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RESEARCH ARTICLE

The relationship between cognitive engagement and better memory in midlife

Lisa Bransby[1] | **Rachel F. Buckley**[2,3,4] | **Emily Rosenich**[1] | **Katherine H. Franks**[1,2] | **Nawaf Yassi**[5,6] | **Paul Maruff**[7,8] | **Matthew P. Pase**[1,9] | **Yen Ying Lim**[1]

[1] Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University, Clayton, Victoria, Australia

[2] Melbourne School of Psychological Sciences, University of Melbourne, Parkville, Victoria, Australia

[3] Department of Neurology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

[4] Center for Alzheimer Research and Treatment, Department of Neurology, Brigham and Women's Hospital, Boston, Massachusetts, USA

[5] Department of Medicine and Neurology, Melbourne Brain Centre at the Royal Melbourne HospitalUniversity of Melbourne, Parkville, Victoria, Australia

[6] Population Health and Immunity Division, The Walter and Eliza Hall Institute of Medical Research, Parkville, Victoria, Australia

[7] Florey Institute of Neuroscience and Mental Health, Parkville, Victoria, Australia

[8] Cogstate Ltd., Melbourne, Victoria, Australia

[9] Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

Correspondence
Yen Ying Lim, Turner Institute for Brain and Mental Health, 18 Innovation Walk, Clayton, VIC 3168, Australia
E-mail: yenying.lim@monash.edu

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Abstract

Introduction: Engagement in cognitively stimulating work and activities may slow cognitive decline and dementia. We examined the individual and combined associations of four cognitive engagement indices (educational attainment, occupational complexity, social engagement, and cognitively stimulating leisure activities) with objective and subjective cognition.

Methods: Middle-aged adults (n = 1864) enrolled in the Healthy Brain Project completed the Cogstate Brief Battery, the Cognitive Function Instrument, and self-report questionnaires of cognitive engagement.

Results: Educational attainment and leisure activity engagement were individually associated with memory performance. Participants were classified based on whether they rated highly in zero to four cognitive engagement indices. Compared to participants with no indices, participants with two or more indices performed moderately better on memory.

Discussion: Results suggest that greater variety of cognitive engagement across different areas of life is related to better memory in midlife. Possible explanation for this relationship may be increased opportunity for enhancing cognitive reserve, but further investigations are required.

KEYWORDS
cognition, cognitive engagement, cognitive stimulation, educational attainment, leisure activity, lifestyle, midlife, occupational complexity, protective factor, social engagement

1 | INTRODUCTION

Engagement in cognitively stimulating work and activities is associated with reduced risk of cognitive decline and onset of dementia.[1,2,3] This suggests that behavioral and lifestyle characteristics or choices may influence age-related change to cognition and provide a potential target for strategies aimed at delaying or preventing dementia.[4,5] Cognitive engagement across work and leisure time may not influence disease pathology directly but may contribute to increases in brain capacity or plasticity so that individuals with greater cognitive engagement may be able to preserve cognitive abilities after insult or injury, a construct termed cognitive reserve (CR).[6] However, while cognitive engagement is considered an important dimension of CR the construct remains ill-defined. Thus, brain–behavior models of CR would benefit from a greater understanding and refinement of models of cognitive engagement.

Most studies investigating associations between cognitive engagement and cognition have defined cognitive engagement using a single index, most commonly years of formal education.[3,7] However, the use of years of education is limited as it ignores education or skills acquired after an individual completes their formal schooling and is subject to bias of opportunity.[8] Other definitions have sought to capture post-schooling experience through young adulthood into midlife by quantifying occupational attainment or occupational complexity.[9,10] However, such indices are also subject to bias due to sex, socioeconomic status, and opportunity.[11] Cognitive engagement has also been inferred from measures of social engagement based on the assumption that cognitive stimulation arises from complex communication and interactions that can occur within social groups.[12,13]

Some studies have defined cognitive engagement using more direct measures such as participation in cognitively stimulating leisure activities.[14,15] For example, social leisure activities such as volunteering or participation in community groups and more individual activities such as reading, arts and crafts, or music have been classified as cognitively stimulating in surveys.[16] Summary or composite scores are then computed to represent frequency of engagement in these leisure activities.[14–16] A recent study in cognitively normal older adults found that participating in a variety of cognitively stimulating leisure activities, as well as high frequency of engagement was significantly associated with a reduced risk of incident mild cognitive impairment (MCI) over a median of 5 years.[17] As implementing engagement in cognitively stimulating leisure activities adds more precision to the definition of cognitive engagement, it is also important to understand whether different aspects of engagement, such as frequency (i.e., how often) and variety (i.e., number) of engagement, have differential associations with cognition.

One approach to defining and understanding cognitive engagement more comprehensively would be to consider information about characteristics that have been used in studies as indirect indices of the construct (i.e., educational attainment, occupational complexity) as well as those that have been used as direct indices of cognitive engagement, such as social engagement and engagement in cognitively stimulating leisure activities. These indices of cognitive engagement can then be examined to determine the extent to which they, individually or in combination, are related to cognition. While these indices of cognitive engagement have been shown to be associated with reduced risk of cognitive impairment and incident dementia in older adults,[18,19] the extent to which they are also related to cognition in middle-aged adults is less clear. In middle-aged adults, pathological changes associated with Alzheimer's disease (AD) have been shown to have begun, although individuals are unlikely to reach thresholds of abnormality.[20] As such, there is now increasing interest in identifying factors that may influence risk of cognitive dysfunction or decline in this middle-age epoch. The Healthy Brain Project (HBP) has recruited a large sample of middle-aged adults enriched for family history of dementia and therefore may be at risk of cognitive decline but are unlikely to present with clinically classified cognitive impairment and dementia. Investigating these relationships in the HBP cohort may therefore provide a basis to increase understanding of how early individual differences in cognitive engagement could influence cognition, and risk for cognitive decline and dementia later in life.

The first aim of this study was to explore the extent to which frequency or variety of cognitively stimulating leisure activities was related to cognition. With this established, the second aim was to determine the associations between each index of cognitive engagement (educational attainment, occupational complexity, social engagement, cognitively stimulating leisure activities) with cognitive performance and subjective ratings of cognition. Based on previous observations,[18,19] we hypothesized that each index of cognitive engagement would be individually associated with better cognitive test performance, and lower subjective ratings of cognitive concerns. The third aim was to determine the association between the combination of multiple indices of cognitive engagement with cognitive performance and subjective ratings of cognition. We hypothesized that greater cognitive engagement across all indices would be associated with better cognitive performance and lower subjective ratings of cognitive concerns.

2 | METHODS

2.1 | Participants

The sample for this study was drawn from baseline data from cognitively normal middle-aged participants enrolled in the HBP,

who completed measures of all four cognitive engagement indices (N = 1864) and have additionally completed measures of cognitive performance (N = 1500) and subjective ratings of cognition (N = 1719; Figure 1). The HBP is a prospective cohort study seeking to understand midlife risk factors for dementia using an online remote assessment platform.[21] HBP participants may complete as many assessments as they choose in a single engagement and therefore may not complete all assessments. This has led to varying sample sizes for each test and survey (Figure 1). The HBP recruitment process has been detailed previously.[21] Briefly, participants were included if they live in Australia, were fluent in English, and were aged between 40 and 70 years. Participants were excluded if they reported a history of major traumatic brain injury or other major neurological disease or insult; psychiatric condition (i.e., schizophrenia, uncontrolled current major depression, or other uncontrolled Axis I psychiatric disorder); any prior use of Therapeutic Goods Administration–approved medications for AD (e.g., donepezil, memantine, or other approved medications); or a diagnosis of MCI, AD, Parkinson's disease, or other known diagnosis of dementia. Family history of dementia is not an inclusion criteria for HBP but as a result of targeted recruitment, 69.58% of our sample has a first- or second-degree family history of dementia (Table 1). The HBP was approved by the human research ethics committee at Melbourne Health and all participants provided informed consent prior to their participation. Recruitment for the HBP is ongoing so the current study uses data collected from inception of the study (February 2017) up to the third formal DataFreeze (May 2020).

RESEARCH IN CONTEXT

1. Systematic review: The authors reviewed the literature using traditional sources (e.g., PubMed). Studies reporting on the cognitive engagement indices and their relationship with cognition were included. Studies investigating potential mechanisms or the theoretical construct for these relationships were also reviewed.
2. Interpretation: Our results suggest a relationship between several cognitive engagement indices and better memory in midlife. This supports a multi-index approach to defining cognitive engagement and provides a more comprehensive understanding of its relationship with cognition, as opposed to the singular approach used by most previous studies.
3. Future directions: As our study was cross-sectional, future longitudinal studies should investigate the relationship between multiple cognitive engagement indices and cognitive decline and risk for dementia in later life. Further, future studies are required to examine how these indices of cognitive engagement inform models of cognitive reserve by investigating whether cognitive engagement moderates cognitive outcomes in the presence of brain pathology or insult.

2.2 | Measurement of cognitive engagement

Educational attainment was measured as self-reported years of formal education. Occupational complexity was quantified using a combination of occupational type and employment fraction. Specifically, participants were required to indicate their employment status (i.e., full time, part time) and select the most appropriate occupational role from several provided options (e.g., upper management, skilled laborer, administrative staff, etc.). If a participant had retired, they then indicated a role that best described their main occupation during their working life. A protocol used previously[22] guided our occupational complexity classification (Supplementary 2 in supporting information). Frequency of social engagement was assessed using the General Social Survey Cycle 17 (GSS).[23] Participants were requested to report how often they see their close friends and relatives in person and communicate with them via phone or internet. Cognitively stimulating leisure activities were assessed using a previously developed survey[24] that was modified to ensure relevance to middle-aged participants in HBP (Supplementary 1 in supporting information). The main outcomes of interests were frequency of engagement in each cognitively stimulating leisure activity as well as the variety of leisure activities. Although some of the cognitively stimulating leisure activities were social in nature (e.g., community activities), these indices were associated only weakly with frequency of social engagement (r = 0.22–0.24) indicating that these scores on these measures reflected different aspects of cognitive engagement. Scoring information for the measures of cognitive engagement can be found in Supplementary 2.

2.3 | Assessment of cognition

Participants completed unsupervised online cognitive testing using the Cogstate Brief Battery (CBB).[25] Delivery and instructions for the CBB have been adapted for remote assessment and the psychometric properties of the online version have been demonstrated previously.[25,26] The CBB consists of four tests: Detection (DET), Identification (IDN), One Card Learning (OCL), and One-Back (OBK), which have been described previously.[27] Briefly, the DET test is a simple reaction time paradigm that measures psychomotor function. The IDN test is a choice reaction time paradigm that measures visual attention. The OBK test is a one-back paradigm that measures working memory. The primary outcome measure for the DET, IDN, and OBK tasks is reaction time in milliseconds (speed), which was normalized using a logarithmic base 10 ($\log_{10}$) transformation. The OCL test is a continuous visual recognition learning paradigm that measures visual learning within a pattern separation model. The primary outcome measure for this task is the proportion of correct answers (accuracy), which is normalized using an arcsine square-root transformation. The raw scores for the outcome measures were standardized to z-scores using the baseline mean and standard deviation of the current sample. All outcomes of speed were

TABLE 1 Demographic characteristics for HBP participants who completed all four measures of cognitive engagement and rated highly in zero to four cognitive engagement indices (educational attainment, occupational complexity, frequency of social engagement, and variety of leisure activities)

		Number of cognitive engagement indices				
	Total	0	1	2	3	4	
	M(SD) or N%	M(SD) or N%	M(SD) or N%	M(SD) or N%	M(SD) or N%	M(SD) or N%	*P*
N	1864	117	463	723	452	109	
Age (years)	57.21 (7.16)	61.36 (5.98)	58.42 (6.94)	56.88 (7.25)	56.34 (7.07)	53.43 (6.02)	<**.001**
Sex, female	1412 (75.75%)	82 (70.09%)	335 (72.35%)	539 (74.55%)	362 (80.08%)	94 (86.24%)	**.002**
Education (years)	15.98 (3.46)	10.85 (1.15)	15.13 (3.57)	16.42 (3.10)	17.13 (2.94)	17.45 (3.07)	<**.001**
European ethnicity	1517 (81.38%)	81 (69.23%)	358 (77.32%)	603 (83.40%)	385 (85.18%)	90 (82.57%)	<**.001**
Family history of dementia	1297 (69.58%)	85 (72.65%)	303 (65.44%)	511 (70.68%)	318 (70.35%)	80 (73.39%)	.212
HADS depression, score units	3.07 (2.78)	3.83 (3.01)	3.34 (2.93)	3.09 (2.83)	2.78 (2.51)	2.25 (2.26)	<**.001**
HADS anxiety, score units	3.69 (3.24)	4.46 (4.17)	4.13 (3.48)	3.59 (3.12)	3.34 (2.97)	3.21 (2.54)	<**.001**

Notes: High educational attainment was defined as >12 years of formal education, and high occupational complexity, high frequency of social engagement, and high variety of leisure activities were defined as scoring above the median (12, 19, and 2, respectively).
Abbreviations: HBP, Healthy Brain Project; HADS, Hospital Anxiety and Depression Scale; SD, standard deviation.

reverse scored such that higher values indicate better cognitive performance. A Memory composite was computed by averaging the standardized OCL and OBK scores, and an Attention composite was computed by averaging the standardized DET and IDN scores.

2.4 | Assessment of subjective ratings of cognition

The Cognitive Function Instrument (CFI)[28] was administered to measure subjective ratings of cognition. As the original CFI was designed for an older adult population, some items were modified to better reflect subjective assessment of cognition in midlife, such as in an occupational setting.[21] The CFI total score (as the sum of all responses) was used as an outcome of subjective ratings of cognition and was standardized to a z-score using the baseline mean and standard deviation derived from the current sample. The standardized score was then reverse scored so that higher values indicate better subjective ratings of cognition.

2.5 | Data analysis

All analyses were conducted using R version 4.0.1. Cognitive engagement indices were considered both continuously and categorically in separate models. A participant was considered to have high educational attainment if they reported greater than 12 years of formal education. High occupational complexity (> 12), high frequency of social engagement (> 19), and high frequency (> 1) and variety (> 2) of engagement in leisure activities were classified using a median split procedure. A median split procedure was used to categorize participants into low and high engagement groups as there are currently no predefined or logical cut-offs for these indices.

A series of analyses of variance and Chi-square tests of independence were conducted to determine any demographic differences between groups of participants that rated highly in zero to four cognitive engagement indices. Any characteristics that were significantly different between groups were added as covariates to subsequent analyses. Pearson's correlations were used to determine the extent to which cognitive engagement indices were associated with each other.

To explore whether frequency or variety of engagement in cognitively stimulating leisure activities was more strongly related to cognition, both frequency and variety scores were entered simultaneously into a linear regression model with each cognitive outcome. The aspect of engagement determined to be most strongly associated with cognitive outcomes was used for subsequent analyses.

To determine the associations between each cognitive engagement index with cognitive performance and subjective ratings of cognition, linear regression models were performed. Educational attainment, occupational complexity, frequency of social engagement, and engagement in leisure activities were entered as simultaneous predictors with each cognitive outcome.

To determine the combined association of all cognitive engagement indices with cognitive performance and subjective ratings of cognition, participants were grouped according to whether they scored highly in zero to four cognitive engagement indices. Analyses of covariance were conducted to investigate the combined association of cognitive engagement indices with each cognitive outcome. Estimated marginal means (EMMs) were calculated for each group and the magnitude of difference between groups was expressed as Cohen's d, with participants with zero cognitive engagement indices as the reference group.

All statistical analyses were adjusted for age, sex, ethnicity, and self-reported depression and anxiety symptomatology (as measured using the Hospital Anxiety and Depression scale[29]) as they were significantly different between cognitive engagement groups. Statistical

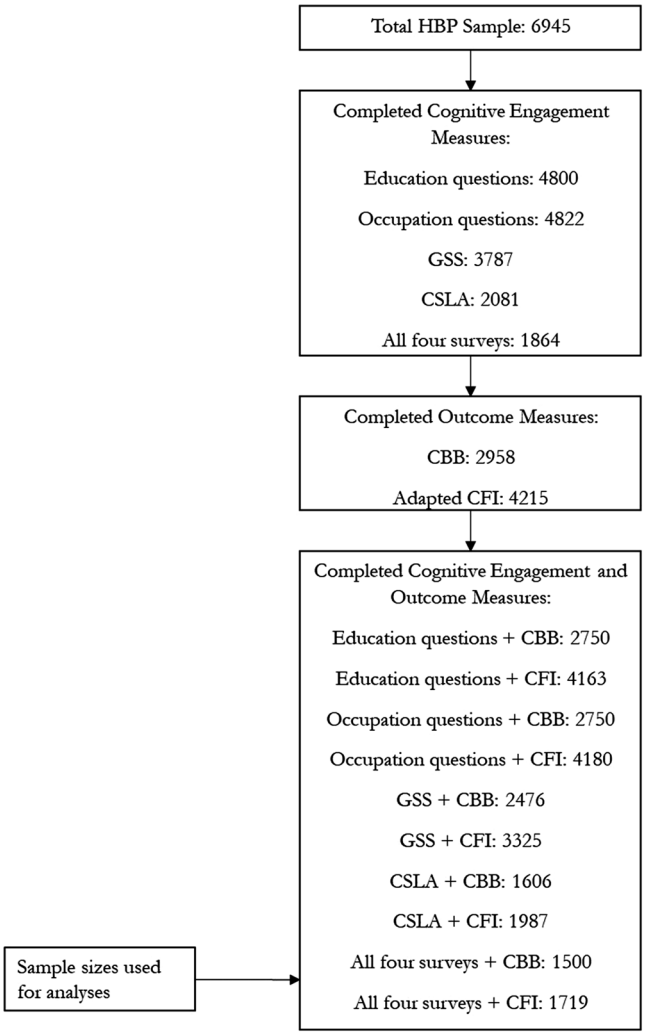

FIGURE 1 Number of participants (N) who completed baseline cognitive engagement surveys and outcome measures and were thus included in analyses. CBB, Cogstate Brief Battery; CFI, Cognitive Function Instrument; CSLA, cognitively stimulating leisure activities survey; GSS, Global Social Survey; HBP, Healthy Brain Project

significance for all comparisons was set at $P < .05$. No corrections for Type I error were instituted because of the novel and experimental nature of this study and the large sample size. Measures of effect sizes were used to contextualize results with comparisons to an estimated effect size (i.e., Cohen's d) of < 0.2 defined as trivial and not interpreted.

3 | RESULTS

3.1 | Demographic characteristics

Table 1 summarizes the demographics characteristics of the sample. Overall, participants with higher cognitive engagement were younger, more likely to be female, have more years of education, have lower levels of depression and anxiety symptomatology, and were more likely to be of European ethnicity than participants with fewer cognitive engagement indices.

The strongest correlation observed was between frequency and variety of engagement in cognitively stimulating leisure activities (r = 0.309, $P < .001$). Significant, but weak, correlations were also observed between other cognitive engagement indices (ranging from −0.078–0.243), except for between occupational complexity with variety of leisure activities (r = 0.028, $P = .211$) and frequency of social engagement (r = −0.007, $P = .648$).

3.2 | Frequency versus variety of engagement in cognitively stimulating leisure activities

When frequency and variety of engagement in leisure activities were considered simultaneously in linear regression models, variety of leisure activities was significantly associated with better performance on the Attention composite (β standard error [SE] = 0.050 [0.022], $P = .025$) and the Memory composite (β [SE] = 0.068 [0.020], $P = .001$), but not with subjective ratings of cognition (β [SE] = 0.009 [0.022], $P = .679$). Frequency of engagement was not associated with any outcome; Attention (β [SE] = −0.016 [0.022], $P = .472$), Memory (β [SE] = 0.017 [0.021], $P = .397$) or subjective ratings of cognition (β [SE] = 0.015 [0.022], $P = .499$). Thus, only variety of engagement in cognitively stimulating activities was considered in subsequent analyses.

3.3 | Associations of individual cognitive engagement factors with cognitive performance and subjective ratings of cognition

Higher levels of educational attainment and greater variety of engagement in leisure activities were each associated with better performance on the Memory composite, but not with performance on the Attention composite or subjective ratings of cognition (Table 2). Occupational complexity and frequency of social engagement were not associated with any aspect of cognition (Table 2).

3.4 | Effect of a composite measure of cognitive engagement on cognitive performance and subjective ratings of cognition

A statistically significant association was observed between the cognitive engagement composite (educational attainment, occupational complexity, frequency of social engagement, and variety of leisure activities) and the Memory composite, but not the Attention composite or subjective ratings of cognition (Table 3). Compared to the zero cognitive engagement indices group, individuals who rated highly in two, three, or four cognitive engagement indices performed significantly better on the Memory composite, with a moderate magnitude of difference between groups (Table 3, Figure 2). Exclusion of participants

TABLE 2 Relationships between individual cognitive engagement indices and Attention and Memory composites and subjective ratings of cognition

	β (SE)	P
Attention composite		
Educational attainment	−0.033 (0.023)	.149
Occupational complexity	−0.006 (0.025)	.797
Frequency of social engagement	−0.012 (0.023)	.621
Variety of leisure activities	−0.035 (0.023)	.127
Memory composite		
Educational attainment	**0.054 (0.021)**	**.010**
Occupational complexity	0.032 (0.022)	.153
Frequency of social engagement	0.027 (0.021)	.198
Variety of leisure activities	**0.057 (0.020)**	**.005**
CFI total		
Educational attainment	−0.001 (0.023)	.971
Occupational complexity	0.019 (0.025)	.421
Frequency of social engagement	−0.023 (0.023)	.313
Variety of leisure activities	0.007 (0.023)	.759

Notes: Beta coefficients are standardized and each model has been adjusted for age (years), sex, ethnicity, and score units for depression and anxiety on the Hospital Anxiety and Depression Scale. Bolded values are statistically significant at $P < .05$.
Abbreviations: CFI, Cognitive Function Instrument; SE, standard error.

who completed assessments during the COVID-19 pandemic (n = 93) did not change these results substantially (d = 0.31–0.54).

4 | DISCUSSION

This study aimed to examine the relationship between multiple indices of cognitive engagement and cognition in a large cohort of middle-aged adults enriched for family history of dementia. We first explored whether frequency or variety of engagement in cognitively stimulating leisure activities was related to cognition and observed that variety, and not frequency, of engagement was associated with better attention and memory. With this established, we examined the extent to which each index of cognitive engagement would be individually associated with cognitive performance and subjective ratings of cognition. The first hypothesis that each index of cognitive engagement would be associated with better cognition, and lower subjective ratings of cognitive concerns was supported partially. Only educational attainment and variety of leisure activities were associated with better memory, although for both indices the magnitude of this relationship was only small ($\eta^2 < 0.1$). This observation is consistent with previous studies conducted in older adults.[30,31] The second hypothesis that greater cognitive engagement across all indices would be associated with better cognitive performance and lower subjective ratings of cognitive concerns was also supported partially. Compared to individuals who rated low on the multidimensional cognitive engagement index, participants who rated highly in two or more indices of cognitive engagement had better memory performance, with the magnitude of this difference moderate (d = 0.30–0.49), and qualitatively increasing with each additional cognitive engagement index. Together, these results suggest that, in middle-aged adults at risk of cognitive decline, high cognitive engagement across several domains of life is associated with better memory.

Our finding that variety, and not frequency, of engagement in cognitively stimulating leisure activities was associated with better cognition in middle-aged adults is consistent with previous findings in older adults.[17,31,32] Others have observed that higher frequency of engagement is associated with better cognition;[14,15,33] however, they did not also consider variety of leisure activities. The results of this study highlight the importance of considering more than one aspect of engagement. Engaging in a greater variety of leisure activities may be associated with better cognition because it introduces the opportunity for greater and more complex stimulation across multiple cognitive domains or abilities.[31] Further, engaging in fewer activities at a higher frequency may become less cognitively demanding over time due to mastering of the activity that may occur with repetition.

When considered simultaneously, only high education and high variety of engagement in leisure activities, but not occupational complexity and social engagement, were associated with cognitive performance. While increased occupational complexity has often been used as a proxy for cognitive engagement, it is also commonly associated with other factors related to poor cognitive performance, such as stress.[34,35] As such, further research is required to clarify the contribution of occupational complexity to cognitive performance, and the extent to which other risk factors may mediate this relationship. Our observation that frequency of social engagement was not associated with cognitive function was also inconsistent with previous studies;[36,37] however, these studies did not simultaneously consider other indices of cognitive engagement. Further, even after the removal of two items reflecting leisure activities that were social in nature (e.g., community activities) from the variety of leisure activities score, the results remained comparable (Supplementary 2), supporting our previous observation that social engagement did not substantially contribute to cognitive performance. Thus, these results suggest that in midlife, cognitive engagement occurring through participation in cognitively stimulating activities may be more strongly associated with better cognitive performance than when occurring through socially stimulating activities. However, our results showing a stronger relationship between better memory and high engagement across multiple indices suggests that greater variety of opportunities for cognitive engagement is important. Previous studies in older adults have shown that high engagement across several cognitively stimulating activities during work and leisure time was associated with a reduced risk of cognitive impairment and incident dementia.[18,19,38] In this study, we extended understanding of this relationship by showing that moderate differences in memory are already apparent in midlife between individuals who are highly engaged across multiple cognitively stimulating activities during work and leisure and those who are not. Further, this relationship was observed through the simultaneous consideration

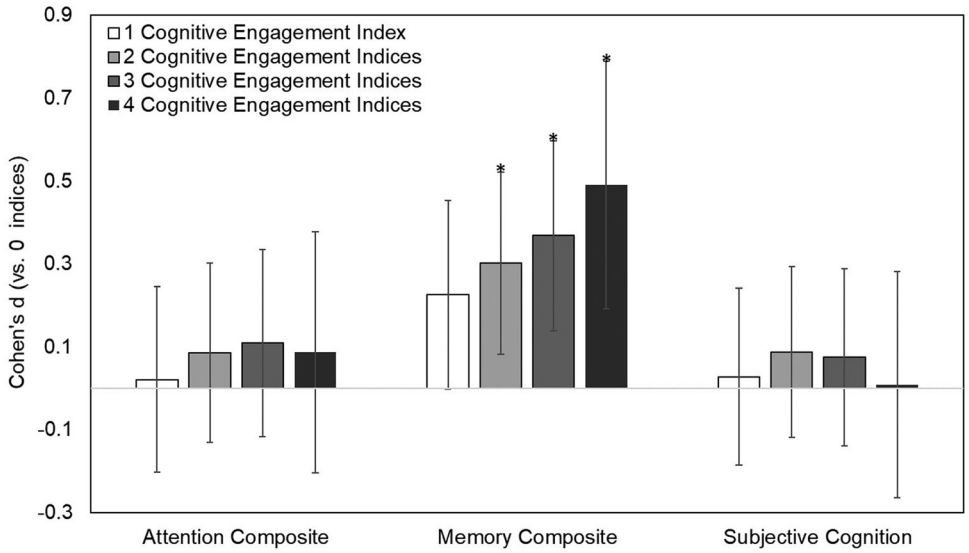

FIGURE 2 The magnitude of difference between individuals who rated highly in zero cognitive engagement indices (educational attainment, occupational complexity, frequency of social engagement, and variety of leisure activities) versus those who rated highly in one, two, three, or four cognitive engagement indices on Attention and Memory composites and subjective ratings of cognition. Note: Error bars are 95% confidence intervals. Effect sizes marked by * are statistically significant at $P < .05$

TABLE 3 Groups that rated highly in zero to four cognitive engagement indices and differences in attention and memory composites and subjective ratings of cognition

			Number of cognitive engagement indices				
			0 (N = 117)	1 (N = 463)	2 (N = 723)	3 (N = 452)	4 (N = 109)
	β (SE)	*P*	EMM (SE)	EMM (SE)	EMM (SE)	EMM (SE)	EMM (SE)
Attention composite	0.042 (0.023)	.069	−0.069 (0.089)	−0.089 (0.048)	0.019 (0.043)	0.036 (0.052)	0.008 (0.096)
Memory composite	**0.080 (0.021)**	**<.001**	−0.225 (0.081)	−0.037 (0.044)	0.052 (0.039)	0.091 (0.047)	0.161 (0.087)
CFI total	−0.013 (0.023)	.570	0.031 (0.090)	0.003 (0.048)	−0.063 (0.042)	−0.045 (0.051)	0.023 (0.094)

Notes: A higher EMM indicates better performance on the Attention or Memory composite, and fewer subjective cognitive concerns; beta coefficients are standardized and each model has been adjusted for age (years), sex, ethnicity, score units for depression and anxiety on the Hospital Anxiety and Depression Scale (HADS). Bolded values are statistically significant at $P < .05$.
Abbreviations: EMM, estimated marginal means; CFI, Cognitive Function Instrument; SE, standard error.

of multiple validated indices of cognitive engagement. Consideration of the relationships between each of these different cognitive engagement indices found that they were only weakly related to each other (r = −0.08–0.24), suggesting that they measure unique elements of the cognitive engagement construct. Together, these results support that a multi-index approach to cognitive engagement is important to enable a more comprehensive understanding of the contribution of cognitive engagement to cognition.

Engagement in cognitively stimulating work and activities may reflect socio-behavioral proxies of CR and may therefore contribute to enhancing CR.[39] However, as this study did not have a measure of brain pathology, the extent to which these results inform CR models of the brain's capacity to withstand pathological insult or injury were limited and will need to be investigated in future studies. Rather, the results of this study contribute to a more comprehensive understanding of cognitive engagement, which in turn provides a foundation for refining the measurement of cognitive engagement in models of CR. Late-life animal studies seeking to understand the role of environmental enrichment indicated that compared to mice in standard housing, mice exposed to environmental enrichment from 12 to 18 months of age had better memory despite having abnormal amyloid beta (Aβ) levels.[40] Other rodent studies have shown associations between environmental enrichment and increased proliferation of neurons in the hippocampus and dentate gyrus, brain-derived neurotrophic factors, nerve growth factors, synaptic proteins, and expression of molecules associated with neuroplasticity and improved cognition.[40–43] In humans, cognitive engagement may boost the efficiency of neural networks, which enables an individual to maintain function despite being affected by

neuropathology, or to compensate for damaged networks, translating to better preservation of cognition.[39] This is supported by *post mortem* studies demonstrating that some older adults remain cognitively normal until death despite having abnormal Aβ levels at autopsy.[44] In vivo studies have also shown greater abnormal Aβ and tau levels and brain atrophy as well as reduced cerebral blood flow in participants with higher cognitive engagement despite having similar levels of cognitive performance to less engaged participants.[45–47] Given the potential benefit of engaging in cognitively stimulating activities on memory, engaging in a greater variety of cognitively stimulating activities during both work and leisure may be akin to greater environmental enrichment in animal models. This suggests that increased neural compensatory ability may be present in individuals with high cognitive engagement, although this needs to be formally tested in behavioral intervention studies.

There are several strengths and limitations associated with this study. An important strength is the large sample of cognitively normal middle-aged adults, the majority of which have a family history of dementia. While this renders the HBP sample not representative of the general population, it does provide important insights into relationships between engagement in a broad range of cognitively stimulating activities and cognition in at-risk middle-aged adults. Additional limitations include the cross-sectional and observational design of the current study. It is thus not possible to determine whether cognitive engagement leads to improved cognitive outcomes. It is also possible that individuals with better cognition are more likely to engage in a broader range of cognitively stimulating activities at work and during leisure time (i.e., reverse causality). As such, the effect of engaging in cognitively stimulating activities on improved cognitive function will need to be tested in future behavioral intervention studies. Further, while a comprehensive range of cognitive engagement measures were used in this study, all assessments relied on self-report, and were completed remotely via the HBP platform. The CBB was also used to measure cognition in this study as it has been adapted for remote assessment. The CBB has been validated extensively, although the breadth of cognitive functions assessed is restricted and not as comprehensive as standard neuropsychological assessments. Nonetheless, the results of this study accord with that of previous studies that have been conducted in person.[18,19] Another important consideration is that opportunity to participate in cognitively stimulating activities during work and leisure can often be associated with cultural and socioeconomic determinants.[8] As such, it will be important for future studies to examine the extent to which socioeconomic factors (e.g., race, socioeconomic neighborhood advantage) may add to or interact with cognitive engagement indices to impact cognition.

These limitations notwithstanding, our results indicate that engagement in a high variety of cognitively stimulating leisure activities, rather than frequency of engagement, is more strongly related to cognitive performance. This study also supports a multi-index approach to defining cognitive engagement and indicates potential for a beneficial effect of a greater variety of cognitive engagement indices on memory function in midlife. These findings provide insight into the contribution of cognitive engagement to cognition in middle-aged adults at risk of cognitive decline and dementia, inform models of CR, and have implications for behavioral interventions seeking to increase cognitive engagement to prevent age-related cognitive decline or reduce dementia risk.

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CONFLICTS OF INTEREST

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SUPPORTING INFORMATION

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