (−51.61, 2.00) | −25.46 (−52.34, 1.42) |
| *P* value | | 0.078 | 0.077 |
| Change in smoking: | | | |
| Non-smoker | 744 (73.0) | 0.00 | 0.00 |
| Increase | 55 (5.4) | −13.08 (−30.17, 4.00) | −12.78 (−30.02, 4.45) |
| Decrease | 79 (7.7) | −2.70 (−17.06, 11.64) | −2.65 (−17.09, 11.78) |
| Constant med/heavy | 140 (13.7) | −6.71 (−18.09, 4.67) | −5.82 (−17.44, 5.79) |
| *P* value | | 0.374 | 0.455 |
| Physical activity at age: | | | |
| 36 y | | | |
| Inactive | 324 (31.8) | 0.00 | 0.00 |
| Moderately active | 275 (27.0) | 2.69 (−7.29, 12.68) | 3.20 (−6.80, 13.20) |
| Most active | 419 (41.1) | 8.00 (−1.12, 17.13) | 8.47 (−0.70, 17.65) |
| *P* value | | 0.081 | 0.067 |
| 43 y | | | |
| Inactive | 475 (46.6) | 0.00 | 0.00 |
| Moderately active | 251 (24.6) | −3.93 (−13.57, 5.69) | −4.37 (−14.03, 5.28) |
| Most active | 292 (28.6) | 11.84 (2.55, 21.12) | 11.18 (1.78, 20.58) |
| *P* value | | 0.022 | 0.034 |
| Midlife score: | | | |
| Inactive | 221 (21.7) | 0.00 | 0.00 |
| Moderate | 608 (59.7) | 8.32 (−1.33, 17.97) | 8.76 (−0.95, 18.47) |
| Most active | 189 (18.5) | 16.71 (4.32, 29.10) | 17.00 (4.50, 29.51) |
| *P* value | | 0.008 | 0.008 |
| Change in activity: | | | |
| Inactive | 221 (21.7) | 0.00 | 0.00 |
| Increase | 164 (16.1) | 14.45 (1.83, 27.07) | 13.78 (1.05, 26.50) |
| Decrease | 354 (34.7) | 7.58 (−2.87, 18.03) | 7.80 (−2.72, 18.34) |
| Constant mod/active | 279 (27.4) | 10.51 (−0.74, 21.77) | 10.46 (−0.92, 21.84) |
| *P* value | | 0.127 | 0.157 |
| Diet at age: | | | |
| 36 y | | | |
| Low-quality diet | 564 (55.4) | 0.00 | 0.00 |
| High-quality diet | 454 (44.6) | −0.52 (−8.39, 7.34) | −1.74 (−9.67, 6.19) |
| *P* value | | 0.896 | 0.667 |
| 43 y | | | |
| Low-quality diet | 521 (51.1) | 0.00 | 0.00 |
| High-quality diet | 497 (48.8) | 0.59 (−7.23, 8.42) | −1.03 (−8.91, 6.84) |
| *P* value | | 0.881 | 0.797 |

Table 3: Continued.

| | N (%) | Visual search decline 43 to 60+ (95% CI) Model 1 | Model 2 |
|---|---|---|---|
| Midlife score: | | | |
| Low-quality diet | 234 (22.9) | 0.00 | 0.00 |
| High-quality diet | 784 (77.0) | 1.59 (−7.89, 11.09) | −0.64 (−10.28, 9.00) |
| *P* value | | 0.741 | 0.896 |
| Change in diet: | | | |
| Low-quality | 234 (22.9) | 0.00 | 0.00 |
| Increase in quality | 330 (32.4) | 1.53 (−9.04, 12.12) | −0.69 (−11.45, 10.06) |
| Decrease in quality | 94 (9.2) | −1.23 (−16.11, 13.64) | −3.22 (−18.18, 11.74) |
| Constant high-quality | 360 (35.3) | 1.63 (−9.09, 12.36) | −1.39 (−12.31, 9.57) |
| *P* value | | 0.972 | 0.978 |

Model 1: model adjusted for sex, childhood social class, childhood cognition at age 8, SEP (own occupation and education), and depression.
Model 2: model 1 plus other lifestyle behaviors.

polyunsaturated fats) [56], is now giving way to studies of global diet quality indices, for guidance in modeling dietary risk in relation to cognitive performance [57, 58]. In this context general recommendations are made for high fruit and vegetable consumption and moderation of high-glycemic index foods as cardioprotective, with secondary benefits to cognitive ageing [59]. The reason for the specificity of the diet memory association is unclear. Healthy dietary choice is protective of dementia [60], and evidence shows that dementia is predicted by memory impairment in particular [61, 62]. However, physical exercise, which was specifically associated with search speed, is also protective of dementia [63]. As already noted, however, the apparent loss of the exercise memory association reported by Richards et al. (2003) may be a consequence of not adjusting for non physical leisure activities here [51].

Our results for diet differ to those of The Nutrition et Cognition (NutCog) study, where diet quality was not independently associated with cognitive change over 3-year period. However, cognitive decline in this study was measured over a much shorter interval, although this study did report an association between diet quality and risk factors for nutrition-related chronic diseases, which are also considered to be risk factors for cognitive decline [56].

There are several plausible biological mechanisms underlying associations between physical activity and cognitive decline. Physical activity reduces cardiovascular risk [64], increases cerebral perfusion, and facilitates neurogenesis [65–67]. In contrast, impaired blood flow in the midbrain [68, 69] is a risk factor for subsequent cognitive impairment and dementia. Of interest, physical activity was specifically associated with a slower decline in psychomotor speed, which is consistent with evidence that highly fit individuals respond faster to stimuli [70].

*4.2. Conclusions and Implications.* In conclusion, our results support evidence that physical activity and healthy dietary choice are protective of aspects of cognitive ageing. These mutually adjusted associations were observed over a 20-year period, in analyses additionally controlling for socioeconomic status, sex, educational attainment, prior cognitive ability, and symptoms of anxiety and depression. Further work on interactions between lifestyle behaviors is recommended. For example, evidence suggests that smokers have poorer dietary choices than nonsmokers [71]; the Mediterranean diet only appears to be an effective protective factor for Alzheimer's disease in those who also exercise [72]. Overall, however, and in view of the enormous financial and societal burden of neurodegenerative diseases, public health interventions based on modifiable lifestyle behaviors across the life course represent high level priorities around the world.

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*Research Article*

# Social Networks and Memory over 15 Years of Followup in a Cohort of Older Australians: Results from the Australian Longitudinal Study of Ageing

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The purpose was to examine the relationship between different types of social networks and memory over 15 years of followup in a large cohort of older Australians who were cognitively intact at study baseline. Our specific aims were to investigate whether social networks were associated with memory, determine if different types of social networks had different relationships with memory, and examine if changes in memory over time differed according to types of social networks. We used five waves of data from the Australian Longitudinal Study of Ageing, and followed 706 participants with an average age of 78.6 years (SD 5.7) at baseline. The relationships between five types of social networks and changes in memory were assessed. The results suggested a gradient of effect; participants in the upper tertile of friends or overall social networks had better memory scores than those in the mid tertile, who in turn had better memory scores than participants in the lower tertile. There was evidence of a linear, but not quadratic, effect of time on memory, and an interaction between friends' social networks and time was apparent. Findings are discussed with respect to mechanisms that might explain the observed relationships between social networks and memory.

## 1. Introduction

Over recent decades, there has been an accrual of evidence concerning the beneficial effects of social relationships on physical and mental health in older people, including longer survival [1], reduced risk of disability [2, 3], and reduced risk of dementia [4]. Cross-sectional [5] and longitudinal studies [6–11] have generally shown that older people with better social relationships also have higher levels of cognitive function. The influence of social relationships is broad.

In the conceptual model proposed by Berkman et al. [12], social *networks* underpin the ways in which social relationships affect health outcomes. Social networks were hypothesised by these authors to influence health through the provision of social support, social influence, social engagement and attachment, and access to material goods and resources. In turn, these aspects of social relationships affect health via behavioural and physiological pathways.

In the extant literature concerning cognitive function, there is considerable variability in the ways that social networks have been defined, which may partly explain differences in results across studies. For example, no association between overall social networks (defined as number of children, relatives, and friends seen at least monthly) and cognitive function was found in a recent cross-sectional study [5]. In a study of higher-functioning older persons [10], no effect of the total number of close social ties with children, relatives, and friend on cognitive performance at baseline and over 7.5 years of followup was observed. In contrast to these results, larger overall social networks have been demonstrated in other studies to be associated with a higher level of cognitive function at baseline [8] and with reduced rates of cognitive decline over 5 years [6] and 12 years of followup [8].

Different social roles are potentially fulfilled by different relationships with various people [13], and it has been argued that different types of social networks—that is, networks with children, relatives, friends, and confidants—may have differential effects on health [14]. For instance, there is longitudinal evidence of different impacts of network types on disability, residential relocation, and death [3, 15, 16]. Other authors have characterised the composition of individuals' social networks (diverse; friend, neighbour, or family focussed; restricted) and shown beneficial effects of diverse social networks on well-being [17, 18], physical activity [19], and survival [20]. However, relatively few studies have investigated the effects of different types of social networks on cognitive function. Zunzunegui et al. [11] showed less frequent contact with relatives, but not friends, was associated with cognitive decline over 4 years of followup. In a separate small study of 200 older adults, statistically significant effects of larger social networks with family and with friends were shown on global cognition over 5 years of followup [9]. However, participants with cognitive impairment at baseline were included in [11], so the possibility that poorer cognitive function leads to smaller social networks cannot be excluded as an explanation for the results. Furthermore, these results are equivocal with respect to the influence of different types of social networks, and followup duration was relatively short (4-5 years) in both studies.

Based on the observation by Hughes et al. [9] that different cognitive domains show similar patterns of response to a variety of social resources, we selected episodic memory as the outcome measure in the present study (but see also [5]). The purpose of our study was to examine the relationship between different types of social networks and memory over 15 years in a large cohort of older Australians who were cognitively intact at study baseline. Our specific aims were to investigate whether social networks were associated with memory, determine if different types of social networks had differential effects on memory, and examine how any effects changed over time.

## 2. Methods

*2.1. Study Sample and Data Collection.* We drew data from the Australian Longitudinal Study of Ageing (ALSA) that began in 1992 in Adelaide, South Australia. ALSA has been described in detail elsewhere [21]. ALSA's major objectives were to assess the effects of social, biomedical, behavioural, economic, and environmental factors upon age-related changes in the health and well-being of older persons [22]. The primary sample was randomly selected from the South Australian Electoral Roll, and stratified by local government area, gender, and age group (70–74, 75–79, 80–84, and ≥85 years). Older men were over-sampled to ensure sufficient numbers of males for longitudinal followup. Persons were eligible for the study if they were resident in the Adelaide Statistical Division and aged ≥70 years on December 31, 1992.

We used five waves of data collection in the present study, taking all available data for the primary participants who completed an interview at baseline. Data relevant to the present study were collected at baseline, then at followup interviews approximately 2, 8, 11, and 15 years after baseline. The relevant ethics committee approved the study, and each participant (or their proxy) gave written informed consent at each wave.

The Minimental State Examination (MMSE) was administered at each study wave and used as a dementia screen in the present study. Participants scoring below 24 at baseline were considered possibly cognitively impaired [23] and excluded from analyses to prevent inclusion of pre-clinical cases of dementia [24].

*2.2. Episodic Memory.* The outcome measure in the present study was an episodic memory measure calculated for each wave from a composite of recalled items that covered symbols, pictures, and words [25]. Recall of symbols from the Digit Symbol Substitution (DSS) subscale of the Wechsler Adult Intelligence Scale-Revised (WAIS-R; Wechsler 1991) was the basis for incidental symbol memory [26]. The total number of symbols correctly recalled out of a possible 9 was used as a measure of incidental symbol memory at each wave. A 15-item short form of the Boston Naming Task [27] gave a basis for the incidental picture recall measure in this study [26]. Participants were asked to recall the 15 pictures immediately after the task. Each participant was assigned a score based on the number of pictures they correctly recalled. The number of words correctly recalled from the three word-recall items of the MMSE was calculated for each participant, with a maximum possible score of three. The number of correctly recalled symbols, pictures, and words was then summed and each participant was assigned a memory score out of a maximum possible of 27.

Picture and symbol components of the memory composite were completed as part of a separate clinical assessment conducted at each of the waves considered here, and not all participants agreed to take part in these further assessments. In total, at baseline there were memory composite scores from 706 participants who had an MMSE ≥ 24.

*2.3. Social Networks.* Social networks with children, other relatives, friends, and confidants were hypothesised as predictors of memory. Measures of these four social network types were developed by Glass et al. [14] and have been previously validated for the ALSA sample using confirmatory factor analysis [28]. The children network combined information on the number of children, proximity of children, and frequency of personal and phone contact with children. The relatives network was calculated from the number of relatives (apart from spouse and children) the participant felt close to, and the frequency of personal and phone contact with these relatives. The friends network captured the number of close friends, personal contact, and phone contact. The confidant network reflected the existence of confidants and whether the confidant was a spouse. A total social network score was calculated as the sum of the children, relatives, friends, and confidant network scores. All component variables were standardized before the derivation of the social network variables. Each participant was then classified as being in the lower, mid, or upper tertile for each of the four social network types and the total social network variable according to the distribution of responses to each variable. These categorized network variables were used in subsequent analyses.

*2.4. Demographic, Health, and Lifestyle Variables.* To incorporate the effects of potential confounding variables in the analyses, a range of demographic and health variables were also considered. Age group (in five-year age bands), gender, current marital status (partnered or not), age left full-time education (≤ 14, > 14 years of age), number of chronic conditions (self-report, based on a list of 10 common conditions), mobility disability [29], depressive symptoms based on the CES-D scale [30] with cut-point of 17, alcohol use [31], and smoking status were considered in the adjusted analyses.

*2.5. Statistical Analyses.* We used all available data to fit random effects models [32] so as to assess the effects of each of the social network types on the memory composite over time. Such models characterize the overall pattern of change in the outcome, but allow for different coefficients for each individual, reflecting the correlation among observations for an individual [33].

We considered the effect of the different social network variables in separate models, and we also examined the interaction of the social network variables with time and time$^2$ in the models. The most complex model included an interaction between linear (time) and quadratic (time$^2$) functions of time in study and each type of social network, as well as the demographic, health, and lifestyle covariates indicated above. A similar approach was used by Ertel and colleagues [34]. A series of nested models that sequentially omitted the interaction between the time$^2$ and social networks, time and social networks, and then the main effects of time$^2$, time and social network variables were fit. We used likelihood ratio tests to compare between complex and simpler models. Stata version 12.1 was used in all analyses.

Table 1: Summary statistics for 706 participants with no cognitive impairment at baseline of ALSA.

| Characteristic | Summary[1] |
|---|---|
| Age years mean (SD[2]) | 78.6 (5.7) |
| Gender | |
| Male | 476 (67.9) |
| Female | 230 (32.1) |
| Place of residence | |
| Community | 673 (95.3) |
| Institution | 33 (4.7) |
| Marital status | |
| Married/De facto | 413 (58.5) |
| Widowed | 244 (34.6) |
| Single | 49 (6.9) |
| Age left school | |
| ≤14 years | 360 (51.0) |
| >14 years | 346 (49.0) |
| Number morbid conditions mean (SD) | 1.6 (1.1) |
| Mobility | |
| No disability | 512 (72.3) |
| Disability | 194 (27.7) |
| Depressive symptoms | |
| CES-D < 17 | 621 (88.0) |
| CES-D ≥ 17 | 85 (12.0) |
| Alcohol problem | |
| AUDIT score < 8 | 671 (95.0) |
| AUDIT score ≥ 8 | 35 (5.0) |
| Smoking status | |
| Never smoker | 320 (45.3) |
| Ex smoker | 340 (48.2) |
| Current smoker | 46 (6.5) |
| Children social network score mean (SD) | 0.05 (0.75) |
| Relatives social network score mean (SD) | 0.02 (0.77) |
| Friends social network score mean (SD) | 0.13 (0.74) |
| Confidants social network score mean (SD) | 0.08 (0.75) |
| Total social network score mean (SD) | 0.27 (1.64) |
| Mini-mental state exam mean (SD) | 28.3 (1.7) |
| Memory composite mean (SD) | 15.7 (3.4) |

[1]Shown is the number (%) of participants unless otherwise indicated.
[2]SD is standard deviation.

## 3. Results

As shown in Table 1, the average age at baseline of the 706 participants who were cognitively intact and had a baseline episodic memory score was close to 80 years; 18% of the cohort was initially aged ≥ 85 years. Two-thirds of the men in the study were married at baseline, while the majority of women were widowed. The prevalence of morbid conditions was relatively high, and the most common conditions were osteoarthritis, heart conditions, hypertension, diabetes, and cancers. More than one quarter of participants reported difficulty in climbing stairs or walking half a mile, and 12% of participants reported symptoms possibly indicative of clinical depression at the baseline interview. Five per cent of participants reported problem alcohol consumption, while more than half of the participants were current (7%) or ex-smokers (48%). The average times between baseline interview and each of the subsequent waves considered in the present study were 2.0 years (SD 0.1), 8.0 years (SD 0.2), 11.0 years (SD 0.2), and 15.2 years (SD 0.2), respectively.

Figure 1 presents trajectories of memory composite scores across 15 years of followup of ALSA participants. As is evident from this figure, there is considerable heterogeneity between participants in terms of memory over time.

The random effects models showed that for the memory composite, there were significant main effects of time and total social networks. However, the interaction between time

Table 2: Summary of effects of friends and total social networks on cognitive function[1].

| Covariate | | | | | | | Males | | | Females | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $\beta^1$ | se[2] | $P$-value | $\beta^3$ | se | $P$-value | $\beta^3$ | se | $P$-value | $\beta^3$ | se | $P$-value |
| Total[1] | | | | | | | | | | | | |
| Time | −0.16 | 0.02 | <0.001 | −0.15 | 0.02 | <0.001 | −0.17 | 0.02 | <0.001 | −0.15 | 0.04 | <0.001 |
| Network mid tertile | 0.77 | 0.26 | 0.004 | 0.62 | 0.22 | 0.005 | 0.59 | 0.30 | 0.052 | 1.00 | 0.49 | 0.040 |
| Network upper tertile | 1.09 | 0.26 | <0.001 | 0.83 | 0.23 | <0.001 | 0.68 | 0.31 | 0.029 | 1.38 | 0.71 | 0.004 |
| Friends[1] | | | | | | | | | | | | |
| Time | −0.23 | 0.04 | <0.001 | −0.25 | 0.04 | <0.001 | −0.21 | 0.04 | <0.001 | −0.38 | 0.10 | 0.001 |
| Friends mid tertile | 0.13 | 0.28 | 0.646 | 0.00 | 0.28 | 0.986 | 0.51 | 0.32 | 0.112 | −0.99 | 0.55 | 0.073 |
| Friends upper tertile | 0.38 | 0.28 | 0.170 | 0.25 | 0.28 | 0.359 | 0.37 | 0.32 | 0.246 | −0.03 | 0.54 | 0.959 |
| Friends mid tertile × time | 0.10 | 0.05 | 0.052 | 0.11 | 0.05 | 0.034 | 0.05 | 0.06 | 0.418 | 0.32 | 0.12 | 0.010 |
| Friends upper tertile × time | 0.08 | 0.05 | 0.107 | 0.10 | 0.05 | 0.054 | 0.07 | 0.06 | 0.193 | 0.22 | 0.11 | 0.051 |

[1]Model also includes sex, age group.
[2]se is standard error.
[3]Model also includes sex, age group, education, marital status, disability status, chronic conditions, depressive symptoms, alcohol consumption and smoking status.

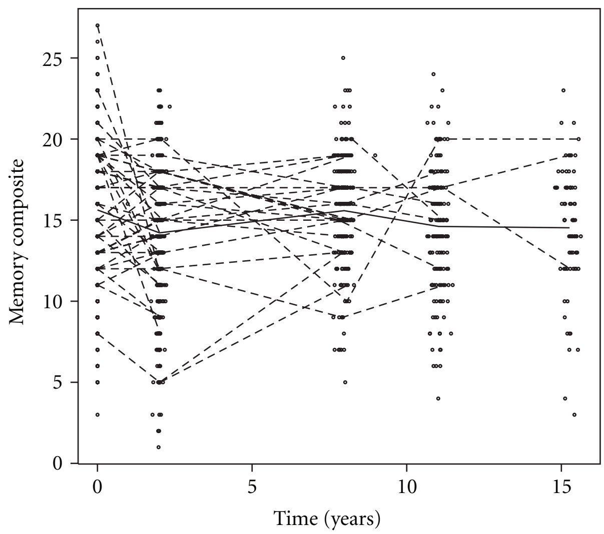


Figure 1: Trajectories of memory composite over fifteen years of followup in ALSA participants who were not cognitively impaired at baseline. Trajectories for a randomly selected 10% of participants are shown (connected dashed line segments). The mean memory composite score at each time of measurement is also shown (bold line).

and total social networks was not statistically significant, suggesting that the changes in memory over time were parallel for the tertile groups of overall social networks. The coefficients in the models that adjusted for the range of demographic, health, and lifestyle covariates (shown in Table 2) demonstrate that the predicted memory composite scores of participants in the mid tertile of total social networks were 0.62 units (standard error (se) 0.22) higher than those in the lower tertile (Table 2). For those participants in the upper tertile of social networks versus the lower tertile, the effect was even larger (0.83, se 0.23). The effect of time was such that for every year, the memory composite scores declined by an estimated 0.15 (se 0.02) units. As shown in Table 2, these results were similar to those from the models which adjusted for sex and age group only. We also fit the final model for total social networks controlling for friends networks (see below), and the coefficients changed little from those presented in Table 2 (i.e., mid total social networks tertile $\beta$ 0.66 se 0.27; upper total social networks tertile $\beta$ 0.84; se 0.30 in the friends adjusted model). There was no evidence of a quadratic effect of time (either as a main effect or as an interaction with total social networks) on the memory composite variable. Separate analyses for males and females also showed broadly similar results for total social networks (Table 2), with effects of social networks on memory slightly larger for the women in our study than for the men.

The suite of models that were fit investigating each type of social network showed that only the effect of friends networks on the memory composite was statistically significant. A significant interaction between friends networks and time was also observed. The interaction effect was such that the rate of decline in memory composite with every year (i.e., the slope) was steeper (0.25 units, se 0.04) for those in the lower tertile of friends networks, and the annual decline in memory composite was less for those in the mid tertile (−0.14 (i.e., −0.25 + 0.11), se 0.05) and upper tertile (−0.15, se 0.05) of friends networks. Separate analyses for males and females suggested the effect of friends social networks differed between the sexes, with a larger effect of friends social networks observed for females than for males. There were no statistically significant effects of the children, relatives, or confidants social networks at baseline on memory in our study, either as main effects or in interaction with time or time$^2$.

## 4. Discussion

We have demonstrated that larger friends social networks and overall social networks had significant benefits for memory in a population-based cohort of participants who were cognitively intact at baseline and followed for an average of 15 years. The results suggested a gradient in the effect of social networks, so that participants in the upper tertile of friends or total social networks had better memory scores than those in the mid tertile, who in turn had better memory scores than participants in the lower tertile of social network. The results also suggested that the observed effects of total and friends social networks were slightly larger for females than for males. Notably, we did not find any significant effects of social networks with children, relatives, or confidants on memory. The five occasions of measurement also allowed us to estimate the rate of decline, which showed that while consistent, the effect of time is small. Our findings point to the importance of disaggregating kin and nonkin networks, rather than considering only aggregate measures of social networks that do not distinguish between different types of social ties.

The mechanisms through which different types of social networks affect cognitive function remain unclear. Berkman et al. [12] contend that social networks influence health in four main ways, through the provision of social support, social influence, social engagement and attachment, and access to material goods and resources. In turn, these psychosocial mechanisms influence health through health behavioural, psychological, and physiological pathways. For memory specifically, social networks and memory may be related in several ways. Social networks are the basis for social engagement, which is cognitively stimulating and may enhance neural plasticity in ageing, thereby maintaining cognitive reserve [35]. Thus better social networks might lead to continued psychological stimulation, delaying cognitive decline, or impairment. An alternative possible mechanism is that the stronger social networks may serve to buffer against stress, through modifying its effects on the activation of the hypothalamic-pituitary-adrenal axis of the central nervous system [12]. This affects neuronal functioning, and in this way individuals with better social networks are protected from some of these neuroendocrine processes [36]. Another possibility is that social networks facilitate access to health care, indirectly forestalling brain pathology and other disease processes that affect cognition [37, 38]. Finally, it is also possible that changes in cognitive function affect social networks. Cognitive impairment may lead to withdrawal from social activities, because of difficulties in participation or in maintaining relationships. These mechanisms could apply equally to friends and total social networks. Reasons for why other types of social networks are not as beneficial remain unclear.

The finding in the present study that social networks with friends had specific effects on memory suggests other ways that social relationships may promote cognitive function. Friends may encourage health seeking and health promoting behaviour, such as physical activity, which may in turn have beneficial sequelae for cognitive health. It is possible that health advice is better received by individuals when it is offered by friends, rather than family or confidants. It is well established that friends can have effects on other psychological measures including depression, self-efficacy, self-esteem [39], coping and morale [18], and sense of personal control [40]. It is possible that these effects are due to the reinforcement of social roles, or because interactions with friends can become increasingly discretionary with age [41]. The friendship networks that are retained in late life may offer high levels of socioemotional support, and thus confer benefit to individuals. It is also possible that less discretionary social networks, such as those with children and relatives, do not only involve positive social interactions, and interactions involving conflict may negate any beneficial effects on cognitive function. However, there is some evidence that negative social interactions are associated with better cognitive ability [9, 10], possibly due to greater cognitive stimulation from negative interactions. Further research to disentangle the mechanisms through which social networks with kin and nonkin affect health in later life is clearly warranted. Further work with the ALSA databank is also needed to investigate if the observed relationships between memory and social networks hold across other measures of cognitive function.

The findings from this study must be interpreted with some caveats borne in mind. While a range of potential confounders were included in the analyses, we cannot discount the possibility that residual confounding could have affected our results, as not all aspects of social engagement or lifestyle were taken into account. Furthermore, ALSA was not explicitly designed to examine the effects of social networks on memory, and the analyses are based on self-reported predictor variables and covariates measured at baseline. We also cannot discount the possibility that for some participants, previous declines in memory and other aspects of cognitive function led to lower social networks scores at baseline. In turn, these lower baseline social networks may then be associated with lower memory scores at subsequent followup times. Social networks may change over time, but the social networks considered in the present study were defined using only baseline data and so cannot reflect social networks at other points—either earlier or later—in the life course. However, total network size has been demonstrated as relatively stable over a long followup period in a study of older Dutch people [42]. Alternative derivations of the memory composite measure (e.g., with differential weightings of the items in the measure or with data reduction techniques such as principal components analysis) could have been applied. However, the interpretation of results based on more complex composite measures is more difficult, off-setting any potential advantages from such derivations of a memory measure. The nonrespondents to ALSA may also have been more socially isolated than participants, although nonresponse bias has generally been demonstrated as minimal in other analyses of ALSA data [26, 43]. We did not explicitly model the risk of dropout or death in this study. A recent study concerning education and cognitive decline [44] suggests this modelling approach may be a worthy avenue for future investigation in this area. A final point is that the MMSE is a crude screening tool for dementia. However, it is very widely used and while it may not eliminate all those with preclinical dementia, the inclusion of participants with possible cognitive impairment in the study would only have added to the variation in observed memory scores. This would serve to attenuate any true association between social networks and memory, so it is likely that the associations we observed would also be found in a more strictly cognitively intact sample. It must be noted, however, that the limitations identified above are true of the majority of longitudinal studies that have considered social relationships and cognitive function in older adults.

We believe these restrictions are balanced by ALSA's strengths, which include the richness of the data, the Australian setting, and the inclusion of residents in aged care facilities. ALSA also included a more heterogeneous population-based sample than many other longitudinal studies of ageing. An additional strength is that the present findings are drawn from five repeated measurements of memory, spanning 15 years of followup, which allowed us to examine whether there was evidence of a nonlinear relationship between cognitive function and time. We have not identified any other studies that considered social networks and memory with as many repeated assessments or the duration of followup that we have presented.

In summary, we have shown that friends and total social networks are associated with memory over 15 years of followup in a large cohort of older Australian men and women who were cognitively intact at baseline. Having a larger social network with more frequent contacts, especially with friends, appears important for preserving cognitive function and slowing the rate of decline.

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*Research Article*

# Do Depressive Traits and Hostility Predict Age-Related Decline in General Intelligence?

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Certain personality traits are likely to be associated with stress and distress through the lifespan, and as a consequence these traits may influence the rate of age-related cognitive decline. The present study uses data from the Glostrup 1914 cohort to analyze potential effects of personality on decline in general intelligence over a 30-year period. The Minnesota Multiphasic Personality Inventory was administered at a 50-year baseline exam, and from this inventory the Obvious Depression Scale and an abbreviated version of the Cook-Medley Hostility Scale were derived. At the 50-year baseline and at the 60-, 70-, and 80-year followups the full version of Wechsler's Adult Intelligence Scale (WAIS) was administered to 673, 513, 136, and 184 participants. Mixed effects statistical models were used to evaluate both the effect of the personality scores on level of intelligence and the interaction between the personality scores and the time since followup. Analyses were adjusted for demographic background and a wide range of lifestyle factors. Both obvious depression and hostility were negatively associated with level of intelligence, but personality scores did not influence rate of decline in general intelligence.

## 1. Introduction

Recent decades have seen a widespread interest in personality and health [1]. This interest partly reflects an increasing focus on personality in a lifespan perspective and on personality and aging. Although personality, aging, and well-being have been investigated in several studies [2], there is very little research on the associations between personality and age-related changes in cognition. This is remarkable because much evidence suggests that stress may impact brain structures involved in cognition [3], and that personality traits associated with increased vulnerability to stress may influence cognition over the lifespan [4]. Thus, Crowe et al. [4] suggested that personality traits associated with stress, depression, and anxiety may be associated with age-related cognitive decline and risk of Alzheimer's disease and demonstrated that the broad personality dimension of neuroticism was in fact associated with higher risk of cognitive impairment. The study was limited by lack of early-life assessment of cognition and by the use of a relatively rough binary measure of cognition based on a telephone interview. However, neuroticism is known to be associated with increased reactivity to environmental stress [5] and has been found to be associated with psychopathology [6], including depression, which is a relatively well-documented risk factor for dementia [7]. If associations between neuroticism and normal age-related cognitive decline could be demonstrated over a wide range of the lifespan, the public health implications would be substantial since normal cognitive decline as a consequence of personality-related vulnerability to stress would affect a much larger part of the general population and presumably would affect individuals over a larger part of their life-span.

Obviously, risk factors for Alzheimer's disease or other forms of dementia are not necessarily risk factors for normal age-related decline. However, studies of personality and normal age-related cognitive decline involve a number of methodological challenges. Thus, cross-sectional studies of old age samples are unable to separate effects of personality on age-related cognitive decline from the associations between personality and cognitive performance which can be demonstrated in younger adults [8]. Studies with short followup intervals will usually observe relatively small age-related changes and may consequently not have sufficient power to detect associations between personality and cognitive decline.

In this perspective, the Glostrup 1914 cohort offers an unusual opportunity to analyze potential associations between personality and cognitive decline as the Minnesota Multiphasic Personality Inventory (MMPI) was administered at age 50 and the cohort was repeatedly assessed with the same cognitive tests for up to 45 years [9]. Among the many scales which can be derived from the MMPI, the Obvious Depression Scale and a short version of the Cook-Medley Hostility Scale have previously been analyzed as predictors of morbidity and mortality [10, 11]. Both scales have been shown to predict cardiovascular disease in the 1914 cohort, and there is a large literature on associations between cardiovascular factors and cognitive decline [12]. Consequently, associations between the two scales and age-related cognitive decline may be hypothesized.

Several findings in nonclinical samples suggest that the Obvious Depression Scale primarily reflects stable aspects of neuroticism and to a smaller extent symptoms of depressive states. In the 1914 cohort 10- and 30-year retest correlations were 0.71 and 0.48 for the Obvious Depression Scale [13], and in another Danish sample of 584 healthy twins, the Obvious Depression Scale was demonstrated to correlate 0.69 with the Neuroticism Scale of the NEO-PI-R [14]. Trait anxiety and trait depression are core components of neuroticism as a broad dimension of personality, and consequently effects on cognitive decline of state anxiety and state depression must be separated from effects of personality. In a cross-sectional study the NEO personality factors explained up to 7% of the variance in cognition, while the state anxiety and state depression scales of the State-Trait Personality Inventory explained very little additional variance [15]. However, a study including a 3-year followup observed no associations between neuroticism and cognitive performance [16].

Hostility may be associated with a tendency to perceive the social environment as stressful and to elicit antagonistic reactions from other people [17]. However, few studies have investigated associations between hostility and age-related cognitive decline. A study using an abbreviated version of the Cook-Medley Hostility Scale found that hostility, in particular hostile attributions, predicted cognitive decline [18]. A more recent study of a community sample used 8 cynicism items from the Cook-Medley Hostility Scale and found that hostility was associated with baseline level of cognitive functioning, but did not influence decline over a 6-year period [19]. However, it is still possible that hostility would influence decline over a longer followup period, and the main aim of the present study was to investigate the obvious depression and Cook-Medley hostility scores at age 50 as predictors of cognitive decline over the following three decades of the lifespan.

Many previous studies have focused on tests of specific cognitive functions, such as reaction time [20], perceptual speed [21], and memory [22]. Studies of the Glostrup 1914 cohort incorporated the full Wechsler Adult Intelligence Scale (WAIS) and consequently, the data provide a unique opportunity to evaluate potential associations between personality and age-related decline in general intelligence. Previous analysis of the 1914 cohort has shown substantially more decline for the performance than for the Verbal IQ [23, 24], and consequently we expected the Performance IQ to be more sensitive to any effects that personality may have on age-related cognitive decline.

Measures of intelligence are usually strongly associated with demographic factors such as education and social status and to some extent this may also be the case for personality measures of depressive traits and hostility. Both intelligence and personality traits may also be associated with lifestyle factors [25], and consequently any observed association between personality and decline in intelligence may reflect confounding by demographic and lifestyle factors. Fortunately, the available data for the 1914 cohort made it possible to control for a range of these potentially confounding factors.

## 2. Materials and Methods

*2.1. Participants.* In 1964, the Copenhagen County Hospital and the County Mental Hospital initiated a population study of all people born in 1914 and living in a predefined administrative area close to the two hospitals in Glostrup. A total of 976 individuals were eligible for the study, and of these 802 50-year olds participated in the medical and 698 in the psychological part of the study. Follow-up studies were conducted during the next 45 years, the most recent being a 95-year followup.

In 1964 673 of the 698 participants (384 men and 289 women) completed both the WAIS and the Danish version of the MMPI. The present study sample comprises these 673 individuals and the subsamples participating in the 60-, 70- and 80-year followups conducted in 1974 ($n = 513:293$ men and 220 women), 1984 ($n = 136:71$ men and 65 women), and 1995 ($n = 184:91$ men and 93 women). Details about the medical [26] and psychological studies [9] of the cohort are provided elsewhere.

### 2.2. Measures

*2.2.1. Cognitive Assessment.* In the 50-, 60-, and 80-year studies the complete WAIS [27] was administered to all participants. When the 50-year-baseline study of the Glostrup

1914 cohort was initiated in 1964, the original version of the WAIS had just been translated into Danish. It consists of six verbal subtests (information, comprehension, similarities, arithmetic, digit span, vocabulary) and five performance subtests (digit-symbol, picture completion, block design, picture arrangement, and object assembly). Testing procedures and scoring criteria have previously been described in detail [28, 29]. To permit comparison between successive WAIS followups, all IQs are based on the Danish 50-year norms [30]. Only one tester was available for the 70-year followup, and consequently the complete WAIS was only administered to 141 participants, of whom 136 had completed the MMPI and were included in the present study sample. At the 80-year followup 329 of the 698 50-year participants were still alive, and of these 189 participated in the followup (184 had completed the MMPI and are included in the present study sample). As described previously, the 189 participants in the 80-year study obtained higher mean full-scale IQ at the 50-year baseline than the remaining participants in the 50-year study [23].

*2.2.2. Obvious Depression Scale.* The Danish version of the MMPI [31] consists of 408 true-false items, although "don't know" is a third answer category in the Danish version. The Obvious Depression Scale comprises 40 items: 8 items potentially reflecting physical health and 32 items reflecting mood, feelings of well-being, and self-esteem [11]. Coefficient alpha for the Danish 50-year sample was 0.78 for the Obvious Depression Scale.

*2.2.3. Cook-Medley Hostility Scale.* The Danish version of the MMPI did not include all the 566 items of the complete inventory. Consequently, the present study included only 27 of the 39-item abbreviated Cook-Medley Hostility Scale: 11 items on cynicism, 9 on hostile attributions, 4 on aggressive responding, and 3 items on hostile affect [32]. Coefficient alpha for the Danish 50-year sample was 0.82 for the 27 item Hostility Scale.

*2.2.4. Demographic Covariates.* These included sex, education, and social status assessed at the 50-year study. School education was coded on a 3-point scale (primary to upper secondary) and vocational training on a 5-point scale (no vocational training to academic). The two scores were combined into an overall ordinal index of educational level with a 2–8 point range [23]. Social status was ranked in 6 ordinal levels based on educational level, job position, and number of subordinates [33].

*2.2.5. Lifestyle Factors.* These included measurement of systolic blood pressure, smoking (as a binary variable), physical activity at work and at leisure (both four-level ordinal measures, recoded into three categories) [11], obesity (measured by body mass index (BMI)), and measures of total serum cholesterol, triglycerides, and insulin [26] analyzed in blood samples obtained in the morning after a 13-hour fast.

*2.3. Data Analysis.* Mixed-effects models were used to test associations between the two personality traits and level of WAIS performance and to test associations between personality traits and change in cognitive function. Data were analyzed using the xtmixed procedure of Stata version 12 (StataCorp LP, College Station, TX, USA). At the 50-year baseline, information on BMI, blood pressure, total serum cholesterol, triglycerides, and insulin was missing for 2, 13, 27, 29, and 27 individuals, respectively. To avoid diluting the sample in multivariate analyses including these variables, the relatively few missing values were imputed using the multivariate normal regression imputing facilities of Stata.

A basic growth curve model, including time since the 50-year baseline as both a fixed and random effect and assuming both random intercept and slope, was used in preliminary analyses of the WAIS full-scale IQ. Since decline in WAIS IQs was nonlinear, time squared was included to allow for non-linear change. Sex, education, and social status were considered core confounders explaining substantial variance in full-scale IQ, and these variables were included in a series of models, which for each continuous covariate tested linear and quadratic regression, and for all covariates tested the significance of the interaction with the time since baseline variable. None of the interactions with the time variable was significant, and significant quadratic effects were only observed for social status and insulin level. Consequently, mean-centered squared variables were included in models with these two variables.

For the obvious depression and hostility scales both main effects and interactions with the time variable were tested in the following models: Model 1 was the basic model including time since the baseline (and the squared time variable). Model 2 also included the sociodemographic variables of sex, education, and social status, including the centered squared status variable. Finally, model 3 further included the lifestyle variables of systolic blood pressure, serum cholesterol, triglycerides, insulin (including a quadratic term), BMI, work and leisure physical activity, and smoking. All three models were analyzed with the full-scale, verbal, and Performance IQs as outcome and with time since the 50-year baseline as both a fixed and random effect and assuming both random intercept and slope, corresponding to assuming random variation in level and form of the individual growth curves.

There was some evidence of selective attrition, and consequently the main analyses were repeated on a reduced longitudinal sample comprising the 184 individuals who participated in both the 50-year and 80-year studies.

The growth curve models provide random effect estimates of interindividual variance in level and slope of the decline curves. By comparing variance estimates for models with and without the obvious depression or the Cook-Medley Hostility Scale, it is possible to calculate the reduction in variance associated with including each of the MMPI scales in the models.

All statistical tests were two-sided and determined significant at the 5% level.

## 3. Results

The sample characteristics for the 50-year baseline and the three followups are shown in Table 1. The percentage of men and smokers decreased at the later followups, and the mean systolic blood pressure and triglycerides level fell. Notably, the mean educational level was higher at the 80-year followup, while the mean social status was lower. For all these variables, significant differences were observed when the 50-year baseline values of the 80-year sample was compared with the baseline values of the remaining 50-year sample. This difference was not significant for any of the remaining variables in Table 1.

Table 2 presents means and standard deviations for the two MMPI scales at the 50-year baseline. For both scales most of the possible score range was used. The distributions were reasonably symmetric with a positive skewness of 0.80 for the Obvious Depression Scale and 0.22 for the abbreviated Cook-Medley Hostility Scale. Women scored significantly higher than men on the Obvious Depression Scale and significantly lower than men on the Cook-Medley Hostility Scales.

Table 3 displays the observed mean IQs at baseline and the three full followup samples as well as means for the subsample comprising the 184 individuals who participated in both the 50- and 80-year studies. Table 3 also presents the mean difference between the results of the 50-year baseline and the 80-year followup. The relatively large standard deviations of this difference illustrate the substantial individual differences in decline which have previously been described [23], and which were further confirmed by the variance in slope (decline in intelligence) observed in all growth-curve models in the present study. Table 3 also shows the high retest correlations which should be compared with the 20-year retest correlations reported previously (for the full-scale IQ, the retest correlations were 0.94 from 50 to 60 years and 0.90 from 50 to 70 years) [9, 24].

For all three WAIS IQs, little decline was observed from age 50 to age 60, but decline was obviously increasing and was substantial from age 70 to age 80, particularly for the Performance IQ. Thus, the means in the table indicate that any model describing cognitive development during the 30-year followup period should include a quadratic trend.

Table 4 presents the analyses of the Obvious Depression Scale. The table shows coefficients for the scale in models only including a term for the main effect and in models adding a term for the interaction between the scale and the time since baseline variable. The table shows relatively large effects of obvious depression on all three IQs in the unadjusted models, corresponding to a 5-6 percent reduction in the estimated variance of the curve level. However, the effects became dramatically smaller (and nonsignificant for Verbal IQ) when adjusted for demographic background variables (1 percent or less reduction in curve level variance), while adjustment for the set of lifestyle factors hardly changed the estimates. None of the tests of interaction with the time since baseline variable was approaching significance, and these models accordingly showed negligible reduction in the estimates of slope variance. Thus, it must be concluded that obvious depression did not influence the form of the cognitive decline curve, while it was associated with the level of the curve (see Figure 1).

Table 5 presents the analyses of the Cook-Medley Hostility Scale. Compared with obvious depression smaller effects of Hostility on all three IQs were observed in the unadjusted models, corresponding to about 3 percent reduction in the estimated variance of the curve level. Although the coefficients became smaller when adjusted for demographic background variables, they remained significant for all three IQs both in models without and with adjustment for the lifestyle factors. For these models, the inclusion of the Cook-Medley Hostility Scale was associated with about 2 percent reduction in curve level variance. None of the tests of interaction with the time since baseline variable was approaching significance, and these models showed negligible reduction in the estimates of slope variance. Thus, scores on the Cook-Medley Hostility Scale were associated with the level of the cognitive performance, but did not influence the form of the decline curve (see Figure 2).

The models in Tables 4 and 5 only tested the linear effects of obvious depression and hostility. However, models including a quadratic term and testing both its main effect and interaction with time since baseline found no significant quadratic effects of either scale. Correlation coefficients can be used to express the size of the linear associations between the MMPI scales and intelligence. In the 50-year-baseline sample the bivariate correlations of the Obvious Depression Scale were −0.24, −0.22, and −0.24 with the full-scale, the verbal and the Performance IQs, but when adjusted for demographic variables, the corresponding partial correlations were only −0.09, −0.05 and −0.10. For the Cook-Medley Hostility Scale, the correlations were −0.19, −0.17, and −0.17, and the adjusted partial correlations were −0.15, −0.13, and −0.13, confirming a stronger adjusted association with WAIS performance for this scale compared with the Obvious Depression Scale.

The correlation between the Obvious Depression Scale and the Cook-Medley Hostility Scale was 0.30. When both MMPI scales were included in the same model, only the main effect of the Cook-Medley Hostility Scale remained significant in all models. Thus, the regression coefficients for the two scales were −0.10 ($P = 0.25$) and −0.27 ($P = 0.003$) in the fully adjusted model while the regression coefficients were −0.19 ($P = 0.023$) and −0.31 ($P < 0.001$) in the corresponding models including either the Obvious Depression Scale or the Cook-Medley Hostility Scale.

Since significant sex differences were observed on both scales, it is possible that the influence of obvious depression and hostility is different in men and women. If this were the case, the three-factor interaction between sex, time since baseline, and each of the two personality scales should be significant. However, this interaction was not found to be significant in supplementary analyses adjusting for demographic variables and also analyses adjusting for lifestyle factors.

The supplementary analyses based on the reduced longitudinal sample showed fewer significant associations

Table 1: Sample characteristics at 50-year baseline and the three followups[1].

| Variable | 50-year baseline | 60-year followup | 70-year followup | 80-year followup |
|---|---|---|---|---|
| Number of participants | 673 | 513 | 136 | 184 |
| Demographic variables | | | | |
| Men (%, *n*) | 57 (384) | 57 (293) | 52 (71) | 49 (91)* |
| Education (mean, SD) | 3.6 (1.4) | 3.6 (1.4) | 3.6 (1.3) | 3.8 (1.4)* |
| Social status (mean, SD) | 4.5 (1.1) | 4.5 (1.1) | 4.5 (0.9) | 4.3 (1.0)* |
| Lifestyle factors | | | | |
| Smokers (%, *n*) | 69 (461) | 67 (339)* | 66 (90) | 55 (101)* |
| Sedentary work activity (%, *n*)[2] | 27 (183) | 27 (139) | 24 (32) | 32 (58) |
| Sedentary leisure activity (%, *n*) | 18 (124) | 17 (89) | 15 (20) | 17 (31) |
| BMI (mean, SD) | 25.2 (4.0) | 25.2 (3.8) | 25.4 (4.1) | 25.0 (3.3) |
| Systolic BP (mean mmHG, SD) | 138.7 (20.4) | 137.9 (19.4) | 134.9 (18.2)* | 135.2 (18.0)* |
| Total cholesterol (mean mg/dL, SD) | 285.7 (49.5) | 285.6 (49.9) | 286.0 (47.9) | 288.9 (47.7) |
| Fasting insulin (mean units/mL, SD) | 22.6 (7.1) | 22.5 (7.2) | 23.4 (8.6) | 22.7 (7.8) |
| Triglycerides (mean mM/liter, SD) | 111.2 (68.4) | 110.0 (70.5) | 113.0 (76.1) | 101.6 (50.9)* |

[1]An* indicates that there was a significant difference on the variable between the followup subsample and the remaining part of the 50-year baseline sample.
[2]This percentage includes about 11% of the participants who reported no work.

Table 2: Score distributions on obvious depression and Cook-Medley Hostility Scales at age 50.

| MMPI scale | *N* | Mean | SD | Range |
|---|---|---|---|---|
| Obvious depression scale[1] | 673 | 11.48 | 5.38 | 1–34 |
| Men | 384 | 10.21 | 4.99 | 1–34 |
| Women | 289 | 13.18 | 5.42 | 4–30 |
| Cook-Medley hostility scale[2] | 673 | 10.43 | 4.92 | 0–25 |
| Men | 384 | 10.97 | 5.04 | 1–23 |
| Women | 289 | 9.72 | 4.67 | 0–25 |

[1]Women scored significantly higher than men ($P < 0.001$).
[2]Men scored significantly higher than women ($P = 0.001$).

between the MMPI scales and intelligence level, but otherwise showed essentially the same results as the analyses of the full sample.

## 4. Discussion

The present study based on multiple administrations of the full WAIS and a 30-year followup period showed that the personality traits obvious depression and hostility were associated with the level of WAIS performance, but did not influence the rate of decline in general intelligence during the 30-year followup period. The association with level of WAIS performance to some extent reflected confounding by demographic factors such as sex, education, and social status, but, except for Verbal IQ, the effects remained significant when these covariates were included in the statistical models. The effect estimates hardly changed when the models also included a wide range of lifestyle related variables.

While the low, but significant, negative correlation between obvious depression and intelligence is consistent with the relatively well-documented negative association between neuroticism and intelligence [8, 34], to our knowledge few—if any—studies exist on the relationship between personality and decline in general intelligence. Many studies have investigated depressive symptoms as a risk factor for dementia [7], while fewer studies have investigated associations between depressive symptoms and cognitive decline [35, 36]. A study based on a large sample and comprehensive assessment of cognitive functions observed no association [37], while another large-sample study observed an association between average depressive symptom score and cognitive decline over varying followup intervals with a mean length of 4.4 years [38]. Among the available studies, the present study is unique because of the young age of the participants at baseline, the long followup period, and the instruments used to assess depression and cognitive function: The participants were only 50 years old at baseline, the followup interval was exceptionally long, and our study used general intelligence as outcome. It is true that many studies have evaluated associations between depression and cognition, but these studies have typically assessed symptoms of depression within the last week in much older individuals, and they have typically focused on depression as a risk factor for dementia over much shorter followup intervals.

Personality traits reflect stable characteristics of an individual and the distinction between state and trait can

Table 3: Mean WAIS IQs during the lifespan from 50 to 80.

| Followup<br>Full samples | N | Full scale IQ<br>Mean | <br>SD | Verbal IQ<br>Mean | <br>SD | Performance IQ<br>Mean | <br>SD |
|---|---|---|---|---|---|---|---|
| 50-year baseline | 673 | 98.96 | 14.40 | 98.19 | 14.21 | 99.12 | 14.22 |
| 60-year followup | 513 | 98.84 | 14.33 | 99.21 | 14.59 | 97.65 | 13.80 |
| 70-year followup | 136 | 94.90 | 14.12 | 96.22 | 13.71 | 93.40 | 14.37 |
| 80-year followup | 184 | 87.66 | 15.49 | 92.27 | 15.64 | 83.46 | 14.78 |
| *80-year sample*[1] | 184 | | | | | | |
| 50-year baseline | | 102.10 | 13.79 | 100.85 | 13.84 | 102.31 | 13.28 |
| 80-year followup | | 87.66 | 15.49 | 92.27 | 15.63 | 83.46 | 14.78 |
| Difference | | 14.44 | 8.88 | 8.58 | 8.75 | 18.85 | 10.43 |
| Retest correlation | | 0.82 | | 0.83 | | 0.73 | |

[1] Data are for the 184 participants who completed the WAIS at both the 50- and 80-year studies.

Table 4: Obvious depression scale: effects on WAIS IQs from 50 to 80.

| Model | Coefficient[1] | 95% CI | *P* for main effect | Interaction[2] coefficient | *P* for interaction |
|---|---|---|---|---|---|
| Full-scale IQ | | | | | |
| Model 1: unadjusted[3] | −0.639 | (−0.83)–(−0.44) | <0.001 | 0.003 | 0.319 |
| Model 2: demographics[4] | −0.184 | (−0.35)–(−0.02) | 0.029 | 0.003 | 0.291 |
| Model 3: lifestyle factors[5] | −0.190 | (−0.36)–(−0.03) | 0.023 | 0.003 | 0.294 |
| Verbal IQ | | | | | |
| Model 1: unadjusted[3] | −0.572 | (−0.77)–(−0.38) | <0.001 | 0.002 | 0.638 |
| Model 2: demographics[4] | −0.119 | (−0.28)–(0.05) | 0.156 | 0.002 | 0.613 |
| Model 3: lifestyle factors[5] | −0.125 | (−0.29)–(0.04) | 0.131 | 0.002 | 0.616 |
| Performance IQ | | | | | |
| Model 1: unadjusted[3] | −0.595 | (−0.78)–(−0.41) | <0.001 | 0.005 | 0.227 |
| Model 2: demographics[4] | −0.223 | (−0.40)–(−0.05) | 0.012 | 0.005 | 0.236 |
| Model 3: lifestyle factors[5] | −0.228 | (−0.40)–(−0.06) | 0.009 | 0.005 | 0.236 |

[1] Fixed effect coefficient from a model only including the main effect of the depression scale. See Section 3 for description of the effects of obvious depression on the estimates of the random effects.
[2] Interaction coefficient from a model including a term for interaction between the obvious depression scale and time since baseline. Additionally all relevant main effects are included in the model.
[3] Model includes linear and quadratic time since baseline and the obvious depression scale.
[4] Model additionally includes sex, education, and social status.
[5] Model additionally includes sex, education, social status, systolic blood pressure, smoking, BMI, total cholesterol, triglycerides, insulin, and leisure and work physical activity.

only be made by empirical studies of stability over time. The high long-term stability of the obvious depression score described in the introduction suggests that this scale should primarily be considered a measure of depressive traits, but in addition there are important differences between the Obvious Depression Scale and scales assessing acute depressive states: typical measures of depressive symptomatology such as the SCL-90-R [39] and the CES-D [40] ask the respondent about symptoms within the last week, while the MMPI does not specify any time period, but asks the respondent to indicate whether the item is characteristic of the respondent which—in the context of items asking about self-confidence, being tense at work, liking parties, and about being happy most of time—is likely to be interpreted by the respondent as questions about his or her personality. Thus, the instruction to the respondent and the item content differentiate trait and state measures, and in the case of the Obvious Depression Scale make the high correlation with the Neuroticism Scale of the NEO-PI-R understandable [14].

For hostility, a recent study observed a measure of cynical hostility to be associated with lower cognitive function, but not with decline in cognition [19]. We observed essentially the same results with a longer followup period and with a measure of general intelligence as cognitive outcome.

Generally, few predictors of cognitive decline have been identified based on strong evidence [12] which may partly reflect complex methodological problems. In spite of the comprehensive assessment of intelligence, and in spite of the long followup period sample attrition is an obvious limitation of our study since, for each outcome, the study was based on 1506 observations, of which only 136 and 184 were from the 70- and 80-year followups. Thus, statistical power

Table 5: Abbreviated Cook-Medley hostility scale: effects on WAIS IQs from 50 to 80.

| Model | Coefficient[1] | 95% CI | P formain effect | Interaction[2] coefficient | P for interaction |
|---|---|---|---|---|---|
| Full Scale IQ | | | | | |
| Model 1: Unadjusted[3] | −0.524 | (−0.74)–(−0.31) | <0.001 | 0.003 | 0.378 |
| Model 2: Demographics[4] | −0.320 | (−0.49)–(−0.15) | <0.001 | 0.003 | 0.386 |
| Model 3: Lifestyle factors[5] | −0.311 | (−0.48)–(−0.14) | <0.001 | 0.003 | 0.391 |
| Verbal IQ | | | | | |
| Model 1: Unadjusted[3] | −0.496 | (−0.71)–(−0.28) | <0.001 | 0.002 | 0.655 |
| Model 2: Demographics[4] | −0.283 | (−0.45)–(−0.11) | 0.001 | 0.001 | 0.690 |
| Model 3: Lifestyle factors[5] | −0.266 | (−0.44)–(−0.10) | 0.002 | 0.001 | 0.699 |
| Performance IQ | | | | | |
| Model 1: Unadjusted[3] | −0.451 | (−0.66)–(−0.24) | <0.001 | 0.005 | 0.269 |
| Model 2: Demographics[4] | −0.295 | (−0.48)–(−0.11) | 0.002 | 0.005 | 0.272 |
| Model 3: Lifestyle factors[5] | −0.297 | (−0.48)–(−0.12) | 0.001 | 0.005 | 0.280 |

[1]Fixed effect coefficient from a model only including the main effect of the hostility scale. See Section 3 for description of the effects of hostility on the estimates of the random-effects.
[2]Interaction coefficient from a model including a term for interaction between the abbreviated Cook-Medley Hostility Scale and time since baseline. Additionally all relevant main effects are included in the model.
[3]Model includes linear and quadratic time since baseline and the abbreviated Cook-Medley hostility scale.
[4]Model additionally includes sex, education and social status.
[5]Model additionally includes sex, education, social status, systolic blood pressure, smoking, BMI, total cholesterol, triglycerides, insulin and leisure and work physical activity.

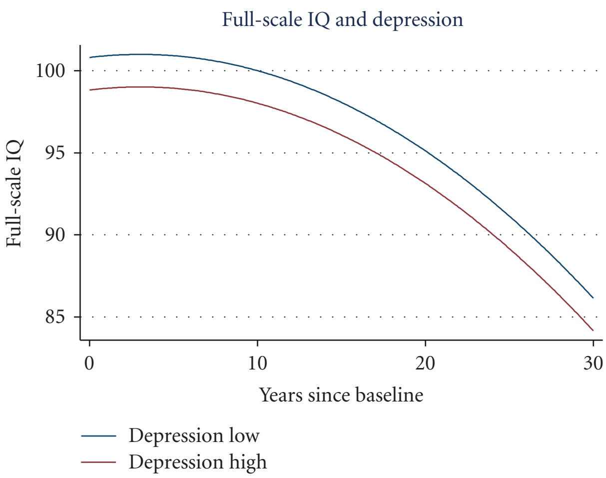


Figure 1: Obvious depression and decline in full-scale IQ from age 50 to age 80. The curves correspond to 1 SD below and above the mean on the Obvious Depression Scale. Adjusted for sex, education and social status.

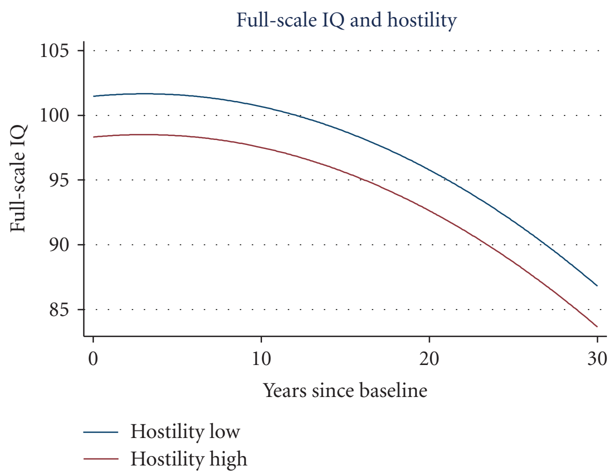


Figure 2: Hostility and decline in full-scale IQ age 50 to age 80. The curves correspond to 1 SD below and above the mean on the abbreviated Cook-Medley Hostility Scale. Adjusted for sex, education, and social status.

may not have been sufficient to detect weak associations between personality and decline in intelligence, particularly since cognitive change was only substantial at the last two followups.

If the negative findings with respect to influence of personality on the rate of cognitive decline reflect a statistical power problem, stronger effects may be expected on the outcome showing the most substantial decline. Over the 30-year followup period Table 3 shows about 1 standard deviation decline for Performance IQ, but only about half a standard deviation for Verbal IQ. Thus, clearer evidence of effects on decline was anticipated for the Performance IQ, but Tables 4 and 5 show no significant interactions for the Performance IQ. Furthermore, separate analyses of each of the WAIS subtests as outcome also showed no significant interactions between the MMPI scales and time since baseline (data not shown). However, potential effects of personality on age-related decline in specific cognitive functions should be further investigated.

The MMPI scales were not available for all followups, which is one of the reasons that we decided to conduct a prediction study based on the MMPI and covariate data from the 50-year baseline study. However, this may be considered a weakness of the study, to the extent that the traits assessed by the two MMPI scales may change during the long followup interval and to the extent that the 50-year scores were influenced by variance in the mental state of the participants. In particular, scores on the Obvious Depression Scale may reflect both trait and state components, although high retest correlations have previously been reported for this scale [13]. We observed substantial ten-year retest correlations from the 50-year baseline to the 60-year followup: 0.74 for the Cook-Medley Hostility Scale and 0.67 for the Obvious Depression Scale, and lack of stability is unlikely to be a major problem since the scales have previously been demonstrated to predict morbidity and mortality over long followup periods [10, 11].

Interpretations of the associations between low intelligence and traits such as obvious depression and hostility are ambiguous because they do not necessarily reflect effects of personality on intelligence or cognitive development since reverse causation—that is, effects of intelligence on personality or personality development—is also a possibility. Indeed, the associations need not reflect a causal relationship since both cognitive development and personality development may be related to factors such as adverse social conditions in childhood [41]. We were unable to control childhood history and social circumstances, but we did adjust for educational level and social status at the 50-year baseline. Tables 4 and 5 clearly show that a substantial part of the covariance between the MMPI scales and WAIS performance reflects association with education and social status. However, intelligence is likely to be one of the factors influencing achieved educational level, and therefore controlling for education may eliminate part of the variance in the association between personality and intelligence that is not due to confounding. In contrast, the tables show remarkably small effects of including a wide range of lifestyle-related factors in the statistical models. As discussed elsewhere, it has proven difficult to identify consistent effects of lifestyle factors on the rate of cognitive decline in the 1914 cohort [9], which is in line with the relatively small effects observed in major longitudinal cohort studies [42, 43].

To the extent that depression and hostility reflect stable personality characteristics, they are likely to be associated with stress and distress across the lifespan. This is the main rationale for the hypothesis that these personality traits influence cognitive decline since increased levels of stress may either influence brain functioning and cognition directly or indirectly through an association with cardiovascular dysfunction or disease [4, 19]. If effects of personality on decline in general intelligence cannot be demonstrated, this may be because the brain is less vulnerable to high levels of stress than expected, or because personality is only one out of a multitude of determinants of cognitive decline. Future studies should focus on the interaction between personality and other determinants of cognitive decline and track changes in personality and cognition across the lifespan to illuminate the direction of causality.

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*Research Article*

# Neighborhood Influences on Late Life Cognition in the ACTIVE Study

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Low neighborhood-level socioeconomic status has been associated with poorer health, reduced physical activity, increased psychological stress, and less neighborhood-based social support. These outcomes are correlates of late life cognition, but few studies have specifically investigated the neighborhood as a unique source of explanatory variance in cognitive aging. This study supplemented baseline cognitive data from the ACTIVE (Advanced Cognitive Training for Independent and Vital Elderly) study with neighborhood-level data to investigate (1) whether neighborhood socioeconomic position (SEP) predicts cognitive level, and if so, whether it differentially predicts performance in general and specific domains of cognition and (2) whether neighborhood SEP predicts differences in response to short-term cognitive intervention for memory, reasoning, or processing speed. Neighborhood SEP positively predicted vocabulary, but did not predict other general or specific measures of cognitive level, and did not predict individual differences in response to cognitive intervention.

## 1. Introduction

The neighborhood has emerged as a prominent level of analysis in studies of contextual influences on health and well-being in human development. This owes to the social organization of life within neighborhoods, and to the availability of data at neighborhood-like levels of analysis (i.e., census tracts). Neighborhood context has also received greater attention due to ecological psychology's conceptualization of human development as the product of a dynamic interaction between the individual and multiple nested environments, of which the neighborhood is one of the most immediate environments [1]. Contemporary scholarship on neighborhood factors has also highlighted the importance of understanding whether neighborhood variables add explanatory variance above and beyond individual differences.

Neighborhood socioeconomic status (SES) is the most consistently reported neighborhood-level predictor of cognitive outcomes—certainly in childhood, and potentially across the life span [2]. SES is also the strongest and most consistently reported neighborhood-level predictor of health outcomes among older adults—a relationship which may have a cumulative effect across the life span [3]. The association of neighborhood-level SES with health is in fact stronger among adults aged 60–69 than among young and middle-aged adults, and during these years its association with health is comparable to or stronger than the relationship of individual SES to health [4]. In addition to predicting poorer physical health, lower neighborhood SES is also associated with reduced rates of physical activity, increased incidence of depression and psychosocial stress, and less neighborhood-based social support and social engagement [3]. Many of these outcomes have also been identified as correlates of late life cognition [5], yet few studies to date have specifically investigated the role of the neighborhood in cognitive aging.

While neighborhood effects on late life cognition have received less attention, neighborhood effects on early-life cognitive development are relatively well documented. Neighborhood SES is positively correlated with cognitive development across the entire spectrum of child development, from the prenatal stages (in the form of reduced rates of congenital anomalies and neural tube defects among higher-SES neighborhoods, presumably due to reduced risk of exposure to environmental toxins; [6, 7]) and preschool years [8, 9] to academic achievement in the school age [10, 11] adolescent, and young adulthood years (e.g., high school graduation rates and college attendance [12]).

Four recent studies explored relationships between late life cognition and the neighborhood context on a broad scale. Wight and colleagues [13] found that after controlling for individual-level education and area-level median household income, elders living in areas with low neighborhood-level educational attainment (defined by census tract area) achieved lower cognitive status scores compared to elders living in areas with high neighborhood-level educational attainment (as assessed using the mini-mental state examination or MMSE [14]). A United Kingdom study [15] reported a clear and significant downward trend in cognitive performance on the MMSE and tests of verbal fluency and memory for older individuals living in neighborhoods with greater deprivation, after controlling for individual-level wealth, income, and education, across all age and gender groups. These effects were also robust after adjusting for the effects of individual systolic blood pressure, history of stroke, and duration of residence in the current neighborhood. Sheffield and Peek [16] moved beyond cross-sectional analysis to examine how neighborhood SES and ethnic composition (proportion Mexican American) predicted 5-year change in MMSE score in a US national sample. Independent of individual-level risk factors, odds and rate of incident cognitive decline increased as a function of lower neighborhood SES and decreased with the proportion of Mexican American neighborhood residents. Finally, recent findings from the Baltimore Memory Study suggest that the relationship between neighborhood and late life cognition may also depend on genotype [17]. Specifically, neighborhood psychosocial hazards were not found to be related worse cognitive performance. However, apolipoprotein E4 genotype was found to interact with high neighborhood psychosocial hazards, resulting in poorer cognitive performance on measures of processing speed and executive functioning after controlling for individual-level covariates. This suggests evidence of a gene-environment interaction in neighborhood's relation to late life cognition.

The existing studies focused on broad differences in late life cognitive *status* (i.e., MMSE score), but did not investigate the effect of neighborhood on different cognitive domains (see recommendations by Cullum et al. [18]). Furthermore, the use of the MMSE in these studies was not an ideal measure of cognition, as they targeted samples of initially healthy, independent elders. The MMSE is not sensitive to differences among healthy older adults, having been designed to screen for dementia [14]. Cognitive aging research has instead focused increasingly on the use of confirmatory factor analysis (CFA) and structural equation modeling (SEM) to explore whether differences in late life cognitive performance are related to general or specific processes. It has also been noted that conceptualizing late life cognition using a single general factor ("*g*") is a simplistic approach to a complex and dynamic cognitive system [19]. This suggests neighborhood influences should be investigated at both general and domain-specific levels. Neighborhood effects may support some dimensions of cognition more strongly than others, in addition to influencing general cognitive status.

The present study aimed to identify whether neighborhood effects on cognition were global, or specifically related to particular cognitive domains such as memory, reasoning, processing speed, everyday cognition, or vocabulary. Another innovation of the present study is the capacity to address whether neighborhood effects might also influence the magnitude of potential benefit from cognitive intervention. No study, in part because of a lack of data availability, has examined this question. Elucidating both the specificity of neighborhood effects on particular domains of cognition and the extent to which neighborhood affects cognitive training response may provide additional hints toward potential mechanisms by which the neighborhood exerts influence. For example, effects on the fluid cognitive abilities such as processing speed, memory, and reasoning (and their response to cognitive training) would suggest a more biologically mediated influence given their sensitivity to brain integrity. In contrast, effects on measures of crystallized cognitive abilities, especially vocabulary, might hint toward a more socioculturally mediated, and possibly lifespan accumulative influence, as crystallized cognitive abilities are developed with the accumulation of verbal knowledge, developed over a lifetime of experience in engaging with culture [20]. As this lifelong accumulation is strongly influenced during childhood, adolescence, and young adulthood, effects of current neighborhood SEP on crystallized abilities may also reflect, in part, effects of early-life neighborhood SEP.

The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study was a randomized, controlled clinical trial examining the effects of three cognitive interventions for community-dwelling older adults [21]. In ACTIVE, older adults from six US catchment areas (Baltimore/coastal Maryland; the metropolitan areas of Birmingham, Boston, Detroit, and Indianapolis; central Pennsylvania) completed a baseline assessment including multiple cognitive measures. Participants were then randomized to one of three ten-session cognitive intervention programs or a no-contact control condition.

The present study sought to examine whether neighborhood socioeconomic position (SEP) shows bivariate relationships with baseline cognitive level and immediate response to cognitive training, beyond individual-level predictors of cognition. If so, we aimed to discern whether neighborhood effects were significant for general cognitive ability ("*g*"), and whether effects were differential for specific cognitive abilities (memory, reasoning, speed, everyday cognition, and vocabulary). We hypothesized that the potential effect of neighborhood SEP may most likely occur by way of sociocultural processes, and therefore would have significant positive associations with general cognitive ability and with crystallized cognitive domains, including vocabulary. Neighborhood SEP was hypothesized to have relatively weaker, if detectable, associations with fluid cognitive domains, including memory, reasoning, speed, and everyday cognition.

## 2. Method

*2.1. Study Design.* The primary objective of ACTIVE was to test the effectiveness and durability of three cognitive interventions. The initial trial randomized individuals to one of three 10-session cognitive interventions designed to improve memory, reasoning, or processing speed performance or to a no-contact control condition [21]. Following training there was an immediate posttest and follow-up assessments at 1-, 2-, 3-, and 5-years after intervention. The current study sought to examine only the immediate pretest-posttest data, focusing on the proximal outcome measures used. The initial clinical trial enrolled participants and collected baseline data between 1997 and 2000. Information on potential covariates was collected, including demographic variables, MMSE, recent depressive symptoms, and general health. Testers at all six sites were trained in standardized assessment protocols and quality control by both study investigators, and the coordinating center ensured fidelity to testing procedures.

*2.2. Participants.* The initial sample of 2,802 participants was recruited through on-site presentations, letters to interested persons, newspaper advertisements, introductory letters, and follow-up telephone calls. Participants were cognitively healthy, community-dwelling older adults aged 65 to 94 years (mean age = 73.6 years, mean years of education = 13.5, mean MMSE = 27, 75.8% female, 72% Caucasian, 26% African American, and 2% other minority groups). The majority of participants (64%) were not married, and most reported good to excellent health (84.3%). Efforts were aimed at recruiting older adults independent of care at enrollment, as well as recruiting a diverse sample especially inclusive of African Americans, who were previously underrepresented in most cognitive training research. Exclusion criteria included (a) being under age 65 at the start of the study, (b) significant functional and/or cognitive decline at enrollment (e.g., impaired activities of daily living, MMSE < 23, and diagnosis of Alzheimer's disease), (c) having a medical condition disposing the participant to imminent cognitive decline or to mortality within the next 2 years, (d) severe sensory or communicative difficulties precluding participation in assessments and training, (e) having had cognitive training, or (f) planning to be unavailable during the testing and training periods of the study.

*2.3. Relationship of the Present Study to the Parent Study.* ACTIVE included multiple assessments of participants, but the present paper restricted itself to baseline cognitive performance and the immediate post-test. Neighborhood-level socioeconomic data from publicly available geographic datasets were then merged with ACTIVE data at the individual level. ACTIVE did not aim *a priori* to include multiple measures of individual-level socioeconomic position. Education (highest level achieved) was assessed for all participants, but other person-level socioeconomic indices (e.g., income, occupation) were not collected at baseline; occupational status was collected at the second annual follow-up occasion.

*2.4. ACTIVE Cognitive Data.* The cognitive domains measured in ACTVE included memory, inductive reasoning, processing speed, everyday cognition, and vocabulary; descriptive statistics on the sample performance for measures within each domain are illustrated in Table 1. Memory was measured using the Hopkins Verbal Learning Test (HVLT, [22]), a 12-word list memory task assessing immediate and delayed recall over 3 learning trials, the Rey Auditory Verbal Learning Test (AVLT, [23]), a 15-word list memory task assessing immediate and delayed recall over 5 consecutive learning trials, and the Rivermead Behavioral Memory Test [24], a paragraph recall task assessing immediate verbal episodic memory. Reasoning was measured using letter series [25], a task requiring accurate identification of the next logical letter group in a series of letters (e.g., a m b a n b a o b), letter sets [26], an inductive reasoning task requiring participants to identify which of 4 sets of letters is unrelated to the others (e.g., eef hhi llm ysy), and word series [27], a task requiring accurate identification of the next logical word in a series. Processing speed was measured using the useful field of view test (UFOV, [28]), a computer-administered task measuring visual sustained, selective, and divided attention through four subtasks, and the complex reaction time test [29], a computer-administered task measuring the time taken to perform various motor behaviors and to complete each task. Everyday cognition was measured using the Everyday Problems Test [30], a performance-based test of ability to solve everyday problems including medications, nutrition, phone use, shopping, and management of finances and household, the Observed Tasks of Daily Living (OTDL) [31], a timed task of problem solving in medication use, telephone use, and financial management, and the Timed Instrumental Activities of Daily Living (TIADL) [32], a timed test of ability to complete daily living tasks (e.g, find telephone number, make change, find and read ingredients on a can, find food items on a shelf, read instructions on medicine bottle). Vocabulary was measured using a multiple-choice measure of vocabulary attainment in which the participant is presented with a word and must choose one of four possible synonyms [26].

*2.5. Combining ACTIVE and Census Data.* Geocoding [33] is a process by which a location (e.g., street address) is assigned Cartesian mathematical coordinates, allowing for other levels of geographic information to be linked with that location. GeoLytics [34], a commercial provider of geocoding services and census demographic data, (1) geocoded the ACTIVE participant addresses, and (2) appended to these addresses data from the 2000 U.S. Census and 2002 Economic Census, creating a dataset that could be used to characterize the neighborhood environment. Following recommendations by prior U.S. neighborhood research [35], ACTIVE participant addresses were geocoded and linked with their associated census tract numbers, which allowed for census tract-level data from the 2000 U.S. Census to be appended to the individual-level ACTIVE data. Geocodes were checked for quality assurance. Participants receiving mail by post office boxes were excluded as such addresses cannot be verified

Table 1: Minimum, maximum, and mean scores (SD: standard deviation) for the ACTIVE sample on measures of baseline cognition.

| Measure | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|
| HVLT total | 4 | 36 | 26.05 | 5.50 |
| AVLT total | 0 | 73 | 48.45 | 10.63 |
| Rivermead total | 0 | 17.0 | 6.30 | 2.76 |
| Word series total correct | 0 | 30 | 9.45 | 4.91 |
| Letter series total correct | 0 | 30 | 9.99 | 5.55 |
| Letter sets total correct | 0 | 15 | 5.72 | 2.80 |
| UFOV task 1 | 16 | 500 | 30.99 | 40.71 |
| UFOV task 2 | 16 | 500 | 132.86 | 124.61 |
| UFOV task 3 | 43 | 500 | 321.09 | 134.12 |
| UFOV task 4 | 170 | 500 | 456.46 | 68.64 |
| CRT score 1 | 0.81 | 17.0 | 1.85 | 0.81 |
| CRT score 2 | 0.91 | 18.75 | 2.25 | 0.87 |
| OTDL total | 1 | 28 | 17.58 | 4.34 |
| EPT total | 0 | 28 | 18.62 | 5.76 |
| Vocabulary total correct | 0 | 18 | 12.37 | 3.95 |

to represent the participant's actual place of residence. Addresses with invalid house numbers, street names, and ZIP codes were flagged for followup; invalid addresses or poorly matched addresses were dropped from the analysis (93% of the ACTIVE addresses accurately matched to a US Geological Survey (USGS) geocode; final sample size = 2,521).

Census tracts are subdivisions of a county, with an average size of approximately 4,000 residents designed to capture collectively agreed-upon areas approximating neighborhoods. That is, the boundaries of census tracts were agreed upon by local officials knowledgeable of the area and were intended to be homogenous with respect to population characteristics, economic status, and living conditions [35]. Smaller measurement units of area-level SES (e.g., block group) have been shown to correlate highly with census-level measures of SES, and variability in SES among block groups is small relative to variability within their census tract [35]. The association of area-level SES with the cognitive measures was tested at three different levels of area measurement (block group, census tract, and ZIP code), with no significant difference in the strength of associations across levels. Because the census tract has traditionally been the most frequently used and most strongly recommended unit of measurement for area-level effects in health research [36], especially in terms of SEP [3, 35], and because it differed very little in model fit or regression coefficients from the other geographic levels, the census tract level of aggregation was selected for all final analyses involving SEP.

Neighborhood socioeconomic position was measured by creating a socioeconomic position (SEP) index [37]. Because SES variables such as income, education, and occupation are often strongly correlated and have been found to load onto a common factor at the census level [38], census-level data on these variables were combined into a weighted factor score to create a neighborhood SEP index that parsimoniously represented multiple socioeconomic variables.

*2.6. Statistical Analysis.* The analytical framework for the study involved exploratory and confirmatory factor analysis, structural equation modeling, and repeated measures mixed effects modeling. In keeping with "best practice" in conducting neighborhood research [38], individual- and area-level effects would ideally have been examined using a multilevel modeling (MLM) approach, with samples of individuals clustered in neighborhoods allowing formal assessment of random variation within neighborhoods. However because ACTIVE was not originally designed to sample data stratified by neighborhood but sampled widely across each region, the insufficient sample size within each neighborhood measured precluded the use of MLM. In keeping with recent scholarship, the current study can instead be classified as ecologic, in which neighborhood variables are measured for each person [39]. Statistical Package for the Social Sciences (SPSS) 18.0 and Analysis of Moment Structures (AMOS) 18.0 were used to conduct all statistical analyses. Prior to analysis, all variables were inspected for consistency with the assumption of multivariate normality (to permit maximum likelihood estimation). Where that assumption was not met, Blom transformations [40] were applied to those variables to improve the normality of their distributions. While no data were missing for any neighborhood-level variables, in a few instances data were missing from the ACTIVE dataset's cognitive variables (e.g., due to failure to complete a task or attrition between the baseline and posttraining testing occasions). Models were estimated using full information maximum likelihood (FIML), which uses all available data (thereby not eliminating participants with incomplete data).

Preparatory to examining the relationship of neighborhood SEP to ACTIVE cognitive outcomes, factor analytic constructs representing neighborhood SEP and baseline cognition were developed. Criteria for acceptable model fit indices included root mean square error of approximation (RMSEA) <0.06, comparative fit index (CFI) >0.95, normed fit index (NFI) >0.95, and Tucker-Lewis Index (TLI) >0.95

[41]. Exploratory factor analyses were first conducted on the neighborhood SEP variables, using Promax rotation to allow optimal fit to the data. A weighted composite measure of SEP was then estimated and optimized in AMOS based on a common factor identified in the exploratory factor analysis. The cognitive measurement model for the present study dimensionalized cognition into several domains, for which the ACTIVE dataset was well designed, having captured at least three measures each of specific cognitive domains including memory, reasoning, processing speed, and everyday cognition, or measures of cognition related to everyday abilities. ACTIVE also collected a measure of vocabulary.

As stated in the introduction, cognitive aging research has increasingly emphasized conceptualization of cognition as both a general ability ("*g*"), and a multifaceted system of specific cognitive domains which may respond differently to neighborhood effects. Therefore the model also estimated effects on each of the above cognitive domains, as well as effects on a higher-order factor representing general cognition or "*g*", which captures the shared variance among the five cognitive domains in the measurement model. The SEP and cognition factor models were combined in a structural equation model estimating regression paths from SEP to the each of the cognitive factors. Model covariates included age, quadratic age, years of education, gender, and race (White, African American). Measures of individual wealth and duration of residence in neighborhood were not collected in ACTIVE, and could not be included as covariates.

Neighborhood SEP as a predictor of training gains was estimated as repeated-measures mixed effects models [42] rather than as structural equation models because this provided a more flexible interface for the analysis of training gains, which was operationalized as a two-occasion difference score (and thus would not significantly benefit from a latent variable approach) while still permitting FIML estimation for maximum power in the presence of missing data (i.e., using all available cases). Model covariates included age, years of education, gender, and race. Separate models were estimated for each domain trained (memory, reasoning, or speed) to examine the gains of each training group relative to other participants who did not receive that training (i.e., the other two training groups and the no-contact controls). Each model tested SEP as a continuous predictor and occasion (baseline, posttest) and training group (received training on the ability being examined or not) each as class variables. Each model also tested all possible two-way interactions and the three-way interaction of SEP, occasion, and group. Interactions were estimated as residualized interaction terms to correct for collinearity with the model's main effects.

## 3. Results

Neighborhood SEP was initially developed using exploratory factor analysis (EFA) to combine 8 indicators of area-level SES: median household income, % households with income ≥ $150,000, % persons in poverty, % with ≤9th grade education, % with ≤ high school education, % with ≥ Bachelor's degree, % unemployed, and % working in management or higher. The EFA indicated all 8 variables loaded strongly onto one factor (eigenvalue = 5.97), explaining 71% of the variance (factor loadings ranged from 0.71 – 0.94). All indicators were then included in a confirmatory factor analysis, where modification indices (MI) suggested high intercorrelations of error variances among variables (e.g., ranging up to MI = 1325.42). To derive an optimally-fit, parsimonious set of variables capturing the shared variance of characteristics on which SEP is typically based (e.g., income, education, and occupational attainment), redundant variables were progressively removed from the model.

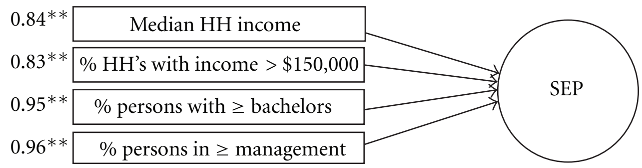


Figure 1: SEP factor structure model. Standardized loadings (ß) to the left of each indicator; $^{**}p < 0.001$; HH = household.

The final SEP factor model (Figure 1) consisted of four variables measuring socioeconomic advantage in income, education, and occupation (median household income, % with income ≥ $150,000, % with ≥ Bachelor's degree, and % in management or higher). As two indices of area-level income would be expected to correlate, a correlation path was estimated between the error variances of median household income and % income ≥ $150,000 and was retained in all subsequent models. Model fit was good (CFI = 0.999, NFI = 0.999, TLI = 0.996, $\chi^2/df$ ratio = 8.23 ($p = 0.004$), and RMSEA = 0.05 ($p = 0.36$)). Notably, the variables loading on the latent SEP factor are all indicators of neighborhood affluence or advantage rather than disadvantage; prior neighborhood research has suggested that measures of social advantage, compared to social disadvantage, may be especially important protective factors in neighborhood influences on development [2]. Mean SEP factor scores were found to differ across ACTIVE catchment sites ($F(5, 2515) = 184.30$, $p < .001$; Table 2). Reestimating the models with catchment site as an additional covariate did not alter the pattern of effects, but reduced the fit of the model to an unacceptable extent. Thus, ACTIVE catchment site was tested but not retained in the study models as a covariate.

*3.1. Measurement Model of Baseline Cognition.* The present paper sought to characterize both general and specific domains of late life cognition. The measured variables (Figure 2) related to memory were combined to represent a memory factor; measures of reasoning combined to form a reasoning factor; guided by preliminary exploratory analyses, measures of processing speed optimally first combined into separate factors based on test, which were then combined to form a speed factor, and individual measures of everyday cognition combined on a factor representing everyday cognition. Because these cognitive domains were represented

Table 2: Mean, (standard deviation), and range of SEP indicators and factor scores for the overall study sample and by catchment site.

| Site | Median household income | % of households with income > $150,000 | % with bachelor degree or higher | % in management positions or higher | SEP factor score |
|---|---|---|---|---|---|
| All | 44,680.96<br>(22,448.78)<br>7,610–170,790 | 5.7<br>(8.44)<br>0–54.0 | 28.45<br>(21.48)<br>1.0–90.0 | 36.19<br>(16.15)<br>4.0–84.0 | 2.91<br>(0.93)<br>0.28–5.76 |
| UAB ($N = 435$) | 51,900<br>(21,214)<br>7,610–143,968 | 7.97<br>(9.18)<br>0–49.0 | 37.74<br>(21.85)<br>1.0–81.0 | 42.61<br>(15.35)<br>13.0–69.0 | 3.31<br>(0.81)<br>1.04–5.18 |
| IU ($N = 450$) | 45,630<br>(18,390)<br>12,154–133,479 | 5.03<br>(6.33)<br>0–42.0 | 30.6<br>(19.26)<br>1.0–75.0 | 36.18<br>(14.93)<br>4.0–69.0 | 2.94<br>(0.91)<br>0.36–5.14 |
| HRCA ($N = 346$) | 62,359.64<br>(23,438.77)<br>18,917–148,257 | 11.46<br>(10.54)<br>0–50.0 | 48.59<br>(21.93)<br>5.0–9.0 | 52.13<br>(15.49)<br>6.0–84.0 | 3.78<br>(0.74)<br>0.93–5.76 |
| JHU ($N = 415$) | 32,791.54<br>(10,699.90)<br>10,408–84,832 | 2.0<br>(2.89)<br>0–25.0 | 17.39<br>(12.38)<br>2.0–75.0 | 29.35<br>(10.4)<br>10.0–75.0 | 2.46<br>(0.64)<br>0.95–4.59 |
| WSU ($N = 459$) | 48,034.58<br>(28,051.51)<br>9,615–170,790 | 7.28<br>(10.77)<br>0–54.0 | 26.42<br>(21.27)<br>1–75.0 | 34.93<br>(17.83)<br>7.0–76.0 | 2.83<br>(1.03)<br>0.28–5.41 |
| PSU ($N = 416$) | 29,345.72<br>(8,620.85)<br>10,101–53,096 | 1.17<br>(1.01)<br>0–6.0 | 12.72<br>(6.30)<br>3.0–28.0 | 24.30<br>(8.01)<br>15.0–44.0 | 2.27<br>(0.51)<br>1.35–3.29 |

Note: UAB: University of Alabama; IU: Indiana University; HRCA: Hebrew Rehabilitation Centre for Aged; JHU: Johns Hopkins University; WSU: Wayne State University; PSU: Pennsylvania State University.

by latent factors (making them "purer" representations of their domains), the vocabulary measure was also represented as a factor by using odd and even scores as indicators loading on a single vocabulary factor; this effectively transforms that factor into a construct representing the odd-even split half reliable variance of the measure. Model covariates included linear age, the quadratic effect of age, years of education, gender, and race. The disturbance terms of all cognitive factors were permitted to correlate with one another. The error variances of the UFOV 2 and 4 subtests, and the Everyday Problems Test and vocabulary were also allowed to correlate in the process of optimizing model fit (Table 3). As the first-order cognitive factors all correlated with one another ($p < 0.001$), and as discussed earlier, the model included a second-order factor, "$g$", capturing the variance shared by the cognitive factors (Table 4). Model fit was acceptable (CFI = 0.98, NFI = 0.97, RFI = 0.96, TLI = 0.97, RMSEA = 0.046, ($p = 1.00$), $\chi^2/df$ ratio = 6.40, and ($p < 0.001$)).

*3.2. Neighborhood SEP Predicting Baseline Cognitive Level.* The SEP and cognitive measurement models were combined in a structural equation model (Figure 2) estimating regression paths from neighborhood-level SEP to the cognitive constructs of "$g$", reasoning, speed, everyday cognition, and vocabulary (a path could not be estimated for SEP or any covariates to memory). Model covariates included linear age, the quadratic effect of age, years of education, gender, and race. Model fit was adequate (CFI = 0.96, NFI = 0.96, TLI = 0.95, $\chi^2/df$ ratio = 6.52, ($p < 0.001$), and RMSEA = 0.05 ($p = 0.99$)). After controlling for individual-level predictors, SEP remained a significant predictor of vocabulary alone ($p < 0.01$; Table 5).

*3.3. Response to Cognitive Training.* Repeated-measures mixed effects analyses of variance were used to estimate whether neighborhood SEP predicted differences in training-related gains, beyond practice-related gains, on posttraining measures of memory, reasoning, and speed. Three separate models examined the gains of each training group relative to all other participants (control group plus members of other training groups) who did not receive that particular training (i.e., for the reasoning outcome, the reasoning training group was compared to the control plus memory plus speed training groups). Each model tested SEP as a continuous predictor and occasion (baseline, posttest) and training group (received training on the ability being examined or not), all possible two-way interactions, and the three-way interaction of SEP, occasion, and group. Significant effects for occasion, training group, and their interaction were observed as previously reported in the parent study. A main effect was found for SEP, but for SEP to predict differences in response to ACTIVE training the three-way interaction would have to be significant; this was not found for any of the trained abilities (Memory: $F(1, 4594) = 0.66, p = 0.42$; Reasoning: $F(1, 4847) = 0.001$, $p = 0.98$; Speed: $F(1, 4793) = 0.001$, $p = 0.97$).

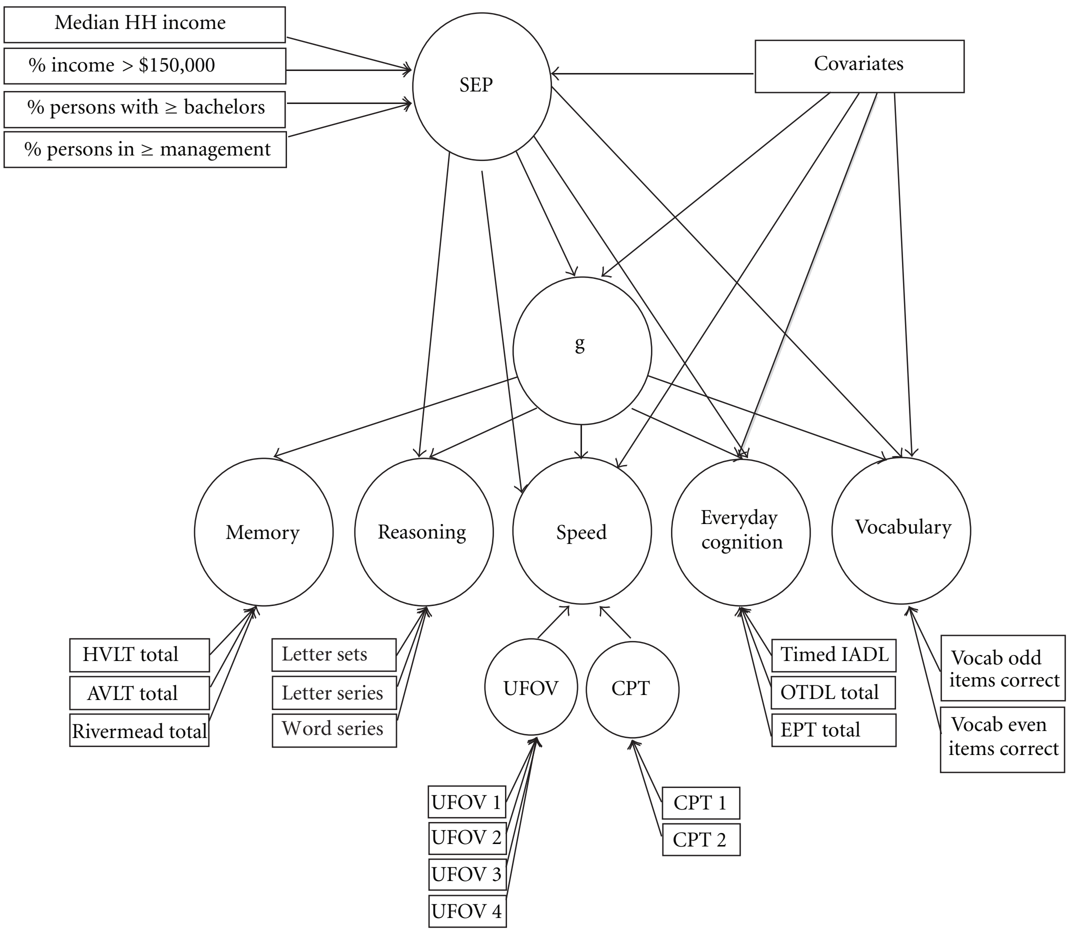


Figure 2: Schematic of the predictive model of baseline cognition. Regression paths were estimated from all covariates (gender, age, education, and race) to g, reasoning, speed, everyday cognition, and vocabulary, and could not be estimated for memory. Model covariates included age, quadratic age, education, gender, and race. HH = Household.

## 4. Discussion

The present study sought to examine the relationship between current neighborhood-level socioeconomic position (SEP) and cognitive level, including several specific cognitive domains in the ACTIVE study, and response to cognitive training. The findings demonstrated that, after controlling for individual-level demographic predictors, census-defined neighborhood socioeconomic position independently predicted differences in late life vocabulary as measured in ACTIVE, but not differences in general cognition ("*g*"), reasoning, everyday cognition, or speed. These findings differed from the similar prior study by Brandt [22], which found neighborhood SES effects on a composite cognitive measure capturing cognitive status, verbal fluency, verbal learning, and prospective memory. The results also demonstrated that neighborhood SEP does not predict individual differences in the immediate response to cognitive training in memory, reasoning, or processing speed.

The lack of effect for neighborhood SEP on any fluid cognitive ability (memory, reasoning, speed, and everyday cognition) or on cognitive plasticity (i.e., response to training) is somewhat surprising given the extensive research documenting neighborhood effects on factors affecting brain health, such as cardiovascular fitness and chronic diseases (e.g., [43, 44]). It would be reasonable to hypothesize that neighborhood could indirectly affect fluid cognitive abilities and training gains, which are more sensitive to compromised brain health than vocabulary [45], through differences in access to health care, nutrition, and opportunities for exercise; however, results suggest that if these indirect effects are present they may be relatively weak. Given the relatively good health of this cohort at baseline testing, the majority of respondents reported "good" or "excellent" health, and all were independent of care, there also may not have been sufficient variability in baseline fluid cognition scores for neighborhood effects to be detectable.

The specific association of neighborhood SEP with vocabulary suggests neighborhood influences cognition more through sociocultural mechanisms, as vocabulary captures crystallized cognitive abilities, the dimension of cognition related to stored verbal knowledge, developed over a lifetime of engaging with culture [20]. Vocabulary is accumulated socially through acculturation. Crystallized knowledge is also the only domain that continues to improve

Table 3: Standardized loadings ($\beta$) of cognitive indicators on first-order cognitive factors. $^{**}p < 0.001$.

| Indicator variable | Interim factor | Cognitive factor* | $\beta$ |
|---|---|---|---|
| UFOV1 | UFOV | | 0.53** |
| UFOV2 | UFOV | | 0.78** |
| UFOV3 | UFOV | | 0.80** |
| UFOV4 | UFOV | | 0.65** |
| CRT1 | CRT | | 0.93** |
| CRT2 | CRT | | 0.91** |
| | *UFOV* | Speed | 0.77** |
| | *CRT* | Speed | 0.77** |
| AVLT total recall | | Memory | 0.78** |
| HVLT total recall | | Memory | 0.82** |
| Rivermead total recall | | Memory | 0.62** |
| Letter series score | | Reasoning | 0.92** |
| Letter sets score | | Reasoning | 0.70** |
| Word series score | | Reasoning | 0.90** |
| Everyday problems test | | Everyday cognition | 0.83** |
| Timed Instrumental Activities of Daily Living (reverse-coded) | | Everyday cognition | 0.68** |
| Observed Tasks of Daily Living | | Everyday cognition | 0.69** |
| Vocabulary, odd items | | Vocabulary | 0.83** |
| Vocabulary, even items | | Vocabulary | 0.87** |

Note: Speed is defined as a second-order factor since better fit was yielded when local associations among UFOV and CRT measures were captured in a first-order factor. These first-order factors were then allowed to load on a second-order speed factor. See Section 2 for full names of tests used.

Table 4: Standardized coefficients ($\beta$) for loadings of domain-specific cognitive factors on "$g$". $^{**}p < 0.01$.

| Cognitive construct | $\beta$ |
|---|---|
| Reasoning | 0.91** |
| Speed | −0.85** |
| Memory | 0.79** |
| Everyday | 0.96** |
| Vocabulary | 0.64** |

in the presence of advancing age, compared to fluid cognitive abilities which become less efficient with age [46]. A review of vocabulary in aging [20] reported increasing vocabulary scores with advancing age, as well as with higher education (although in the present study neighborhood SEP predicted vocabulary independent of education). Vocabulary measures like the one used in this study, requiring multiple-choice word recognition rather than production of word meanings, are especially robust to the effects of aging [20].

Neighborhood may influence vocabulary by facilitating or constraining one's capacity for, and influencing the results of, sociocultural engagement in the community. It may do so by providing resources or facilities [47] encouraging cultural interaction or by encouraging acculturation through modeling and social comparisons. That is, high-SEP neighborhoods may support vocabulary because more neighbors with high educational and occupational attainment provide more social models of high achievement. This modeling may foster upward social comparisons [48, 49], pressuring or evoking desire in an individual to be more like his or her neighbors, resulting in greater engagement in activities enhancing cognitive skills and abilities. Positive community social processes may also foster sociocultural interaction. Certainly, other researchers have hinted toward social processes (i.e., social norms, interactions and ties, and collective efficacy) as the mechanism linking neighborhoods with developmental outcomes [2, 47].

While vocabulary is related to current neighborhood SEP, it is important to consider that vocabulary is also highly correlated with childhood cognitive level [45]. Vocabulary often reflects both cognitive reserve and premorbid ability level [50], as it is most robust to not only aging but physical insults to the brain, including head trauma, medical conditions, and exposure to neurotoxins [45]. Expressed differently, when cognition is measured in late life, vocabulary is the strongest index of early life cognitive ability [51]. Therefore, the current neighborhood-vocabulary association found in this study may reflect both historical and current relationships between neighborhood context and cognition; the well-established relationship between neighborhood and cognition in childhood supports this hypothesis. Thus, a part of the late life neighborhood effects on cognition observed here may represent an "echo" of this earlier relationship during a critical period of development. There is evidence

Table 5: Standardized coefficients ($\beta$) for prediction of cognitive domains by SEP and covariates. $^{**}p < 0.01$.

| | Cognitive factors | | | | |
|---|---|---|---|---|---|
| | "g" | Speed | Reasoning | Everyday cognition | Vocabulary |
| SEP | 0.02 | 0.02 | 0.03 | −0.02 | 0.07** |
| Education | 0.37** | 0.11** | 0.03 | 0.09** | 0.21** |
| Age | −0.49** | 0.14** | 0.11** | 0.13** | 0.36** |
| Gender | 0.34** | 0.40** | −0.27** | −0.26** | −0.15** |
| Race | 0.35** | 0.02 | 0.01 | 0.02 | 0.13** |

Note: Beta weights to general cognition, or *g*, are predicting total variance in that factor. Beta weights to the remaining cognitive factors represent additional significant predictor effects after controlling for *g*.

that early life socioeconomic indicators also predict late life cognitive outcomes. Berkman and Glymour [52] found that the county of residence during primary schooling, by way of the laws guiding educational requirements in that county, predicted individual differences in both educational attainment and late life cognitive performance. Similarly, Wilson and colleagues [53] reported that parental education during childhood independently predicted cognitive activity across the lifespan and into old age. Therefore, it is likely that childhood SEP, had it been collected in ACTIVE, may be associated with both late life vocabulary and late life neighborhood SEP.

Finally, it was reported in the results that there were catchment site-level differences in mean SEP. Clearly, an individual's neighborhood SEP is also part of the general SEP of the region in which that individual lived; the interaction between neighborhood and regional SEP may influence how a neighborhood's SEP relates to cognition. For example, in regions with lower overall SEP, it may be more "normal" to live in a lower-SEP neighborhood; this experience might differ from the experience of living in a low-SEP neighborhood within a high-SEP region, and might differently affect cognition. Such issues have been explored on the level of individual SES-to-neighborhood SES interactions (e.g., low individual education predicts worse cognition for those living in low-education neighborhoods versus high-education neighborhoods, [13]), but neighborhood-region SEP interactions affecting cognition have not been described to our knowledge.

*4.1. Study Limitations and Future Directions.* This study was limited in several ways due to its nature as a secondary analysis. Several covariates would ideally have been included had they been collected in the parent study, including individual-level income and occupation (although this may later be examined in for the subset present at the 2nd-annual followup) and the length of time lived at current residence. As a consequence, this study included only a single measure of individual-level socioeconomic status. This is an important limitation, as the observed neighborhood association may be attributable, partially or completely, to unmeasured differences in individual-level socioeconomic status. The possibility that the relationship between vocabulary and neighborhood SEP can be explained by childhood neighborhood SEP must also remain speculation, as this data was not originally collected in ACTIVE. This study therefore was unable to examine measures of childhood socioeconomic status (e.g., mother's or father's education and income, neighborhood SEP in childhood). It is likely that childhood SEP is associated with both vocabulary and late life SEP, in which case vocabulary's relationship with current neighborhood SEP would be expected to diminish or disappear if childhood SEP was accounted for in the study.

The cross-sectional nature of effects also limits discussion to relationships among variables at a particular time rather than to causal or temporal relationships between variables. Longitudinal assessment of these relationships is an important next step that will be attempted in future studies. At the time this study was conducted, ACTIVE collected its 10th annual follow-up testing occasion, allowing examination of the interaction between 2000 neighborhood and cognition with 2010 neighborhood and cognition. Future studies will also attempt to examine (a) neighborhood effects on change trajectories, and (b) whether there were neighborhood moves for participants, and whether such moves were associated with functional changes. Furthermore, at this follow-up data was collected documenting participant's county of primary schooling. National historical data will allow investigators to use county information to explore whether and how distal environmental influences (i.e., county-level SEP and educational laws during primary schooling years) might predict contextual neighborhood characteristics and cognitive outcomes later in life.

## 5. Conclusions

This paper adds to the body of research examining neighborhood-cognition associations in late life, and extends previous findings by looking beyond general cognition or cognitive status to examine effects of neighborhood across specific cognitive domains. The finding that neighborhood SEP predicts crystallized cognitive abilities (specifically, vocabulary) suggests that neighborhood effects may be most related to sociocultural influences on cognitive development. There was a lack of association between neighborhood SEP and fluid cognitive abilities, as well as between neighborhood SEP and immediate cognitive change following training. As discussed above, future research should investigate how associations between early life neighborhood context and cognitive development may influence cognitive function and neighborhood selection in late life.

## Acknowledgments

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*Research Article*

# The Role of Education and Intellectual Activity on Cognition

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Although educational attainment has been consistently related to cognition in adulthood, the mechanisms are still unclear. Early education, and other social learning experiences, may provide the skills, knowledge, and interest to pursue intellectual challenges across the life course. Therefore, cognition in adulthood might reflect continued engagement with cognitively complex environments. Using baseline data from the Baltimore Experience Corps Trial, multiple mediation models were applied to examine the combined and unique contributions of intellectual, social, physical, creative, and passive lifestyle activities on the relationship between education and cognition. Separate models were tested for each cognitive outcome (i.e., reading ability, processing speed, memory). With the exception of memory tasks, findings suggest that education-cognition relations are partially explained by frequent participation in intellectual activities. The association between education and cognition was not completely eliminated, however, suggesting that other factors may drive these associations.

## 1. The Role of Education and Intellectual Activity on Cognition

Cognitive enrichment early in life may account for some of the variation in cognitive ability in adulthood. Consistently, higher educational attainment is associated with greater levels of cognitive performance [1–5], as well as with a reduced risk of dementia and Alzheimer's disease [6–9]. Although the exact mechanisms are unclear, one possibility is that educational experiences provide the foundation for continued intellectual stimulation across the life course, resulting in improved cognitive functioning in late adulthood. Prior research findings contribute to the plausibility of this assumption. First, educational attainment is often associated with greater participation in various lifestyle activities [10, 11], especially those that are cognitively demanding [12–14]. Second, the beneficial effects of maintaining an engaged lifestyle have been demonstrated across several studies, even when activities are introduced later in life [15–19].

Education may cultivate the knowledge, skills, and ability necessary for continued participation in intellectually demanding activities (e.g., reading, taking courses) well into later adulthood. According to the engagement hypothesis, in-dividuals who continuously place significant demands on their intellectual resources (i.e., through multiple and complex decisions, ill-defined problem solving) may maintain or even enhance cognitive potential [3, 20, 21]. Therefore, compared to other forms of lifestyle activity, greater participation in intellectually demanding activities may be especially beneficial for cognitive function [3, 10, 14, 20–24]. For instance, Hultsch et al. [10] found that individuals who more frequently participated in novel information processing were less likely to show cognitive declines over time. Likewise, Ghisletta and colleagues [25] found that activities such as reading a book and playing games were related to changes in perceptual speed, whereas other forms of engagement (e.g., physical, social, and religious activities) were not associated with such changes. Conversely, activities low in cognitive stimulation, such as watching television, have been related to an increased risk of cognitive impairment [26]. Moreover, activities low in cognitive demand may be more prevalent among those with lower educational attainment [27].

Although several studies have explored the independent contributions of education or activity on cognition, few studies have explored these factors in combination. The current study examines whether educational attainment and late-life activities contribute independently to cognitive performance or if education-cognition relations can be at least partly explained by participation in activities in adulthood. Specifically, our work is driven by the following assumptions: (1) education will be associated with cognition, such that individuals with higher levels of educational attainment will demonstrate better performance on cognitive measures; (2) older adults with higher levels of educational attainment will report being more active, especially in intellectually demanding activities; (3) intellectual activities will influence cognition, such that participation in intellectually demanding activities (as compared to other forms of activity) will be related to better cognitive performance, independent of education. Consequently, we expect that the association between education and cognition will be attenuated (not completely eliminated) once participation in a wide variety of lifestyle activities is considered [28, 29]. Further, we also expect that the effects will be greatest for intellectually demanding activities, as these may be more strongly associated with both education and cognition [1–5, 10, 12–14].

We wish to be clear that this cross-sectional, correlational research does not allow us to establish the temporal ordering among variables and acknowledge that reciprocal relationships could be possible. Therefore, we cannot draw any conclusions regarding causal relationships between education, activity and cognition as implied by our theoretically based model (i.e., education leads to greater participation in activities, which in turn, promotes cognition). However, in the absence of longitudinal data, establishing associations among education, activity, and cognition allows us to better conceptualize plausible mechanisms for the promotion of cognitive health in adulthood.

## 2. Methods

We report data collected as part of the Baltimore Experience Corps Trial (see Fried and colleagues [30] for detailed description of recruitment procedures and study design), a community-based volunteer program designed as a health promotion model for older adults while simultaneously addressing the academic needs of elementary school children [30, 31]. Briefly, in this program older adults (age 60 and older) are trained and placed into elementary school classrooms (kindergarten to third grade) to serve as mentors and tutors for young children. To be eligible to serve as a volunteer, individuals had to meet screening criteria for general cognitive status (as indicated by a score of greater than 23 on the Mini-Mental State Exam (MMSE)) [32] and perform at a sixth grade reading level or higher on a measure of functional literacy, the Wide Range Achievement Test (WRAT-4) [33]. The data we report are based on baseline scores for measures before participants ($N = 702$) were randomly assigned to one of two conditions: to the intervention (Experience Corps program) or to a low-activity control group.

Table 1: Demographic characteristics of sample.

| | % | M | SD |
|---|---|---|---|
| Age (years) | | 67.49 | 5.95 |
| Education (years) | | 13.85 | 2.94 |
| Elementary school (K-8) | 2.3 | | |
| High school/equivalent (9–12) | 40.2 | | |
| College (13–16) | 41.2 | | |
| Postgraduate | 13.1 | | |
| Other | 1.1 | | |
| Income (past 12 months) | | | |
| Less than $5,000 | 6.1 | | |
| $5,000–14,999 | 23.1 | | |
| S15,000–34,999 | 35.2 | | |
| $35,000–74,999 | 27.4 | | |
| $75,000 or greater | 6.8 | | |
| Sex | | | |
| Male | 15.4 | | |
| Female | 84.6 | | |
| Race | | | |
| African American | 90.5 | | |
| European American | 5.1 | | |

*2.1. Sample.* For purposes of the present analyses, individuals were included ($n = 675$) if they completed the Lifestyle Activities Questionnaire (LAQ) [16] and cognitive measures as part of the baseline assessment. Participants were, on average, 67 years of age (SD = 5.95, range = 60–89 years), had 13.9 years of education (SD = 2.94, range = 6–22 years), and were predominantly female (84.6%) and African American (90.5%) (Table 1). In addition, participants reported their current health as excellent, very good, or good (89.1%) and displayed very low levels of depressive symptoms (as indicated by a score less than 5 on the 15-item Geriatric Depression Scale; M = 1.5 symptoms; SD = 1.7) [34]. We have reported elsewhere that individuals who did not complete the LAQ at baseline tended to be older, reported poorer health, and demonstrated lower cognitive performance (as measured by the MMSE and WRAT-4) ($P$'s $< 0.05$). There were no differences in educational attainment between those who completed and those who did not complete the LAQ measure at baseline [35].

*2.2. Measures*

*2.2.1. Education.* Educational attainment was defined as the self-reported number of years of formal education completed.

*2.2.2. Activity.* Frequency of participation in a wide range of activities was assessed via the Lifestyle Activities Questionnaire [16]. Participants rated their typical frequency of participation in various daily activities (e.g., cooking, singing, gardening, listening to music, reading) over the past year. Responses were made on a 6-point scale (never/less often than once a month, once a month, 2 to 3 times a month, once a week, a few times a week, and every day).

For analyses, we classified lifestyle activities into five activity domains to examine the effects of participation in specific types of activity on education-cognition relations (Table 2; also see Parisi et al. [35] for detailed information on activity items and domains). These activity domains were theoretically based on a comprehensive review of the existing literature [10, 12, 14, 16, 22, 36, 37] and have been used in our previous research [35]. Specifically, individual activity items were classified into *intellectual* (6 items: reading a book, reading a newspaper, balancing checkbook, using a computer, crossword puzzles, taking courses/classes), *social* (7 items: discussing local or national issues, visiting, clubs/organizations, attending church/religious service, playing cards/games, going to movies, going to plays/concerts), *physical* (3 items: shopping, gardening, hunting/fishing/camping), *creative* (4 items: singing, playing an instrument, cooking, drawing or painting, sewing/mending/fixing things), and passive (4 items: watching TV, listening to music, listening to the radio (not music), looking at art) activity domains (Table 2). The frequency of participation was calculated within each activity domain by averaging frequency responses to individual activity items, with lower numbers reflecting less participation.

*2.2.3. Cognition.* Measures were selected to assess global cognitive status (MMSE) [32] and several distinct cognitive processes, such as reading ability, processing speed, and memory performance. *Reading ability* was assessed using the reading subtest of the Wide Range Achievement Test, version 4 (WRAT-4) [33]. To complete this test, participants are asked to read aloud a list of 15 letters and 55 words increasing in difficulty level (from cat to terpsichorean). Higher scores reflect a greater number of correctly pronounced words. *Processing speed* was assessed by the pattern comparison task [38] in which participants are asked to make "same" or "different" judgments as quickly as possible (for 30 seconds) for sequences of pairs of patterns. Higher scores reflect a greater number of correct responses. *Memory performance* was assessed by the Rey Auditory Verbal Learning Test (AVLT) [39, 40], capturing both immediate and delayed recall. Using a word-list learning paradigm, participants are first presented with a 15-word list (List A) and asked to recall the list (this process is repeated for five trials). Next, participants are presented with one trial of a second 15-word list (List B; interference) and asked to recall the list. Finally, participants are asked to recall the words on the initial list (List A) after a 20-minute delay (delayed recall trial). For scoring, immediate recall reflects the sum of words recalled on trials 1 to 5 (on List A) and delayed recall reflects total number of words recalled after a 20-minute delay. For each of these outcome measures, higher scores reflect greater memory ability.

Table 2: Activity domains from the lifestyle activities questionnaire.

| Activities | Percentage of individuals reporting activity | M | SD |
|---|---|---|---|
| Intellectual | | | |
| Reading a book | 88.7 | 3.1 | 1.8 |
| Reading a newspaper | 87.7 | 3.6 | 1.7 |
| Balancing checkbook | 82.6 | 2.0 | 1.5 |
| Using a computer | 57.0 | 2.2 | 2.2 |
| Crossword puzzles | 49.0 | 1.6 | 2.0 |
| Taking courses or classes | 25.7 | 0.6 | 1.2 |
| Social | | | |
| Discussing local or national issues | 96.0 | 3.9 | 1.3 |
| Attending church religious service | 91.3 | 3.0 | 1.3 |
| Visiting | 87.2 | 2.3 | 1.4 |
| Clubs/organizations | 78.6 | 2.2 | 1.6 |
| Playing cards or games | 49.4 | 1.2 | 1.5 |
| Going to movies | 33.9 | 0.5 | 0.9 |
| Going to plays concerts | 33.5 | 0.4 | 0.7 |
| Physical | | | |
| Shopping | 98.8 | 3.3 | 1.0 |
| Gardening | 46.9 | 1.5 | 1.8 |
| Hunting, Fishing, Camping | 3.7 | 0.1 | 0.3 |
| Creative | | | |
| Preparing food | 97.6 | 4.2 | 1.1 |
| Sewing, mending, fixing things | 78.2 | 2.2 | 1.6 |
| Singing, playing instrument | 66.6 | 2.5 | 2.0 |
| Drawing or Painting | 21.0 | 0.5 | 1.1 |
| Passive | | | |
| Watching TV | 99.1 | 4.8 | 0.6 |
| Listening to music | 99.1 | 4.6 | 0.9 |
| Listening to radio (not music) | 89.3 | 3.8 | 1.6 |
| Looking at art | 58.9 | 1.4 | 1.6 |

Note: Averages based on 6-point scale; 1 = never, 6 = everyday.

*2.2.4. Covariates.* Final models adjusted for demographics (e.g., age, sex, ethnicity/race), household income (for the past 12 months), self-reported health status (5-point scale; 1 = poor to 5 = excellent), and depressive symptoms as measured by the Geriatric Depression Scale (15-item) [34].

*2.3. Data Analysis.* Multiple mediation models were applied to determine the following: (1) whether frequent participation in a wide range of lifestyle activities could partially explain the relationship between education and cognition, or (2) whether the relationship between education and cognition could be better explained by participation in specific activity domains (see Figure 1) [41, 42]. As we were

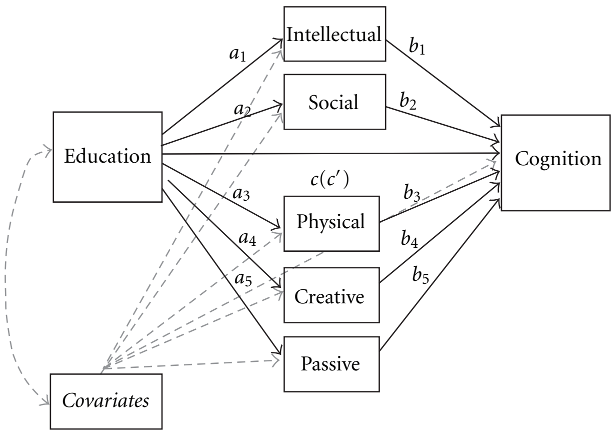


Figure 1: Example of multiple mediator model.

interested in exploring the relative contributions of education and activities on distinct cognitive abilities, multiple mediation models were conducted separately for each cognitive outcome (e.g., reading ability, processing speed, memory; Figure 1). Analyses were conducted with IBM Statistical Package for the Social Sciences (SPSS) software, version 19 (see http://www.quantpsy.org/ for the SPSS macro command set for multiple mediation) [42].

Following the procedures defined by Preacher and Hayes [42], we examined both the *total* and *specific* indirect effects using 5,000 bootstrap samples to calculate the 95% bias-corrected and accelerated bootstrap confidence intervals (CI). These nonparametric bootstrapping techniques are often considered more statistically robust than traditional approaches (e.g., Sobel test, causal steps approach) because they do not assume normality in the sampling distribution [42–45]. The *total* indirect effect explains the *combined* contribution of activity domains (intellectual, social, physical, creative, passive) on education-cognition relations; whereas, the *specific* indirect effect tests the *unique* contribution of each activity domain, above and beyond participation in other domains. Point estimates were considered significant when zero was not included in the confidence interval.

## 3. Results

*3.1. Correlations.* As expected, greater educational attainment was related to better performance on cognitive measures (ranging from $r = 0.09$ for processing speed to $r = 0.46$ for reading ability), as well as with overall frequency of activity ($r = 0.14$) (Table 3). Educational attainment was also related to greater participation in intellectual and physical activities ($r = 0.26$ and 0.14, resp.). Additionally, greater participation in intellectual activities was consistently associated with performance on cognitive tasks (ranging from $r = 0.11$ for delayed memory recall to $r = 0.22$ for reading ability).

*3.2. Multiple Mediation Models.* The results from the bootstrapping analyses showed that the total indirect effect (i.e., aggregate effect of participation across the five activity domains) was significant for the measures of global cognition (point estimate = 0.120; $\text{CI}_{.95}$ = 0.000, 0.025), reading ability (point estimate = 0.062; $\text{CI}_{.95}$ = 0.014, 0.120), and processing speed (point estimate = 0.075; $\text{CI}_{.95}$ = 0.033, 0.131) (Table 4). It is important to note that in each of these models, education-cognition relations were not completely eliminated (i.e., the association between education on cognition remained significant). These findings indicate that, taken as a set, frequent participation in a wide range of lifestyle activities partially accounts for the effects of education on these cognitive abilities. Further inspection of the specific indirect effects (e.g., $a_1b_1$ versus $a_2b_2$ in Figure 1) indicated that this effect only held true for intellectually challenging activities (point estimate = 0.014; $\text{CI}_{.95}$ = 0.000, 0.025 for global cognition; point estimate = 0.070; $\text{CI}_{.95}$ = 0.027, 0.125 for reading ability; point estimate = 0.078; $\text{CI}_{.95}$ = 0.040, 0.134 for processing speed; Table 4), controlling for all other activity domains. Thus, these findings suggest that greater participation in social, physical, creative, or passive activity did not contribute to the total indirect effect above and beyond participation in intellectual activity for measures of global cognition, reading ability, and processing speed. We did not find similar associations (neither the total nor specific indirect effects were significant) for the AVLT immediate or delayed memory task.

## 4. Discussion

The goal of the present study was to examine whether participation in a wide range of activities (intellectual, social, physical, creative, and passive) could account for the relationship between education and cognition in adulthood. Generally, our findings suggest that education-cognition relations can be partially explained by frequent participation in intellectual demanding activities [19, 29, 46].

As suggested earlier, educational experiences may provide the necessary knowledge, understanding, skills, and competencies for establishing a lifetime of participation in cognitive challenges. In fact, individuals with higher levels of educational attainment tend to allocate more time and put forth more effort when engaging in intellectually complex activities [47]. As a result, the accumulated exposure to cognitively charged environments may have a direct beneficial effect on brain structure and function, resulting in greater neurological development (e.g., increase in synaptic density) or more efficient use of existing brain networks [48–50]. In addition to such neuroprotective effects, continued practice of cognitive skills may develop compensatory strategies to help maintain cognition in the face of age-related declines [51] or may bolster perceptions of confidence and competence in one's skills and abilities, potentially leading to more frequent engagement in cognitively demanding environments [36, 52].

It is important to mention, however, that the association between education and cognition was not completely eliminated by participation in intellectually demanding activities, suggesting that both educational attainment and intellectual endeavors may independently benefit late-life cognitive

Table 3: Unadjusted correlations among education, activity, and cognition.

| | | | | Cognition | | |
|---|---|---|---|---|---|---|
| | Education | MMSE | WRAT-4 | Speed | Memory: immediate | Memory: delayed |
| Education | 1.00 | 0.17** | 0.46** | 0.09* | 0.10** | 0.11** |
| Activity level | | | | | | |
| Frequency, overall | 0.14** | 0.08* | 0.05 | 0.15** | 0.12** | 0.10* |
| Activity type | | | | | | |
| Intellectual | 0.26** | 0.12** | 0.22** | 0.16** | 0.14** | 0.11** |
| Social | −0.04 | −0.01 | −0.13** | 0.08* | 0.05 | 0.03 |
| Physical | 0.14** | −0.03 | 0.08* | 0.04 | 0.04 | 0.01 |
| Creative | 0.01 | 0.02 | −0.06 | 0.06 | 0.12** | 0.10* |
| Passive | 0.07 | −0.02 | −0.02 | 0.03 | −0.01 | −0.01 |

Note: * $P < 0.05$. ** $P < 0.01$. MMSE: Mini-Mental State Exam; WRAT: Wide Range Achievement Test-4.

performance [29]. In other words, although education may provide a foundation for continued engagement in intellectually demanding environments across the life course, it is also the "choices we make, not chance, that determines our fate" [53].

The few studies that have previously investigated these hypothesized pathways have yielded mixed findings. Similar to our findings, Kleigel and colleagues [29] also demonstrated the importance of both education and intellectual stimulation for cognitive performance among the oldest old. A more recent study by Soubelet [54], however, failed to find such associations. The discrepancies may be attributable, in part, to differences in the selected sample, exclusively among centenarians (M = 100.21 years; SD = 0.40) [29] or across a large range of ages (18–96 years) [54]. Further, the definition of intellectual activity differed across studies, potentially impacting the significance of findings. For instance, some of the intellectual activities used in the study by Soubelet [54] were included in our social domain (e.g., theater, cinema, religious participation), for which we did not find significant associations. It should also be noted that the few reports examining whether education-cognition associations could be explained by intellectual activities did not simultaneously consider participation in other forms of engagement. In fact, there is very little work that has examined the relations between education and the types of lifestyle activities that were measured in the current study. The application of multiple mediation models allowed us to test the effects of participation in a wide range of activities (*total indirect* effect), as well as independent associations with specific activity domains (*specific indirect* effect), on cognitive performance. To our knowledge, no other study has explored whether participation in various forms of activity can potentially explain the association between education and cognition.

Although our findings contribute to the relatively few studies that have examined education-cognition pathways, several limitations need to be addressed. First and foremost, as our data were cross-sectional, we were unable to distinguish whether variation in cognition resulted from age-related decline or from earlier life experiences. We also were unable to establish temporal precedence between activity and cognition. As such, it is also likely that cognitive ability could lead to greater activity [23, 55], rather than activity driving cognition as suggested in the current study. With this said, while correlation does not imply causation, establishing covariation among variables is a necessary (albeit insufficient) condition for causality. In the literature, several questions reg4rding the determinants and effects of an active lifestyle have yet to be answered [15]. Even though we cannot draw causal assumptions from cross-sectional data, our correlational findings help define what causal models are plausible. More longitudinal investigations are needed to test these competing models, as well as to determine how engaging in cognitively complex challenges across different periods of the lifespan impacts cognition in adulthood [21, 56].

We also acknowledge that investigating these associations within the context of a school-based, intensive volunteer program attracted a relatively healthy, active group of volunteers potentially limits the generalizability of our findings to other populations. However, individuals included in this study reported a high prevalence of chronic health conditions (e.g., diabetes, stroke, hypertension, and vascular disease) and comorbidity, placing them at a disproportionately greater risk for cognitive and physical impairments [57]. We also recognize that the *number of years* of education does not directly translate to the *quality* of these educational experiences [58, 59]. This is especially salient given that many of the individuals enrolled in the Baltimore Experience Corps Trial were educated prior to desegregation, a time when the quality of and access to education was not equal for African Americans.

Lastly, our measure of activity (LAQ) was developed to capture participation in a broad range of lifestyle activities (e.g., cognitive, social, physical), with a limited number of items reflecting each activity domain. This is especially true for physical activities, which have demonstrated associations with both education and cognition in prior research [48]. However, these neurobiological findings have not translated as well to epidemiologic studies of dementia risk, where self-reported frequency of physical activity is the standard [60, 61]. For instance, Wang and colleagues [62] did not observe an association between physical activity and dementia incidence after accounting for participation in social, cognitive, and productive activities. Nonetheless, findings may have differed if more extensive activity measures were

Table 4: Indirect effects of education on cognition through activity.

| Indirect effects | Estimate | SE | BCa 95% Cl Lower | BCa 95% Cl Upper |
|---|---|---|---|---|
| MMSE | | | | |
| Total | .012 | .006 | .000 | .025 |
| Intellectual | .014 | .006 | .003 | .027 |
| Social | .000 | .001 | −.003 | .003 |
| Physical | −.002 | .002 | −.008 | .002 |
| Creative | −.001 | .001 | −.005 | .001 |
| Passive | −.001 | .002 | −.006 | .001 |
| WRAT-4 | | | | |
| Total | .062 | .027 | .014 | .120 |
| Intellectual | .070 | .024 | .027 | .125 |
| Social | .000 | .004 | −.010 | .009 |
| Physical | .003 | .009 | −.011 | .027 |
| Creative | −.004 | .008 | −.029 | .005 |
| Passive | −.007 | .009 | −.033 | .004 |
| Processing speed | | | | |
| Total | .075 | .025 | .033 | .131 |
| Intellectual | .078 | .024 | .040 | .134 |
| Social | .000 | .004 | −.007 | .007 |
| Physical | .001 | .008 | −.016 | .018 |
| Creative | .001 | .004 | −.007 | .012 |
| Passive | −.004 | .007 | −.025 | .003 |
| Memory: immediate recall | | | | |
| Total | .043 | .033 | −.015 | .112 |
| Intellectual | .050 | .031 | −.004 | .119 |
| Social | .002 | .005 | −.009 | .012 |
| Physical | −.004 | .012 | −.033 | .017 |
| Creative | .004 | .010 | −.006 | .036 |
| Passive | −.008 | .010 | −.041 | .004 |
| Memory: delayed recall | | | | |
| Total | .005 | .012 | −.017 | .030 |
| Intellectual | .010 | .012 | −.012 | .034 |
| Social | .000 | .002 | −.005 | .004 |
| Physical | −.005 | .005 | −.018 | .002 |
| Creative | .001 | .003 | −.002 | .012 |
| Passive | −.001 | .003 | −.012 | .002 |

Note: IV: independent variable (education, in years); DV: dependent variable (cognitive outcomes); BCa 95% Cl: bias-corrected and accelerated confidence intervals. Total indirect effect represents the sum of the indirect effects for specific activity pathways. All models were adjusted for age, sex, race, household income (past 12 months), health, and depression.

implemented. Further, education and lifestyle activities are not the only forms of experiential richness. For instance, occupational complexity has been consistently linked to cognition in later life [56, 63]. Moreover, occupational status is often associated with other factors (e.g., finances, time) that may impact selection and participation in activities over the life course [64]. Unfortunately, we did not have a reliable measure of occupational history or complexity and were unable to explore these relations in our dataset.

Consistent with the engagement hypothesis [3, 10], remaining actively engaged in activities may provide a protective mechanism against cognitive decline and dementia in later life. Although there was some evidence that education-cognition relations could be partially explained by greater participation in intellectual activities, both education and activities uniquely contributed to cognition in adulthood. As such, interventions such as the Experience Corps program which promote broad-based engagement may help older adults maintain, or potentially enhance, cognitive function. Further research is recommended to replicate these important findings with similar activities in varied populations.

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*Research Article*

# Caudate Nucleus Volume Mediates the Link between Cardiorespiratory Fitness and Cognitive Flexibility in Older Adults

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The basal ganglia play a central role in regulating the response selection abilities that are critical for mental flexibility. In neocortical areas, higher cardiorespiratory fitness levels are associated with increased gray matter volume, and these volumetric differences mediate enhanced cognitive performance in a variety of tasks. Here we examine whether cardiorespiratory fitness correlates with the volume of the subcortical nuclei that make up the basal ganglia and whether this relationship predicts cognitive flexibility in older adults. Structural MRI was used to determine the volume of the basal ganglia nuclei in a group of older, neurologically healthy individuals (mean age 66 years, $N = 179$). Measures of cardiorespiratory fitness ($VO_{2max}$), cognitive flexibility (task switching), and attentional control (flanker task) were also collected. Higher fitness levels were correlated with higher accuracy rates in the Task Switching paradigm. In addition, the volume of the caudate nucleus, putamen, and globus pallidus positively correlated with Task Switching accuracy. Nested regression modeling revealed that caudate nucleus volume was a significant mediator of the relationship between cardiorespiratory fitness, and task switching performance. These findings indicate that higher cardiorespiratory fitness predicts better cognitive flexibility in older adults through greater grey matter volume in the dorsal striatum.

## 1. Introduction

Age-related cognitive decline is an unfortunate, but nearly ubiquitous, characteristic of late life that is preceded by atrophy of several brain regions including the prefrontal cortex, medial temporal lobe, and basal ganglia [1, 2]. Because of the expected increase in the proportion of adults over the age of 65 in the next forty years, it has become a major public health initiative to identify methods to prevent or reverse regional brain atrophy with the hope that this might concurrently improve cognitive performance [3]. Randomized trials of aerobic exercise have proven promising from this regard, with participation in exercise programs leading to greater prefrontal [4] and hippocampal volumes [5]. Nonrandomized longitudinal studies of physical activity [6, 7] and cross-sectional studies of cardiorespiratory fitness [8–10] have shown similar results, with more physical activity and higher fitness levels associated with greater volumes.

Unfortunately, few studies have examined whether cardiorespiratory fitness levels in older adult humans are associated with brain areas other than the prefrontal cortex and hippocampus [4–6, 8–10]. The striatum is of particular interest because it shows relatively early and rapid age-related atrophy, [2, 11] is a critical node in motor circuitry, supports task coordination and attentional control processes, and disruption of its dopamine circuits is linked to common age-related disorders such as Parkinson's disease [12, 13]. Yet, there is emerging evidence that exercise directly influences dopamine circuitry, angiogenesis, and cell signaling cascades in the striatum. For example, rodent research has found that voluntary wheel running increases the production of dopamine and brain-derived neurotrophic factor in the dorsal striatum [14–16]. Exercise is also considered to be one of the more promising treatments for attenuating dopamine deficiency in 6-hydroxydopamine models of Parkinson's disease [17, 18]. In concert with this, exercise ameliorates motor and cognitive deficits in adults with Parkinson's disease [19, 20]. Finally, higher cardiorespiratory fitness levels are associated with larger caudate nucleus and putamen volumes in children and these volume differences were in turn associated with better performance on a measure of attentional control [21]. Yet, the possible link between fitness levels and basal ganglia structure in older adults has not been investigated despite the accumulation of research suggesting an association.

In this study, we examined the association between the volume of basal ganglia and cardiorespiratory fitness levels in older adults. Given the extant rodent literature and one study in humans [21], we predicted that the size of the dorsal striatum, including the caudate nucleus and putamen, and the size of the ventral striatum (i.e., nucleus accumbens) would be positively associated with cardiorespiratory fitness compared to the output nucleus of this system, the globus pallidum, which has been less frequently associated with exercise. Furthermore, we predicted that any association between fitness and dorsal striatum volume would have implications on cognitive tasks that are supported by these structures. Specifically, cognitive flexibility and attentional control paradigms have been closely linked to the function of the dorsal striatum [21–23]. Therefore, using mediation modeling, we predicted that the volume of the dorsal striatum, but not the ventral striatum, would mediate the association between higher cardiorespiratory fitness levels and elevated performance on attentional control and task switching paradigms.

## 2. Methods

*2.1. Participants.* One hundred and seventy-nine older adults (109 females; 56 males) between 59 and 81 yrs of age (mean age = 66.6 years; standard deviation = 5.6 years) participated in this study. Participants were recruited for a 1-year randomized controlled trial examining the effect of aerobic training on brain and cognition. We report here results from the initial baseline MR session. Subjects were recruited through community advertisements and physician referrals and were screened for dementia by the revised and modified Mini-Mental Status Examination [24]. Participants were excluded from participation if they did not reach the required cutoff of 51 (high score of 57).

Additional inclusion criteria have been described elsewhere [5, 9, 25–27]. In brief, participants were required to be 60+ years of age during the trial, capable of performing physical exercise, successfully complete a graded exercise test, have normal or corrected-to-normal vision, absence of clinical depression (as measured by the Geriatric Depression Scale [28]), and a low-active lifestyle at time of baseline assessment. All participants have received a physician's clearance to engage in a maximal graded exercise test and signed an informed consent approved by the University of Illinois.

In addition to these criteria, all participants met or surpassed criteria for participating in a magnetic resonance imaging (MRI) study including no previous head trauma, no previous head or neck surgery, no diagnosis of diabetes, no neuropsychiatric or neurological condition including brain tumors, and no metallic implants that could interfere with or cause injury due to the magnetic field.

The current study focused on participants that had both high-resolution MRI data and completed the cognitive assessments described below. All analyses were performed in a pairwise manner with the subjects who had relevant data points. The specific degrees of freedom are reported for each test.

*2.2. Cardiorespiratory Assessment.* Aerobic fitness ($VO_{2max}$) was assessed by graded maximal exercise testing on a motor-driven treadmill. The participant walked at a speed slightly faster than their normal walking pace (approximately 30–100 m/min) with increasing grade increments of 2% every 2 min. A cardiologist and nurse continuously monitored measurements of oxygen uptake, heart rate and blood pressure. Oxygen uptake was measured from expired air samples taken at 30 s intervals until a maximal $VO_2$ was attained or to the point of test termination due to symptom limitation and/or volitional exhaustion. $VO_{2max}$ was defined as the highest recorded $VO_2$ value when two of three criteria were satisfied: (1) a plateau in $VO_2$ peak between two or more workloads; (2) a respiratory exchange ratio >1.00; (3) a heart rate equivalent to their age predicted maximum (i.e., 220-age).

*2.3. Body Mass Index (BMI).* Height and weight were measured using a Seca electronic scale and stadiometer (model 763 1321139). Participants were measured while wearing light clothing and without shoes. BMI was calculated using the standard formula of weight (kg)/[height (m)]$^2$.

*2.4. MRI Acquisition and Volumetric Analysis.* High-resolution T1-weighted brain images were acquired within two weeks of the cardiorespiratory fitness tests using a 3D Magnetization Prepared Rapid Gradient Echo Imaging (MPRAGE) protocol with 144 contiguous axial slices, collected in ascending fashion parallel to the anterior and posterior

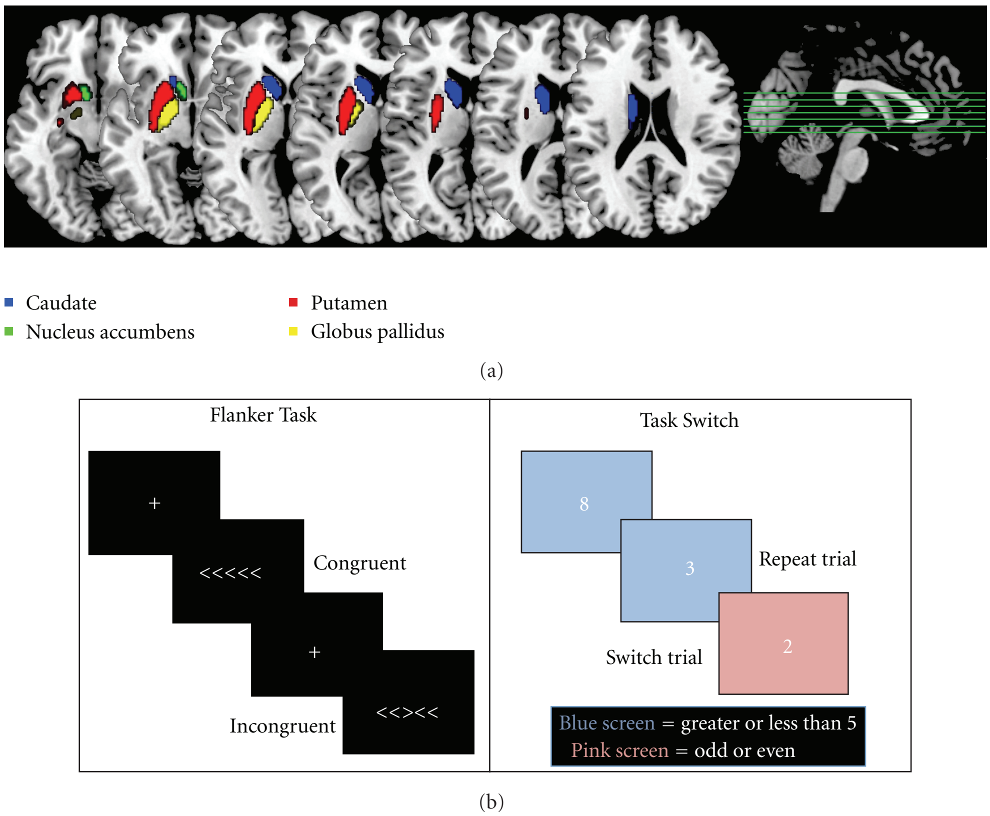


FIGURE 1: (a) Template maps for the four regions of interest used in this study. While only left hemisphere regions are shown here, data from both hemispheres was collapsed together in the final analyses. (b) Illustration of the two behavioral paradigms tested.

commissures, echo time $(TE) = 3.87$ ms, repetition time $(TR) = 1800$ ms, field of view (FOV) = 256 mm, acquisition matrix 192 mm × 192 mm, slice thickness = 1.3 mm, and flip angle = 8. All images were collected on a 3T head-only Siemens Allegra MRI scanner.

For segmentation and volumetric analysis of the basal ganglia we employed FMRIB's Integrated Registration and Segmentation Tool (FIRST) in FMRIB's Software Library (FSL) version 4.1. FIRST is a semiautomated model-based subcortical segmentation tool utilizing a Bayesian framework from shape and appearance models obtained from manually segmented images from the Center for Morphometric Analysis, Massachusetts General Hospital, Boston, MA, USA. Structural and landmark information was obtained from 317 manually segmented and labeled T1 weighted images of the brain from normal children, adults, and pathological populations (including schizophrenia and Alzheimer's disease) and were modeled as a point distribution model in which the geometry and variation of the shape of the structure are submitted as priors. Volumetric labels are parameterized by a 3D deformation of a surface model based on multivariate Gaussian assumptions. FIRST then searches through linear combinations of shape modes of variation for the most probable shape given the intensity distribution in the T1-weighted image (see Patenaude et al. [29], for further description of this method).

This method first runs a two-stage affine registration to a standard space template (MNI space) with 1 mm resolution using 12 degrees of freedom and a subcortical mask to exclude voxels outside the subcortical regions. Second, the left and right basal ganglia including the caudate nucleus, putamen, pallidum, and nucleus accumbens are segmented with 30, 40, 40, and 50 modes of variation, respectively. The modes of variation are optimized based on leave-one-out cross-validation on the training set and increase the robustness and reliability of the results [29]. Finally, boundary correction takes place for each structure that classifies the boundary voxels as belonging to the structure or not based on a statistical probability ($z$-score $> 3.00$; $P < 0.001$). Figure 1(a) shows the template masks for these nucleus volumes in the left hemisphere. Although volumes were estimated separately for the left and right hemispheres the volumetric estimates were highly correlated between the hemispheres for the nucleus accumbens ($r(139) = 0.552$, $P < 0.001$), caudate nucleus ($r(151) = 0.638$, $P < 0.001$), putamen ($r(151) = 0.542$, $P < 0.001$), and globus pallidus ($r(151) = 0.806$, $P < 0.001$). Therefore, a total volume estimate was generated for each nucleus by summing the values for the two hemispheres together.

Intracranial volume (ICV) is frequently used to adjust the regional volumes for sex and height (e.g., [1]). Here, we calculated ICV as the sum of gray, white, and cerebrospinal fluid using FMRIB's automated segmentation tool in FSL version 4.1 [30, 31]. In accordance with other volumetric studies, ICV was used as a covariate in all analyses reported below [5, 9, 32].

*2.5. Behavioral Tasks.* Figure 1(b) shows the time line of each trial for the two behavioral paradigms utilized in this study. Results from the full battery of cognitive tasks have been reported in previous studies [5, 9, 25–27]. Given the *a priori* interest in the basal ganglia, we analyzed the flanker and task switching batteries because they both have been associated with basal ganglia function in animal and human studies. Cognitive tasks for which we did not predict *a priori* to be associated with the basal ganglia were not analyzed in this study.

*2.5.1. Task Switching.* This task provided a measure of executive function by testing participants' abilities to flexibly switch their focus of attention between multiple task sets. In this task participants had to switch between judging whether a number (1, 2, 3, 4, 6, 7, 8, or 9) was odd or even and judging whether it was low or high (i.e., smaller or larger than 5). Numbers were presented individually for 1500 ms against a pink or blue background at the center of the screen, with the constraint that the same number did not appear twice in succession (see Figure 1(b)).

If the background was blue, participants used one hand to report as quickly as possible whether the letter was high ("*X*" key) or low ("*Z*" key). If the background was pink, participants used their other hand to report as quickly as possible whether the number was odd ("*N*" key) or even ("*M*" key). Participants completed four single task blocks (2 blocks of odd/even and 2 blocks of high/low) of 24 trials each. Due to the difficulty of this task, participants were provided with a practice block in which they switched from one task to the other for 120 trials. This practice block allowed participants to become acquainted with the switching block and ensured compliance with task instructions. Finally, they completed a switching block of 120 trials during which the task for each trial was chosen randomly.

For the current study, we examined local switch cost, which refers to the difference in performance for trials when the preceding trial involved the same task (nonswitch trial) and those when the preceding trial was of the other task (switch trial), and represents a measure of attentional set reconfiguration and inhibition, two subcomponents of executive function [33]. Reaction time measures (based on mean reaction time) were used for computing local switch cost. Consistent with prior studies using this paradigm [27], we used accuracy rates (percent correct) as an outcome measure and also calculated an accuracy cost score that reflects the difference in accuracy rates between switch and repeat conditions within the switching block.

*2.5.2. Flanker Task.* A modified flanker paradigm required participants to identify the orientation of a central arrow cue that was flanked by arrows that were in either a congruent (e.g., >>>>>) or incongruent (e.g., >><>>) orientation. We used reaction times for both conditions in addition to proportional cost. Cost was calculated by subtracting the reaction times of congruent trials from those of incongruent trials and dividing by the reaction time of congruent trials. Such an approach accounts for individual differences in perceptual speed (see Figure 1(b)).

*2.6. Data Analysis*

*2.6.1. Partial Correlations.* Initial analyses examined the distribution of the variables for skew using Q-Q plots. All variables were confirmed to be normally distributed by both visual inspection of the Q-Q plots and a resulting $r$-squared value to the simulated distribution of >0.95. Any missing values were eliminated from calculations. This resulted in degrees of freedom ranging from 139 to 178 in this sample, depending on the variables used in each analytical comparison. Bivariate analyses examined the correlation between $VO_{2max}$ and age, sex, education, ICV, and BMI using Pearson's correlation coefficients. These variables were then used as covariates in all subsequent analyses looking at $VO_{2max}$, task and brain volume relationships.

Once the covariate relationships were determined, partial correlations were then used to test the relationship between $VO_{2max}$ and pallidum, putamen, nucleus accumbens, and caudate nucleus volumes. Next, the direct effect of $VO_{2max}$ on the cognitive tasks described above was estimated. Partial correlations were then conducted to assess the association between basal ganglia volumes and cognitive tasks.

*2.6.2. Mediation Analysis.* To determine indirect pathways, we conducted a bootstrapped mediation analysis. The main requirement for mediation is that the *indirect effect* of the independent variable ($VO_{2max}$) through the mediator (e.g., caudate nucleus volume) on the dependent variable (e.g., task switch % accuracy) be significant.

Mediation analyses were conducted using the *indirect macro* designed for SPSS [34]. This macro uses bootstrapped sampling to estimate the indirect mediation effect of volume on the relationship between $VO_{2max}$ and Flanker Task or task switching performance. In this analysis, 5,000 bootstrapped samples were drawn with replacement from the dataset to estimate a sampling distribution for the indirect mediation pathway. Indirect effects and 95% confidence intervals are reported. Mediation indirect effects can be interpreted as the strength of the relationship between the independent variable ($VO_{2max}$) and dependent variable (e.g., Task Switching performance) when accounting for the mediating pathway [35]. We report adjusted $R^2$ values for an estimate of the effect size. Each outcome measure was used as a dependent variable in separate analyses. All models controlled for the variance from age, education, BMI, ICV, and sex.

## 3. Results

*3.1. Covariate Effects.* We first examined the association between cardiorespiratory fitness and other factors that may act as sources of noise in the analyses. These relationships are illustrated in Figure 2 (Covariates section). As expected, there were significant negative correlations between $VO_{2max}$ and BMI ($r(178) = -0.242$, $P = 0.001$), sex (logistic beta = $-1.034$, $r(178) = -0.480$, $P < 0.001$), and age ($r(178) = -0.391$, $P < 0.001$). Thus, cardiorespiratory fitness levels were lower in overweight and obese subjects, lower in women than men, and lower in older aged participants. We also found positive correlations between $VO_{2max}$ and years of

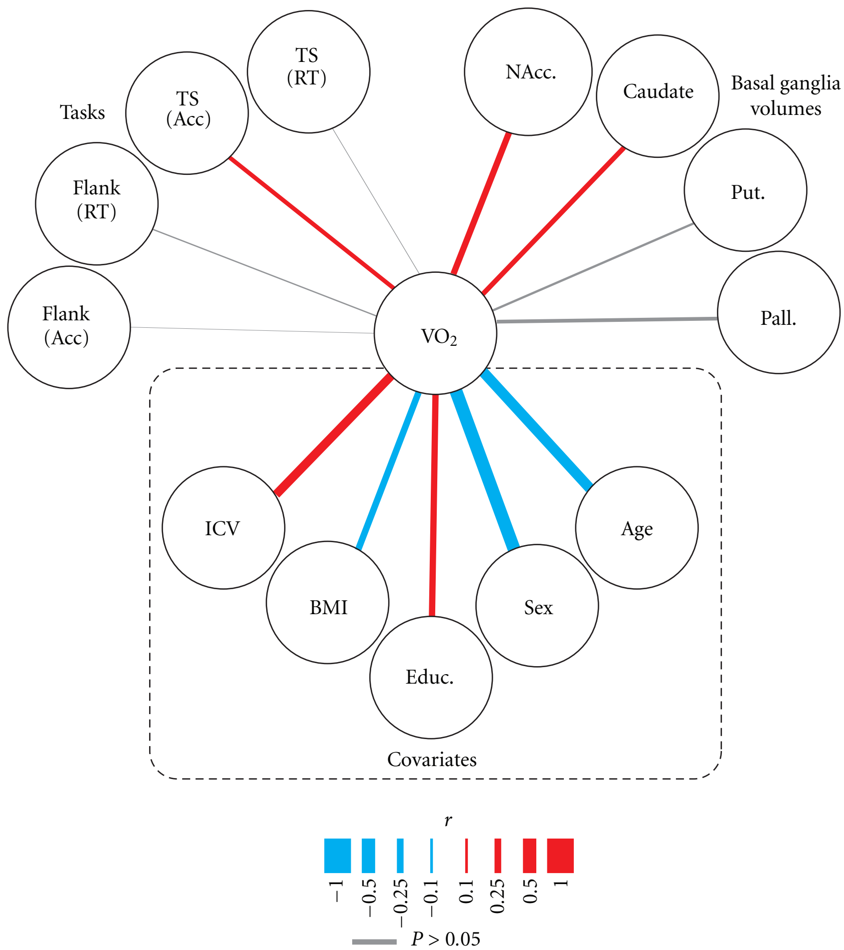


FIGURE 2: Correlation paths relating directly to measures of cardiorespiratory integrity ($VO_{2max}$). Colored lines show significant correlations and the width of the line reflects the strength of the relationship. All correlation values are reported in the text. Variables highlighted in the "Covariates" section were used as control factors in the partial correlation analyses for the other pathways. Behavioral results reflect between condition changes in performance (i.e., costs). $VO_{2max}$: $VO_2$, Task Switching: TS, Flanker Task: Flank, accuracy: Acc, reaction time: RT, nucleus accumbens: NAcc., putamen: Put. globus pallidus: Pall. education: Educ., body mass index: BMI, intracranial volume: ICV.

education ($r(178) = 0.234$, $P = 0.002$) as well as intracranial volume ($r(178) = 0.322$, $P < 0.001$). Thus, cardiorespiratory fitness increased with educational attainment and overall body size. This latter association is presumably driven by the sex effects since men had significantly larger intracranial volumes than women ($t(156) = 7.86$, $P < 0.001$). These five factors were included in all subsequent analyses as covariates.

*3.2. Associations between Cardiorespiratory Fitness and Task Performance.* Next, we examined relationships between cardiorespiratory fitness and performance in the two behavioral tasks. These relationships are illustrated in Figure 2 (Tasks region). To get a full appreciation of relationships to the behavioral tasks, Table 1 shows the simple bivariate correlations between all demographic variables, cardiorespiratory fitness, and behavioral task performance. However, our core analysis centers on relationships specific to cardiorespiratory fitness, therefore we used a partial correlation analysis to control for noncardiorespiratory effects (see Section 2).

Unlike the results from previous studies [15, 21, 36, 37], we did not see an association between cardiorespiratory fitness and performance in the Flanker Task. After adjusting for covariate effects, there was no significant correlation between $VO_{2max}$ scores and percent interference for reaction times in the Flanker Task ($r(149) = 0.049$, $P = 0.546$). We also failed to detect a significant association between $VO_{2max}$ and response times on either the congruent ($r(149) = 0.035$, $P = 0.669$) or incongruent ($r(149) = 0.001$, $P = 0.994$) conditions. This effect does not appear to be due to a lack of sensitivity in the overall behavioral responses, as there was a significant group-level increase in response times to incongruent trials, compared to congruent trials (mean percent interference $= 14.9\%$, std $= 10.4$, $t(166) = 18.55$, $P < 0.001$).

We also failed to detect a significant association between fitness levels and accuracy rates in the Flanker Task. After controlling for covariate effects, there was no significant correlation between $VO_{2max}$ scores and differences in accuracy between the incongruent and congruent conditions

Table 1: Simple bivariate Pearson correlations between demographic variables, cardiorespiratory fitness, and behavioral data. *Significant at $P < .05$; **significant at $P < .01$.

| | $VO_2$ | Age | Sex | Education | BMI |
|---|---|---|---|---|---|
| Flanker | | | | | |
| Con RT | −.178* | .283** | .207** | .009 | −.036 |
| Inc RT | −.144 | .162* | .211** | .042 | −.056 |
| Cost (RT) | .020 | −.179* | .064 | .023 | −.034 |
| Con Acc | .199** | −.277** | −.133 | .092 | .060 |
| Inc Acc | .112 | −.168* | −.022 | .052 | .009 |
| Cost (Acc) | −.055 | .099 | .084 | −.015 | −.060 |
| Task-switch | | | | | |
| Repeat RT | −.021 | .006 | .135 | −.034 | .005 |
| Switch RT | −.082 | −.011 | .173* | −.105 | .020 |
| Cost (RT) | −.071 | −.004 | .151 | −.088 | .025 |
| Repeat Acc | .174* | −.224** | .001 | .040 | .135 |
| Switch Acc | .231** | −.270** | −.032 | .061 | .130 |
| Cost (Acc) | .190* | −.281** | −.027 | .022 | .154 |

($r(149) = 0.008$, $P = 0.925$). As with response times, there was no significant association between $VO_{2max}$ scores and response accuracy during either the congruent ($r(149) = 0.053$, $P = 0.521$) or incongruent conditions ($r(149) = 0.041$, $P = 0.648$). However, these null effects may be driven by a ceiling effect in accuracy rates in this sample (congruent: mean = 95.89%, std = 9.40%; incongruent: mean = 93.43%, 13.00%).

We also failed to detect significant associations between cardiorespiratory fitness and local switch costs in the Task Switching experiment. That is, after adjusting for covariate effects, $VO_{2max}$ was not significantly correlated with the delayed reaction times that result from switching between trial types ($r(150) = 0.025$, $P = 0.398$). Although, there was a significant positive correlation between $VO_{2max}$ and response times for the repeat condition such that individuals with higher $VO_{2max}$ had slightly slower response times ($r(150) = 0.312$, $P < 0.001$). This correlation was not seen with response times during switch trials ($r(150) = 0.019$, $P = 0.815$). The lack of a correlation between fitness and switch costs does not appear to be due to a floor effect in the switching costs because across all subjects the average response times were significantly slower after a switch relative to a repeat condition (mean difference = 530.5, std = 225.94, $t(162) = 29.976$, $P < 0.001$).

In contrast to response times, we did observe a small, but significant, association between cardiorespiratory fitness and accuracy in the Task Switching experiment. After adjusting for covariate effects, $VO_{2max}$ scores were positively correlated with task-switch accuracy for switch trials after subtracting the accuracy rates from repeat trials ($r(150) = 0.160$, $P = 0.048$). In general, switching accuracies were negative (mean $= -0.167$, std $= 0.228$, $t(165) = -9.42, P < 0.001$) meaning that more errors occurred on switch trials compared to repeat trials. Within each condition used to calculate the accuracy cost, we also found a positive correlation between $VO_{2max}$ scores and accuracy rates for repeat trials ($r(150) = 0.176$, $P = 0.030$) and switch trials ($r(150) = 0.177$, $P = 0.029$). Thus, individuals with higher $VO_{2max}$ scores were both more accurate in general and were better able to maintain accurate responses immediately following a change in task goals.

*3.2.1. Associations between Cardiorespiratory Fitness and Basal Ganglia Volumes.* We next set out to identify relationships between cardiorespiratory fitness and volumetric measures of the subcortical nuclei that compose the basal ganglia system. These relationships are illustrated in the "Basal Ganglia Volumes" region of Figure 2.

Our first analysis focused on the nuclei that compose the major input of the basal ganglia system, the striatal nuclei. Partial correlations, after adjusting for covariate effects, revealed significant associations between cardiorespiratory fitness and the volume of nuclei that compose the caudal sections of the striatum. Specifically, $VO_{2max}$ scores positively correlated with the volume of the nucleus accumbens ($r(138) = 0.232$, $P = 0.006$) and caudate nucleus ($r(151) = 0.186$, $P = 0.022$). In both cases, individuals with higher cardiorespiratory fitness also had larger volumes of these striatal nuclei. In contrast, we did not observe this same correlation with the volume of the putamen ($r(151) = 0.085$, $P = 0.296$).

We next looked at the principal output nucleus of the basal ganglia, the globus pallidus. Although we found a trend for a positive association between $VO_{2max}$ scores and pallidal volume, this relationship did not reach statistical significance ($r(151) = 0.139$, $P = 0.086$). Thus, although $VO_{2max}$ had significant associations with sections of the input to the basal ganglia, the relationship between cardiorespiratory fitness and the globus pallidus remains uncertain.

*3.2.2. Associations between Basal Ganglia Volumes and Task Performance.* According to current methods of mediation analysis, detecting direct pathway effects (i.e., $VO_{2max}$ to task performance) is not a necessary condition for indirect pathway effects (i.e., $VO_{2max}$ to brain volume to task performance) [34]. However, in order to identify possible indirect mediating pathways between cardiorespiratory fitness and task performance through basal ganglia volumes, the direct pathways between brain volumes and behavior must also be established. These pathways are illustrated in Figure 3.

For performance in the Flanker Task, we failed to observe any significant associations between basal ganglia volume and task performance. Specifically, the partial correlation analysis failed to detect a significant relationship between response interference in the Flanker Task and the volume of either the nucleus accumbens ($r(138) = 0.031$, $P = 0.721$), caudate nucleus ($r(150) = 0.062$, $P = 0.446$), putamen ($r(150) = 0.131$, $P = 0.106$), or globus pallidus ($r(150) = 0.087$, $P = 0.284$). There was also a lack of significant relationships between accuracy in the Flanker Task and the volume of either the nucleus accumbens ($r(138) = 0.078$, $P = 0.361$), caudate nucleus ($r(149) = -0.074$, $P = 0.368$), putamen ($r(149) = 0.028$, $P = 0.732$), or globus pallidus ($r(149) = 0.054$, $P = 0.511$). This same pattern was also present when the partial correlations were run against

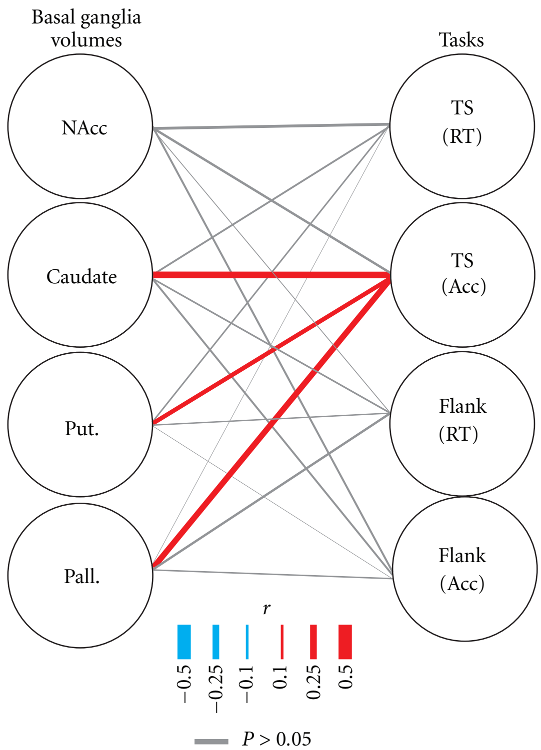


FIGURE 3: Correlation paths between basal ganglia regions of interest volume and behavioral costs for both tasks. Same plotting convention as Figure 2.

TABLE 2: Partial correlations between nuclear volumes and components of the behavioral scores.

| | Nucleus accumbens | Caudate nucleus | Putamen | Pallidum |
|---|---|---|---|---|
| Flanker | | | | |
| Con RT | −.114 | −.015 | −.054 | .013 |
| Inc RT | −.096 | −.037 | −.127 | −.035 |
| Cost (RT) | .031 | .062 | .131 | .087 |
| Con Acc | .132 | .122 | .045 | −.034 |
| Inc Acc | .176 | .013 | .069 | −.012 |
| Cost (Acc) | .078 | −.074 | .028 | .054 |
| Task-switch | | | | |
| Repeat RT | .010 | −.238** | −.018 | .089 |
| Switch RT | .079 | −.103 | .081 | .016 |
| Cost (RT) | .107 | −.069 | .058 | −.003 |
| Repeat Acc | .120 | .286** | .115 | .176* |
| Switch Acc | .133 | .274** | .153 | .217** |
| Cost (Acc) | .089 | .247** | .164* | .218** |

the congruent and incongruent scores in the Flanker Task separately (Table 2). Therefore, we can rule out any possible indirect pathway effects in the Flanker Task in our sample.

Similarly, we failed to detect any significant associations between Task Switching costs in response times and basal ganglia volumes. The partial correlation analysis failed to detect a significant correlation between switching and the volume of the nucleus accumbens ($r(138) = 0.102$, $P = 0.209$), caudate nucleus ($r(148) = -0.069$, $P = 0.398$), the putamen ($r(148) = 0.059$, $P = 0.477$), or the globus pallidus ($r(148) = -0.003$, $P = 0.973$). We did detect a negative correlation between caudate volume and reaction times in the repeat trial condition (see Table 2), suggesting that greater caudate nucleus volume predicted overall faster reaction times in the simpler condition. However, the speed cost of changing between conditions was not predicted by caudate volume. Therefore, similar to performance in the Flanker Task, we can rule out the possibility of indirect mediating pathways between cardiorespiratory fitness and response times in the Task Switching experiment in our sample.

We did, however, observe significant associations between the volume of basal ganglia nuclei and accuracy in the Task Switching experiment. While the volume of the nucleus accumbens failed to have a significant partial correlation ($r(138) = 0.089$, $P = 0.293$), we observed significant positive correlations between the volumes of the caudate nucleus ($r(150) = 0.247$, $P = 0.002$), the putamen ($r(150) = 0.164$, $P = 0.044$) and the globus pallidus ($r(150) = 0.218$, $P = 0.007$) with accuracy rates in the switch condition. When we look at the components of the accuracy cost score, we see that both repeat and switching trials were negatively correlated with the volume of the caudate nucleus and the globus pallidus, but not the putamen (see Table 2). Thus, these two nuclei had predictive value for both overall accuracy rates

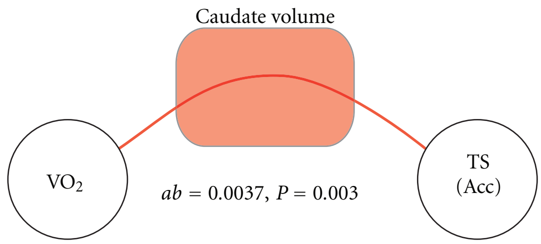


Figure 4: Indirect mediating pathway between cardiorespiratory fitness and Task Switching performance via the volume of the caudate nucleus.

and accuracy costs in switching between conditions. Taken together, these results suggest that, in our sample, the size of the two largest striatal nuclei and the output nucleus of the basal ganglia were predictive of better accuracy during Task Switching conditions. This leaves open the possibility of indirect mediating pathways of the basal ganglia in the relationship between cardiorespiratory fitness and accuracy in the Task Switching experiment.

*3.2.3. Mediating Pathways.* The presence of significant relationships between (a) $VO_{2max}$ and caudate nucleus volume and (b) caudate nucleus volume and accuracy in the Task Switching experiment, suggests that the caudate nucleus may be a candidate mediator for the relationship between cardiorespiratory fitness and task switch performance. We set out to determine the degree to which the caudate nucleus volume mediated the relationship between $VO_{2max}$ and task performance. We tested this using a bootstrapped mediation analysis approach [34] and included all the covariate terms in the regression model. This analysis revealed a significant indirect mediation pathway between $VO_{2max}$ and accuracy through caudate nucleus volume (Figure 4; *ab* coefficient = 0.0037, $P = 0.003$, 95%CI = 0.0009–0.0085, df = 150). The effect size of this mediation effect was small ($R^2 = 0.1661$), however including the caudate volume in the calculation of the direct pathway from $VO_{2max}$ to Task Switching accuracy accounted for approximately 33% of the total effect ($c$ coefficient = 0.0106, $c'$ coefficient = 0.0070). Thus, caudate nucleus volume was a significant, partial mediator of the relationship between cardiorespiratory fitness and task performance.

## 4. Discussion

Our results show that similar to our previous findings in cortical regions [5, 9], increased cardiorespiratory fitness, that is, higher $VO_{2max}$, in older adults is associated with larger volumes of several core basal ganglia nuclei, specifically the caudate nucleus and nucleus accumbens. The putamen and globus pallidus were not significantly associated with $VO_{2max}$. Cardiorespiratory fitness levels were also positively associated with accuracy rates in a Task Switching paradigm that assesses cognitive flexibility. While several basal ganglia nuclei were positively associated with Task Switching accuracy, only the caudate nucleus met the assumptions necessary to perform subsequent mediation analyses. This subsequent analysis found that the caudate nucleus volume was a partial mediator of the relationship between fitness and Task Switching accuracy. These results highlight a key candidate pathway by which differences in cardiorespiratory fitness may regulate cognitive flexibility in older adults.

Our results are consistent with previous studies demonstrating that dopamine receptor pathways in the nucleus accumbens and mesolimbic circuitry mediate the rewarding aspects of exercise in rodents [38–40]. In addition, rodents that are provided access to running wheels show attenuated effects of methamphetamine and cocaine in the nucleus accumbens [41–43] and increased gene expression in both the dorsal and ventral striatum for D1 and D2 receptors and associated G-proteins [40]. Exercise attenuates the neurotoxic effects of 6-hydroxydopamine on dopaminergic circuitry in the dorsal striatum [16, 44], possibly through BDNF pathways [44]. Hence, results from rodent studies of exercise are in line with our finding that cardiorespiratory fitness levels in humans are positively associated with the size of basal ganglia. The results from rodent models also provide potential molecular mechanisms by which fitness is associated with greater volume of the basal ganglia. Although the cellular and molecular correlates of MRI-based volumetric estimates remain unknown, our finding of larger volumes as a function of cardiorespiratory fitness is interesting in the light of this previous literature in rodents.

To the extent that cardiorespiratory fitness is modifiable by participation in regular aerobic exercise [5], our results suggest that age-related loss in volume of the caudate nucleus and nucleus accumbens may be remediable by exercise. In relation to this, however, a recent study by our group [5] reported that a randomized 1-year aerobic exercise intervention failed to significantly increase caudate nucleus volume, despite a significant increase in the size of the hippocampus. Hence, the results from the cross-sectional analysis reported here are not in line with the results from the randomized exercise intervention. There are several potential explanations for this apparent discrepancy. First, the sample size in the current study ($N = 179$) was larger than the results from the Erickson et al. [5] study ($N = 60$ per group) suggesting that the intervention might have been underpowered to detect exercise-induced changes in volume of the caudate nucleus. Such a conclusion is strengthened by a closer examination of the Erickson et al. [5] intervention results that showed a trend for the volume of the caudate nucleus to be different between the exercise and stretching groups at post-assessment, but the difference did not reach significance. Longer randomized trials with larger sample sizes are needed to confirm whether an exercise intervention is capable of increasing the size of the caudate nucleus and nucleus accumbens.

A second explanation for the apparent discrepancy between our results and those of Erickson et al. [5] is the inherent limitation in all cross-sectional study designs. Specifically, it is possible that an uncontrolled third variable, correlated with both cardiorespiratory fitness and caudate nucleus volume, but not with exercise participation *per se*, explains the discrepancy between our results and those of Erickson et al. [5]. In fact, there is a genetic component to $VO_{2max}$ [45] that might explain both the link to the volume of the basal ganglia and cognitive flexibility. Again, these results suggest that randomized trials with larger sample sizes and longer periods of an exercise treatment are necessary to disentangle the possible explanations for the discrepancy between the cross-sectional results reported here and the intervention results reported in Erickson et al. [5]. In fact, a larger scale intervention study could attempt to replicate the cross-sectional results that we describe here in addition to testing whether an exercise regimen could alter the size of the basal ganglia. Another method of testing these hypotheses would be to recruit individuals with dysfunction or deficits of the basal ganglia into an exercise intervention to examine whether volume could be altered in these at-risk or impaired populations.

To our knowledge, there is only one other cross-sectional neuroimaging study examining the volume of the basal ganglia in relation to cardiorespiratory fitness levels [21]. In that study of 55 preadolescent children (9-10 years old) higher fitness levels were associated with greater volume of the caudate nucleus, putamen, and globus pallidus, but not the nucleus accumbens. Interestingly, the volume of the putamen and globus pallidus was also correlated with performance on a Flanker Task. The results we report here are clearly only partially consistent with the results from Chaddock et al. [21]. First, we failed to find any associations with Flanker Task performance and the size of the basal ganglia, and second, we only find associations with fitness for the caudate nucleus and nucleus accumbens, not the putamen or pallidum. One possible explanation for the inconsistency between our study and that of Chaddock et al. [21] is that there are maturational differences in the growth and later atrophy of the basal ganglia [46] such that fitness effects emerge on different brain structures at different time points throughout the lifespan. In fact, such an explanation is likely given developmental trajectories of brain growth, pruning, and myelination [47] earlier in development in contrast to atrophy and volumetric loss late in life [2]. Of course another possible explanation for these between-study differences could simply result from the inter-subject variability inherent in all cross-sectional experimental designs.

Here we were able to demonstrate that greater volume of the caudate nucleus is a significant indirect pathway between cardiorespiratory fitness and cognitive flexibility as assessed by a Task Switching paradigm. Switching abilities and reversal learning are supported by the basal ganglia, medial frontal cortex, and dorsolateral prefrontal cortex in both rodents and humans [48, 49]. Our results, therefore, are consistent with this literature and suggest that variation in cardiorespiratory fitness levels might explain significant individual variability in correlations between volume and task-switch performance. Interestingly, we failed to find associations with performance on the Flanker Task, despite previous studies showing links with attentional control and function of the basal ganglia circuits [21, 50]. This dissociation between the task-switch and flanker paradigms suggests some specificity of the function of the basal ganglia circuits in late adulthood. One explanation might be that tasks involving attentional control and response conflict, like the flanker paradigm, might be more dependent on prefrontal structures than basal ganglia in late life. This hypothesis is supported by a recent study demonstrating that older adults had less activity in the dorsal striatum during performance of a Stroop task compared to a younger group [50]. Given the presence of cortico-striatum loops, it is likely that a distributed circuit of frontal, parietal, and striatum is involved in mediating both attentional and switching behaviors, but that the relative importance of these structures changes with age.

In addition, we failed to find significant associations between Flanker Task performance and fitness levels despite numerous other studies finding significant associations throughout the lifespan [15, 21, 36, 37, 51–53]. It is likely that our limited range of cardiorespiratory fitness levels precluded our ability to detect significant associations and that the correlations with Task Switching performance are more robustly associated with fitness levels. In any case, it will be important for future studies with a wider range of fitness levels to examine the links between Flanker performance and caudate nucleus volume.

Finally, as alluded to earlier, there are several limitations to the current study that warrant further exploration in future work. First, our study was cross-sectional in nature so causal conclusions about how increased cardiorespiratory fitness might influence the size of the basal ganglia are inherently limited. It will be critical for randomized exercise interventions conducted with a large well-characterized cohort to determine whether it is possible to alter the size of these structures. Second, we did not have any tasks (i.e., reward-based) that might be considered to be dependent on the nucleus accumbens, so we were unable to examine the behavioral importance of greater nucleus accumbens volume with higher fitness levels. However, despite these limitations we were able to detect associations using a relatively large and homogeneous sample of older adults and cognitive tasks that have been previously linked to the function of the dorsal striatum. In sum, we find that cardiorespiratory fitness levels are positively associated with volume of the caudate nucleus and nucleus accumbens in late adulthood and that the size of the caudate nucleus is a significant mediator between fitness and performance in the Task Switch paradigm.

## Authors' Contribution

T. D. Verstynen, B. Lynch, and K. I. Erickson equally contributed to this work.

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*Research Article*

# Investment Trait, Activity Engagement, and Age: Independent Effects on Cognitive Ability

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In cognitive aging research, the "engagement hypothesis" suggests that the participation in cognitively demanding activities helps maintain better cognitive performance in later life. In differential psychology, the "investment" theory proclaims that age differences in cognition are influenced by personality traits that determine when, where, and how people invest their ability. Although both models follow similar theoretical rationales, they differ in their emphasis of behavior (i.e., activity engagement) versus predisposition (i.e., investment trait). The current study compared a cognitive activity engagement scale (i.e., frequency of participation) with an investment trait scale (i.e., need for cognition) and tested their relationship with age differences in cognition in 200 British adults. Age was negatively associated with fluid and positively with crystallized ability but had no relationship with need for cognition and activity engagement. Need for cognition was positively related to activity engagement and cognitive performance; activity engagement, however, was not associated with cognitive ability. Thus, age differences in cognitive ability were largely independent of engagement and investment.

## 1. Introduction

In cognitive aging research, the "engagement hypothesis" predicts that engagement in physical, social, and intellectual activity contributes to reducing age-related cognitive decline and the risk of neurodegenerative disorders [1, 2]. That is, frequent participation in cognitively demanding activities is thought to "exercise" the brain with more cognitively engaged people having better cognition over time because of practice benefits. Thus, the preservation of cognition is thought to depend on the extent to which "a diverse behavioral repertoire is integrated into daily life" [3, page 487]. In differential psychology, the "investment theory" suggests that age-related changes in cognitive development are influenced by personality traits that determine where, when, and how people apply their mental ability [4, 5]. Thus, investment traits are thought to predispose individuals to seek cognitively stimulating environments that in turn prompt the development, application, and practice of cognitive strategies [3, 5]. That said, investment traits may also lead to approaching even mundane experiences in a cognitively stimulating manner, thereby enhancing intellectual development (cf. [6]).

In spite of their native disciplines' differential emphasis on decline versus growth, the engagement hypothesis and investment theory have a lot in common. First, both models propose that individual differences in intellectual engagement are reflected in lifespan trajectories of cognitive development [1, 5]. Second, both models have received some empirical support (e.g., [7–9]), as well as some rejections (e.g., [10–12]). Third, both are subject to the same criticism that the effects of engagement or investment on cognitive change (i.e., differential preservation) are explained by alternative factors, in particular by prior cognitive ability (i.e., preserved differentiation, cf. [2]). That said, the engagement hypothesis and investment theory also differ in one crucial point: cognitive aging researchers tend to assess differences in engaging in substantively complex environments, while investment theorists measure latent traits of personality that refer to "the tendency to seek out, engage in, enjoy, and continuously pursue opportunities for effortful cognitive activity" [13, page 225]. That is, activity engagement is typically assessed with reference to a specific set of activities or environments, such as going to the theatre, while investment traits refer to the intrinsic motivation to think, and corresponding scales assess, for example, one's preference of complex over simple problems. Despite following different rationales, investment and engagement measures rely equally on self-reports, and neither construct has a gold standard scale or equivalent (cf. [2, 13]). Cognitive aging measures of activity engagement vary in their foci, ranging between the frequency of an activity (e.g., regular versus sporadic; [14]), its intensity (e.g., gentle versus vigorous exercise; [15]), life-stage-specific activities (e.g., educational attainment in young adulthood versus occupational achievements in later life; [16]), and specific activity domains (e.g., social versus physical; [11]). Conversely, theoretical and psychometric definitions of investment range from comparatively narrow investment trait scales (e.g., need for cognition; [17]) to broad trait dimensions (e.g., openness to experience; [18]), to even broader trait complexes [5]. To systematically address the role of engagement and investment for cognitive performance, the current study compares the need for cognition scale and a measure of cognitive activity engagement, as well as their relationship with age differences in cognitive ability.

Two previous studies that assessed a wide range of activities, including, for example, housework and religious service attendance, found little support for the notion that activity engagement mediated the effects of an investment trait on cognitive performance [3, 19], which may have been due to the breadth of the included investment and engagement measures. Here, a narrowly focused scale was developed to assess the frequency of participating in typical cognitive activities (e.g., reading a novel; visiting a museum). To measure individual differences in intellectual investment, the need for cognition scale was selected. It refers to the "tendency to engage in and enjoy thinking" [17, page 116] and is a widely used, well-validated and precise measure of investment (cf. [20–22]). Need for cognition scale items makes no reference to specific cognitive activities or environments but measure the extent to which a person enjoys deliberating, abstract thinking and problem solving [17].

In line with previous research [3, 23], it was hypothesized that need for cognition was not meaningfully associated with age because it is a relatively stable trait dimension. Conversely, the frequency of activity engagements is likely to change according to age. That is, during some life periods that allow for the time and financial resources (e.g., young adulthood or early retirement), activity levels can be expected to be relatively high compared to others that are more restricted (e.g., adolescence and parenthood). It follows that activity engagement may have a nonlinear relationship with age.

With respect to age differences in cognitive ability, the so-called fluid abilities (i.e., reasoning capacity) were expected to be negatively correlated with age, while the crystallized abilities (i.e., vocabulary) were expected to be positively associated with age (cf. [4, 5]). Accordingly, age differences in fluid and crystallized ability may be mediated or moderated by cognitive activity engagement and need for cognition (cf. [24, 25]; Figure 1). In a mediation model, the effect of age on cognition is accounted for by activity engagement, which in turn should be positively associated with need for cognition. Thus, the predisposition to seek cognitively stimulating environments is thought to result in a greater frequency of activity engagement, which explains part of the association between age and cognition. By comparison in a moderation model, strength and direction of the relationship between age and cognition is expected to depend on the level of activity engagement and need for cognition (cf. [24]). Thus, people with high need for cognition and subsequently frequent cognitive activity engagements may show smaller age differences in fluid ability and greater ones in crystallized ability than those with low need for cognition and few activity engagements. Because mediation and moderation models are equally plausible in this research context, the current study explores both alternatives.

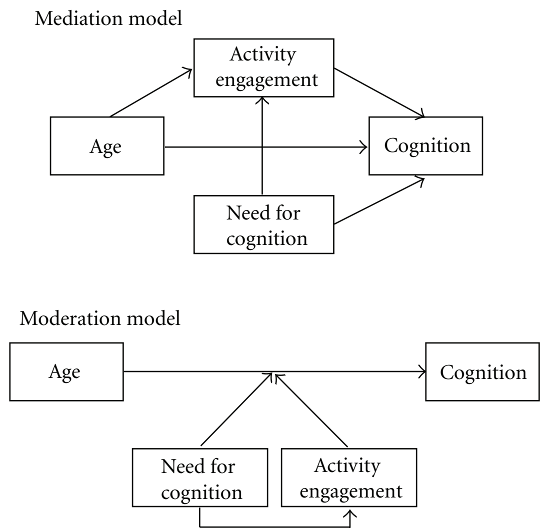


Figure 1: Mediation and moderation models.

## 2. Methods

*2.1. Sample.* 200 British adults (97 men) were recruited with an average age of 34.6 years (SD = 11.8; range from 18 to 69 years; two participants did not report their age). As their highest educational qualification, 14% participants had completed general certificates of secondary education (10th grade); 15% A-levels (12th grade); 18% a vocational qualification or equivalent; 33.5% an undergraduate degree, and 19% a postgraduate degree. About half of the sample reported to earn less than £15.000 ($22,500) per annum, while about 8% declared to earn more than £35.000 ($52,000) per annum.

*2.2. Measures*

*Need for Cognition (see [17]).* The 18-item scale measures the desire to engage in effortful cognitive activity on a 5-point Likert scale, ranging from strongly disagree, disagree, somewhat agree, agree, to strongly agree. An example item

Table 1: Descriptives of cognitive activity engagement items.

| | Item | $N$ | $M$ | SD |
|---|---|---|---|---|
| 1 | Read a book? | 198 | 135.13 | 141.54 |
| 2 | Read the newspapers? | 199 | 203.59 | 137.46 |
| 3 | Attend a music event or concert? | 199 | 29.38 | 56.88 |
| 4 | Attend evening classes? | 197 | 18.71 | 43.91 |
| 5 | Write for pleasure? | 200 | 63.16 | 109.54 |
| 6 | See a play at the theatre? | 197 | 17.76 | 37.32 |
| 7 | Go to a museum or gallery? | 198 | 29.45 | 44.59 |
| 8 | Attend a public talk or lecture? | 196 | 22.03 | 50.23 |
| 9 | Visit the cinema? | 199 | 35.70 | 64.12 |
| 10 | Google things? | 200 | 273.56 | 126.51 |

Note: activity engagement was recorded on a 5-point scale and recoded in days per annum (i.e., every day = 365; every other day = 182; every week = 52; once or twice a month = 18; never = 0).

reads: "I would prefer difficult to simple problems." Internal consistency typically ranges from .83 to .97 [20].

*Cognitive Activity Engagement.* Nine items that were most frequently used in previous studies to assess cognitive activity engagement were adapted [7, 14, 26] and complemented by one addressing the use of modern information technology (i.e., google; Table 1). Participants indicated on a Likert-type scale how often they engaged in the activities listed ranging from 1 to 5, including never, once or twice a month, every week, every other day, and every day.

*Cognitive Ability.* Fluid and crystallized abilities were assessed with three tests each, including Raven's matrices [27] and five other tests [28]. *Fluid ability:* (1) Raven's progressive matrices: 12 items showed grids of 3 rows × 3 columns, each with the lower right-hand entry missing. Participants chose from 8 alternatives the one that completed the 3 × 3 matrix figure. The test was timed at 4 minutes. (2) Lettersets: in 5 sets of 4 letters, participants identified the set that did not fit a rule that explained the composition of the other 4 lettersets. The test had 15 items and was timed at 6 minutes. (3) Nonsense syllogisms: participants judged if a conclusion that followed two preceding statements (premises) showed good (correct) reasoning or not. The test had 15 items and was timed at 4 minutes. *Crystallized ability:* (1) verbal reasoning: participants had to identify the correct pair of words from five options to complete a comparison sentence, whose first and last works were missing. The test had 14 items and was timed at 7 minutes. (2) Vocabulary: participants had to identify the correct synonym for a given word out of five answer options. The test had 18 items and was timed at 4 minutes. (3) Verbal fluency: participants had to write down as many words as possible that started with the prefixes "sub" and "pro." For each prefix, 60 seconds were allowed.

*2.3. Procedure.* Participants were recruited in London, England, with online and flyer advertisement. Inclusion criteria were as follows: native English speakers; normal or corrected to normal vision, hearing, and motor coordination; having lived in the United Kingdom for at least 10 years. These criteria were self-reported by the participants prior to testing. No university students were recruited. Participants completed a two-hour testing session in groups of up to twenty in designated research laboratories. The ability tests were administered in 40 minutes, then participants completed a range of other measures (not reported here), and finally, they completed the cognitive activity engagement and need for cognition scale, as well as a demographic background questionnaire in their own time (approximately 15 minutes). They received monetary compensation.

*2.4. Analysis.* The intelligence tests' $z$-scores were added to form unit-weighted composite scores of fluid and crystallized ability. The cognitive activity responses were weighted on a linear frequency scale of days per annum (i.e., every day = 365; every other day = 182; every week = 52; once or twice a month = 18; never = 0); the psychometric properties of the scale were subsequently analyzed. The study variables were investigated for sex differences in means and variances, and then, their intercorrelations were computed. Next, a series of path models tested if age differences in cognition were mediated or moderated by need for cognition and cognitive activity engagement. To test for mediation, a path model was fitted in line with Figure 1, including fluid and crystallized ability as correlated outcome variables. To test for moderation, all variables were $z$-transformed. A series of regression models tested two-way interactions (need for cognition × age, activity engagement × age, and need for cognition × activity engagement) and a three-way interaction (age × need for cognition × activity engagement) separately for fluid and crystallized ability. That is, a first set of models (one for fluid, one for crystallized ability) included age and need for cognition in a first step and in a second, their interaction term. A second set of models included age and activity engagement in a first step and then their interaction. A third set of models included first age, activity engagement, and need for cognition, next their two-way interactions, and finally the three-way interaction term.

## 3. Results

Table 1 shows the descriptives for the cognitive activity engagement items after recoding the Likert scale into days per annum. Item endorsement frequencies did not vary meaningfully with age. A unit-weighted composite score was formed; the corresponding coefficient alpha was .58. The activity engagement score was normally distributed, and so were the test scores of all cognitive ability tests. No meaningful sex differences were observed in the study variables, and thus, data from men and women were analyzed together.

The scatterplot suggested that age was not associated with cognitive activity engagement, neither in a linear nor in a nonlinear fashion. Table 2 shows the descriptives of and correlations between age (in years), need for cognition, activity engagement, and fluid and crystallized ability. Age was significantly negatively associated with fluid and positively with crystallized ability. Furthermore, fluid and crystallized ability were intercorrelated ($r = .66$), and so were cognitive

Table 2: Correlations and descriptives for study variables.

| | | $N$ | $M$ | SD | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|---|---|---|
| 1 | Fluid ability | 200 | 0.00 | 2.31 | — | | | |
| 2 | Crystallized ability | 189 | −0.01 | 2.52 | .66* | — | | |
| 3 | Age (years) | 198 | 34.58 | 11.84 | −.14* | .18* | — | |
| 4 | Activity engagement | 193 | 830.32 | 357.84 | .08 | .10 | .00 | — |
| 5 | Need for cognition | 189 | 3.46 | 0.60 | .34* | .35* | .00 | .25* |

*$P < .05$.
Note: need for cognition was recorded on a 5-point Likert scale, ranging from strongly disagree, disagree, somewhat agree, agree, to strongly agree. Activity engagement was also recorded on a 5-point scale and recoded in days per annum (i.e., every day = 365; every other day = 182; every week = 52; once or twice a month = 18; never = 0).

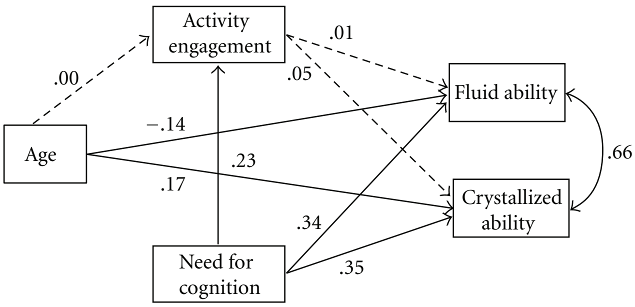


Figure 2: Mediation model of age differences in cognitive ability with standardized path parameters. Note: error terms for activity engagement, fluid and crystallized ability have been omitted to sustain graphical clarity. Dashed paths represent nonsignificant pathways ($P > .05$). The double-headed arrow indicates a correlation.

activity engagement and need for cognition, albeit to a much smaller extent ($r = .25$). Cognitive activity engagement was not correlated with age, fluid or crystallized ability, while need for cognition had a significant, positive associations ability but not with age.

Figure 2 shows the mediation model results. As before, age was positively associated with crystallized ability and negatively with fluid intelligence, while need for cognition had positive relationships with activity engagement, fluid and crystallized ability. Activity engagement did not mediate any of the age or need for cognition effects on cognitive ability. Thus, need for cognition and age had only direct effects on fluid and crystallized ability, accounting for 13% and 15% of their total variance, respectively.

Table 3 shows the results of the moderation models. In the first step, age was positively associated with crystallized and negatively with fluid ability, while need for cognition was positively associated with both, and activity engagement was not meaningfully related to ability. Neither two-way nor three-way interaction yielded any significant results. Thus, the level of activity engagement or investment did not interact with age differences in fluid and crystallized abilities. Overall, the results suggest that while investment traits and cognitive activity engagement are moderately associated, neither affects age differences in cognition. That said, need for cognition was significantly correlated with cognitive ability, while activity engagement was not.

## 4. Discussion

The current study explored the relationship of an investment personality trait (i.e., need for cognition) and a cognitive activity engagement scale with age differences in cognitive performance. In line with earlier research [3, 19], need for cognition and cognitive activity engagement were positively interrelated, albeit weakly so. Therefore, a predisposition to deliberate and think abstractly is somewhat different to actively pursuing cognitively stimulating engagement, such as reading a novel or going to the theatre. Also consistent with previous findings [1, 5], age was negatively associated with fluid and positively with crystallized ability, as well as unrelated to the investment trait need for cognition (cf. [17, 23]). Contradicting the current hypotheses, however, no meaningful age differences were observed in cognitive activity engagement. Thus, while the frequencies of activity engagement were slightly elevated in age groups that are likely to experience the most advantageous conditions for engagement (i.e., financial security and time), these differences were not significant.

Confirming previous research [20, 21, 29], need for cognition was positively associated with both fluid and crystallized ability, while no such association was observed for cognitive activity engagement (cf. [3, 19]). Furthermore, cognitive activity engagement did not mediate the association between age and cognition. That is, age and need for cognition had direct, independent effects on cognition, which were unrelated to cognitive activity engagement. It seems plausible that need for cognition contributes to constructing everyday experiences in an intellectually enriching way, and thus, the effect of need for cognition on cognitive performance is direct and not mediated by engagement (cf. [3, 6]). Future research must establish how need for cognition affects perception and perhaps even intellectual exploitation of daily working and living routines, and how such experiences contribute to cognitive development and aging.

The current study has several limitations. First, the study design was cross-sectional, and all causal inferences are speculative. Second, the recruitment methods of the study may have led to a biased sample composition by attracting

Table 3: Standardized regression parameters for two-way and three-way moderation models.

| Step | Model 1 | | | | | | Model 2 | | | | | | Model 3 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fluid ability | | | Crystallized ability | | | Fluid ability | | | Crystallized ability | | | Fluid ability | | | Crystallized ability | | |
| | $\beta$ | CI (95%) | | $\beta$ | CI (95%) | | $\beta$ | CI (95%) | | $\beta$ | CI (95%) | | $\beta$ | CI (95%) | | $\beta$ | CI (95%) | |
| 1 | | | | | | | | | | | | | | | | | | |
| Age | **−.14** | **−0.63** | **−0.01** | **.17** | **0.08** | **0.77** | −.11 | −0.59 | 0.07 | **.19** | **0.12** | **0.86** | −.13 | −0.63 | 0.03 | **.19** | **0.12** | **0.86** |
| NFC | **.34** | **0.44** | **1.05** | **.35** | **0.51** | **1.16** | — | — | — | — | — | — | **.32** | **0.39** | **1.02** | **.35** | **0.50** | **1.18** |
| CAE | — | — | — | — | — | — | .07 | −0.18 | 0.48 | .09 | −0.13 | 0.59 | .03 | −0.27 | 0.38 | .05 | −0.22 | 0.48 |
| 2 | | | | | | | | | | | | | | | | | | |
| NFC × age | −.03 | −0.37 | 0.24 | −.04 | −0.41 | 0.24 | — | — | — | — | — | — | −.05 | −0.43 | 0.23 | −.01 | −0.38 | 0.32 |
| CAE × age | — | — | — | — | — | — | −.05 | −0.43 | 0.20 | −.05 | −0.45 | 0.24 | −.05 | −0.46 | 0.23 | .01 | −0.36 | 0.39 |
| CAE × NFC | — | — | — | — | — | — | — | — | — | — | — | — | −.09 | −0.43 | 0.10 | .00 | −0.28 | 0.29 |
| 3 | | | | | | | | | | | | | | | | | | |
| CAE × NFC × age | — | — | — | — | — | — | — | — | — | — | — | — | .09 | −0.13 | 0.36 | .13 | −0.07 | 0.45 |

Note: the regressions were stepwise conducted, entering the respective set of independent variables in step 1, and their corresponding interaction terms in step 2 and 3. All models were run separately for fluid and crystallized ability as dependent variables. Model 1 shows the results for the two-way interaction of age and need for cognition; model 2 shows the two-way interaction of age and cognitive activity engagement; model 3 shows the results of testing for the three-way interaction. Significant parameters are shown in bold. Keys: age = age in years; NFC = need for cognition; CAE = cognitive activity engagement.

particularly active or cognitively engaged individuals. Also, the age range of participants (18 to 69 years), about half of whom were aged between 18 and 30 years, is possibly not ideal for detecting age differences in cognition. Indeed, the modesty of the observed associations between age and cognition is likely to be due to the relative youth of the current sample. The latter is unlikely, however, to account for the observed zero-order associations of age with investment and engagement because the sample spanned several life periods. Third, the current study assessed only one dimension of activity engagement (i.e., cognitive), but it may be that other engagement aspects, such as physical or social activity, are more important for age differences in cognition [7]. Also, only the frequency of cognitive activity engagement but not its duration nor the complexity of the activity was assessed here. Finally, the assessment instruments of intellectual investment and cognitive activity both relied on self-reports, which are known to be influenced by social desirability and self-serving bias (cf. [30]).

Notwithstanding these shortcomings, the current study contributes to understanding the role of investment and engagement for age differences in cognition. Echoing previous research (e.g., [7, 9, 11, 12]), it seems as if intellectual engagement—regardless of being assessed in terms of activity participation or trait disposition—has little effect on age differences in cognition. That said, the predisposition to invest (i.e., need for cognition) in one's cognitive competence contributed overall to better cognitive performance and a higher frequency of cognitive activity engagement (cf. [3, 9]). To explain the relationship between investment and cognition, mechanisms other than activity engagement must be explored, for example, individual differences in constructing experiences within daily living routines.

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