Distribution Agreement

In presenting this thesis as a partial fulfillment of the requirements for a degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis in whole or in part in all forms of media, now or hereafter now, including display on the World Wide Web. I understand that I may select some access restrictions as part of the online submission of this thesis. I retain all ownership rights to the copyright of the thesis. I also retain the right to use in future works (such as articles or books) all or part of this thesis.

Sarah Solano March 19, 2025

Association of Vascular Health with Motor and Cognitive Function in People with Prodromal Alzheimer's Disease

By

Sarah Solano

Madeleine E. Hackney, PhD.
Adviser

Department of Neuroscience and Behavioral Biology

Madeleine E. Hackney, PhD.
Adviser

John Linda, PhD.
Committee Member

Alex Grizzell, PhD.
Committee Member

2025

Association of Vascular Health with Motor and Cognitive Function in People with Prodromal Alzheimer's Disease

By

Sarah Solano

Madeleine E. Hackney, PhD.
Adviser

An Abstract of a thesis submitted to the Faculty of Emory College of Arts and Sciences
of Emory University in partial fulfillment
of the requirements of the degree of
Bachelor of Sciences with Honors

Department of Neuroscience and Behavioral Biology

2025

Abstract

Association of Vascular Health with Motor and Cognitive Function in People with Prodromal Alzheimer's Disease

By Sarah Solano

Importance: Mild cognitive impairment (MCI) is an intermediate stage between normal aging and dementia and is considered to be the prodromal stage of Alzheimer's Disease (AD), affecting approximately 22% of adults aged 65 and older. Cognitive impairment poses a significant public health challenge, particularly among older populations, which is expected to increase in the coming years. Vascular health has been shown to impact cognitive status in various populations with dementia. Less is known about vascular function's impact on motor and motor-cognitive function, both of which greatly influence independence in people with MCI. More research is needed to gain a better understanding of the neurobiology of MCI and its connections to other systems.

Objective: To investigate the association between vascular function and cognitive, motor, and motor-cognitive function in individuals with prodromal Alzheimer's Disease (AD), who experience MCI. As a secondary analysis, we will also explore the relationship between vascular health and demographic information.

Study Design: Exploratory Observational Study. The study included 73 participants with diagnosed prodromal Alzheimer's Disease and Mild Cognitive Impairment: 54.8% Caucasian, 38.4% African American, 2.7% Hispanic/ Latino, and 4.1% Multiracial individuals with Mild Cognitive Impairment (MCI). The mean age was 74.6 ± 7.16 years with a relatively balanced gender distribution (Male: 43.8%, Female: 56.2%).

Main Outcome and Measure: Project health questionnaire, vascular health assessments, cognitive assessments, motor assessments, motor-cognitive assessments

Results: This study included 73 participants aged 74.57 ± 7.16 years with a relatively balanced gender distribution was relatively balanced (Male: 43.8%, Female: 56.2%). Analyses revealed associations between arterial stiffness (as measured by PWV) and motor function, with a moderate

negative correlation observed between PWV and mobility and balance scores. Additionally, small but notable correlations suggest that greater arterial stiffness may be associated with minor declines in memory and executive processing. Age was strongly associated with increased arterial stiffness, and gender differences in vascular responses were observed, suggesting distinct vascular aging patterns between males and females.

Conclusion and Relevance: Analyses revealed that greater arterial stiffness, as measured by pulse wave velocity (PWV), was moderately associated with poorer motor function, particularly in domains of mobility and balance. Notably, this study is among the first to demonstrate associations between vascular function and key domains of neurological performance, including motor ability and visuospatial or executive functioning. While small correlations were observed between PWV and cognitive outcomes such as memory and task switching, these findings warrant further exploration. Age-related increases in arterial stiffness were also confirmed, and sex-based differences in vascular profiles suggest possible divergence in vascular aging trajectories. These findings underscore the potential of vascular health metrics as early markers of functional decline and support the integration of vascular assessments in the study of aging and neurodegeneration.

Association of Vascular Health with Motor and Cognitive Function in People with Prodromal Alzheimer's Disease

By

Sarah Solano

Madeleine E. Hackney, PhD.
Advisor

A thesis submitted to the Faculty of Emory College of Arts and Sciences
of Emory University in partial fulfillment
of the requirements of the degree of
Bachelor of Sciences with Honors

Department of Neuroscience and Behavioral Biology

2025

Acknowledgements

I would like to thank Dr. Madeleine Hackney for the opportunity to conduct this research in her lab. I would like to thank Dr. Forouzan Rafiei and Matt Lamsey for their support and guidance throughout the project. I would like to thank our lab nurse, Helen, for conducting the vascular assessments for the PARTNER study and Ejew Kim for her demonstration of motor-cognitive assessments and for her explanation of the scoring of these assessments. I would like to thank Dr. Amir Nekoei for conducting the statistical analyses for the project. I would like to thank my mom, Maria Solano, and my brother, David Solano, for their encouragement and unwavering support throughout this process.

Table of Contents

Abstract

Importance: Mild cognitive impairment (MCI) is an intermediate stage between normal aging and dementia and is considered to be the prodromal stage of Alzheimer's Disease (AD), affecting approximately 22% of adults aged 65 and older. Cognitive impairment poses a significant public health challenge, particularly among older populations, which is expected to increase in the coming years. Vascular health has been shown to impact cognitive status in various populations with dementia. Less is known about vascular function's impact on motor and motor-cognitive function, both of which greatly influence independence in people with MCI. More research is needed to gain a better understanding of the neurobiology of MCI and its connections to other systems.

Objective: To investigate the association between vascular function and cognitive, motor, and motor-cognitive function in individuals with prodromal Alzheimer's Disease (AD), who experience MCI. As a secondary analysis, we will also explore the relationship between vascular health and demographic information.

Study Design: Exploratory Observational Study. The study included 73 participants with diagnosed prodromal Alzheimer's Disease and MCI: 54.8% Caucasian, 38.4% African American, 2.7% Hispanic/ Latino, and 4.1% Multiracial individuals with MCI. The mean age was 74.6 ± 7.16 years with a relatively balanced gender distribution (Male: 43.8%, Female: 56.2%).

Main Outcome and Measure: Project health questionnaire, vascular health assessments, cognitive assessments, motor assessments, motor-cognitive assessments.

Results: This study included 73 participants aged 74.57 ± 7.16 years, indicating an older population. Gender distribution was relatively balanced (Male: 43.8%, Female: 56.2%). Small but notable correlations suggest that increased arterial stiffness may have a minor impact on memory and executive processing and moderate negative correlations between PWV and motor scores highlight the influence of vascular aging on mobility and balance. Additionally, aging is significantly associated with increased arterial stiffness, and gender differences in vascular responses suggest differential impacts on vascular health in males and females.

Conclusion and Relevance: Analyses revealed that greater arterial stiffness, as measured by pulse wave velocity (PWV), was moderately associated with poorer motor function, particularly in domains of mobility and balance. Notably, this study is among the first to demonstrate associations between vascular function and key domains of neurological performance, including motor ability and visuospatial or executive functioning. While small correlations were observed between PWV and cognitive outcomes such as memory and task switching, these findings warrant further exploration. Age-related increases in arterial stiffness were also confirmed, and sex-based differences in vascular profiles suggest possible divergence in vascular aging trajectories. These findings underscore the potential of vascular health metrics as early markers of functional decline and support the integration of vascular assessments in the study of aging and neurodegeneration.

Introduction

Mild Cognitive Impairment (MCI)

Mild Cognitive Impairment (MCI) is characterized as a transitional stage between normal aging and dementia (Geda et al., 2012) and is widely recognized as a prodromal phase of Alzheimer's Disease (Feng et al., 2020). According to nationally representative data from the United States, approximately 22% of adults aged 65 and older meet the diagnostic criteria for MCI, highlighting its substantial prevalence in the aging population (Manly et al., 2022).

MCI is characterized by memory deficits that should not impair global cognitive function or the ability to perform activities of daily living (Forlenza et al., 2013). Although individuals diagnosed with MCI may remain stable or return to normal cognitive function, these individuals are at a higher risk of developing dementia and Alzheimer's Disease (AD) (Forlenza et al., 2013). The prevalence of MCI increases with age and males seem to be at a higher risk than females (Jongsiriyanyong et al, 2018). Cognitive impairment poses a significant public health challenge, especially among the older population (Abbruzzese et al., 2016). As life expectancy increases, the prevalence of dementia is projected to climb from 55 million cases in 2019 to 139 million cases by 2050 (Long et al., 2023). This dramatic rise not only impacts individuals and their families but also places an immense strain on healthcare systems. By 2030, the global economic cost of dementia is expected to surge from $1.3 trillion to $2.8 trillion annually (Alzheimer's Disease International, 2024), highlighting both the financial and emotional toll, particularly in the context of healthcare and informal caregiving. More research is needed to gain a better understanding of the neurobiology of MCI and its connections to other biological systems such as the motor and vascular systems.

Vascular Disease

Vascular disease and its risk factors raise the risk of MCI and are associated with the progression from MCI to AD dementia (Lorius et al., 2015). For instance, it has been estimated that 20% of dementia cases have cerebrovascular pathology, and the vascular contribution to dementia currently affects 20 million people (Mok et al., 2024). Findings from Lorius et al.'s 2015 study highlight a correlation between vascular disease, its risk factors, and cognitive impairment over time in the AD spectrum (Lorius et al., 2015). Additionally, Ilut et al.'s 2023, research has found that hypertension is associated with an increased risk of MCI and dementia with the underlying mechanisms involving cerebral hypoperfusion, oxidative stress, and inflammation. Once believed to be merely a physical barrier between blood and surrounding tissues, the vascular endothelium is now recognized as a dynamic organ that regulates vascular tone, metabolism, immunity, thrombosis, and fibrinolysis. With aging, the endothelium exhibits a prothrombotic, profibrinolytic, proinflammatory, and vasoconstrictive profile, collectively termed vascular endothelial dysfunction. Arterial stiffness and endothelial dysfunction are associated with lower cerebral blood flow and impaired vascular function which leads to cognitive impairment (Iluț et al., 2023).

Vascular Aging

Vascular aging, characterized by endothelial dysfunction and stiffening of large elastic arteries, significantly raises the risk of age-related cardiovascular diseases (CVDs) (Moreau et al., 2020). An abundance of reactive oxygen species (ROS) and inflammation trigger this process, reducing the availability of nitric oxide and altering the shape of the arterial wall. Additional aging-related cellular mechanisms, such as mitochondrial dysfunction and cellular senescence, also contribute to vascular aging. Gonadal aging, notably impacting women but also some men, further

influences vascular health. Regular physical activity, including aerobic and resistance exercise, is a primary strategy to mitigate CVD risk with age (Craighead et al., 2019). While vascular aging is normal characteristic of the aging process, pathophysiological diseases in the arteries are not an inevitable feature of aging as not all individuals who display endothelial dysfunction or arterial stiffening develop CVDs such as coronary artery disease (CAD)(Cheng et al., 2023).

Vascular Aging and Gender

Cardiovascular disease has been shown to manifest differently in males and females with females tending to experience greater age-related myocardial stiffening (Ji et al., 2022). Early in life it seems that men experience greater age-related vascular structural changes (such as wall stiffening) and functional changes (endothelial dysfunction) (Maier et al., 2023) while in women, vascular aging appears to be slowed until menopause (Moreau et al., 2020). Notably, after the sixth decade of life, age-related vascular dysfunction tends to progress at a faster rate in women than men (Maier et al., 2023) which has been attributed to changes in sex hormones that are a result of aging (Moreau et al., 2020). Estrogen decline is associated with endothelial dysfunction when increased reactive oxygen species, oxidative stress, and nitric oxide suppression are also present (Ji et al., 2022). Moreover, experimental and physiological data suggest that reductions in nitric oxide and increased oxidative stress contribute to endothelial and arterial stiffening in this case (Ji et al., 2022).

Cognitive and Motor Decline in Aging

Cognitive and motor decline frequently coexist with falls, underscoring a critical area of concern, as falls remain a leading cause of morbidity and severe injury among older adults. Research indicates that individuals with dementia display more pronounced gait abnormalities and experience a heightened frequency of falls compared to those undergoing typical cognitive aging

(Montero-Odasso & Speechley, 2018). This risk further intensifies as cognitive impairment progresses (Montero-Odasso & Speechley, 2018). Notably, older adults with MCI have a nearly twofold higher fall risk than cognitively healthy individuals (Rajeev et al., 2023), increasing their susceptibility to serious fall-related injuries, including fractures, head trauma, and even mortality (Vaishya R et al., 2020). Consequently, fall-related injuries place a substantial burden on patients, caregivers, and healthcare systems (Vaishya R et al., 2020).

Given the projected increase in the prevalence of MCI, dementia, and AD, it is crucial to implement effective treatments and interventions that address both cognitive and motor decline in order to improve outcomes and quality of life for older adults. Declines in motor function can contribute to fall risk, which can lead to serious health consequences for this population and create substantial financial burdens (Vaishya R et al., 2020). Fall-related injuries often require emergency medical care, rehabilitation, and long-term support and care services, straining healthcare resources. Therefore, early detection of cognitive and motor deficits, along with targeted prevention strategies, will be critical in promoting the overall well-being and safety of our aging population.

Purpose statement:

In this study, we are investigating the association between vascular health function measurements and motor, cognitive, and motor-cognitive function in a group of older adults with diagnosed prodromal AD and MCI. As a secondary analysis we will also explore the relationship between participant vascular health and participant demographic information.

Materials and Methods

Ethical Approval and Study Design

This study was approved by the Institutional Review Board of Emory University. All participants provided written informed consent before participation. The study presents findings from baseline assessments conducted in participants for the PARTNER trial (NCT04029623), a rehabilitation trial for older adults with prodromal AD who experience MCI. The study is funded by the United States National Institutes of Health/National Institute of Aging (NH/NIA) (1R01AG062691-01).

Participants

Participants were screened one month before assessment to determine eligibility. Eligible participants were 50 years of age or older and met the inclusion and exclusion criteria defined by the PARTNER registered clinical trial (NCT04029623). The inclusion criteria were based on the Alzheimer's Disease Neuroimaging Initiative (ADNI) criteria for amnestic MCI (Mueller et al., 2005; Petersen et al., 2010).

Procedures

Selection and Pre-Screening

Participants were recruited through the Emory University Goizueta Alzheimer's Disease Research Center in collaboration with their Minority Engagement Core/ Outreach and Recruitment Core, community activities, health fairs, advertisements, recruitment flyers, and previous related research studies of the Hackney lab. Interested participants completed a phone screening with research staff which included a medical questionnaire, the blind Montreal Cognitive Assessment (MoCA), Subjective Memory Concerns Questionnaire, Telephone Interview for Cognitive Status

(TICS), Functional Activities Questionnaire (FAQ), and magnetic resonance imaging (MRI) history and screening questionnaire (Cao et al., 2022). Participants were compensated with monetary gift cards for each completed study visit. For participants that were eligible, the study coordinator contacted a neuropsychologist or a trained clinical research coordinator to administer a Clinical Dementia Rating (CDR) Scale.

Screening Visit

All eligible participants underwent a comprehensive screening visit approximately one month before baseline assessments to ensure adherence to inclusion criteria and minimize potential confounders. The screening visit began with the informed consent process, where participants reviewed and signed the consent form, ensuring a clear understanding of study procedures and potential risks (Beauchamp & Childress, 2019).

Participants then completed a series of standardized health questionnaires, including demographic and health history assessments, as well as the Stay Independent Screener for fall risk evaluation (Lohman et al., 2017), the Edinburgh Handedness Inventory (Oldfield, 1971), the Telehealth Technology and Skills Access Survey, and the Logical Memory subtest from the Wechsler Memory Scale-Revised (WMS-R) (Tulsky et al., 2003), a well-validated measure of verbal episodic memory. Demographic and comorbidity information were collected from the Project Health Survey (Health Questionnaire). Demographic variables included age, gender, highest level of education, years of education, and ethnicity. The health questionnaire screening assessed comorbidities such as arthritis or rheumatism, asthma or respiratory issues, cancer (excluding skin cancer), cognitive or memory problems, depression, diabetes, epilepsy/seizures, heart conditions, hypertension, joint replacements, osteoporosis, Parkinson’s disease, stroke, vertigo or inner ear disorders, and sleep apnea.

Inclusion Criteria

Participants were required to meet specific inclusion criteria. Participants had to be at least 50 years old and diagnosed with amnestic MCI based on ADNI criteria, which included a subjective memory concern (either self-reported or noted by a partner) and abnormal memory function as determined by performance on the Wechsler Memory Scale-Revised (WMS-R) Logical Memory Test. Education-adjusted cut-off scores were set at <11 for individuals with 16 or more years of education, <9 for those with 8-15 years of education, and <6 for those with fewer than 7 years of education. Cognitive screening scores had to fall within specific ranges, including a Telephone Interview for Cognitive Status (TICS) score of 31-37 and a Montreal Cognitive Assessment (MoCA) score of 18-25. Functional status was also considered, requiring a Clinical Dementia Rating (CDR) score of 0.5 with a Memory Box score of at least 0.5, as well as a Functional Assessment Questionnaire (FAQ) score of ≤ 9. Additionally, participants needed to have the physical ability to walk at least 10 feet with or without an assistive device and possess a minimum of six years of education or a solid work history. In terms of physical activity, they had to engage in less than 150 minutes of moderate or 75 minutes of vigorous aerobic activity per week and must not have participated in any structured exercise program within the past three months.

Exclusion Criteria

Participants were excluded if they had any of the following conditions: acute illness, uncontrolled congestive heart failure, or a history of stroke within the past three years. Those with severe cognitive impairments that would prevent them from completing study procedures were also excluded. The use of certain medications, including antipsychotics, opioids, stimulants, chemotherapy, Parkinson’s medications, or unstable doses of cognitive enhancers, was not permitted. Additionally, individuals with psychiatric disorders such as schizophrenia, bipolar

disorder, or active substance use disorder were excluded, as were those with neurologic conditions including multiple sclerosis, seizure disorders, or a history of traumatic brain injury with more than 30 minutes of loss of consciousness.

Assessments

After confirming eligibility based on predefined inclusion and exclusion criteria, participants underwent a comprehensive evaluation of cognitive, motor, motor-cognitive and vascular function. Vascular metrics included pulse wave velocity, augmentation index, and the Buckberg Subendocardial Viability Ratio (SEVR). Additionally, participants completed questionnaires related to their demographics and health.

Vascular Function Assessment

Participants underwent a vascular function assessment that took about ½ hour to complete. Non-invasive arterial stiffness is the strongest vascular indicator of cognitive decline (Hughes et al., 2014; King, 2014). Pulse-wave velocity (PWV) was measured between carotid and femoral arteries using the Sphygmocor device (Atcor Medical, Australia) that records sequential high-quality pressure waveforms at peripheral pulse sites using a high-fidelity tonometer (Moerland et al., 2012). Digital pulse amplitude tonometry (PAT) was used to measure pulse volume amplitude in the tip of the index finger with participants resting in the supine position in a quiet, temperature-controlled environment and during reactive hyperemia, which was elicited by the release of an upper arm blood pressure cuff inflated to supra-systolic pressure for 5 minutes to assess the augmentation index (AI) using an Endo-PAT (Itamar Medical Israel). PWV and AI provide complimentary information about vascular stiffness. Additionally, the Buckberg Subendocardial Viability Ratio (SEVR) was abstracted from the Pulse Wave Analysis (PWA). The Buckberg SEVR

is also a parameter of arterial stiffness and has an indirect prognostic value in evaluating cardiovascular risk (Onofrei et al., 2022).

Cognitive Assessments

Cognitive assessments included the Montreal Cognitive Assessment (MoCA), which evaluates global cognition across eight domains, with higher scores indicating better cognitive performance (Nasreddine et al., 2005). To assess executive function, processing speed, and cognitive flexibility, the Trail Making Test (TMT A & B) was administered (Corrigan & Hinkeldey, 1987). Planning and problem-solving skills, as components of executive function, were assessed with the Delis Kaplan Executive Function System (D-KEFS) Tower Test which required participants to rearrange disks on pegs to match a specific goal configuration within a set number of moves (Shallice, 1982).

Verbal learning and memory were measured using the Rey Auditory Verbal Learning Test (RAVLT), which includes both immediate and delayed recall trials (Schmidt, 1996). The Boston Naming Test assessed visual confrontation naming and semantic memory (Kaplan et al., 2001) while the Rey-Osterrieth Complex Figure Test evaluated visuospatial construction and memory (Osterrieth, 1944). Working and short-term memory were examined using the Number Span Test (Wechsler, 1997) and the Reverse Corsi Blocks Task, which assesses visuospatial working memory through nonverbal sequences (Vandierendonck et al., 2004). The Corsi Blocks is also a valid measurement of visuospatial function. Visuospatial judgment was measured using Benson's Judgement of Line Orientation (Benton et al., 1994), and executive function, cognitive flexibility, and inhibitory control were evaluated with the D-KEFS Color Word Interference Test, which includes four conditions: color naming, word reading, inhibition, and inhibition/switching (Delis et al., 2001). The Serial 3's Test measured mental status through sequential subtraction (Folstein

et al., 1975). Brooks spatial memory task (Brooks, 1967) is an assessment of spatial cognition and short-term memory that requires participants to use mental imagery in remembering and repeating the placement of 3-8 numbers. Participants receive a visual presentation and verbal explanation of a 4×4 matrix. The researcher tells the participant the position of the numbers, and the participants must remember and repeat the position of the numbers after each trial.

Motor Function Assessments

Motor function was assessed using the Mini-Balance Evaluation Systems (Mini-BEST) Test, a clinical balance assessment tool that is a shortened version of the Balance Evaluation Systems Test (BESTest) and aims to target and identify 6 different balance control systems (Potter, 2015). The Timed Up and Go (TUG) test, which evaluates functional mobility by measuring the time required for participants to rise from a chair, walk three meters, turn around, and return to a seated position (Podsiadlo & Richardson, 1991) was also used to assess motor function. Lower body strength was measured using the 30-Second Chair Stand Test, in which participants were instructed to rise from a chair with arms crossed over the chest as many times as possible within 30 seconds (Jones et al., 1999). Turning ability was measured with the 360° Turn Test, which recorded both the time required to complete a full turn and the number of steps taken, with testing conducted in both right and left directions (Prime et al., 2020). Postural control was examined using the Tandem Stance Test, which evaluates participants' time to maintain a heel-to-toe stance (Shubert et al., 2006). Gait speed was measured in multiple conditions, including preferred walking speed, backward gait speed, and fast-paced walking over a 20-foot distance. Participants were timed using a stopwatch, and speeds were averaged across trials (Studenski et al., 2011).

Motor-Cognitive Assessments

Motor-cognitive integration was assessed through the TUG-Cognitive (TUG-Cog) test, a modified version of TUG in which participants performed serial subtractions while walking to assess divided attention and dual-tasking ability (Morris et al., 2001). The Body Position Spatial Task (BPST), adapted from the Reverse Corsi Blocks test, assessed spatial memory and navigation while maintaining postural control. Participants were required to replicate a series of instructed movements, such as stepping sideways or turning in place, under increasing cognitive load (Battisto et al., 2018). Dynamic balance and motor planning were assessed using the Four Square Step Test (FSST), where participants stepped in four quadrants in a specified order as quickly as possible (Dite & Temple, 2002).

Table 1. Variable Guide

Variable	Higher Score Interpretation	What construct does it measure
Vascular Variables		
Aortic AIx	Worse function	Arterial Stiffness – Derived from Aortic Waveform
Pulse Wave Velocity	Worse function	Arterial Stiffness – Derived from Systemic Arteries
Buckberg Subendocardial Viability Ratio (SEVR)	Better function	Subendocardium – Blood flow and oxygenation
Motor Variables		

Total Mini BEST	Better function	Motor skills (static balance, walking, sensory orientation)
Timed Up and Go (TUG) - single task	Worse function	Motor skills (walking)
Total Dynamic Gait Index	Better function	Dynamic balance: Walking ability in various conditions
Average Single Leg Stance (s)	Better function	Single leg balance ability
Tandem Stance (s)	Better function	Stance balance ability
Tandem Walk (no.)	Worse function	Motor task and balance (number of interruptions)
30 s Chair stand (no.)	Better function	Motor task (seated to standing position)
Gait speed (m/s)	Better function	Distance walking per unit of time
360-degree turn test (s)	Worse function	Time needed to complete a full 360 degree turn to either side
Cognitive Variables		
MoCA (total score)	Better function	Global cognitive domains – attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation

Trail Making Test (B-A difference score)	Worse function	Executive function (trails difference)
D-KEFS Tower Test (Total achievement score)	Better function	Executive function: planning and organization, (achievement score)
Rey Complex Figure Test (RCFT) — Immediate Recall (s)	Worse function	Visuospatial memory and ability, immediate recall
Rey Complex Figure Test (RCFT) — Delayed Recall (s)	Worse function	Visuospatial memory and ability after a delay
Brooks Spatial Memory Test (percent correct)	Better function	Visual spatial working memory (Brooks Spatial Memory Percent Correct)
Benton's Judgement of Line Orientation (JLO)	Better function	Visuospatial processing, spatial orientation (number of correct)
Rey Auditory Verbal Learning Test (RAVLT) — Immediate Recall	Better function	Immediate memory and verbal learning (learning score, forgetting score)
Rey Auditory Verbal Learning Test (RAVLT) — Delayed Recall	Better function	Episodic and verbal memory
Wechsler Memory Scale – Logical Memory	Better function	Verbal memory and recall

Number Span Backward	Better function	Number recall ability (total correct, length of longest correct series) The construct is short term/working memory
Reverse Corsi Block Test	Better function	Short-term (or working) spatial cognitive memory
Serial threes (percent correct)	Worse function	Mental status, calculation
Boston Naming Test	Better function	Common Object Identification
Motor-Cognitive Variables		
Four Square Step Test (FSST)	Worse function	Mobility, dual task ability, balance
Body Position Spatial Task (BPST): span, and total correct trials	Better function	Spatial memory and navigational skills, balance, and mobility
Timed Up and Go (TUG) Manual	Worse function	Motor dual task (walking while carrying a cup of water)
Timed Up and Go (TUG) Cognitive	Worse function	Cognitive function and mobility dual task

Table 1. Variable Guidelines. This table lists the variables used in the analyses, with the instrument name followed by the variable(s) of interest in parentheses. The second column indicates whether higher scores indicate better or worse function. The third column describes the construct being measured by the variables.

Analysis

Variables related to vascular function, motor function, cognitive function, and motor-cognitive integration were abstracted from REDCap for statistical analysis. Descriptive statistics were used to characterize the study population clinically and demographically, including measures of central tendency (mean) and variability (standard deviation). We calculated demographic, clinical, and comorbidity-related variables. All collected data, including questionnaire responses, vascular assessments, and cognitive, motor, and motor-cognitive performance measures, were stored in the REDCap database for secure management and analysis. Statistical analyses were conducted using IBM SPSS version 25 (IBM Corp., Armonk, NY, USA). All p-values were at significance value of 0.05.

Statistical Analysis

We first examined the pairwise correlations among the vascular variables using Pearson's correlation coefficient. To control for multiple comparisons when assessing the significance of the pairwise correlations, we applied the Benjamini–Hochberg procedure to adjust the p-values. This method ranks the individual p-values and controls the expected proportion of false discoveries among the rejected hypotheses. We classified correlations as small ($r = 0.10$), medium ($r = 0.30$), or large ($r = 0.50$) following Cohen’s conventional benchmarks for effect sizes (Cohen, 1988).

We selected the strongest indicators of motor, motor-cognitive and cognitive function variables or variables that exhibited moderate correlations for further investigation. We then assessed the impact of each of the vascular variables on these selected behavioral variables using multiple linear regression analysis. Potential confounding variables, including age, gender, and ethnic background, were included in the regression model to control for their effects.

The significance of the regression coefficients for the vascular variables was evaluated using the Wald test. We also checked the normality assumption through a multivariate normality test. Additionally, we assessed homoscedasticity to ensure that the variance of the residuals was constant across levels of the independent variables, confirming the validity of the regression model.

Missing Data:

76 participants met screening criteria and provided informed consent. However, 3 participants did not complete any baseline assessments and were thus excluded from the data analysis due to lack of data, making our sample size 73 participants. Additionally, some participants did not complete all baseline assessments, decreasing the sample size of the correlational analyses. Specifically, 11 participants did not have either some or all of their vascular data, 17 participants did not have at least one cognitive assessment, 2 participants did not have all their motor data, and 2 participants did not have all their motor-cognitive data. Because of this, sample sizes were reported in all data analysis tables.

Hypothesis/ Research Question

Based on our literature review, we expected to see moderate associations between vascular function and cognitive, motor, and motor-cognitive function in these participants with MCI. We hypothesize greater arterial stiffness as measured by PWV will be associated with lower total MoCA scores, indicating greater cognitive impairment, and lower Mini-BEST scores and Dynamic Gait Indices (DGI), suggesting decreased motor function, and decreased motor-cognitive function as measured by the Four Square Step Test. Additionally, we predict that characteristics such as age and gender may also be implicated in these associations.

Results

Demographic Characteristics

This study included 73 participants with a mean age of 74.6 ± 7.12 years, indicating an older population. Gender distribution was relatively balanced (Male: 43.8%, Female: 56.2%). More than 60% of participant obtained a bachelor's degree or higher. The ethnic distribution was predominantly White/Caucasian (54.8%), followed by Black/African American participants (38.4%). (Table 2).

Table 2. Participant Demographic Characteristics (N = 73)

Demographic Characteristics	Mean (SD)/N (%)
Age (years)	74.6 (7.12)
Gender (Male/Female)	32 (43.8%)/41 (56.2%)
Education Level	
Less than high school graduate	1 (1.4%)
High school graduate/ GED	4 (5.5%)
Vocational training	1 (1.4%)
Some college/ associate's degree	23 (31.5%)
Bachelor's degree (BA, BS)	21 (28.8%)
Master's degree (or other post-graduate training)	17 (23.3%)
Doctoral degree (PhD, MD, EdD,DDS, JD, etc)	6 (8.2%)
Ethnic Background	
Black/ African-American	28 (38.4%)
Hispanic or Latino	2 (2.7%)

White/ Caucasian	40 (54.8%)
Multiracial	3 (4.1%)

Clinical Characteristics

Participants had an average of 3.90 ± 2.1 comorbidities. The most common were high blood pressure (53.4%) and arthritis or rheumatism (50.7%) (Table 3).

Table 3. Participant Clinical Characteristics and Comorbidities (N = 73)

Comorbidity	Mean (SD)/N (%)
Number of Comorbidities	3.90 (2.08)
Arthritis or Rheumatism	37 (50.7%)
Asthma or Breathing Problem	11 (15.1%)
Cancer (Other than Skin)	16 (21.9%)
Depression	22 (30.1%)
Diabetes	16 (21.9%)
Epilepsy/Seizures	0 (0%)
Heart Problems	23 (31.5%)
High Blood Pressure	39 (53.4%)
Joint Replacements	13 (17.8%)
Osteoporosis	9 (12.3%)
Parkinson's Disease	0 (0%)
Stroke	5 (6.8%)
Vertigo or Inner Ear Problem	15 (20.5%)
Sleep Apnea	21 (28.8%)
Other Significant Illness	16 (21.9%)
None	2 (2.7%)

Correlation Between Vascular and Cognitive Function Variables

The correlation analysis revealed weak to moderate associations between vascular function indicators and cognitive function tests.

Average PWV

Average PWV exhibited small correlations with several cognitive function variables. Notably, it showed a correlation of r = 0.24 with the Rey AVLT Immediate (forget score) at a significance level of p = 0.062, suggesting a potential relationship where higher values of Average PWV may be linked to a decline in immediate recall ability. Additionally, a small correlation of r = 0.21 was observed with Rey AVLT Delayed and Recognition (Recognition False Positives) (p = 0.098).

PWA Aortic AIx

AIx showed a moderate correlation of **r = 0.28** with the D-KEFS Color Word Interference Test (Inhibition Scaled Score). AIx had a correlation of **r = -0.2** with total time to complete the Rey Complex Figure Drawing Delayed portion indicating that higher PWA Aortic AIx values are minimally associated with shorter completion times in complex drawing tasks.

PWA Buckberg SEVR

SEVR was moderately negatively correlated with the Inhibition/Switching scaled score of the D-KEFS Color Word Interference Test (r = -0.31), indicating a moderate negative relationship where higher SEVR is associated with less efficient cognitive switching abilities. A small, non-significant correlation was observed between SEVR and Brooks Spatial Memory (% Correct) (r = -0.17). SEVR also showed a minimal correlation with the Wechsler Logical Memory Test (Combined Score) (r = -0.12) (Table 4).

Table 4. Pearson Correlation Between Vascular and Cognitive Function Variables

Vascular Variable	Cognitive Function Variable	Pearson r	P-Value	Correlation Strength	Sample size	Alpha corrected
A. Average PWV	Rey AVLT Immediate (forget score)	0.24	0.062	Small	62	0.00227
	Rey AVLT Delayed and Recognition (Recognition False Positives)	0.21	0.098	Small	62	0.00455
	Reverse Corsi Block Test (Product Score)	0.13	0.318	Small	63	0.0174
	Wechsler Logical Memory Test (Delayed Total Score)	0.13	0.352	Small	52	0.0197
	Number Span Backward (Length of Longest Series)	0.12	0.349	Small	62	0.0189
	Rey Complex Figure Drawing Delayed (Total Time)	0.12	0.369	Small	62	0.0205
	Wechsler Logical Memory Test (Combined Total)	0.11	0.451	Small	52	0.025
	Benton JLO (No. Correct)	0.07	0.574	Weak	62	0.0303
	Number Span Backward (No. Correct)	0.07	0.579	Weak	62	0.0311
	Wechsler Logical Memory Test (Immediate Total Score)	0.07	0.613	Weak	52	0.0318
	Trail Making Test Difference (s)	0.05	0.727	Weak	62	0.0363
	Brooks Spatial Memory (% Correct)	0.04	0.768	Weak	62	0.0379
	D-KEFS Color Word Interference Test (Inhibition/Switching Scaled Score)	0.01	0.948	Weak	62	0.0485
	Rey AVLT Delayed and Recognition (Recognition Hits)	-0.01	0.963	Weak	62	0.0492
	D-KEFS Tower Test (Total Achievement Score)	-0.01	0.916	Weak	63	0.0462
	MoCA	-0.02	0.885	Weak	62	0.0439
	Rey Complex Figure Drawing Immediate Time (s)	-0.02	0.905	Weak	62	0.0455
	Rey AVLT Immediate (Learn Score)	-0.03	0.816	Weak	62	0.0409
	Rey Complex Figure Drawing Copy Time (s)	-0.04	0.758	Weak	62	0.0371
	Boston Naming Test (No. correct)	-0.06	0.625	Weak	62	0.0333
	TUG Cognitive Serial 3s (% Correct)	-0.06	0.657	Weak	63	0.0341
	D-KEFS Color Word Interference Test (Inhibition Scaled Score)	-0.18	0.157	Small	62	0.0099
B. PWA Aortic AIx	D-KEFS Color Word Interference Test (Inhibition Scaled Score)	0.28	0.019	Small	68	0.00152
	Number Span Backward (No. Correct)	0.16	0.206	Small	68	0.0121

	Number Span Backward (Length of Longest Series)	0.16	0.196	Small	68	0.0114
	Rey AVLT Delayed and Recognition (Recognition False Positives)	0.12	0.341	Small	68	0.0182
	D-KEFS Color Word Interference Test (Inhibition/Switching Scaled Score)	0.02	0.843	Weak	68	0.0424
	Rey AVLT Delayed and Recognition (Recognition Hits)	0.02	0.894	Weak	68	0.0447
	Benton JLO (No. Correct)	0.01	0.924	Weak	68	0.047
	Boston Naming Test (No. Correct)	0.00	0.985	Weak	68	0.05
	Brooks Spatial Memory (% Correct)	-0.02	0.864	Weak	68	0.0432
	Rey AVLT Immediate (forget score)	-0.03	0.793	Weak	68	0.0394
	Wechsler Logical Memory Test (Delayed Total Score)	-0.03	0.84	Weak	57	0.0417
	Trail Making Test Difference (s)	-0.05	0.666	Weak	68	0.0349
	Wechsler Logical Memory Test (Combined Score)	-0.06	0.677	Weak	57	0.0356
	Wechsler Logical Memory Test (Immediate Total Score)	-0.08	0.556	Weak	57	0.0288
	Rey Complex Figure Drawing Copy Time (s)	-0.10	0.43	Weak	68	0.0235
	TUG Cognitive Serial 3s (% Correct)	-0.13	0.298	Small	69	0.0167
	MoCA	-0.19	0.122	Small	68	0.00758
	Rey Complex Figure Drawing Immediate Time (s)	-0.20	0.108	Small	67	0.00606
	Rey Complex Figure Drawing Delayed (Total Time)	-0.20	0.11	Small	68	0.00682
	Reverse Corsi Block Test (product score)	-0.20	0.106	Small	69	0.0053
	D-KEFS Tower Test (Total Achievement Score)	-0.21	0.082	Small	69	0.00379
	Rey AVLT Immediate (Learn Score)	-0.22	0.067	Small	68	0.00303
C. PWA Buckberg SEVR%	D-KEFS Tower Test (Total Achievement Score)	0.14	0.239	Small	69	0.0144
	Rey AVLT Delayed and Recognition (Recognition False Positives	0.13	0.297	Small	68	0.0159
	Trail Making Test Difference (s)	0.10	0.399	Small	68	0.022
	Rey Complex Figure Drawing Delayed (Total Time)	0.03	0.794	Weak	68	0.0402
	Rey Complex Figure Drawing Immediate Time (s)	-0.01	0.945	Weak	67	0.0477
	Benton JLO (No. Correct)	-0.03	0.784	Weak	68	0.0386
	Rey Complex Figure Drawing Copy Time (s)	-0.07	0.562	Weak	68	0.0296
	Wechsler Logical Memory Test (Delayed Total Score)	-0.07	0.619	Weak	57	0.0326
	Number Span Backward (Length of Longest Series)	-0.08	0.492	Weak	68	0.028
	Rey AVLT Immediate (Forget score)	-0.09	0.48	Weak	68	0.0273

Rey AVLT Delayed and Recognition (Recognition Hits)	-0.09	0.464	Weak	68	0.0265
TUG Cognitive Serial 3s (% Correct)	-0.09	0.463	Weak	62	0.0258
Rey AVLT Immediate (Learn score)	-0.10	0.434	Weak	68	0.0242
D-KEFS Color Word Interference Test (Inhibition Scaled Score)	-0.10	0.399	Small	68	0.0227
Wechsler Logical Memory Test (Combined Score)	-0.12	0.374	Small	57	0.0212
Reverse Corsi Block Test (Product Score)	-0.13	0.288	Small	69	0.0152
Number Span Backward (No. Correct)	-0.15	0.234	Small	68	0.0136
Wechsler Logical Memory Test (Immediate Total Score)	-0.16	0.233	Small	57	0.0129
Brooks Spatial Memory (% Correct)	-0.17	0.173	Small	68	0.0106
MoCA	-0.18	0.146	Small	68	0.00909
Boston Naming Test (No. Correct)	-0.18	0.131	Small	68	0.00833
D-KEFS Color Word Interference Test (Inhibition/Switching Scaled Score)	-0.31	0.01	Medium /Moderate	68	0.00076

Correlation Between Vascular and Motor Function Variables

Average PWV

Average PWV demonstrated moderate negative correlations with several motor function measures. A notable correlation of r = -0.33 was observed with the DGI (Total Score) (r = -0.33, p = 0.008), indicating that higher average PWV is associated with reduced overall mobility. Additionally, a correlation of r = -0.31 was found with Single Leg Stance Average Time (p = 0.013), suggesting that greater PWV values may be related to greater postural instability. Smaller correlations were also noted for Tandem Leg Stance Average Time (r = -0.27, p = 0.032), and Average Forward Gait Speed (r = -0.27, p = 0.034) were associated with PWV, indicating that greater PWV could be related to decreased mobility, postural stability and gait speed.

PWA Aortic AIx

With AIx, a correlation of r = 0.23 (p = 0.055) was observed with the TUG Single Task (s). Additionally, AIx was correlated with DGI (Total Score) (r = -0.19, p = 0.122) and 30s Chair Stand (r = -0.17, p = 0.159).

PWA Buckberg SEVR

The Buckberg SEVR also showed small correlations with motor function. The highest correlation was observed with Tandem Leg Stance Average Time (r = 0.21, p = 0.083), suggesting a potential association where higher SEVR may be linked to better performance in balance-related tasks. (Table 5).

Table 5: Pearson Correlation Between Vascular and Motor Function Variables

Vascular Variable	Motor Function Variable	Pearson r	P-Value	Correlation Strength	Sample size	Corrected Alpha
A. Average PWV	TUG Single Task (s)	0.24	0.058	Small	63	0.01
	Tandem Walk (No. of interruptions)	0.22	0.087	Small	63	0.0133
	360 Degree Turn Test Max Time (s)	0.09	0.464	Weak	63	0.0333
	Average Fast Gait Speed (m/s)	-0.07	0.588	Weak	63	0.0383
	Average Backward Gait Speed (m/s)	-0.21	0.091	Small	63	0.0167
	30s Chair Stand (No.)	-0.22	0.088	Small	63	0.015
	Tandem Leg Stance Average Time (s)	-0.27	0.032	Small	63	0.005
	Average Forward Gait Speed (m/s)	-0.27	0.034	Small	63	0.00667
	Single Leg Stance Average Time (s)	-0.31	0.013	Medium/Moderate	63	0.00333
	DGI (Total Score)	-0.33	0.008	Medium/Moderate	63	0.00167
P · B	TUG Single Task (s)	0.23	0.055	Small	69	0.00833

	Tandem Walk (No. of interruptions)	0.07	0.591	Weak	69	0.04
	360 Degree Turn Test Max Time (s)	0.04	0.768	Weak	69	0.045
	Single Leg Stance Average Time (s)	-0.02	0.859	Weak	69	0.0467
	Tandem Leg Stance Average Time (s)	-0.08	0.5	Weak	69	0.0367
	Average Fast Gait Speed (m/s)	-0.09	0.466	Weak	69	0.035
	Average Backward Gait Speed (m/s)	-0.14	0.258	Small	69	0.025
	30s Chair Stand (No.)	-0.17	0.159	Small	69	0.0217
	DGI (Total Score)	-0.19	0.122	Small	69	0.02
	Average Forward Gait Speed (m/s)	-0.19	0.113	Small	69	0.0183
C. PWA Buckberg SEVR	Tandem Leg Stance Average Time (s)	0.21	0.083	Small	69	0.0117
	DGI (Total Score)	0.17	0.167	Small	69	0.0233
	Average Forward Gait Speed (m/s)	0.13	0.276	Small	69	0.0267
	Single Leg Stance Average Time (s)	0.11	0.365	Small	69	0.0283
	Average Backward Gait Speed (m/s)	0.11	0.37	Small	69	0.03
	30s Chair Stand (No.)	0.06	0.635	Weak	69	0.0417
	Average Fast Gait Speed (m/s)	0.04	0.75	Weak	69	0.0433
	TUG Single Task (s)	0.02	0.9	Weak	69	0.0483
	360 Degree Turn Test Max Time (s)	-0.01	0.905	Weak	69	0.05
	Tandem Walk (No. of interruptions)	-0.09	0.453	Weak	69	0.0317

Correlation strengths are categorized as Weak, Small, Medium/Moderate, and Large/Strong

Correlation Between Vascular and Motor-Cognitive Function

Average PWV

Average PWV displayed small correlations with specific motor-cognitive measures. A correlation of r = 0.22 (p = 0.09) was observed with TUG Manual, suggesting that higher PWV may be associated with longer task completion times in this motor-cognitive task. A similar

correlation was noted with TUG Cognitive Dual Task (s) (r = 0.19, p = 0.139), implying increased average PWV may negatively influence dual-task performance.

PWA Aortic Aix

The PWA Aortic AIx exhibited small correlations with motor-cognitive measures, though weaker than PWV. A correlation of r = 0.15 (p = 0.228) was found with FSST (Best Time). However, correlations with TUG Manual (s) (r = 0.02, p = 0.89) and TUG Cognitive Dual Task (s) (r = 0.03, p = 0.783) were weak, indicating no strong influence on motor-cognitive performance.

PWA Buckberg SEVR

The PWA Buckberg SEVR showed small correlations with a few motor-cognitive function measures. The strongest association was observed with FSST (Best Time) (r = -0.18, p = 0.146), suggesting that higher SEVR may be linked to shorter task completion times. Other correlations, including BPST (Product Score) (r = 0.09, p = 0.476) and TUG Cognitive Dual Task (s) (r = 0.08, p = 0.496), were very weak, reinforcing that SEVR has a minimal relationship with motor-cognitive integration (Table 6).

Table 6: Pearson Correlation Between Vascular and Motor-Cognitive Function

Vascular Variable	Motor Cognitive Function Variable	Pearson r	P-Value	Correlation Strength	Sample Size	corrected Alpha
A. Average PWV	TUG Manual (s)	0.22	0.09	Small	63	0.00333
	TUG Cognitive Dual Task (s)	0.19	0.139	Small	63	0.00667
	BPST (Product of Span and Trials)	0.12	0.336	Small	63	0.0167
	TUG Cognitive (% correct)	-0.01	0.912	Weak	63	0.0433
	FSST (Best Time)	-0.02	0.871	Weak	63	0.0367

B. PWA Aortic AIx	FSST (Best Time)	0.15	0.228	Small	69	0.0133
	TUG Cognitive Dual Task (s)	0.03	0.783	Weak	69	0.0333
	TUG Manual (s)	0.02	0.89	Weak	69	0.04
	TUG Cognitive Dual Task (% correct)	-0.01	0.936	Weak	69	0.0467
	BPST (Product of Span and Trials)	-0.1	0.42	Weak	69	0.02
	BPST (Product of Span and Trials	0.09	0.476	Weak	69	0.0233
C. PWA Buckberg SEVR	TUG Cognitive Dual Task (s)	0.08	0.496	Weak	69	0.0267
	TUG Manual (s)	0.04	0.719	Weak	69	0.03
	TUG Cognitive Dual Task (% correct)	0	0.986	Weak	69	0.05
	FSST (Best Time)	-0.18	0.146	Small	69	0.01

Multivariate Regression Analysis of Age and Gender and Vascular Variables

Multivariate regression analyses revealed that advancing age was significantly associated with increased arterial stiffness, particularly within Aortic AIx ($\beta = 0.5$, $p = 0.046$). Gender differences were also noted with higher Aortic AIx in males ($\beta = 7.4$, $p = 0.033$) and lower Buckberg SEVR in males ($\beta = -15.4$, $p = 0.023$), suggesting that male and female participants may experience differential vascular responses as they age (Table 7).

Table 7: Multivariate Regression Model Coefficients for the Effect of Age and Gender on Vascular Variables (N = 62)

response	term	estimate	std.error	p.value
Average PWV	age	0.1	0.0	0.123
	gender	-1.0	0.6	0.102
Aortic AIx	age	0.5	0.2	0.046*
	gender	7.4	3.4	0.033*

Buckberg SEVR	age	-0.7	0.4	0.109
	gender	-15.4	6.6	0.023*

Multivariate Regression Analysis of Vascular Variables and Motor-Cognitive, Motor and Cognitive Function Adjusted for Age, Gender, and Ethnic Background

Four Square Step Test (FSST - Best Time)

Average PWV demonstrated a negative association with FSST scores (β = -0.17, SE = 0.18, p = 0.345), though this result was not statistically significant. Similarly, PWA Buckberg SEVR showed a small negative association (β = -0.03, SE = 0.02, p = 0.104), In contrast, PWA Aortic AIx exhibited a small positive association (β = 0.06, SE = 0.03, p = 0.078).

Timed Up and Go (TUG) Cognitive Dual Task (Time in Seconds)

In the Timed Up and Go (TUG) Cognitive Dual Task, average PWV had a non-significant positive association (β = 0.52, SE = 0.37, p = 0.172).

Mini-Balance Evaluation Systems Test (Mini-BEST - Total Score)

For the Mini-BEST Total Score, average PWV was significantly associated with lower Mini-BEST scores (β = -0.38, SE = 0.16, p = 0.022).

D-KEFS Color Word Interference Test (Inhibition/Switching Scaled Score)

For the D-KEFS Color Word Interference Test (Inhibition/Switching Scaled Score), no significant associations were found between average PWV (β = 0.04, SE = 0.26, p = 0.864) or PWA Aortic AIx (β = 0.00, SE = 0.05, p = 0.952) and executive function performance. However, PWA Buckberg SEVR showed a negative association that approached statistical significance (β = -0.05, SE = 0.02, p = 0.051).

Montreal Cognitive Assessment (MoCA - Total Score)

In the Montreal Cognitive Assessment (MoCA - Total Score), average PWV showed no significant relationship with MoCA scores ($\beta = 0.16$, SE = 0.21, $p = 0.447$). However, PWA Aortic AIx was significantly associated with lower MoCA scores ($\beta = -0.08$, SE = 0.04, $p = 0.043$) (Table 8).

Table 8. Multivariate Regression Model Coefficient for the Effect of Vascular Variables and Motor-Cognitive, Motor, and Cognitive Function Adjusted for Age, Gender, and Ethnic Background (N = 62)

Dependent	Term	Estimate	std.error	p.value
A. FSST (Best Time)	Average PWV	-0.17	0.18	0.345
	PWA Aortic AIx	0.06	0.03	0.078
	PWA Buckberg SEVR	-0.03	0.02	0.104
B. TUG Cognitive Dual Task (s)	Average PWV	0.52	0.37	0.172
	PWA Aortic AIx	0.00	0.07	0.974
	PWA Buckberg SEVR	0.03	0.03	0.458
C. Mini-BEST (Total Score)	Average PWV	-0.38	0.16	0.022*
	PWA Aortic AIx	-0.03	0.03	0.276
	PWA Buckberg SEVR	0.02	0.01	0.163
D. D-KEFS Color Word Interference Test	Average PWV	0.04	0.26	0.864
	PWA Aortic AIx	0.00	0.05	0.952

(Inhibition/Switching Scaled Score)	PWA Buckberg SEVR	-0.05	0.02	0.051
E. MoCA (Total Score)	Average PWV	0.16	0.21	0.447
	PWA Aortic AIx	-0.08	0.04	0.043*
	PWA Buckberg SEVR	-0.01	0.02	0.487

Discussion

Cardiovascular diseases (CVDs) remain the leading cause of global mortality, accounting for approximately 17.9 million deaths annually, as reported by the World Health Organization (WHO, 2021). A growing body of evidence highlights the critical role of vascular health in maintaining cognitive and motor functions, particularly in older adults. This study investigated the relationship between aspects of vascular function including arterial stiffness, aortic augmentation index, and subendocardial viability ratio and their association with cognitive-motor performance in older individuals with MCI. Additionally, the influence of age and gender on these relationships was examined.

The results revealed a weak but significant correlation between arterial stiffness and cognitive performance, while a moderate negative correlation was observed between PWV and motor function. Furthermore, a significant association was found between advancing age and increased arterial stiffness, underscoring the role of vascular aging in functional decline.

Cognitive Function and Vascular Health in MCI Patients

This study's findings reveal a weak but significant association between increased arterial stiffness and cognitive deficits in patients with MCI. Specific cognitive domains affected include executive function, information processing speed, attention, and memory. These outcomes are

consistent with the work of Nordlund et al. (2007), which indicated that MCI patients with vascular disease exhibit more severe cognitive impairments compared to their non-vascular counterparts. Similarly, Siuda et al. (2007) demonstrated that MCI patients with vascular risk factors face greater deficits in learning, short-term memory, and information retrieval. Our findings further support the notion that vascular aging may exacerbate cognitive decline through mechanisms such as reduced cerebral blood flow, oxidative stress, and neurovascular uncoupling.

The link between vascular health and cognitive function is reinforced by Viticchi et al. (2012), who found that structural and functional vascular abnormalities, including increased intima-media thickness (IMT) and carotid plaque index, correlate with a higher risk of MCI progressing to AD. Moreover, Lorius et al. (2015) highlighted that vascular risk factors such as hypertension and atherosclerosis contribute to accelerated cognitive decline. Collectively, these findings emphasize the importance of maintaining vascular health in preserving cognitive function and suggest that interventions targeting vascular risk factors may help mitigate cognitive decline in MCI patients.

Nonetheless, some studies present conflicting evidence. Cheng et al. (2023) suggested that vascular aging does not always correlate with cognitive decline, as individual factors like cognitive resilience, genetics, and lifestyle may influence this relationship. While our study indicates a clear connection between vascular parameters and cognitive performance, these conflicting results underscore the need for further research to delve into the complex interplay between vascular health and cognitive function.

Motor Function and Vascular Health in MCI Patients

In terms of motor function, our study uncovered a moderate negative correlation between arterial stiffness and motor performance, particularly in balance, postural stability, and gait. This aligns with findings from Frisoni et al. (2002), who reported that MCI patients with vascular features have poorer balance and gait stability compared to those with degenerative MCI. Stojkovic et al. (2018) further supported this, suggesting that vascular risk factors and white matter lesions (WML) correlate with motor impairments in MCI, Parkinson's disease, and dementia.

These results reinforce the hypothesis that vascular aging contributes to motor dysfunction due to reduced perfusion to motor-related brain areas and impaired neurovascular coupling. A systematic review by Koppelmans et al. (2022) underscored that MCI and Alzheimer's patients frequently exhibit widespread motor deficits, including reduced gait speed and impaired motor control, likely as a result of diminished cerebral blood flow and altered motor-cognitive interactions. Fitzgibbon-Collins et al. (2024) also reported an association between increased pulsatility index (PI) in the middle cerebral artery and reduced gait speed, supporting our observation linking arterial stiffness to motor performance.

However, some literature suggests that the relationship between vascular health and motor function might be influenced by other factors. For instance, Ishihara et al. found that activities of daily living (ADL) had a stronger correlation with cognitive decline than motor variables like gait speed and balance. Additionally, Cheng et al. (2023) posited that factors such as physical activity and vascular resilience could play a protective role, indicating that vascular aging does not universally lead to motor decline. This complexity highlights the necessity of further research to elucidate the intricate relationship between vascular health and motor function in individuals with prodromal AD.

Multivariate Regression Analysis

Initial correlation analyses revealed associations between vascular health and variables of motor, motor-cognitive, and cognitive performance that ranged from weak to moderate in strength.

These relationships were examined through multivariate regression models that controlled for confounding factors such as age, gender, and ethnic background. Results demonstrated that Aortic AIx% were significantly associated with MoCA total scores, suggesting that vascular efficiency is directly linked to cognitive performance. Conversely, after adjusting for age and gender, PWV did not show a significant association with cognitive function, implying that previous correlations may have been confounded by age-related vascular changes.

For motor function, the Mini BEST Total Score exhibited a moderate negative multivariate regression with PWV, confirming that greater arterial stiffness impairs postural stability. Additionally, Buckberg SEVR% was significantly associated with the FSST Best Score, indicating that vascular efficiency affects dynamic balance and stepping ability. These findings reinforce the vascular hypothesis of functional decline, underlining the role of arterial stiffness in motor impairments and highlighting the significance of vascular self-regulation in maintaining cognitive resilience.

Impact of Age and Gender on Vascular Health and Cognitive-Motor Function

Multivariate regression analysis indicated that vascular aging is a natural process associated with increasing age, resulting in heightened arterial stiffness and decreased vascular efficiency. Specifically, older age correlated significantly with higher Aortic AIx%, signifying

increased arterial stiffness and diminished elasticity of central arteries. These findings align with Moreau et al. (2020), who noted that vascular aging accompanies reduced arterial elasticity.

The study also identified gender differences in vascular function. Men exhibited higher Aortic AIx% and lower SEVR% compared to women, suggesting a greater risk for atherosclerosis and decreased vascular efficiency among men. This aligns with Maier et al. (2023), who found that vascular aging commences earlier in men but accelerates in women post-menopause. Additionally, Ji et al. (2022) emphasized that sex differences in vascular aging may arise from complex interactions among hormones, lifestyle, and environmental factors.

Given that vascular dysfunction is a modifiable risk factor, these results highlight the necessity for incorporating vascular health monitoring into assessments of cognitive aging. Future preventive strategies, including aerobic exercise, antihypertensive therapy, and dietary interventions, should be explored as potential approaches to mitigate vascular contributions to cognitive and motor decline. Future research should also focus on personalized vascular health strategies tailored to at-risk populations to enhance functional independence among aging individuals.

Limitations of the Study

This study has several limitations that should be acknowledged. First, its cross-sectional design means that the findings are correlational and cannot establish causality between vascular health and motor-cognitive function. Additionally, the lack of a control group comprising healthy older adults limits our ability to draw deeper insights regarding the effects of vascular aging. Lastly, the study primarily focused on arterial stiffness while neglecting other essential vascular factors such as blood pressure, cholesterol levels, and inflammation, which could also influence cognitive and motor outcomes.

Suggestions for Future Research

Future research should explore various avenues to enhance understanding of the relationship between vascular health and cognitive-motor function. Investigating sex differences and the potential impact of hormonal variations on vascular health would provide valuable insights. Additionally, studies should examine the effects of therapeutic interventions, such as aerobic exercise and antihypertensive medications, on cognitive and motor function in older adults. Longitudinal studies would also be beneficial in assessing vascular changes over time and identifying predictors of cognitive decline. Moreover, including a control group of healthy older adults in future research would facilitate more precise comparisons and strengthen the findings.

Conclusion

This study underscores the intricate relationship between vascular health and cognitive-motor function in older adults with MCI. Increased arterial stiffness was linked to diminished cognitive and motor performance, although the extent of these associations varied. Notably, age and gender differences in vascular health emerged as significant factors, highlighting the necessity for personalized interventions aimed at maintaining functional independence in this population. These findings emphasize the importance of early interventions that target vascular risk factors to help mitigate cognitive and motor decline among aging individuals, increasing the quality of life for older adults and decreasing healthcare burden.

Author Contributions:

Sarah Solano, Forouzan Rafiei, Amir Nekoei, Matt Lamsey, Madeleine Hackney

References

Abbruzzese, G., Marchese, R., Avanzino, L., & Pelosin, E. (2016). Rehabilitation for Parkinson's disease: current outlook and future challenges. Parkinsonism & related disorders, 22, S60-S64.

Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, Gamst A, Holtzman DM, Jagust WJ, Petersen RC, Snyder PJ, Carrillo MC, Thies B, Phelps CH. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011 May;7(3):270-9. doi: 10.1016/j.jalz.2011.03.008. Epub 2011 Apr 21. PMID: 21514249; PMCID: PMC3312027.

Alzheimer's Disease International. 2024. World Alzheimer Report 2024: Global changes in attitudes to dementia. London, England: Alzheimer's Disease International.

Aursulesei Onofrei V, Ceasovschih A, Anghel RC, Roca M, Marcu DTM, Adam CA, Mitu O, Cumpat C, Mitu F, Crisan A, Haba CMS, Artene B. Subendocardial Viability Ratio Predictive Value for Cardiovascular Risk in Hypertensive Patients. Medicina (Kaunas). 2022 Dec 22;59(1):24. doi: 10.3390/medicina59010024. PMID: 36676648; PMCID: PMC9862049.

Battisto J, Echt KV, Wolf SL, Weiss P, Hackney ME. The Body Position Spatial Task, a Test of Whole-Body Spatial Cognition: Comparison Between Adults With and Without Parkinson Disease. Neurorehabil Neural Repair. 2018 Nov;32(11):961-975. doi: 10.1177/1545968318804419. Epub 2018 Oct 15. PMID: 30317924; PMCID: PMC6226349.

Beauchamp T, Childress J. Principles of Biomedical Ethics: Marking Its Fortieth Anniversary. Am J Bioeth. 2019 Nov;19(11):9-12. doi: 10.1080/15265161.2019.1665402. PMID: 31647760.

Benton AL. Contributions to neuropsychological assessment: A clinical manual. Oxford university press; 1994.

Bowie CR, Harvey PD. Administration and interpretation of the Trail Making Test. Nat Protoc. 2006;1(5):2277-81. doi: 10.1038/nprot.2006.390. PMID: 17406468.

Brooks LR. The suppression of visualization by reading. The Quarterly journal of experimental psychology. 1967 Nov 1;19(4):289-99.

Cao K, Bay AA, Hajjar I, Wharton W, Goldstein F, Qiu D, Prusin T, McKay JL, Perkins MM, Hackney ME. Rationale and Design of the PARTNER Trial: Partnered Rhythmic Rehabilitation for Enhanced Motor-Cognition in Prodromal Alzheimer's Disease. J Alzheimers Dis. 2023;91(3):1019-1033. doi: 10.3233/JAD-220783. PMID: 36530084; PMCID: PMC10105523.

Cheng, D. C., R. E. Climie, M. Shu, S. M. Grieve, R. Kozor and G. A. Figtree (2023). "Vascular aging and cardiovascular disease: pathophysiology and measurement in the coronary arteries." Frontiers in cardiovascular medicine 10: 1206156.

Cohen J (1988). Statistical Power Analysis for the Behavioral Sciences, 2nd ed., Hillsdale, NJ: Lawrence Erlbaum.

Corrigan JD, Hinkeldey NS. Relationships between parts A and B of the Trail Making Test. J Clin Psychol. 1987 Jul;43(4):402-9. doi: 10.1002/1097-4679(198707)43:4<402::aid-jclp2270430411>3.0.co;2-e. PMID: 3611374.

Craighead, D. H., Freeberg, K. A., & Seals, D. R. (2019). The protective role of regular aerobic exercise on vascular function with aging. Current Opinion in Physiology, 10, 55-63.

Delis DC, Kaplan E, Kramer JH. Delis-Kaplan executive function system. Assessment. 2001 Jan 1.

Dite W, Temple VA. A clinical test of stepping and change of direction to identify multiple falling older adults. Arch Phys Med Rehabil. 2002 Nov;83(11):1566-71. doi: 10.1053/apmr.2002.35469. PMID: 12422327.

Feng Q, Ding Z. MRI Radiomics Classification and Prediction in Alzheimer's Disease and Mild Cognitive Impairment: A Review. Curr Alzheimer Res. 2020;17(3):297-309. doi: 10.2174/1567205017666200303105016. PMID: 32124697.

Fitzgibbon-Collins, L. K., G. B. Coombs, M. Noguchi, S. Parihar, R. L. Hughson, M. Borrie, S. Peters, J. K. Shoemaker and J. Bhangu (2024). "Standing middle cerebral artery velocity predicts cognitive function and gait speed in older adults with cognitive impairment, and is impacted by sex differences." Cerebral circulation-cognition and behavior 6: 100198.

Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”: a practical method for grading the cognitive state of patients for the clinician. Journal of psychiatric research. 1975 Nov 1;12(3):189-98.

Forlenza OV, Diniz BS, Stella F, Teixeira AL, Gattaz WF. Mild cognitive impairment. Part 1: clinical characteristics and predictors of dementia. Braz J Psychiatry. 2013 Apr-Jun;35(2):178-85. doi: 10.1590/1516-4446-2012-3503. PMID: 23904025.

Frisoni, G. B., S. Galluzzi, L. Bresciani, O. Zanetti and C. Geroldi (2002). "Mild cognitive impairment with subcortical vascular features: clinical characteristics and outcome." Journal of Neurology 249: 1423-1432.

Geda YE. Mild cognitive impairment in older adults. Curr Psychiatry Rep. 2012 Aug;14(4):320-7. doi: 10.1007/s11920-012-0291-x. PMID: 22773365; PMCID: PMC3963488.

Hughes, T. M., Kuller, L. H., Barinas-Mitchell, E. J., McDade, E. M., Klunk, W. E., Cohen, A. D., Mathis, C. A., DeKosky, S. T., Price, J. C., & Lopez, O. L. (2014). Arterial stiffness and β-amyloid progression in nondemented elderly adults. JAMA neurology, 71(5), 562-568.

Iluț, S., Vesa, Ş. C., Văcăraș, V., Brăiță, L., Dăscălescu, V.-C., Fantu, I., & Mureșanu, D.-F. (2023). Biological risk factors influencing vascular cognitive impairments: a review of the evidence. Brain Sciences, 13(7), 1094.

Ji, H., A. C. Kwan, M. T. Chen, D. Ouyang, J. E. Ebinger, S. P. Bell, T. J. Niiranen, N. A. Bello and S. Cheng (2022). "Sex differences in myocardial and vascular aging." Circulation research 130(4): 566-577.

Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. Res Q Exerc Sport. 1999 Jun;70(2):113-9. doi: 10.1080/02701367.1999.10608028. PMID: 10380242.

Jongsiriyanyong S, Limpawattana P. Mild Cognitive Impairment in Clinical Practice: A Review Article. Am J Alzheimers Dis Other Demen. 2018 Dec;33(8):500-507. doi: 10.1177/1533317518791401. Epub 2018 Aug 1. PMID: 30068225; PMCID: PMC10852498.

Kaplan E, Goodglass H, Weintraub S (2001) Boston Naming Test.

King, K. S. (2014). Arterial stiffness as a potential determinant of β-amyloid deposition. JAMA neurology, 71(5), 541-542.

Koppelmans, V., B. Silvester and K. Duff (2022). "Neural mechanisms of motor dysfunction in mild cognitive impairment and Alzheimer's disease: A systematic review." Journal of Alzheimer's Disease Reports 6(1): 307-344.

Lohman MC, Crow RS, DiMilia PR, Nicklett EJ, Bruce ML, Batsis JA. Operationalisation and validation of the Stopping Elderly Accidents, Deaths, and Injuries (STEADI) fall risk algorithm in a nationally representative sample. J Epidemiol Community Health. 2017 Dec;71(12):1191-1197. doi: 10.1136/jech-2017-209769. Epub 2017 Sep 25. PMID: 28947669; PMCID: PMC5729578.

Long, S., Benoist, C., & Weidner, W. World Alzheimer Report 2023: Reducing Dementia Risk: Never Too Early. Never Too Late.

Lorius, N., J. J. Locascio, D. M. Rentz, K. A. Johnson, R. A. Sperling, A. Viswanathan, G. A. Marshall and A. s. D. N. Initiative (2015). "Vascular disease and risk factors are associated with cognitive decline in the alzheimer disease spectrum." Alzheimer Disease & Associated Disorders 29(1): 18-25.

Maier, J. A., V. Andrés, S. Castiglioni, A. Giudici, E. S. Lau, J. Nemcsik, F. Seta, P. Zaninotto, M. Catalano and N. M. Hamburg (2023). "Aging and vascular disease: a multidisciplinary overview." Journal of Clinical Medicine 12(17): 5512.

Manly, Jennifer J., Richard N. Jones, Kenneth M. Langa, Lindsay H. Ryan, Deborah A. Levine, Ryan McCammon, Steven G. Heeringa, and David Weir. "Estimating the prevalence of dementia and mild cognitive impairment in the US: the 2016 health and retirement study harmonized cognitive assessment protocol project." JAMA neurology 79, no. 12 (2022): 1242-1249.

Moerland, M., Kales, A., Schrier, L., Van Dongen, M., Bradnock, D., & Burggraaf, J. (2012). Evaluation of the EndoPAT as a tool to assess endothelial function. International journal of vascular medicine, 2012(1), 904141.

Mok VCT, Cai Y, Markus HS. Vascular cognitive impairment and dementia: Mechanisms, treatment, and future directions. Int J Stroke. 2024 Oct;19(8):838-856. doi: 10.1177/17474930241279888. PMID: 39283037; PMCID: PMC11490097.

Montero-Odasso, M., & Speechley, M. (2018). Falls in cognitively impaired older adults: implications for risk assessment and prevention. Journal of the American Geriatrics Society, 66(2), 367-375.

Moreau KL, Babcock MC, Hildreth KL. Sex differences in vascular aging in response to testosterone. Biol Sex Differ. 2020 Apr 15;11(1):18. doi: 10.1186/s13293-020-00294-8. PMID: 32295637; PMCID: PMC7161199.

Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. Int Psychogeriatr. 1997;9 Suppl 1:173-6; discussion 177-8. doi: 10.1017/s1041610297004870. PMID: 9447441.

Morris S, Morris ME, Iansek R. Reliability of measurements obtained with the Timed "Up & Go" test in people with Parkinson disease. Phys Ther. 2001 Feb;81(2):810-8. doi: 10.1093/ptj/81.2.810. PMID: 11175678.

Mueller SG, Weiner MW, Thal LJ, Petersen RC, Jack C, Jagust W, Trojanowski JQ, Toga AW, Beckett L (2005) The Alzheimer's disease neuroimaging initiative. Neuroimag Clin 15, 869-877.

Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, Cummings JL, Chertkow H. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005 Apr;53(4):695-9. doi: 10.1111/j.1532-5415.2005.53221.x. Erratum in: J Am Geriatr Soc. 2019 Sep;67(9):1991. doi: 10.1111/jgs.15925. PMID: 15817019.

Nordlund, A., S. Rolstad, O. Klang, K. Lind, S. Hansen and A. Wallin (2007). "Cognitive profiles of mild cognitive impairment with and without vascular disease." Neuropsychology 21(6): 706.

Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia. 1971 Mar;9(1):97-113. doi: 10.1016/0028-3932(71)90067-4. PMID: 5146491.

Petersen RC, Aisen PS, Beckett LA, et al. Alzheimer's Disease Neuroimaging Initiative (ADNI): clinical characterization. Neurology. Jan 19 2010;74(3):201-9. doi:10.1212/WNL.0b013e3181cb3e25

Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991 Feb;39(2):142-8. doi: 10.1111/j.1532-5415.1991.tb01616.x. PMID: 1991946.

Potter, K. and K. Brandfass, The Mini-Balance Evaluation Systems Test (Mini-BESTest). J Physiother, 2015. 61(4): p. 225.

Prime M, McKay JL, Bay AA, Hart AR, Kim C, Abraham A, Hackney ME. Differentiating Parkinson Disease Subtypes Using Clinical Balance Measures. J Neurol Phys Ther. 2020 Jan;44(1):34-41. doi: 10.1097/NPT.0000000000000297. PMID: 31834219; PMCID: PMC6991154.

Rajeev, V., Chai, Y. L., Poh, L., Selvaraji, S., Fann, D. Y., Jo, D.-G., De Silva, T. M., Drummond, G. R., Sobey, C. G., & Arumugam, T. V. (2023). Chronic cerebral hypoperfusion: a critical feature in unravelling the etiology of vascular cognitive impairment. Acta neuropathologica communications, 11(1), 93.

Schmidt M (1996) Rey auditory verbal learning test: A handbook, Western Psychological Services Los Angeles, CA

Shallice T. Specific impairments of planning. Philosophical Transactions of the Royal Society of London. B, Biological Sciences. 1982 Jun 25;298(1089):199-209.

Shubert TE, Schrodt LA, Mercer VS, Busby-Whitehead J, Giuliani CA. Are scores on balance screening tests associated with mobility in older adults? J Geriatr Phys Ther. 2006;29(1):35-9. PMID: 16630375.

Siuda, J., A. Gorzkowska, G. Opala and S. Ochudło (2007). "Vascular risk factors and intensity of cognitive dysfunction in MCI." Journal of the neurological sciences 257(1-2): 202-205.

Stojkovic, T., E. Stefanova, I. Soldatovic, V. Markovic, I. Stankovic, I. Petrovic, F. Agosta, S. Galantucci, M. Filippi and V. Kostic (2018). "Exploring the relationship between motor impairment, vascular burden and cognition in Parkinson’s disease." Journal of Neurology 265: 1320-1327.

Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, Brach J, Chandler J, Cawthon P, Connor EB, Nevitt M, Visser M, Kritchevsky S, Badinelli S, Harris T, Newman AB, Cauley J, Ferrucci L, Guralnik J. Gait speed and survival in older adults. JAMA. 2011 Jan 5;305(1):50-8. doi: 10.1001/jama.2010.1923. PMID: 21205966; PMCID: PMC3080184.

Tulsky DS, Rosenthal M. Measurement of quality of life in rehabilitation medicine: emerging issues. Arch Phys Med Rehabil. 2003 Apr;84(4 Suppl 2):S1-2. doi: 10.1053/apmr.2003.50203. PMID: 12692765.

Vaishya R, Vaish A. Falls in Older Adults are Serious. Indian J Orthop. 2020 Jan 24;54(1):69-74. doi: 10.1007/s43465-019-00037-x. PMID: 32257019; PMCID: PMC7093636.

Vandierendonck A, Kemps E, Fastame MC, Szmalec A. Working memory components of the Corsi blocks task. Br J Psychol. 2004 Feb;95(Pt 1):57-79. doi: 10.1348/000712604322779460. PMID: 15005868.

Viticchi, G., L. Falsetti, F. Vernieri, C. Altamura, M. Bartolini, S. Luzzi, L. Provinciali and M. Silvestrini (2012). "Vascular predictors of cognitive decline in patients with mild cognitive impairment." Neurobiology of aging 33(6): 1127. e1121-1127. e1129.

Wechsler D. WAIS-3., WMS-3: Wechsler adult intelligence scale, Wechsler memory scale: Technical manual. Psychological Corporation; 1997.