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Understanding Individual Differences in Executive Function in Older Adults

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by

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Under the Direction of Vonetta M. Dotson, PhD

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ABSTRACT

Aging is associated with declines in executive function leading to difficulties performing everyday tasks. To combat aging declines, many studies investigate varying rehabilitation interventions. Although improvement on task performance has been noted, improvement on other tasks remains inconsistent. The current study sought to replicate Miyake and Friedman's (2012) Unity and Diversity (U&D) model including physical activity as a predictor across a sample of older adults. Two models were computed to estimate three latent variables: Common EF, Updating, and Shifting. Model 1 replicated Miyake and Friedman's bifactor model. Model 2 was a structural model that included physical activity as a separate independent variable. Extracted factor scores were used to predict within network connectivity for several resting state networks. We didn't find evidence for a Shifting factor or a relationship between EF factors, physical activity, and within-network connectivity. Future analyses will continue to examine this model and modified versions in older adults.

INDEX WORDS: Executive function, older adults, physical activity, resting-state networks, within-network connectivity, factor analysis

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1 INTRODUCTION

By the year 2060, the number of adults over the age of 65 in the US is expected to double to over 90 million people (National Center for Chronic Disease Prevention and Health Promotion, 2022). Advances in medicine and technology have increased life expectancies of older adults, which unfortunately has also resulted in increased susceptibility to neurological diseases. One-third of the population in the US aged 85 years and older have dementia of Alzheimer's type (Hale et al., 2020). Research has also shown that 11.2% of adults older than 45 years reported subjective cognitive decline (Taylor et al., 2018). These findings are concerning and are already resulting in financial burdens placed on families (Wolff et al., 2016) and the public health system (Kelley et al., 2015). As the number of older adults increases in the population, so does the importance of developing interventions to combat these declines.

Executive functions (EFs), higher-order cognitive processes that regulate lower-level processes to guide goal-directed behavior (Miyake & Friedman, 2012), are particularly affected by aging declines, which is alarming due to the association EFs have with daily functioning. Performance on EF measurements predict older adults' ability to carry out important activities like decision-making, medication management, and driving (Nguyen et al., 2019). Cognitive scientists and interventionists will need to devise cost-effective approaches to improve daily functioning of these individuals. Although most studies find that older adults perform worse on EF tasks compared to younger adults, the mechanisms of EF decline in older adults are not fully understood (Maldonado et al., 2020). Work in resting state brain imaging shows that aging may alter patterns of connectivity, which may account for these behavioral declines (Siman-Tov et al., 2017). Comparisons of otherwise healthy older adults who engage in regular physical exercise or cognitive training against a control cohort reveal group differences in both EF test scores and brain connectivity (Voss et al., 2010). However, we know of no cognitive models that incorporate the effects of specific lifestyle differences as a mitigating factor of these changes. The goal of the present study was to develop a model of aging and changes in EF that incorporates an individual's lifestyle choice, specifically regular physical exercise, which is associated with prophylaxis from neurocognitive declines (Ahlskog et al., 2011). The current research proposal sought to provide evidence of aging-related differences in EF as previously modeled by Miyake & Friedman (2012) in light of assessment of physical activity. Additionally, this project examined functional connectivity as assessed by resting state fMRI to identify potential neurophysiological correlates of this behavioral model.

1.1 Aging and Functional Connectivity

Aging related declines are not only observable in behavioral performance but are also associated with structural and functional changes in the brain. Although alterations in brain structure are important, perhaps ultimately so, the current study focused on functional alterations. Examining functional connectivity (FC) provides insight into how brain regions and networks interact. FC denotes the statistical dependency (correlation, coherence) between certain regions' time courses (Betzel et al., 2014). One method to better understand the impact of functional brain changes on cognitive decline in older adults is through analysis of resting state functional magnetic resonance imaging (rsfMRI). Using rsfMRI to examine FC has led to the identification of resting state networks (RSNs), which give insight to how the brain is organized (Honey et al., 2009). A few of the commonly identified networks include default mode, dorsal attention, ventral attention, frontoparietal, salience, visual, and somato-motor. Aging-related changes in these RSNs offer insight of individual differences in behavioral measures even prior to the presentation of clinical symptomatology (Sala-Llonch, 2015).

Recent work in resting state brain imaging shows that aging may alter patterns of connectivity. For example, Betzel et al. (2014) examined age-related changes in FC and observed that RSNs associated with cognitive functions become less unified with age. FC tended to decrease within RSNs and increased between RSNs. Tsvetanov et al. (2016) found that similar patterns explained significant variability across multiple cognitive domains. Some studies have reported that higher-order RSNs are specifically vulnerable to aging declines. For example, increased within connectivity in the salience network was associated with better fluid cognition (Hausman et al., 2020) and decreased between connectivity in associative networks predicted worse memory performance (Chan et al., 2014). Several models based off imaging data have been proposed to explain the etiology of these FC changes: compensation, scaffolding, dedifferentiation etc. (Reuter-Lorenz & Cappell, 2008). Although an in-depth overview of these models is beyond the scope of the current study, it is useful to keep these models in mind when interpreting the brain-behavior results.

1.2 Rehabilitation Interventions

To combat these behavioral and neuronal age-related declines, many older adults participate in rehabilitation interventions. These interventions include a variety of methods that focus on either cognitive training, physical activity, or a combination of both. Cognitive interventions focus on compensating for cognitive deficits by developing strategies (strategy-based training) or they can restore deficits by repeated task practice that targets specific cognitive domains (process-based training) (Nguyen et al., 2019). Physical activity interventions involve a variety of activities like walking, cycling, or stretching, but most studies have focused on the effects of aerobic exercise. This is because aerobic exercise has been shown to have neuroprotective benefits against aging effects (Aghjayan et al., 2022). There are numerous cellular and molecular mechanisms underlying these improvements. Exercise improves cardiovascular health leading to increases in cerebral blood flow, which is important for providing nutrients to the brain (Mahalakshmi et al., 2019). These benefits of aerobic exercise are also associated with changes in older adults' FC (Won et al., 2021). Studies have found that engagement in aerobic exercise increases the functional coherence of several networks (Stillman et al., 2019). FC of networks gives insight to how regions communicate and how information is processed in the brain (Bamidis et al., 2014). If exercise is truly able to improve these processes in older adults, then consistent behavioral improvements would also be expected. Unfortunately, this is not always the case.

In general, reviews examining cognitive training in older adults have found improvements in task performance, but rarely do these improvements, involving specific executive processes, transfer to the performance of other tasks (Lampit, Hallock & Valenzuela, 2014). There are a few factors that could contribute to these inconsistent results. For instance, type of intervention may predict gains in improvements. A meta-analytic review examined the effects of working memory training (WMT) on older adults and found significant near-transfer effects, but not far-transfer effects (Teixeira-Santos et al., 2019). Near transfer effects are improvements on tasks/skills that involve the same mechanisms/domains and far transfer effects are improvements on tasks/skills that do not involve the same mechanisms/domains (Barnett & Ceci, 2002). This could be because WMT is a type of process-based training where individuals are training specifically on that one EF or task.

Lampit, Hallock and Valenzuela (2014) reviewed the efficacy of computerized cognitive training (CCT) as it relates to cognitive outcomes. It was found that CCT has small improvements in nonverbal memory, WM, and processing speed, but no improvements in attention or EF. Alternatively, the dosage of training should be taken into consideration. Both brief sessions, once a week or sessions lasting less than 30 minutes, and sessions that occur more than three times a week have been seen as inefficient (Lampit, Hallock & Valenzuela, 2014). It can take weeks or months for individuals to show overt behavioral gains. It is likely that individuals have training-related improvements, but they are not yet reflected behaviorally. The issue could be related to which tasks are used to measure training improvements and transfer effects or perhaps the issue is related to how the deficit was defined to begin with.

1.3 Defining Executive Functions

Executive functions can be described as higher-order cognitive processes that regulate lower-level processes to guide goal directed behavior (Miyake & Friedman, 2012). Although there is now a relative consensus on how to define EF, there are conflicting views on how EFs are organized and modeled (Baggetta & Alexander, 2016). Some early models like Spearman's *g* and Baddeley's model of Working Memory describe EF as a unitary construct (Duncan et al., 1996; Baddeley, 1992). Support for these unitary theories comes from frontal lobe lesion studies where damage to the frontal lobe leads to difficulties on a variety of cognitive tasks (Miyake et al., 2000). However, the difficulty of measuring EFs creates a challenge for this interpretation. A score from an individual task measuring EF, Stroop for example, will likely capture variance that is attributable to non-EF processes (Miyake & Friedman, 2012). In contrast, using multiple tasks to define EF is may has its own caveats as tasks usually show low intercorrelations (often referred to as task impurity). Approaches like factor analysis are employed to attempt to resolve this task impurity problem. Factor analysis can evaluate variance structure in the dependent measures of EF tests and affords modeling of constructs (called latent variables or factors) that best fit the data. In more basic terms, factor analysis can test how well measured variables represent latent variables/constructs.

In 2000, Miyake et al. used confirmatory factor analysis (CFA) to develop a unity and diversity framework that defines EF as having common underlying and fully separable abilities. CFA is a type of factor analysis where the number of factors and which measured variables are related to each factor are specified at the start of the analysis. The resulting model (Figure 1a) focused on three EFs and showed how the EFs were correlated with each other (unity), but the correlations were less than 1.0 (diversity). Although this model was replicated in numerous samples, it was later updated to further describe the unity and diversity framework. Friedman et al. (2008) found that adding a general factor (Common EF), comprised of all the measured variables, correlated perfectly with the inhibition factor, indicating there was no unique variance left for inhibition to account for. The resulting bi-factor model (Figure 1b) was made up of three latent variables/factors: Common EF, Updating-specific, and Shifting-specific. The Common EF factor is the general factor onto which all items load and is described as one's ability to maintain goals and use those goals to guide ongoing processing (Friedman & Miyake, 2017). The Updating and Shifting factors are orthogonal (uncorrelated) onto which specific items load. Updating, similar to working memory (WM) updating, represents the gating of new information and retrieval of old information. Shifting represents flexibility and one's ability to switch between different task-sets or mental states.

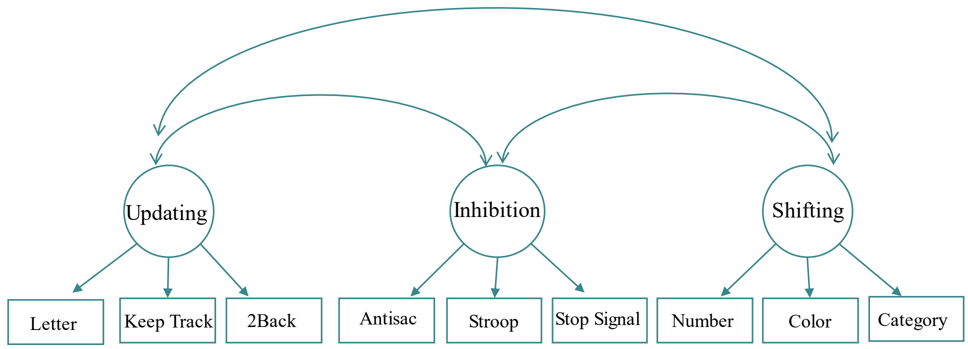

Figure 1 Unity and Diversity Three Factor Model (Miyake & Friedman, 2012)

Note. Circles represent latent variables and squares represent measured variables. The single headed arrows show the relationship between the latent and measured variables. In this model, these arrows show which latent variables are influenced by each measured variable. The double headed arrows represent correlations between factors. Unity is demonstrated by the inter-factor correlations and Diversity is demonstrated when the correlations are closer or further from 1.0, respectively.

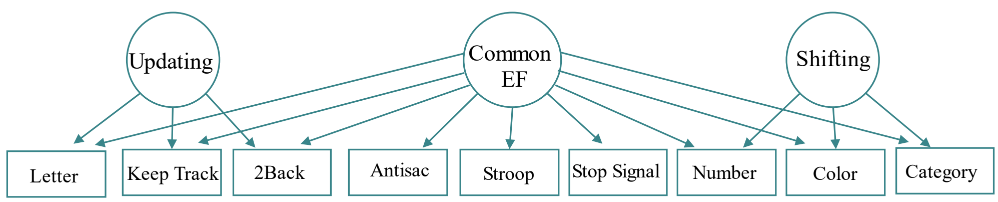

Figure 2 Unity and Diversity Bi-factor Model (Miyake & Friedman, 2012)

Note. Circles represent latent variables and squares represent measured variables. The single headed arrows show the relationship between the latent and measured variables. In this model, these arrows show which latent variables are influenced by each measured variable. Unity is demonstrated by all measured variables loading on the Common EF variable whereas Diversity is demonstrated by specific measured variables loading on the nested Updating and Shifting factors.

Previous studies have replicated this bi-factor model in samples of young adults, but only a few have attempted to replicate this model in a sample of older adults. This represents a significant gap in the literature considering the known deficits in EFs in older adults. There are studies that have replicated the original three factor model (Figure 1a) and modified versions of original and updated model in older adults. The models were modified by having additional latent factors or other measured variables. For example, Glisky et al. (2020) examined the original model (Figure 1a), a one factor version, and varying two factor models in groups of young-old (aged 60-73) and old-old adults (aged 74-98). They found that none of the models showed acceptable fit indices for the young-old group, but a nested two factor model showed exceptional fit for the old-old group. The latent variables in the two-factor model were the Common EF and Shifting.

In another recent study, Seer at al. (2021) examined differential EF contributions to complex motor control in older adults. The investigators ran modified versions of both models (Figure 1a and 1b) that included complex motor control as a dependent variable. These modified models were actually structural models rather than simple CFAs. Structural models allow you to examine regression relationships between latent variables or latent and other measured variables. Seer at al. (2021) was interested in whether the latent factors of the U&D model would predict complex motor control. The authors found that the Updating latent factors in both models and the Common EF significantly predicted complex motor control in older adults.

1.4 The Current Study

While studies continue to identify the utility of Miyake & Friedman's Unity and Diversity (U&D) framework for characterizing EFs in young adults, modeling EFs using the U&D rubric in older adults requires more study, particularly with respect to intervening lifestyle factors. Further, the employ of neurophysiological data to characterize correlates of neural activity could assist in identifying neural mechanisms subserving behavioral data. The current study sought to replicate Miyake and Friedman's (2012) Unity and Diversity model including physical activity as a predictor across a sample of older adults. The study examined the relationship between each EF factor, physical activity, and within-network resting-state connectivity. Combining this model with measures of physical activity and resting state data could give additional insights to the mechanisms underlying EF in older adults.

1.5 Specific Aims and Hypotheses

1.5.1 Specific Aim 1

To identify whether individual differences in executive function in older adults as evaluated by a modified version of Miyake and Friedman's U&D model are associated with physical activity.

1.5.2 Hypothesis 1

We hypothesized that older adults who engage in more physical activity will load on all three EF factors showing both unity and diversity. We also hypothesized that older adults who engage in less physical activity will load more on the Common EF factor compared to the Updating and Shifting factors, which would indicate more unity and less diversity.

1.5.3 Specific Aim 2

To examine the relationship between each EF factor (Common EF, Updating, Shifting), physical activity, and within resting-state network connectivity in older adults.

1.5.4 Hypothesis 2

We hypothesized that older adults who do not engage in regular exercise will show less diversity of EF and a lower degree of coherence in resting state networks, specifically the default mode network, the frontoparietal and the dorsal attention network

2 METHODS

2.1 Participants

A sample of 223 older adults ranging from 60-85 years of age was taken from the Human Connectome Project in Aging (HCP-A). The HCP-A study is a multisite project that collects neurological, behavioral, and biometric data with the goal of creating a normative dataset (Bookheimer et al., 2019). This study used data collected at the baseline visit of the project. Participants went through an initial phone screening to rule out exclusion criteria: (1) current or previous diagnosis of major psychiatric or neurological disorders; (2) individuals with severe depression that required treatment for 12 months or longer; (3) any contraindications for MRI scan; (4) a score of 30 or greater on the Telephone Interview for Cognitive Status modified (TICS-M) (de Jager et al., 2003). Subjects over 80 years old who did not score a 30 or greater on the TICS-M were required to pass critical orientation items.

Following consent, the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) was administered to further determine eligibility. The HCP-A has a liberal age dependent threshold for the MoCA with the goal of having a “typical” aging sample allowing adults ages 60-79 to be eligible with a score of 19 or greater, which may have led to individuals with cognitive impairment to be included (Bookheimer et al., 2019). The original cutoff score for detecting Mild Cognitive Impairment (MCI) was 26 (Nasreddine et al., 2005), which could lead to an increased rate of false positives for older aged individuals and those with less education. Recent meta-analyses using a more culturally and educationally diverse sample found that a cutoff score of 23 shows better accuracy for detecting MCI (Carson et al., 2018). For this project, only subjects with a MoCA score of 23 or greater will be included. A full list of inclusion and exclusion criteria is included in the Appendix.

Table 1 Sample Characteristics

Age (years)	70.98 ± 7.03
Education (years)	17.87 ± 2.09
Sex (number of females)	124
Race (% White)	83%
MoCA	26.72 ± 2.05

Note. MoCA =Montreal Cognitive Assessment

2.2 Behavioral Assessments

Cognitive assessments come from the NIH Cognitive Toolbox. The Rey Auditory Verbal Learning Test (RAVLT) (Rey, 1941) and the Trail Making Test B (Reitan, 1992) were included as supplemental measures in the HCP-A. All assessments were completed on a laptop computer except for the Trails Making Test B, RAVLT and the International Physical Activity Questionnaire (IPAQ) (Booth, 2000), which were completed using pencil and paper and interview.

2.2.1 Inhibition

Flanker Inhibitory Control and Attention Test (Flanker). This task required participants to focus on a target stimulus while inhibiting attention to other stimuli. Participants were presented with a target arrow pointing in a certain direction along with two flanking arrows that either face the same (congruent) or opposite direction of the target arrow (incongruent). The participant selected one of two buttons as quickly and accurately as possible to identify if the arrows were congruent or incongruent. Accuracy and reaction time were combined into a computed score used for the dependent measure. A maximum score of 10 was possible where higher scores indicated a greater ability to inhibit.

Proactive Interference (Pro Int) from Rey Auditory Verbal Learning Test (RAVLT). The RAVLT is used as a verbal learning and memory measurement (Rey, 1941). For the first five trials, participants were read a list of 15 words at the beginning of each trial that they must then immediately recall. On the sixth trial, participants were read a list of different, unrelated words, that they had to immediately recall. For the final trial, participants were asked to recall the words from the first five trails without being prompted. Proactive interference was calculated by subtracting the number of correctly recalled words in trial 1 from number of words correctly recalled in trial six. Because this calculation resulted in some negative values, the values were recoded, so all scores are positive numbers. Proactive interference represented a score of inhibition; it means that previously learned material was interfering with learning new material. A higher score indicated a greater degree of inhibition and less proactive interference.

2.2.2 Updating

List Sorting Working Memory Test (List Sort). Participants were presented with pictures of different foods and animals with accompanying text. The goal was to verbally recall and list the pictures in order from smallest to largest on just one dimension (food OR animals) and then both dimensions (food AND animals). For the two-dimension conditions, participants first listed the food objects and then the animals from smallest to largest. Accuracy scores were obtained and used as the dependent measure. A maximum score of 26 was possible with a higher score indicating greater updating ability.

Picture Sequence Memory Test (Pic Seq). Participants were presented with pictures of objects and activities, along with auditory phrases, in a particular sequence. The goal of the task was to recall the sequence in the correct order. The sequences increased in length from six to 18 pictures. Accuracy scores were obtained and used as the dependent measure. A maximum score of 31 was possible with a higher score indicating greater updating ability.

2.2.3 Switching/Shifting

Trail Making Test B (TrailsB). This test measured switching ability that involved connecting a set of dots that are made up of numbers and letters. Participants were required to connect the dots in ascending order alternating between letters and numbers (1-A-2-B-3-C). Time to complete the task was measured in seconds and used as the dependent measure. The HCP-A did not have a cut-off score and allowed participants to continue until completed. Following Reitan (1992) instructions, a maximum time of 300 seconds was allowed for the current study and any scores that were above 300 seconds were made to be equal to 300 seconds. A lower score indicated greater switching ability.

Dimensional Change Card Sort Test (DCCS). This task measured switching ability as well as cognitive flexibility. Participants were presented with target pictures that vary along two dimensions: shape and color. The goal was to match test pictures with target pictures based on one of the dimensions. Some of the trials required participants to switch which dimension is being matched. Accuracy and reaction time were combined into a computed score used for the dependent measure. A maximum score of 10 was possible where higher scores indicated a greater ability to switch.

2.2.4 Physical Activity

Short International Physical Activity Questionnaire (IPAQ). The IPAQ is an interview survey that calculates minutes of physical activity (Booth, 2000). It asks questions about types of physical activity that individuals have done in last seven days. The questions consider the intensity of the activity (vigorous, moderate, walking), time spent doing the activity (days per week, hours per day, minutes per day) and the amount of time spent sitting. The amount of physical activity per week was represented by MET-minutes (metabolic equivalent intensity levels) per week, which was calculated by weighing the reported minutes per week within each activity category by a MET expenditure estimate (Craig et al., 2003). MET-minutes per week was used as the dependent measure.

2.3 rsfMRI Acquisition and Pre-processing

MRI scans were acquired using a Siemens 3T Prisma scanner and a 32-channel head coil. A high resolution ($0.8mm^3$) multi-echo T1-weighted 3D magnetization prepared rapid acquisition gradient echo (MPRAGE) scan was obtained in the sagittal plane (TE = 1.8/3.6/5.4/7.2 ms; TR = 2500 ms; FOV = 256 x 240 x 166 mm; FA = 8°; voxel size = 0.8 x 0.8 x 0.8 mm^3; matrix size = 320 x 300 x 208 slices; time = 8.22 min). For the resting-state acquisition, participants were instructed to look at a small, white crosshairs on a black background. The rsfMRI time course was acquired with a 2D multiband gradient-recalled echo (GRE) echo-planar imaging sequence (EPI) (volumes = 488; TE = 37 ms, TR = 800 ms, FOV = 208 x 208 x 144 mm; FA = 52°; voxel size = 2.0 x 2.0 x 2.0 mm^3; matrix size = 104 x 104 x 72 slices). Four runs lasting 6.5 min each were acquired resulting in a total resting-state acquisition time of 26 minutes.

Minimally pre-processed images were obtained from the HCP-A project and further processed and analyzed using CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012) (RRID:SCR_009550) release 21.a (Nieto-Castanon & Whitfield-Gabrieli, 2021) and SPM (RRID:SCR_007037) release 12.7771 (Penny et al., 2011). Functional and anatomical data were preprocessed using a flexible preprocessing pipeline including outlier detection and smoothing (Nieto-Castanon, 2020). Potential outlier scans were identified using ART (Whitfield-Gabrieli et al., 2011) as acquisitions with framewise displacement above 0.9 mm or global BOLD signal changes above 5 standard deviations (Power et al., 2011; Nieto-Castanon, n.d.) and a reference BOLD image was computed for each subject by averaging all scans excluding outliers. Last, functional data were smoothed using spatial convolution with a Gaussian kernel of 6 mm full width half maximum (FWHM).

In addition, functional data were denoised using a standard denoising pipeline (Nieto-Castanon, 2020) including the regression of potential confounding effects characterized by white matter timeseries (5 CompCor noise components), CSF timeseries (5 CompCor noise components), motion parameters (12 factors) (Friston et al., 1996), outlier scans (below 98 factors) (Power et al., 2011), session effects and their first order derivatives (2 factors), and linear trends (2 factors) within each functional run, followed by bandpass frequency filtering of the BOLD timeseries (Hallquist et al., 2013) between 0.008 Hz and 0.09 Hz. CompCor (Behzadi et al., 2007; Chai et al., 2012) noise components within white matter and CSF were estimated by computing the average BOLD signal as well as the largest principal components orthogonal to the BOLD average, motion parameters, and outlier scans within each subject's eroded segmentation masks. From the number of noise terms included in this denoising strategy, the effective degrees of freedom of the BOLD signal after denoising were estimated to range from 220.3 to 237.2 (average 235.6) across all subjects (Nieto-Castanon, n.d.).

2.4 Data Analyses

Scores for the behavioral assessments were subjected to trimming and transformation used in previous studies to improve normality and reliability (Friedman et al., 2016) (Reineberg et al., 2018). Scores that were greater than three standard deviations from the mean were replaced with values three standard deviations from the mean for each measure. To avoid problems arising from extreme differences in variable variances, we rescaled Trails B and the IPAQ by taking the square root of the dependent measure.

2.4.1 Aim 1: Confirmatory Factor Analyses

Two models were computed using Mplus 8.0 to estimate the unity and diversity of EF in older adults with three latent variables: Common EF, Updating and Shifting specific (Muthén and Muthén, 1998–2017). Model 1 was based on Friedman et al.'s (2008) bifactor model where all cognitive assessments loaded on the Common EF and updating and shifting assessments loaded on the Updating and Shifting factors. Model 2 was a structural model that was similar to Model 1, but the IPAQ was included as a separate independent variable predicting the three latent factors. Factor scores for the three EF variables in Model 1 were extracted and used in analysis of Aim 2. The factor variance in both models was fixed to 1.0 to set the scale of the variables. Factor loadings were equal for the Updating and Shifting factors to ensure that model identification was present. Several fit indices were examined to assess goodness of fit: the chi-square value (χ^2), confirmatory fit index (CFI), and the root-mean-square error of approximation (RMSEA). A non-significant χ^2 value is considered a good indicator of fit of the data to the model. The χ^2 is known to be sensitive to sample size so the other two fit indices will also be examined. A CFI value greater than 0.9 and a RMSEA value less than 0.06 is considered good fit (McDonald & Ho, 2002).

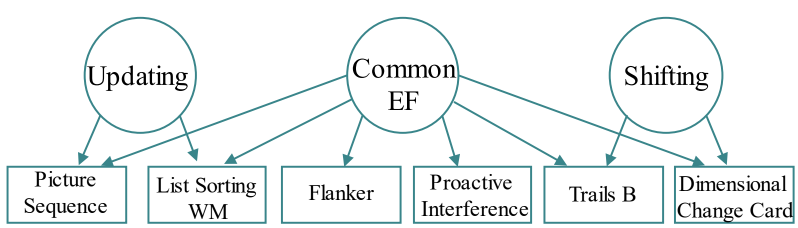

Figure 3 Confirmatory Factor Analysis

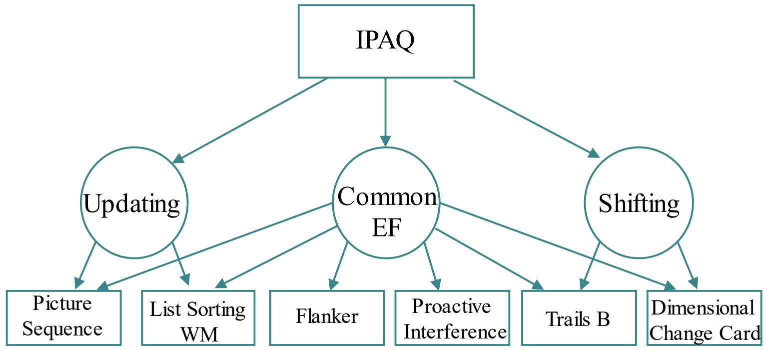

Figure 4 Structural Model

2.4.2 Aim 2: Within-Network rsfMRI

A priori networks based on a publicly available network parcellation of the brain were selected as ROIs (Yeo et al., 2011). This parcellation includes seven main resting-state networks, but only three were examined for this analysis: default mode (10 ROIs), dorsal attention (6 ROIs), and frontoparietal (16 ROIs). ROI-to-ROI connectivity (RRC) matrices were estimated using CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012) (RRID:SCR_009550) release 21.a (Nieto-Castanon & Whitfield-Gabrieli, 2021) that characterized the functional connectivity between each pair of regions among the ROIs for each network. Functional connectivity strength was represented by Fisher-transformed bivariate correlation coefficients from a general linear model (weighted-GLM) (Nieto-Castanon, 2020), estimated separately for each pair of ROIs, characterizing the association between their BOLD signal time series. To compensate for possible transient magnetization effects at the beginning of each run, individual scans were weighted by a step function convolved with an SPM canonical hemodynamic response function and rectified.

The average within-network connectivity for each participant was calculated by computing the mean of the pairwise correlations between the specified ROIs that comprise each resting-state network (Hausman et al., 2020). To examine the relationship between within-network connectivity and EF variables, multiple linear regressions were run predicting within-network connectivity for each network from the latent EF factor scores and the IPAQ using IBM SPSS Statistics (Version 29). Age and sex were included in each regression as covariates.

Table 2 Descriptive Statistics for Dependent Measures

	M	*SD*	Min	Max	Skewness	Kurtosis
Pro Int	6.65	1.98	1.00	12.00	-0.1	0.27
Flanker	7.84	0.68	5.61	9.64	-0.76	1.55
Pic Seq	10.33	6.22	0.00	29.08	0.77	0.3
List Sort	16.28	2.71	8.00	24.00	-0.32	0.16
DCCS	8.03	0.81	5.92	9.88	-0.25	-0.05
Trails B (sqrt)	9.67	3.33	5.38	17.32	1.33	0.68
Trails B	104.60	79.71	28.90	300.00	1.68	1.49
IPAQ (sqrt)	46.81	20.59	0.00	97.24	0.19	-0.11
IPAQ	2613.84	2086.61	0.00	9454.72	1.29	1.69

Note. Pro Int = Proactive Interference, Pic Seq = Picture Sequence Memory Test, List Sort = List Sorting Working Memory Test, DCCS = Dimensional Change Card Sort Test, IPAQ = Short International Physical Activity Questionnaire, (sqrt) = rescaled values by taking the square root.

Table 3 Correlation Matrix for Dependent Measures

	Pro Int	Flanker	Pic Seq	List Sort	DCCS	Trails B	IPAQ
Pro Int	-						
Flanker	0.08	-					
Pic Seq	0.04	0.23**	-				
List Sort	0.04	0.27**	0.21**	-			
DCCS	0.02	0.51**	0.19**	0.31**	-		
Trails B	0.12	-0.09	-0.06	-0.13	-0.15*	-	
IPAQ	0.06	-0.04	-0.08	0.03	0.08	-0.04	-

Note. *$p < .05$; **$p < .01$; Pro Int = Proactive Interference, Pic Seq = Picture Sequence Memory Test, List Sort = List Sorting Working Memory Test, DCCS = Dimensional Change Card Sort Test, IPAQ = Short International Physical Activity Questionnaire.

3 RESULTS

3.1 Aim 1

A summary of descriptive and correlational statistics for the behavioral measures used in the factor analyses is presented in Tables 1 and 2. For Model 1, both factor loadings for the Shifting factor were zero and nonsignificant, which indicated model misspecification. We respecified Model 1 (Model 1a) so the latent factor Shifting was removed, and its indicators only loaded on the Common EF factor. Model 1a had excellent fit indices χ^2 (15) = 7.271, p = .508, CFI = 1.000, RMSEA = .001, where five of the six tasks loaded significantly on the Common EF and the updating tasks loaded significantly on the Updating factor (Figure 3a). Model 2 was adjusted to account for the changes in Model 1a and had good overall fit, χ^2 (12) = 13.266, p = .350, CFI = .989, RMSEA = .022. Model 2 had similar significant loadings as in Model 1a, but the IPAQ did not significantly predict the latent factors (Figure 3b).

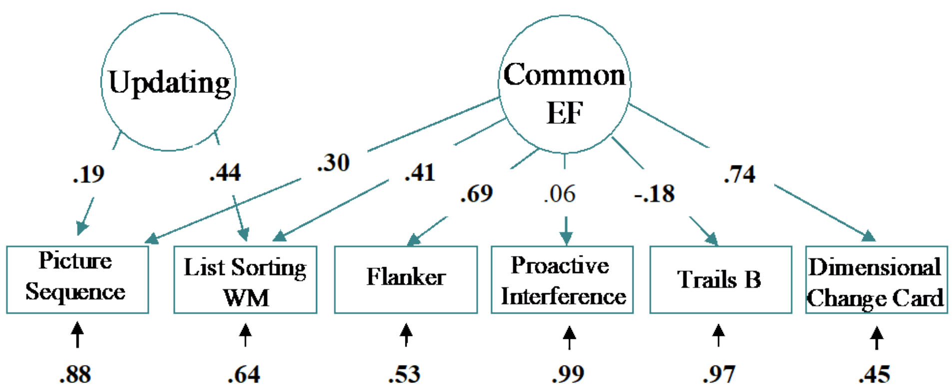

Figure 5 Model 1a: Modified Unity and Diversity Model

Note. Long, blue arrows indicate standardized factor loadings. Small, black colored arrows indicate error variance. Significant indicators are highlighted in boldface at p < .05.

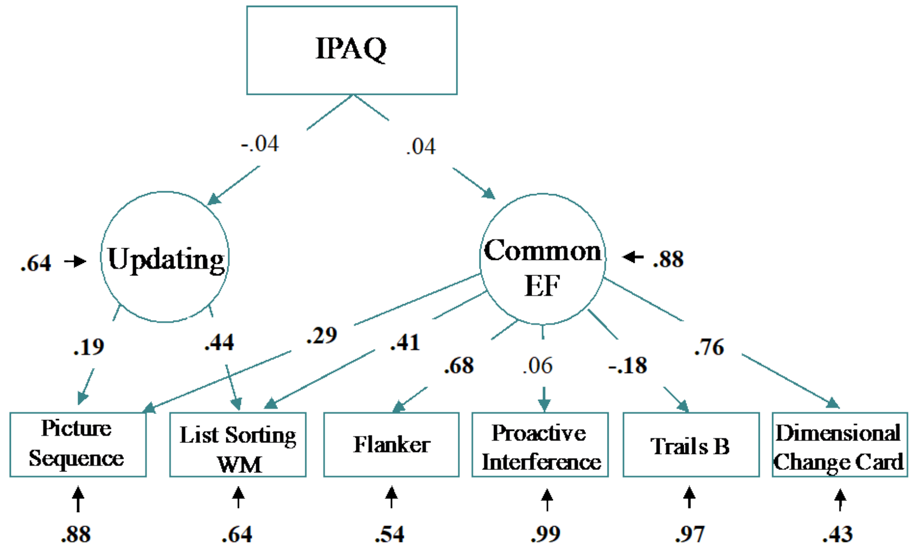

Figure 6 Model 2: Structural Model

Note. Long, blue arrows indicate standardized factor loadings. Small, black colored arrows indicate error variance. Significant indicators are highlighted in boldface at $p < .05$.

3.2 Aim 2

To give further insight to the unity and diversity of EF in older adults, we regressed the Common EF and Updating factor scores, obtained from Model 1a, as well as IPAQ scores on within-network connectivity values, while controlling for age and sex. We found that none of the linear regressions predicting within-network connectivity for the three networks (DMN, DA, FN) were significant.

Table 4 Association between within-network connectivity, EF factors, and physical activity

Network	Variable	Unstandardized Coefficients		Standardized Coefficients	t	*p*	R^2
		B	*SE*	Beta (β)			
DMN	Common	-.018	.010	-.126	-1.728	.085	.018
	Updating	.014	.017	.058	.842	.401	
	IPAQ	.000	.000	-.018	-.268	.789	
	Age	3.70E-05	.001	.002	.031	.976	
	Sex	-.012	.001	-.051	-.748	.455	

DA	Common	-.013	.011	-.089	-1.222	.223	0027
	Updating	.017	.018	.067	.966	.335	
	IPAQ	.000	.000	-.022	-.327	.744	
	Age	.002	.001	.101	1.41	.160	
	Sex	-.009	.017	-.034	-.493	.622	
FP	Common	.002	.005	.025	.341	.733	.015
	Updating	.006	.008	.048	.690	.491	
	IPAQ	.000	.000	.080	1.15	.253	
	Age	.000	.001	.037	.518	.605	
	Sex	.008	.008	.071	1.036	.301	

Note. R^2 represents the overall R^2 for each model. DMN = Default Mode Network, DA = Dorsal Attention Network, FP = Frontoparietal Network.

4 DISCUSSION

The mechanism of EF decline in older adults is not well understood especially when considering certain lifestyle factors. The current study employed a factor analysis approach to investigate aging-related changes in EF and how physical activity may mitigate these changes. We expected to replicate the U&D model in our sample, and we also expected that physical activity would be associated with the three latent factors. We were not able to replicate the U&D model, but instead found that a modified version, only including the Common EF and Updating factors, fit the data. The latent EF factors in this modified model were not associated with amount of physical activity. We also investigated whether the latent factors and physical activity could predict within-network connectivity but found no significant associations.

4.1 Modified Unity and Diversity Model

Unlike Miyake and Friedman's model, we did not observe any evidence of a Shifting-specific factor. One possible explanation for this finding is that the structure of EFs is different in older adults. As previously stated, the U&D model has been successfully replicated in several samples of young adults, but few studies have examined it in older adults. Glisky et al. (2020) examined several different model structures and found evidence of a two-factor model that included the Common EF and Shifting factors. Seer et al. (2021) reported on a modified version of the U&D model where the factors were predicting complex motor control. The structural model had an acceptable fit and showed that the Common EF and Updating factors predicted complex motor control. However, the authors did not report on the baseline CFA model prior to the addition of complex motor control as a dependent variable (Seer et al., 2021). Due to the lack of studies investigating the U&D model in older adults, it would've been useful to examine the baseline CFA model. Even though our models didn't find evidence of a specific Shifting factor, that does not definitively mean it doesn't exist.

Our models did display excellent overall fit, but there are some indications that the local fit of the models may not be as excellent. In both models, one of the six measurements was not a significant indicator (Pro Int), and two of the six (Pro Int and TrialsB) did not have significant R-squared (R^2) values. Also, factor loadings were relatively small in both models for Pro Int, TrailsB, and Pic Seq. Specifically in Model 2, physical activity was not a significant predictor for the latent factors. These results may be due to the specific behavioral measurements selected for the factor analysis. Some tasks used to represent the factors are not commonly used to measure the specific EFs of interest, and show lower relative construct validity. For example, Proactive Interference and the Picture Sequence Memory Task are not typically used to represent inhibition and working memory updating in studies of EF. In a systematic review of studies using latent variables to measure EF, Kar et al. (2019) found that most studies used a Stroop paradigm, Antisaccade task, and a Stop-Signal task to measure inhibition. To measure working memory updating, studies frequently used the *n*-back, Letter Memory task, the Keep Track task, and the Digit Span Backwards task (Karr et al., 2019).

Although four out of the six measurements had significant R^2 values, their numbers ranged from small to moderate (.12-.55). This suggests that there is additional variance in the indicators that has yet to be explained by the model and could be explained by other variables. Several studies have included other latent factors to define EF in older adults. The most common additional latent factors are speed of processing (Hedden & Yoon, 2006; de Frias et al., 2009; Frazier et al., 2015; Bettcher et al., 2016) and long-term memory access (Fisk & Sharp, 2004; Androver-Roig et al., 2012). It is important to note that these studies based their factor structure on the original three-factor model including inhibition, shifting, and updating (Miyake et al., 2000) rather than the bifactor structure (Friedman et al., 2008).

4.2 Within-network Connectivity

The current study investigated whether results from the bifactor model could be related to differences in within-network connectivity of specific resting-state networks. Although the results weren't significant, this study helps address a major gap in the literature. We believe this is the first study to examine the relationship between the U&D model, physical activity, and within-network connectivity of resting-state networks in older adults. Previous studies have examined the relationship between within-network connectivity and EFs citing the U&D model, but none to our knowledge have defined the EFs using factor analysis. In many instances, studies have created composite scores to represent each of the EF factors or used performance on a single task as a comparison (Yang et al., 2018; Hausman et al., 2020; Hausman et al., 2022). While these methods are helpful in gaining a better understanding of brain-behavior relationships in older adults, they don't directly investigate how the U&D model could relate to functional connectivity.

Within-network connectivity was defined as the average of the pairwise correlations between the ROIs that comprised each network. Although this method was reasonable to examine within-network connectivity, it may have overlooked other significant results. For example, we did not further examine the regional connectivity patterns of ROIs in each network, nor did we consider other measures of network connectivity. Previous studies have utilized alternate methods to investigate within-network connectivity changes in older adults, specifically graph theory (Betzel et al., 2014; Chan et al., 2014). Graph theory approaches define a network by parcellating the brain into sets of regions (nodes) and then calculating all possible connections between the regions (edges) (Sala-Llonch et al., 2015). Once a network is defined, several descriptive measures can be calculated to characterize its functional connectivity. Common descriptive measures include network segregation (within-network connectivity), network integration, node centrality (defining hub regions), and network resilience (Rubinov & Sporns, 2010). Examining more than one metric of functional connectivity can provide a better understanding of how the brain is organized.

4.3 Physical Activity

Although physical activity did not significantly predict the EF factors nor within-network connectivity in the current study, it continues to be an important lifestyle factor to consider. It is well known that participating in aerobic exercise and physical activity can lead to positive changes in cognition and brain functioning (Woo et al., 2021). The actual extent of changes can depend on several factors: type of exercise/physical activity, frequency, and intensity. Although these factors are considered when scoring the IPAQ, the IPAQ only asks about physical activity within the last seven days. This can be problematic because it is measuring physical activity at one point in time. The IPAQ is also a self-report measure so individuals may over- or underestimate their levels of physical activity. An alternate lifestyle factor that may be more informative than physical activity is cardiovascular health. A measure of cardiovascular health considers not only physical activity, but also smoking status, diet, body mass index, glucose concentration, blood cholesterol concentration, and blood pressure (Lloyd-Jones et al., 2010). These additional factors provide a more extensive measure of overall health that can impact brain-behavior relationships.

4.4 Limitations and Future Directions

The present study is not without limitations, especially regarding the sample's characteristics, behavioral measurements, and the method of analyses. First, our sample was highly educated ranging from 14-21 years of education and 83% Non-Hispanic White. These characteristics make it difficult to generalize the results to the general population. Future studies should use more educationally and racially diverse samples to increase the generalizability. Second, the choice of and number of behavioral measurements could be improved upon. As previously stated, some of the measurements selected are not typically used to represent the EF factors this study examined. The number of assessments used may have also played a factor into the results. We used a total of six cognitive assessments to create the latent factors, whereas Miyake and Friedman's studies (Miyake et al., 2000; Friedman et al., 2008; Friedman et al., 2016) used nine. Using only two indicators per latent factor can lead to instances of model identification or specification problems (Kline, 2016). To combat this issue, equality constraints are used, but it can still impact the model in small sample sizes.

Although the current study was limited to what the HCP-A project provided, future work should select more common tests to represent the factors and each factor should have a minimum of three indicators. This will increase reliability and allow more direct comparisons to other studies. Third, the ROI-ROI analysis used in this study may have limited the findings. This analysis only examined average within-network connectivity and did not consider the patterns of connectivity between each ROI for a given network. Examining hub regions could help target specific regions for interventions (Hausman et al., 2022). Future studies should include additional analyses to better describe within-network connectivity as well as other network characteristics.

4.5 Conclusions

This study may be the first to examine the U&D model in older adults in combination with physical activity and within-network connectivity of resting-state networks. Unlike Miyake and Friedman's model, factor analyses did not find evidence for a Shifting EF factor. Results also revealed no associations between the EF factors, physical activity, and within-network connectivity. These findings could suggest the presence of an alternate EF structure for older adults but are more likely the result of methodological complications. Further analyses with alternate behavioral measures and additional functional connectivity metrics are required to better understand the mechanisms underlying EF in older adults.

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APPENDICES

Appendix A

Table 5 HCP-A Inclusion and Exclusion Criteria (Bookheimer et al., 2019)

HCP-A Inclusion Criteria	
1.	Age 36-100+
2.	Ability to give informed consent
HCP-A Exclusion Criteria	
1.	During the participant's lifetime:
a.	Neurologic disease including multiple sclerosis, cerebral palsy, Parkinson's disease, or Alzheimer's disease
b.	Brain surgery
c.	Major psychiatric disorder, such as bipolar disorder or schizophrenia
d.	Hospitalization for 2 days or more for alcoholism or drug dependence
e.	Head injury causing any of the following:
i.	Loss of consciousness for >30 minutes
ii.	Amnesia for >24 hours
iii.	Change in mental status for >24 hours
iv.	Neuroimaging findings consistent with traumatic brain injury
v.	Persistent (>3 months) post-concussive symptoms following concussion or mild TBI
f.	Two or more non-provoked (e.g. not due to fever) seizures after age 5 years or a diagnosis of epilepsy
g.	Any brain tumor including meningiomas
h.	Any cancer treated with chemotherapy and/or radiation to the head or neck, and/or any stage 4 (metastatic) cancer even if no treated
i.	Hospitalization for brain aneurysm, brain hemorrhage, subdural hematoma or stroke (except TIA is allowed)
j.	Rheumatoid arthritis, HIV or lupus or another condition requiring long-term use of steroids or other immunosuppressant
k.	If 80 years old or younger: Diagnosis of macular degeneration
l.	Known genetic disorder (e.g. sickle cell disease or cystic fibrosis)

2. Within the last 5 years:
a. Pharmacologic or surgical treatment by a neurologist, or endocrinologist for a period of 12 months or longer, except for thyroid conditions or for back pain or other condition that is clearly not brain-related.
b. Severe depression requiring treatment by a psychiatrist for 12 months or longer
3. Within the last 1 year:
a. Diagnosis of thyroid problems and/or changing doses of thyroid medication
b. Heart attack
4. Current:
a. Diabetes that has been diagnosed within the past 3 years (diabetes is OK if it is stably controlled per participant report of either HbA1c <7.0 or stable control for at least 3 months)
b. Hearing loss sufficient to prevent communication via telephone
c. Vision worse than 20/200
d. Current pregnancy
e. Unsafe metal or devices in body
f. Moderate to severe claustrophobia
g. Use of prescription medication to prevent migraines (migraines allowed if not taking daily preventive medications)
h. Migraine less than 72 hours before the first visit or during the visit
i. Uncontrolled high blood pressure (>170/100) or working with doctor to stabilize blood pressure
j. Severe lung, living, kidney or heart disease or other major organ failure
k. Montreal Cognitive Assessment (MoCA) score of 19 or below for participants aged up to 79 years; MoCA score of 17 or below for participants ages 80-89; MoCA score of 16 or below for participants age 90 and above
l. For participants aged 60 – 79, a score of 29 or below on the TICS-M questionnaire. If participants ages 80 and above score 29 or below on the TICS-M, we give them a secondary screen to determine their eligibility.