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Concurrent and Longitudinal Relationships Between Cognitive Activity, Cognitive Performance, and Brain Volume in Older Adult Women

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Objectives. We investigated (a) cross-sectional associations between cognitive activity, cognitive performance, and MRI measures and (b) longitudinal associations between cognitive activity and change in cognitive performance, using structural equation modeling (SEM).

Method. Women's Health Initiative Memory Study (WHIMS) Extension participants who continued annual neuropsychological assessments by telephone and completed a concurrent questionnaire of cognitive activities and MRI scans were included (mean age = 81.4 years; $N = 393$). Cognitive performance was measured by tests of attention, working memory, verbal fluency, executive function, and memory. Cognitive activity was measured by self-reported participation in a variety of cognitive activities (e.g., reading books, playing games, computer activities; $N = 11$ items) during the previous 12 months. MRI measures included gray and white matter normal and white matter lesion volumes.

Results. SEM demonstrated a significant association between cognitive activity and baseline cognitive performance but not change over 2–3 years. Gray and white matter was associated with cognitive performance but not cognitive activity. All effects remained significant after modeling covariates (age, education, depressive symptoms, WHIMS intervention assignment, and intracranial volume).

Conclusions. Cognitive activity benefits current cognitive performance but is not associated with change over 2–3 years. Cognitive activity and MRI volumes are independently associated with cognitive performance, suggesting distinct cognitive and brain reserve constructs.

Key Words: Cognition—Cognitive activity—Longitudinal change—MRI—SEM.

THE activity engagement hypothesis predicts that engagement in physical, social, and intellectual activities in older adulthood prevents the decline of cognitive abilities, and furthermore, that the action of engaging in activities precedes, and thus affects subsequent improvements in cognitive performance in older adulthood (Hultsch, Hertzog, Small, & Dixon, 1999; Salthouse, 2006). Underlying this hypothesis is the theory of cognitive reserve, which posits that engagement with the environment (including lifestyle activities, education, and lifelong occupation) can influence neural processing and synaptic organization by allowing neurological processes to become more efficient, adaptive, and plastic (Hultsch et al., 1999; Stern, 2002). Recent behavioral and imaging studies suggest that the human brain in old age maintains the capacity to change its structure according to learning and physical or cognitive exercise demands and that activity engagement might serve to stimulate cognitive reserve (Kramer, Bherer, Colcombe, Dong, & Greenough, 2004; Tranter & Koutstaal, 2008; Wilson, Segawa, Boyle, & Bennett, 2012).

Individuals who participate in cognitively stimulating activities are predicted to perform better on cognitive tests, experience less cognitive decline over time, and may have a reduced likelihood of developing neurodegenerative disorders such as Alzheimer's disease (Wang, Karp, Winblad, & Fratiglioni, 2002) or cognitive impairment (Carlson et al., 2009). For example, cross-sectional studies of older adults have found that reading the newspaper predicts stronger memory, fluid, and crystallized abilities (Newson & Kemps, 2006) and that activity-related benefits may consistently be found on perceptual speed (Craik et al., 2007). Similarly, longitudinal research has demonstrated that higher frequencies of participation in activities like reading and playing chess are related to more gradual 5-year declines in perceptual speed (Ghisletta, Bickel, & Lovden, 2006) and that increased cognitive stimulation may decrease annual rates

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of global cognitive decline by up to 20% (Wilson et al., 2003). Although cognitive stimulation at earlier ages is positively associated with current cognitive performance in older adults on measures of perceptual speed, visuospatial ability, and semantic memory (Wilson, Barnes, & Bennett, 2003), the association between current participation in cognitive activities and current cognitive ability may be even stronger. Controlling for current levels of cognitive stimulation has been found to account for the relationship between past activity and current cognition (Wilson et al., 2005), and this is taken as evidence that lifestyle changes can have a beneficial impact even when they are implemented during later years of life. However, longitudinal evidence is mixed, and some studies of normal aging older adults (e.g., Salthouse, 2006; Salthouse, Berish, & Miles, 2002) and older adults at risk for dementia (Woodard et al., 2012) have not found significant effects of activity engagement on cognitive function, perhaps due to choice of activity domain, lag time, or methodology.

Although engagement in cognitive activities has been associated with maintaining cognitive performance and reducing the likelihood of cognitive decline in older adults, neural mechanisms underlying protective effects of these lifestyle behaviors are largely unknown. Potential correlates of effects include morphometric changes such as simple alterations in cell size, growth or atrophy of neurons or glia, and changes in the intracortical axonal architecture (i.e., synaptogenesis). Cognitive stimulation might serve as a reserve mechanism in brain aging because macrostructural brain changes have been demonstrated in older and younger adults in response to cognitive training (May, 2011). Similar to younger adults, older adults show transient gray matter changes in the hippocampus induced by training on motor skill acquisition paradigms (Boyke, Driemeyer, Gaser, Buchel, & May, 2008) and differences in hippocampal gray matter in studies of expertise that compare musical experts to amateurs (Gaser & Schlaug, 2003). In addition, learning-induced structural changes may provide support that activity engagement promotes cognitive reserve. Associations between regional cerebral volumes and performance may be more temporary than previously thought, appearing and disappearing based on the aspect and stage of cognitive skill that is measured (Raz & Rodrigue, 2006), because the relationship between brain structure and performance dynamically changes in the process of skill acquisition. By extension, cognitive activity may mediate the relationship between brain structure and cognitive performance in older adults, in so far as it may enhance, prolong, or solidify temporary volumetric changes.

In the current paper, we investigated concurrent associations between self-reported cognitive activity, MRI measures (brain and lesion volume), and cognitive performance, in addition to a longitudinal model of cognitive activity and cognitive performance, using a linear structural equations approach. Structural equation modeling (SEM) is a form of covariance analysis that allows testing of a priori hypotheses about the causality among variables. SEM assesses the statistical relationships among latent variables (the structural model), which represent theoretical constructs that underlie measured observations (the measurement model). A linear structural equations approach may be used to address issues of reversed causation, confounding variables, and measurement error (Aartsen, Smits, Tilburg, Knipscheer, & Deeg, 2002; MacCallum & Austin, 2000). Latent change score analysis (LCS) is an extension of the SEM framework used to test the latent mean difference between measurement occasions (McArdle & Hamagami, 2001; Steyer, Eid, & Schwenkmezger, 1997). In LCS, change is modeled as a distinct latent construct represented by the difference between adjacent observations. The SEM framework was used to test (a) measurement models of cognitive activity, MRI volumes, and cognitive performance; (b) cross-sectional structural models of these relationships; and (c) configural invariance of longitudinal cognitive performance. LCS was then used to test a longitudinal structural model of baseline cognitive activity and change in cognitive performance. Using these latent variable approaches, we wanted to answer the following questions: (a) what is the bidirectional relationship between cognitive activity and cognitive performance?, (b) what is the relationship between cognitive activity and MRI volumes?, and (c) what is the effect of cognitive activity on latent change in cognitive performance? Because we hypothesized that engaging in cognitive activities has a positive influence on the brain, which in turn has beneficial effects on cognitive performance, we also tested a mediation model of the cognitive activity, MRI volumes, and cognitive performance relationship.

We predicted both a concurrent and a longitudinal beneficial association between cognitive activity and cognitive performance. Based on the literature, we expected education to account for some but not all of this relationship because education is also a measure of cognitive reserve (Christensen et al., 2007). Although we hypothesized, based on the literature, that MRI measures (in particular gray matter volume) would have a positive concurrent association with cognitive performance, we also wanted to explore the relationship between cognitive activity and MRI volumes, which is largely untested. Although studies of expertise demonstrate gray matter plasticity (Gaser & Schlaug, 2003), no studies that we know of examine latent variable relationships between cognitive activity and brain volume. Therefore, we also tested a cross-sectional mediation model (cognitive activity → MRI → cognitive performance), using the latent variable approach (e.g., Selig & Preacher, 2009).

Method

Participants

Seven thousand four hundred fifty-two women between the ages of 65 and 79 years who were participating in the Women's Health Initiative (WHI) Hormone Therapy (HT)

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clinical trials also agreed to participate in the Women's Health Initiative Memory Study (WHIMS), an ancillary study testing the impact of HT on incident dementia (Shumaker et al., 2003). In 2004, the WHI HT trials ended and consenting participants were entered into an observational study. In 2008, WHIMS participants were invited to continue annual cognitive assessments by phone in WHIMS-Epidemiology of Cognitive Health Outcomes (ECHO), and 2901 participants were enrolled. The mean (SD) age of participants at enrollment into WHIMS-ECHO was 81.2 (4.3) years. The WHIMS-MRI 1 and 2 are successive studies of women recruited from the ongoing WHIMS extension. Of the $N = 1403$ women who completed scans in WHIMS-MRI 1, 729 women also had eligible scans collected in WHIMS-MRI 2, which was completed a mean of 4.7 years after the first MRI. Those women who were cognitively normal at MRI 2 (e.g., did not meet study criteria for the classification of mild cognitive impairment or dementia), concurrently completed the cognitive activities measure and the WHIMS-ECHO cognitive battery, and had at least three additional cognitive battery assessments were included in all the analyses ($N = 393$).

Measures

Cognitive performance.—Participants in WHIMS-ECHO are annually administered a brief telephone battery of neurocognitive tests that include measures of global cognitive performance, as well as episodic memory, working memory, verbal fluency, attention, and executive functions (Rapp et al., 2012). It includes (a) the modified Telephone Interview for Cognitive Status (TICS; Knopman et al., 2010), a widely used measure of global cognitive functioning modeled after the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975); (b) the East Boston Memory Test a measure of verbal memory (Albert et al., 1991); (c) the Oral Trail-Making Test, a modified version of the original Trail-Making Test (Reitan, 1992), a measure of attention (Part A) and executive function (Part B); (d) Verbal Fluency-Animals, a measure of verbal fluency (Benton, 1968); and (e) the Digit Span Test a measure of working memory (Wechsler, 1981). Rapp et al. (2012) demonstrated that administering this battery by telephone produced scores similar to face-to-face administration.

Cognitive activity.—The Physical and Cognitive Activities Questionnaire (Wilson et al., 1999) was administered once at the time of the MRI 2 scan. Respondents reported the frequency of engagement (once a month or less = 0, 2–3 times a month = 1, 1–2 times per week = 2, 3–4 times per week = 3, 5–6 times per week = 4, and every day = 5) in a variety of physical activities and cognitive activities (reading the news, reading magazines, reading books, playing games, playing music, art activities, craft activities, group activities, social activities, computer activities, watching television: $N = 11$ items) over the prior 12 months. Only the cognitive activities items were included in these analyses.

MRI volumes.—WHIMS-MRI was designed to contrast neuroradiological outcomes post-trial among WHIMS participants who had been assigned to HT *versus* placebo. Scans were performed, on average, 3.0 years post-trial for the conjugated equine estrogen (CEE) + medroxy progesterone acetate (MPA) trial and 1.4 years post-trial for the CEE-Alone trial; average on-trial follow-up intervals were 4.0 years for CEE + MPA and 5.6 years for CEE-Alone. Exclusion criteria were presence of pacemakers, defibrillators, neurostimulators, prohibited medical implants, and foreign bodies (e.g., bullets, shrapnel, metal slivers) that would pose a hazard during the MRI procedure. Other exclusion criteria were shortness of breath and/or inability to lie flat, as well as conditions that can be exacerbated by stress (e.g., anxiety, panic disorders, claustrophobia, and uncontrolled high blood pressure or seizure disorders) severe enough to preclude an MRI.

Brain MRI scans were conducted at multiple sites and analyzed centrally at the Department of Radiology, University of Pennsylvania using a standardized protocol (Resnick et al., 2009). MRI scanning pulse sequences were performed in the following order: series 1 = 3-plane gradient echo localizer for positioning; series 2 = sagittal T1-weighted spin echo midslice image to demonstrate anatomical location of the anterior–posterior commissure plane (AC-PC) for slice angle and slice position; series 3 = oblique axial spin density/T2-weighted spin echo images from the vertex to skull base parallel to the AC-PC plane; series 4 = oblique axial fluid-attenuated inversion recovery T2-weighted spin echo images, matching slice positions in series 3; series 5 = oblique axial 3-dimensional T1-weighted gradient echo images from the vertex to skull base parallel to the AC-PC plane. To quantify regional brain volumes, the T1-weighted volumetric MRI scans were first preprocessed according to the standardized protocol (Goldszal et al., 1998): (a) alignment to the AC-PC orientation, (b) removal of extracranial material, and (c) segmentation of brain parenchyma into gray matter, white matter, and cerebrospinal fluid (CSF). Regional volumetric measurements of gray matter, white matter, and CSF were subsequently obtained via a validated, automated computer-based template warping method (Shen & Davatzikos, 2002) that summed the number of respective voxels falling within each anatomical region of interest.

Gray and white matter were classified as either "normal" or "ischemic," with areas of ischemia corresponding to what is generally referred to as "small-vessel ischemic disease" (ischemic white matter disease and lacunar infarctions). Ischemic white matter disease represents a non-necrotic, ischemic effect on myelin that is secondary to the effects of aging, hypertension, and other small vessel pathological processes of the brain (Pantoni & Garcia, 1997). Separate volumes (total and ischemic lesion) for gray and white matter were provided for 92 anatomical regions of interest in the cerebrum (Lao et al., 2008). Total volumes for each of these regions were calculated by summing across the smaller subregions. Intracranial volume (ICV) was estimated as the

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total cerebral hemispheric volumes, including ventricular CSF and the CSF within the sulcal spaces. Study analyses included gray and white matter normal volumes and white matter ischemic or lacunar volumes in all participants.

Gray matter volume included frontal, temporal, parietal, occipital, and limbic areas. White matter normal and lesion volumes included frontal, temporal, parietal, occipital, and corpus callosum. Areas were calculated by summing regional volumes in left and right hemispheres. For gray matter, frontal (inferior frontal gyrus, lateral frontal orbital gyrus, medial frontal gyrus, medial orbital frontal gyrus, middle frontal gyrus, precentral gyrus, and superior frontal gyrus), temporal (amygdala, entorhinal cortex, hippocampal formation, inferior temporal gyrus, lingual gyrus, middle temporal gyrus, parahippocampal gyrus, superior temporal gyrus, temporal pole, and uncus), parietal (angular gyrus, postcentral gyrus, precuneus, superior parietal lobule, and supramarginal gyrus), occipital (cuneus, inferior occipital gyrus, lateral occipitotemporal gyrus, medial occipitotemporal gyrus, middle occipital gyrus, occipital pole, and superior occipital gyrus), and limbic (frontal cingulate region, parietal cingulate region, insula, and perirhinal cortex) areas were used. For white matter, frontal (left and right frontal lobe), temporal (left and right temporal lobe), parietal (left and right parietal lobe), occipital (left and right occipital lobe), and corpus callosum areas were used.

Analyses

All analyses were conducted using M-Plus (Muthén & Muthén, 1998–2010). Following standard procedures in SEM, data were screened for missing values, outliers, nonlinearity, and non-normality (Vaughan & Giovanello, 2010). There were zero missing cells for cognitive activity and MRI data and near zero (<0.002%) missing cells for cognitive performance. To improve interpretation, directionality of the cognitive activity and cognitive performance measures was scaled so that larger numbers always indicated better performance, and variables with high kurtosis were transformed. For each model, five steps for SEM analyses were followed (specification, identification, estimation, testing, and modification). The measurement models for cognitive activity, cognitive performance, and MRI measures—gray matter volume (GMV), white matter volume (WMV), and white matter lesion volume (WMLV)—were specified first, followed by the structural models between the latent variables. The longitudinal model of cognitive performance met strong factorial invariance assumptions (factor structure, factor loadings, and intercepts of the factor indicators constant over time), which are a prerequisite for measuring change using an SEM approach. An LCS model was estimated to determine change across 3 time points (Time 1, Time 2, and Time 3), each a year apart. Time 1 was concurrent with cognitive activity and MRI 2 data collection.

First, the overall omnibus fit of the model (e.g., whether or not the sample variance-covariance matrix S is similar to the population variance-covariance matrix) was tested. The overall omnibus fit of the model was evaluated by the nonsignificance of the χ^2 test. A nonstatistically significant χ^2 value indicates similarity between the sample covariance matrix (S) and the model-implied covariance matrix (Σ). In addition, the root mean square error of approximation (RMSEA) and the standardized root mean square residual (SRMR) were evaluated for overall fit. The RMSEA, which is widely reported, estimates the amount of error of approximation (the lack of fit between the hypothesized model and the population covariance matrix) per model degree of freedom, taking sample size into account. A value of less than or equal to 0.05 indicates a good fit. The SRMR is the standardized difference between observed and predicted covariances. Low SRMR values indicate that the residual matrix of S (the sample covariance matrix) used to estimate (the sample-implied covariance matrix) is near zero for a good model. A value less than 0.08 is considered a good fit. The second criteria of model fit were the statistical significance of individual parameter estimates. The significance of the individual parameters (path estimates) was evaluated for their meaningfulness to the model (t values significant at the 0.05 level).

Sample size requirements for SEM depend upon several factors including number of indicators per latent variable, the strength of association between the indicators and the latent variables, degree of multivariate normality, missing data, and reliability and variance-covariance of variables. Recommendations are for the number of indicators (p) per factor (p/f) to be at least three when sample sizes are at a minimum (N = 100) and that the model be identified (e.g., all of the parameters can be uniquely determined because there is enough information in the model). Following these recommendations, sample sizes of 200–400 are found to be adequate for similarly specified cross-sectional and longitudinal analyses (Jackson, 2001).

Results

Participant demographic characteristics are included in Table 1. Descriptive statistics for all measures used in the confirmatory factor analysis models are included in Supplementary data, Appendix A, Table 1. The standard approach used throughout the paper for model building was to first include all uniquely measured variables in the model, then exclude variables with nonsignificant factor loadings, and follow theory as well as output modification indices to improve fit. χ^2 difference tests were used to evaluate the fit of nested models, and where appropriate, are reported below. First, we present the cross-sectional data, and then we present the longitudinal data.

Behavioral Measurement Models

Cognitive activity.—Six items were included in the final measurement model (reading magazines, reading books, craft

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Table 1. Participant Demographic Characteristics ($N = 393$)

Age (years) (mean, SD)	81.21 (4.26)
Years of education (frequency, %)	
<High school	3 (.01)
High school graduate	11 (.03)
Some college	89 (22.65)
College graduate	48 (12.21)
Some graduate school	102 (25.95)
Masters degree	50 (12.72)
PhD/MD/JD	41 (10.43)
Not reported/did not know	46 (11.70)
Missing	3 (.01)
Geriatric Depression Scale (GDS) score (mean, SD)	1.19 (1.66)
HT arm (frequency, %)	
HT	188 (47.84)
Placebo	205 (52.16)

Notes. HT = Hormone Therapy; *SD* = standard deviation.

activities, group activities, social activities, and television; χ^2 difference test for final *versus* all 11 items; $p = <.0001$). The fit indices for the one-factor model are reported here and in Supplementary data, Appendix B, Table 1. A one-factor model fit the data well and produced a nonsignificant χ^2 ($\chi^2 = 7.21$, $df = 8$, $p = .51$, RMSEA = 0.00 [90% confidence interval {CI} = 0.00–0.06], CFI = 1.0, SRMR = 0.02), and all of the factor loadings were significant (all $p \leq .01$).

Cognitive performance.— Four measured variables—global cognition (TICS), verbal fluency (VFA), task-switching (TRAILS-B), working memory (DIGITS-Backwards)—were included in the final measurement model for cognitive performance (χ^2 difference test for final *vs* all 7 items; $p < .0001$). The fit indices for the one-factor model are reported here and in Supplementary data, Appendix B, Table 2. A one-factor model fit the data well and produced a nonsignificant χ^2 ($\chi^2 = 1.62$, $df = 2$, $p = .44$, RMSEA = 0.00 [90% CI = 0.00–0.09], CFI = 1.0, SRMR = 0.01), and all of the factor loadings were significant (all $p < .001$).

MRI Measurement Models

Gray matter normal volumes.—The global model for GMV included frontal, temporal, parietal, occipital, and limbic areas and ICV as a covariate. The fit indices for the one-factor global model are reported here and in Supplementary data, Appendix B, Table 3. This model produced a nonsignificant χ^2 ($\chi^2 = 1.10$, $df = 3$, $p = .79$, RMSEA = 0.00 [90% CI = 0.00–0.05], CFI = 1.0, SRMR = 0.01), and all of the factor loadings were significant (all $p < .001$). ICV was a significant covariate ($p < .001$).

White matter normal volumes.—The global model for ICV included frontal, temporal, parietal, occipital, and corpus callosum areas and ICV as a covariate. The fit indices for the one-factor global model are reported here and in Supplementary data, Appendix B, Table 4. This model produced a nonsignificant χ^2 ($\chi^2 = 7.49$, $df = 3$, $p = .06$, RMSEA = 0.05 [90% CI = 0.00–0.11], CFI = 1.0, SRMR = 0.01), and all of the factor loadings were significant (all $p < .001$). ICV was a significant covariate ($p < .001$).

White matter lesion volumes.—The global model for WMLV included frontal, temporal, parietal, occipital, and corpus callosum areas and ICV as a covariate. The fit indices for the one-factor global model are reported here and in Supplementary data, Appendix B, Table 5. This model produced a nonsignificant χ^2 ($\chi^2 = 12.24$, $df = 6$, $p = .06$, RMSEA = 0.05 [90% CI = 0.00–0.09], CFI = 1.0, SRMR=.02), and all of the factor loadings were significant (all $p < .001$). ICV was a significant covariate ($p < .001$).

Behavioral Structural Linear Regression Models

What is the bidirectional relationship between cognitive activity and cognitive performance?.—Cognitive activity and cognitive performance. The fit indices for the structural model of cognitive activity and cognitive performance are reported in Table 2 and shown in Figure 1. The bidirectional effect of cognitive activity on cognitive performance was tested in a latent regression model. As hypothesized, we detected a positive and significant effect of cognitive activity on cognitive performance that was maintained when we added covariates (age, education, HT, Geriatric Depression Scale score [GDS]; 0.25, $p = .01$; $\chi^2 = 65.10$, $df = 50$, $p = .07$; RMSEA = 0.03 [90% CI = 0.00–0.05], CFI = 0.94, SRMR = 0.04). Significant covariate relationships included the effects of education on cognitive activity (0.35, $p < .001$) and cognitive performance (0.16, $p = .03$) and the effect of GDS on cognitive activity (–0.24, $p = .001$). The reverse effect of cognitive performance on cognitive activity was nonsignificant (0.16, $p > .10$). More education was associated with higher frequencies of cognitive activity and better cognitive scores. Lower depression scores were associated with higher frequencies of cognitive activity. Not controlling for education in the model resulted in a stronger relationship between cognitive activity and cognitive performance (0.29, $p = .002$) but a similar fit (χ^2 diff. test > 0.05), demonstrating that education accounts for only a small amount of the variance between the constructs.

MRI Structural Linear Regression Models

What is the relationship between cognitive activity and MRI volumes?.—Cognitive activity and MRI measures. Cross-sectional models of cognitive activity and MRI measures were tested using ICV as a covariate. There was no significant effect of cognitive activity on any MRI measures (all $p > .10$; tables not shown): GMV: (0.02, $p = .73$, $\chi^2 = 54.26$, $df = 46$, $p = .19$, RMSEA = 0.02 [90% CI = 0.00–0.04], CFI = 1.0,

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Table 2. Fit Indices and Factor Loadings for the Structural Model of Cognitive Activity and Cognitive Performance Including Covariates ($N = 393$)

Model	*df*	χ^2	RMSEA	SRMR	CFI
1. One-factor Cognitive activity/one-factor Cognitive performance	50	65.10, $p = .07$	0.03 (90% CI = 0.00–0.05)	0.04	0.94
Factor and item	Factor loading (*p* value)	Factor and item			Factor loading (*p* value)
Cognitive activity → read magazines	0.28 (.000)	Cognitive performance → TICS			0.73 (.000)
Cognitive activity → read books	0.46 (.000)	Cognitive performance→ VFA			0.48 (.000)
Cognitive activity → craft	0.19 (.006)	Cognitive performance → TRAILS-B			0.32 (.000)
Cognitive activity → group	0.27 (.000)	Cognitive performance → DIGITS-B			0.45 (.000)
Cognitive activity → social	0.22 (.003)				
Cognitive activity → television	0.50 (.000)				
Structural model					
Cognitive activity → Cognitive performance	0.25 (.014)				
Item correlations					
Social ↔ group	0.18 (.000)				
Covariates					
Education → Cognitive activity	0.35 (.000)	Education → Cognitive performance			0.16 (.030)
GDS → Cognitive activity	−0.24 (.001)				

Notes. CFI = comparative fit index; CI = confidence interval; DIGITS-B = Digits Backward score; GDS = Geriatric Depression Scale; RMSEA = root mean square error of approximation; SRMR = standardized mean square residual; TICS = Telephone Interview for Cognitive Status total score; TRAILS-B = Trails Part B time; VFA = Verbal Fluency Animals word count.

SRMR = 0.03); WMV: (0.01, $p = .91$, $\chi^2 = 36.98$, $df = 46$, $p = .83$, RMSEA = 0.00 [90% CI = 0.00–0.02], CFI = 1.0, SRMR = 0.03); WMLV: (−0.05, $p = .55$, $\chi^2 = 59.19$, $df = 49$, $p = .15$, RMSEA = 0.03 [90% CI = 0.00–0.04], CFI = 0.99, SRMR = 0.03. Because there was no association between cognitive activity and MRI measures, assumptions were not met for testing the proposed mediation model (e.g., cognitive activity → GMV → cognitive performance).

MRI measures and cognitive performance.—Cross-sectional structural models of MRI measures (GMV, WMV, and WMLV) and cognitive performance were tested using ICV as a covariate (see Supplementary data, Appendix C, Tables 1–3). There was a significant effect of GMV on cognitive performance (0.29, $p = <.001$, $\chi^2 = 38.01$, $df = 28$, $p = .10$, RMSEA = 0.03 [90% CI = 0.00–0.05], CFI = 1.0, SRMR = 0.04); WMV on cognitive performance (0.18, $p = .01$, $\chi^2 = 32.53$, $df = 27$, $p = .21$, RMSEA = 0.02 [90% CI = 0.00–0.05], CFI = 1.0, SRMR = 0.02); and a marginal effect of WMLV on cognitive performance (−0.13, $p = .06$) $p < .001$: ($\chi^2 = 50.45$, $df = 31$, $p = .02$, RMSEA = 0.04 [90% CI = 0.02–0.06], CFI = 0.99, SRMR = 0.05). Cognitive performance is significantly and positively associated with GMV and WMV and marginally negatively associated with WMLV.

Cognitive Activity and Longitudinal Cognitive Performance

What is the effect of cognitive activity on latent change in cognitive performance?.—Longitudinal cognitive performance. The fit indices for the longitudinal structural model are reported in Table 3. A minimum level of measurement invariance (usually strong factorial invariance) is a prerequisite to evaluating longitudinal change in latent variables in a meaningful way (Widaman & Reise, 1997). Configural invariance requires only the factor structure (the number of patterns and the loading pattern) to be constant across time. Weak factorial invariance requires the factor loadings to be the same for all indicators over time. In addition, strong factorial invariance requires the intercepts of the indicators to be constant across time. A set of models was generated in order to fulfill these conditions: configural factorial invariance ($\chi^2 = 22.97$, $df = 15$, $p = .08$, RMSEA = 0.04 [90% CI = 0.00–0.07], CFI = 0.99, SRMR = 0.03), weak factorial invariance ($\chi^2 = 26.38$, $df = 18$, $p = .09$, RMSEA = 0.03 [90% CI = 0.00–0.06], CFI = 0.97, SRMR = 0.04), and strong factorial invariance ($\chi^2 = 30.47$, $df = 22$, $p = .11$, RMSEA = 0.03 [90% CI = 0.00–0.06], CFI = 0.99, SRMR = 0.04). A model of strong factorial invariance with autocorrelated errors fit the data well and satisfies this condition.

Change in cognitive performance.—We tested an LCS model (McArdle, 2009) of the latent mean difference between cognitive performance at adjacent time points. The latent mean difference between Times 1 and 2 was in the expected direction (−0.16) but not significantly different from zero ($p = .47$, $\alpha = 0.05$ level for a two-tailed test). As expected, the fit was equal to the model of strong factorial invariance ($\chi^2 = 30.47$, $df = 22$, $p = .11$, RMSEA = .03 [90% CI = 0.00–0.06], CFI = 0.99, SRMR = 0.04). The latent mean difference between cognitive performance at Times 2 and 3 was significant (−0.53, $p = .02$); overall model fit for strong factorial invariance for all 3 time points ($\chi^2 = 86.66$, $df = 65$, $p = .04$, RMSEA = 0.03 [90% CI = 0.01–0.04], CFI = 0.99, SRMR = 0.05).

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Table 3. Fit Indices and Factor Loadings for the Longitudinal Structural Model of Cognitively Activity and Change in Cognitive Performance Including Covariates (N = 393)

Model	*df*	χ^2	RMSEA	SRMR	CFI
1. Cognitive activity/Cognitive performance (baseline and time 3)/change in Cognitive performance	87	108.74, p = .06	0.03 (90% CI = 0.00–0.04)	0.04	0.98
Factor and item	Factor loading (p value)	Factor and item (time 1)			Factor loading (p value)
Cognitive activity → read magazines	0.28 (.000)	Cognitive performance → TICS			0.79 (.000)
Cognitive activity → read books	0.47 (.000)	Cognitive performance → VFA			0.46 (.000)
Cognitive activity → craft	0.19 (.008)	Cognitive performance → TRAILS-B			0.29 (.000)
Cognitive activity → group	0.27 (.000)	Cognitive performance → DIGITS-B			0.37 (.000)
Cognitive activity → social	0.22 (.002)	Factor and item (time 2)			
Cognitive activity → television	0.50 (.000)	Cognitive performance → TICS			0.71 (.000)
		Cognitive performance → VFA			0.43 (.000)
		Cognitive performance → TRAILS-B			0.32 (.000)
		Cognitive performance → DIGITS-B			0.37 (.000)
		Factor and item (Time 3)			
		Cognitive performance → TICS3			0.83 (.000)
		Cognitive performance → VFA3			0.51 (.000)
		Cognitive performance → DIGITS-B3			0.34 (.000)
		Cognitive performance → TRAILS-B3			0.47 (.000)
Structural model					
Cognitive activity → T1 Cognitive performance	0.21 (.03)				
Cognitive activity → T2-T1 Cognitive performance	−0.24 (.289)				
Cognitive activity → T3-T2 Cognitive performance	−0.02 (.945)				
Covariates					
Education → Cognitive activity	0.35 (.000)	Education → Cognitive performance (time 1)			0.14 (.000)
		Depression → Cognitive activity			−0.23 (.002)

Notes. CFI = comparative fit index; CI = confidence interval; DIGITS-B = Digits Backward score; GDS = Geriatric Depression Scale score; RMSEA = root mean square error of approximation; SMSR = standardized mean square residual; TICS = Telephone Interview for Cognitive Status total score; TRAILS-B = Trails Part B time; VFA = Verbal Fluency Animals word count.

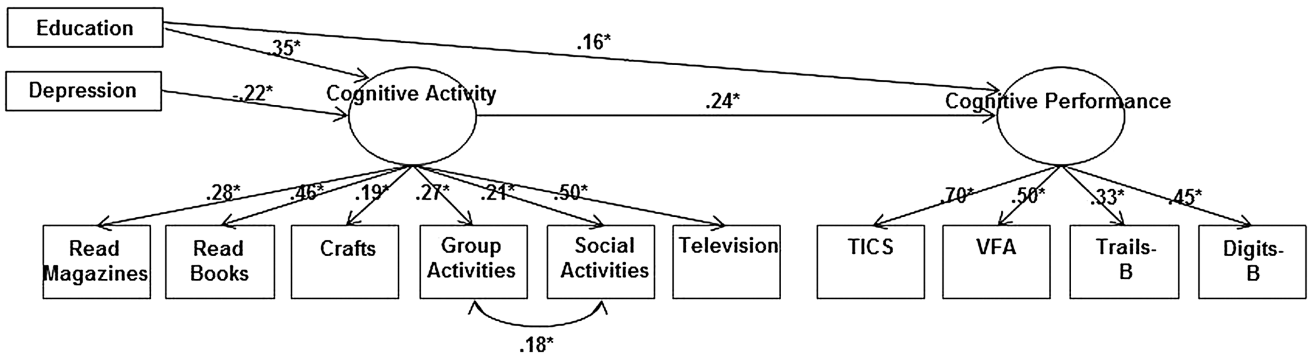

Figure 1. Structural model of cognitive activity and cognitive performance with significant covariates (*significant at α < 0.01). TICS = Telephone Interview for Cognitive Status total score; VFA = Verbal Fluency Animals word count; TRAILS-B = Trails Part B time; DIGITS-B = Digits Backward score; GDS = Geriatric Depression Scale score.

Cognitive activity and change in cognitive performance.—Last, we tested the effect of cognitive activity on latent change in cognitive performance (see Table 3), including covariates. The effect of cognitive activity on change in cognitive performance from T1 to T2 was small and nonsignificant (−0.24, p =.29) as was the effect of cognitive activity on change in cognitive performance from T2 to T3 (−0.02, p =.95); overall model fit for T1, T2, and T3 (χ^2 = 202.52, df = 165, p = .03, RMSEA = .02 [90% CI = 0.01–0.04], CFI = 0.98, SRMR = 0.04). The relationship between education and cognition (0.14, p = .04), education and cognitive activity (0.35, p = .000), and depression and cognitive activity (−0.23, p = .002) was similar to the cross-sectional structural model.

Discussion

We found that increased cognitive activity is significantly associated with better cognitive performance in older women. Engaging in cognitively stimulating activities is

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important to current cognitive performance but seems to have little effect on change in cognitive performance across 2–3 years. Our findings are consistent with other studies that show concurrent positive relationships between cognitive activity engagement and cognitive performance (Bielak, Anstey, Christensen, & Windsor, 2012; Bielak, Hughes, Small, & Dixon, 2007; Mitchell et al., 2012; Wilson, Barnes, & Bennett, 2003; Wilson et al., 2005) and add to a mixed but growing body of literature on how cognitive activity influences longitudinal cognitive performance.

Although few studies examine longitudinal relationships between cognitive activity and cognitive performance, the results of our longitudinal analyses did not demonstrate a direct effect of cognitive activity on change in cognitive performance across 2–3 years. This is in-line with what appears to be stronger evidence for 1–2 year versus >5 years longitudinal relationships between cognitive activity and cognitive performance (Ghisletta et al., 2006; Salthouse et al., 2002; 2006). Significant associations have not been found between cognitive activity and cognitive performance over longer intervals (6 years: Aartsen et al., 2002; 7 years: Mackinnon, Christensen, Hofer, Korten, & Jorm, 2003), although it has been suggested that current cognitive activity may positively influence future cognitive activity, which in turn is expected to have positive concurrent benefits on future cognition (Bielak et al., 2007). In addition, Mitchell et al. (2012) analyzed how baseline and change in cognitive activity predicted longitudinal cognitive outcomes across 4 longitudinal studies of aging and found evidence that change in cognitive activity from one's previous level has a transitory association with concurrent cognitive performance.

Another question involves the direction of the effects, and although the unidirectional nature of the activity engagement and cognition relationship has not been irrefutably proven in studies of normal cognitive aging which is the focus of this paper, (e.g., see Schooler & Mulatu, 2001), it has been demonstrated in several studies (Wilson et al., 2012; Ghisletta et al., 2006; Tranter & Koutstaal, 2008). In agreement with these results, all of our latent variable linear models showed a significant directional relationship between cognitive activity and cognitive performance, but not the opposite pattern, in support of the activity engagement hypothesis.

Significant positive relationships have been noted between cognitively stimulating activity and cognitive performance in highly educated participants (Bielak et al., 2007; Hultsch et al., 1999; Wilson et al., 2005), whereas some (cross-sectional) studies have found that education in particular accounts for this relationship (e.g., Aartsen, Smits, Tilburg, Knipscheer, & Deeg, 2002). We examined the effects of covariates on the latent variables and found that including education as a covariate in our model removed a small amount of the variance in the relationship between cognitive activity and cognitive performance. This relationship remained significant, demonstrating that cognitive activity is a unique measure of reserve. More education was associated with higher cognitive test scores and higher frequencies of cognitive activity engagement, as might be expected if education contributes to cognitive reserve (Kramer et al., 2004; Stern, 2002). Although we found no influence of age on any of the latent variables in the models, a novel finding included significant effects of depressive symptoms on cognitive activity (but not on cognitive performance), which might suggest that cognitive stimulation could moderate the relationship between depressive symptoms and cognitive performance if this were examined in a clinical cohort.

When we examined the relationship between MRI measures and cognitive performance, both GMV and WMV positively influenced cognitive performance, as expected, although GMV demonstrated a stronger association. White matter lesion volumes showed a marginal negative relationship with cognitive performance, and we have previously reported significant relationships in a larger cohort of WHIMS women. Cerebral white matter hyperintensities in normal aging have been associated with decreased performance on tasks of processing speed, memory, executive function, and global cognition (Raz & Rodrigue, 2006), and our findings were in the expected direction.

We also hypothesized that engaging in cognitively stimulating activities might enhance brain volume, which in turn might mediate the relationship between cognitive activity and cognitive performance (e.g., cognitive activity → MRI measures → cognitive performance). Although our structural models showed direct effects of MRI measures (GMV, WMV, WMLV) on cognitive performance as discussed above, there was no relationship between cognitive activity and MRI measures, which precluded testing a mediation model. This finding parallels one study in which there was no mediation of the relationship between brain atrophy and cognitive change by education as a measure of cognitive reserve, although there was a significant effect of education level on cognitive change (Christensen et al., 2007). These findings emphasize the distinctiveness of the brain (MRI volumes) *versus* cognitive (cognitive activity) reserve constructs, which are often used interchangeably.

Cross-sectional analyses of learning and experience comparing extensively practiced skill sets with sex and age-matched controls have documented regional increases in the gray and white matter volumes of professional musicians (Bengtsson et al., 2005; Gaser & Schlaug, 2003), expert players of games such as chess and baduk (Ericsson & Delaney, 1999; Lee et al., 2010), and those with navigational expertise (Maguire et al., 2000). Although recent longitudinal experimental studies of training of visuomotor tasks demonstrating transient regional gray matter increases provide further support for structural brain plasticity in aging (Boyke et al., 2008), it is important to note that the majority of these studies examined specific skills that have an intentional, not merely incidental, memory or learning component (as might be assumed in reading, watching television,

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craft activities, etc.). Therefore, it may be that the complexity, novelty, and modality of the task (e.g., spatial or abstract) have a particular role in influencing brain plasticity over and above the frequency of the task, which is typically measured in studies of activity engagement. In any case, the results we report here, along with experimental studies that manipulate cognitive engagement, highlight the importance of anchoring interpretations of gray matter or white matter volume changes in the context of behavioral outcomes or processes.

Methodological strengths of this study include the use of latent variables to remove unwanted error variance, the inclusion of several key cognitive domains to measure cognitive performance longitudinally, and concurrent collection of cognitive activity and MRI data. In addition, the modeling approach allowed examining the effect of covariates of interest on the latent constructs. To our knowledge, this study is unique in examining cognitive activity and MRI measures collected concurrently in normal aging. The cohort also has several strengths including that older women may engage in a more diverse repertoire of activities associated with roles (e.g., caregiving and social) over a longer life span and, therefore, may experience greater activity variability throughout their life time. Limitations include the lack of a corresponding longitudinal cognitive activity measure, which precluded the examination of how change in cognitive activity might be associated with change in cognitive performance. Additional limitations include the reliance on self-reported cognitive activity, which may make the measure vulnerable to social desirability bias and oversight, as well as the possible limited generalizability of our findings to men and younger adults. The measure does not disentangle the effect of engaging in intellectual activities from a possible socialization effect found in social activities (e.g., it does not distinguish between cognitive activities performed alone or with others); however, group activities and social activities loaded significantly on the cognitive activities construct. In addition, a high percentage of WHIMS participants have a college education, which may also limit the generalizability of our findings (see Rapp et al., 2013 for a related discussion). Although the construct validity of the measure of cognitive activities has been demonstrated (Wilson et al., 1999), it is a challenge to this field in general to capture the full range of cognitive activities, as well as individual differences in activity engagement in an aging cohort. Future studies may benefit from using real-time approaches to data collection of cognitive activity that better capture the variability of daily human activity.

In conclusion, in a large cohort of older adult women, we found that engaging in higher frequencies of cognitive activities had a significant and positive direct effect on concurrent cognitive performance but little effect on cognitive change after 3 years. The relationship between cognitive activity and cognitive performance is not fully accounted for by education, although more educated women engaged in a higher frequency of cognitive activities and had better cognitive function. In addition, women who performed more cognitive activities self-reported less depressive symptomatology. Although MRI measures of normal brain volumes, in particular GMV, were positively associated with cognitive performance, they demonstrated little overlap with cognitive activity, which highlights the distinctness of the brain and cognitive reserve constructs. Further studies should directly examine how engaging in cognitively stimulating activities influences brain structure and function to try and explain the positive relationship between cognitive activity and cognitive performance. Better understanding the longitudinal relationships between cognitive activity and cognitive performance may also lead to interventions that enhance activity participation in older adults and thus promote healthy cognitive aging.

Supplementary Material

Supplementary material can be found at: http://psychsocgerontology.oxfordjournals.org/

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