Predictors of Cognitive Decline in a Multi-Ethnic Sample of Midlife Women: A Longitudinal Study

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A Thesis Presented

by

JASMINE S. DIXON

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Approved as to style and content by:

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Rebecca Ready, Chair

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Elizabeth Harvey, Member

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Nilanjana Dasgupta, Member

____
Caren Rotello, Department Head
Psychological and Brain Sciences

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ABSTRACT

PREDICTORS OF COGNITIVE DECLINE IN A MULTI-ETHNIC SAMPLE OF MIDLIFE WOMEN: A LONGITUDINAL STUDY

FEBRUARY 2020

JASMINE S. DIXON, B.S., HOWARD UNIVERSITY

M.S., UNIVERSITY OF MASSACHUSETTS AMHERST

Directed by: Professor Rebecca E. Ready

Hypertension, diabetes, depressive symptoms, and smoking are predictors of cognitive decline in late life. However, it is not known if these risk factors are associated with cognition during midlife or if the associations between these risk factors and cognition vary by race. This longitudinal study hypothesized that (1) the risk factors would predict cognitive decline in midlife, (2) African Americans would have greater cognitive decline than European Americans and East Asians, and (3) there would be stronger associations between risk factors and cognition for African American women compared to European American and East Asian women. Participants (aged 42-52) were European American (n = 1,000), African American (n = 516), and East Asian (n = 437) women from the Study of Women's Health Across the Nation who were studied for 8 years. Risk factors (i.e., diabetes, hypertension, smoking, and depressive symptoms) and cognitive outcomes (i.e., episodic memory, processing speed, and working memory) were measured at multiple timepoints. Two-level hierarchical linear models tested change in cognition over time controlling for income, education, and age. African Americans had lower scores than European Americans and East Asians on all cognitive outcomes. East

Asian smokers had greater episodic memory decline compared to European American smokers. Depressive symptoms did not adversely impact processing speed for East Asian relative to European Americans. Contrary to our hypothesis, hypertension was associated with improved processing speed over time for African Americans compared to European Americans. Racial disparities in cognition were evident for African American women.

Keywords: racial differences; risk factors; cognitive decline; midlife; women

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CHAPTER 1

INTRODUCTION

Dementia is the sixth leading cause of death in the U.S. (Kochanek, Murphy, & Xu, 2017). In 2018, 5.5 million Americans were estimated to have Alzheimer's Disease (AD) and this number is projected to reach 13.8 million by 2050 (Hebert, Weuve, Scherr, & Evans, 2013). Vascular Dementia (VaD) is responsible for 5-10% of dementia cases, making it the second most common type of dementia (Brenowitz et al., 2017; Kapasi, DeCarli, & Schneider, 2017). More women relative to men have AD, with the disorder affecting 3.3 million women in the United States compared to 2.0 million men (Alzheimer's Association, 2018). Racial differences in dementia prevalence are well known. AD and VaD are more likely to be diagnosed in African Americans compared to non-Hispanic European Americans (Mayeda, Glymour, Quesenberry, & Whitmer, 2016; Mehta & Yeo, 2017; Steenland, Goldstein, Levey, & Wharton, 2015). Thus, women and African Americans deserve particular attention in dementia research. There is some evidence that Asian Americans have lower dementia incidence rates compared to African Americans and European Americans (e.g. Mayeda et al., 2016). Compared to other ethnic minority groups, there is limited data on risk for cognitive decline in Asian Americans, despite the fact that they are the fastest growing racial group in the U.S. population.

The neuropathology of dementia may begin in midlife (Sperling et al., 2011). Midlife is an important developmental period in cognition because it bridges the link between early life and late life age-related changes. For example, knowledge-related and emotion regulation abilities increase, whereas processing speed an working memory start to decrease (Lachman, 2016). Additionally, physical health at midlife sets the foundation for late life cognition (Lachman, Teshale, & Agrigoroaei, 2015; Sabia et al., 2012). By gaining a better understanding of cognitive abilities and predictors of cognition at midlife, prevention and treatment can be directed to persons most at risk for cognitive decline.

Risk factors for cognitive decline and/or impairment in older adults are known and include depressive symptoms, diabetes, hypertension, and smoking (Baumgart et al., 2015). However, it is unknown if these risk factors are equally important in predicting cognitive decline in midlife or if their associations with cognitive decline vary by racial group (Gottesman et al., 2014; D. Knopman et al., 2001; Mayeda et al., 2014). To support the idea that there may be racial group differences in the association between risk factors and cognitive decline, we utilize the cumulative disadvantage hypothesis of health disparities. This theory will be discussed in more detail below.

The current project - using longitudinal data from the Study of Women's Health Across the Nation (SWAN; Sowers et al., 2000) - will fill important gaps in the literature by determining which risk factors (i.e. diabetes, hypertension, smoking, and depressive symptoms) are associated with cognitive decline in midlife women. We will determine if the associations between risk factors and cognitive decline are more adverse for African American women compared to European American and East Asian women. This study will focus on cognitive outcomes that are reliable early signs of AD and/or VaD, namely episodic memory, working memory, and processing speed.

1.1 Early Cognitive Markers of AD and VaD

Common early neuropsychological signs of AD and VaD are decline in episodic memory, working memory, and/or processing speed, and these cognitive abilities may begin to change in midlife (Weintraub, Wicklund, & Salmon, 2012). For AD, a clinical hallmark of the disease is impaired episodic memory, which involves the ability to recall a specific event (Karantzoulis & Galvin, 2012). Verbal episodic memory is often assessed by measures of story recall (i.e., Logical Memory Test; Wechsler, Coalson, & Raiford, 2008) or word list learning (i.e., California Verbal Learning Test; Delis, Kramer, Kaplan, & Ober, 2000); deficits are most robust for delayed recall scores (Weintraub et al., 2012). In contrast to AD, episodic memory impairment is less pronounced in early VaD (Karantzoulis, 2012).

Working memory is part of the executive function domain, which includes other abilities such as inhibition and cognitive flexibility (Diamond, 2014). Working memory not only requires a person to remember information for a limited period of time, but to also manipulate that information (Baddeley, 1992). Neuropsychological assessments that require persons to recall a series of numbers backwards (i.e. Digit Span Backwards; Wechsler et al., 2008) can be used to measure this cognitive ability. Working memory and executive function deficits are a hallmark of VaD (Kandiah, Narasimhalu, Lee, & Chen, 2009; O'Brien & Thomas, 2015). Working memory is also impaired in early AD (Kirova, Bays, & Lagalwar, 2015; Stopford, Thompson, Richardson, Neary, & Snowden, 2010).

Processing speed declines in early VaD and early AD (Karantzoulis, 2012; McGuinness, Barrett, Craig, Lawson, & Passmore, 2010). Processing speed is measured by the time it takes a person to complete a relatively simple task. Thus, in summary, episodic memory, working memory, and processing speed are prominent and early deficits in AD and/or VaD; decline in these abilities in midlife could signal risk for dementia in late life.

1.2 Predictors of Cognitive Decline

Four risk factors for cognitive decline are the focus of this project, namely hypertension, diabetes, depressive symptoms, and smoking. There is longitudinal and cross-sectional evidence that these risk factors are associated with cognition in older adults (Table 1). In addition, several studies link these risk factors with cognitive domains that are early signals of AD and/or VaD (i.e., processing speed, working memory, and episodic memory). That is, there is compelling – although not definitive – evidence that these risk factors are associated with concurrent or longitudinal changes in the cognitive domains of interest. Thus, these four risk factors may be viable signals for cognitive decline in midlife.

We do not have a sufficiently clear picture if diabetes, hypertension, smoking, and depressive symptoms are linked with cognitive decline in midlife. In comparison to older adult studies, there are only a few longitudinal studies that investigated our risk factors and cognitive decline in midlife adult samples (Table 2). Results of these studies are mixed and - with so few studies to draw from - more research is needed.

1.3 Theoretical Framework for Health Disparities

Next, to address why there may be racial group differences in cognition, we will discuss a health disparities theory. This study is guided by the cumulative disadvantage hypothesis for health disparities. The cumulative disadvantage theory states that the adverse effects of risk factors accumulate over the lifespan and early life disadvantages compound with later disadvantages and contribute to increasingly large group differences over time (Dannefer, 1987, 1988, 2003). This theory emphasizes the long-term and additive adverse consequences of risk factors, which result in ever-growing health disparities. This theory implies racial group differences in cognitive outcomes will increase over time. By the midlife developmental period, the adverse effects of risk factors have already accumulated over time. Thus, the negative impact on cognition may be evident for African Americans relative to European Americans in midlife. As described in more detail below, we hypothesize that risk for cognitive decline in our midlife sample will be greater for African American relative to European American and East Asian participants.

1.4 Racial Disparities in Cognitive Decline

Studies of racial differences in cognitive decline are few in number and focus almost exclusively on European Americans and African Americans; the current study will include East Asians as well. Examining differences in health outcomes between three racial groups is important because African Americans - relative to European and Asian Americans - are disproportionately affected by adversities such as lower socioeconomic status (SES), racial discrimination, stressful life events, and poor healthcare access (Assari, 2018; Lewis & Van Dyke, 2018; Mays, Cochran, & Barnes, 2014; Stevens-Watkins, Perry, Pullen, Jewell, & Oser, 2015; Williams, Priest, & Anderson, 2016). Having a racial minority comparison group (i.e., East Asians) allows us to test whether any cognitive disadvantage observed in African Americans may be specific to that racial group compared to simply having racial minority status in comparison to European Americans. According to the cumulative disadvantage theory, adverse conditions experienced by African Americans since early life may make them more vulnerable to risk for cognitive decline in late life relative to European Americans and East Asians. Indeed, African Americans are at greater risk for dementia than European Americans (Barnes & Bennett, 2014). Data are mixed, however, if African Americans exhibit greater cognitive decline than European and Asian Americans at midlife.

That is, African Americans exhibited greater cognitive decline than European Americans in five studies of older adults (Gupta et al., 2016; Lyketsos, Chen, & Anthony, 1999; Sachs-Ericsson & Blazer, 2005; Sawyer, Sachs-Ericsson, Preacher, & Blazer, 2009; Wolinsky et al., 2011). Three of these five studies examined global cognitive decline (Lyketsos et al., 1999; Sachs-Ericsson & Blazer, 2005; Sawyer et al., 2009). When specific cognitive outcomes were studied, African Americans exhibited greater cognitive decline than European Americans in episodic memory (Wolinsky et al., 2011) and in executive functions (Gupta et al., 2016), as measured by the Trail Making Test (TMT; Reitan, 1992).

In contrast, two studies did not find significant racial differences in cognitive decline but found significant baseline performance differences between African Americans and European Americans (Castora-Binkley, Peronto, Edwards, & Small, 2013; Marsiske et al., 2013). It is unclear why results of these two studies differed from the other studies because the average age of participants and follow-up duration were similar. The only difference is that these two studies used composite scores of neuropsychological tests measuring episodic memory, working memory, and processing speed compared to other studies that used global cognition measures.

There is minimal literature examining cognitive decline, cognitive impairment, and dementia in Asian Americans. Our knowledge of Asian American cognitive function comes from longitudinal and cross-sectional studies of Chinese Americans (i.e. Li, Ding, Wu, & Dong, 2017) and Japanese Americans (i.e. Kemmotsu, Enobi, & Murphy, 2013). One of our risk factors - hypertension during midlife - was positively associated with an increased risk of dementia in older Japanese men (Launer et al., 2000). Asian Americans have lower rates of dementia in comparison to African Americans and European Americans (Mayeda, Glymour, Quesenberry, & Whitmer, 2017; Mayeda, Glymour, Quesenberry, & Whitmer, 2016). Thus, we theorize that cognition for East Asians will be more comparable to European Americans than African Americans.

Unlike European Americans and African Americans, there are no data on risk for cognitive decline in midlife for Asian Americans. By including Asian Americans in the present study, we will fill gaps in knowledge about Asian American cognitive decline during midlife, as well as determine how changes in cognition over time are different from and/or similar to a racial minority and majority group.

1.5 Racial Differences in the Associations between Risk Factors and Cognitive Decline

African Americans suffer more adversity than European and Asian Americans and – according to the cumulative disadvantage theory – may subsequently be more vulnerable to the adverse effects of diabetes, hypertension, smoking, and depressive symptoms on cognitive decline over time. Longitudinal and cross-sectional studies have investigated racial differences in the associations between risk factors and cognitive decline in older and midlife adults (Table 3).

Indeed, a stronger association between diabetes and all three of our cognitive outcomes is demonstrated in African Americans relative to European Americans (Table

3). Specifically, diabetes had a stronger association with episodic memory (Rajan et al., 2016) and processing speed (Mayeda et al., 2014; Obidi et al., 2008) in African Americans than European Americans. There is also cross-sectional evidence supporting a significant association between diabetes and working memory for African Americans with low SES compared to European Americans (Dore, Waldstein, Evans, & Zonderman, 2015).

However, studies examining racial group differences in the association between hypertension and cognitive decline find - somewhat surprisingly - a stronger association in European Americans than African Americans. In two longitudinal studies, European American midlife adults with hypertension exhibited greater cognitive decline in processing speed compared to African Americans with hypertension (Gottesman et al., 2014; Knopman et al., 2001). Although a definitive association cannot be determined from only two studies, these longitudinal studies support the notion that further research should be conducted to clarify the nature of the associations between hypertension, race, and cognitive decline.

The data on smoking, cognition, and race are mixed. For African American midlife adults, smoking was significantly associated with poorer processing speed, a result not replicated in European Americans (Knopman et al., 2001). Conversely, smoking was significantly associated with decline in episodic memory for European Americans but not African American older adults (Schneider et al., 2014).

Only one study examined racial differences in the association between depressive symptoms and cognition (Zahodne, Nowinski, Gershon, & Manly, 2014). Depressive symptoms were associated with poor concurrent episodic memory performance in African Americans and with poor processing speed in European Americans.

In summary, there is mixed support for our hypothesis – derived from the cumulative disadvantage theory – that risks for cognitive decline will be stronger in African Americans than European Americans. The fairly small number of studies indicate that further research is needed to clarify how race interacts with risk factors of cognitive decline.

1.6 The Present Study

The present study has three aims. First, the study will determine if diabetes, hypertension, smoking, and depressive symptoms predict cognitive decline in episodic memory, working memory, and processing speed in midlife women. Although there is evidence that these risk factors tend to be associated with cognitive decline in midlife, the data are not entirely consistent (Arvanitakis et al., 2004; Ganguli, Du, Dodge, Ratcliff, & Chang, 2006; Hassing et al., 2004; D. Knopman et al., 2001; Mayeda et al., 2014; Royall, Palmer, Chiodo, & Polk, 2012; Schneider et al., 2014; Vásquez et al., 2016). We predict that diabetes, hypertension, smoking, and depressive symptoms will be associated with longitudinal decline in all cognitive outcomes.

The second aim is to determine if there are racial differences in cognitive decline between European Americans, African Americans, and East Asians. Given that African Americans are more likely to be diagnosed with dementia in late life than European Americans and Asian Americans (Mayeda et al., 2016), and that African Americans experience more cognitive decline compared to European Americans (Gupta et al., 2016; Sachs-Ericsson & Blazer, 2005; Wolinsky et al., 2011; see exceptions Castora-Binkley et al., 2013; Marsiske et al., 2013), this group might be at greater risk for cognitive decline beginning in midlife, when the neurodegenerative disease process typically begins. Thus, African American women are expected to exhibit more cognitive decline over time in processing speed, working memory, and episodic memory compared to East Asians and European American women. We hypothesize that results for East Asians will not be significantly different from European Americans because their dementia prevalence is the lowest of the three racial groups (Mayeda et al., 2017; Mayeda et al., 2016).

The third aim is to test the cumulative disadvantage hypothesis and determine if race moderates the associations between risk factors (i.e. diabetes, hypertension, depressive symptoms, and smoking) and cognitive decline in processing speed, working memory, and episodic memory. African Americans are disproportionately affected by disparities that adversely impact health (Assari, 2018; Lewis & Van Dyke, 2018; Mays et al., 2014; Stevens-Watkins et al., 2015; Williams et al., 2016). We hypothesize that, due to greater adversities earlier in life, the associations between risk factors and cognitive decline in processing speed, working memory, and episodic memory will be stronger for African American women compared to European American and East Asian women.

CHAPTER 2

METHOD

2.1. Participants

Participant (*N* =1,953) data are from the Study of Women's Health Across the Nation (SWAN; Sowers et al., 2000). SWAN is a longitudinal epidemiological study assessing psychological, physical, cultural, and social factors that contribute to the health of American women during midlife. Original eligibility criteria included being 42-52 years old, not taking hormone medications, having a uterus and at least one ovary, and having a menstrual period within the past three months. The primary race of the participants were European American (*n* = 1,000), African American (*n* = 516), and East Asian (*n* = 437; including Chinese Americans and Japanese Americans). Researchers also recruited Hispanic participants, but the sample had high attrition so these data were not included in the present study. Study sites were University of Pittsburgh, University of California-Los Angeles, University of California-Davis/Kaiser Permanente, Rush Presbyterian-St. Luke's Medical Center, Massachusetts General Hospital, and University of Michigan.

2.2. Procedures

Race and educational attainment were collected at the screening visit in 1996-1997. After the baseline assessment, participants completed follow up visits approximately once a year. Visit 10 occurred between 2006-2008 and is the endpoint for the present study because it is the last time data were made publicly available. At the yearly visits, questionnaires were administered to assess depressive symptoms, family income, age, and physical health. Predictor measures of hypertension, diabetes, smoking, and depressive symptoms were collected at baseline, visits 1, 2 (diabetes was not collected at this visit), and 3, and prior to initial cognitive assessments at visit 4. Cognitive measures were collected at visits 4, 6, 7, 8, 9, and 10. Given the diverse ethnicity of the sample, all questionnaires were translated in Japanese and Cantonese. For this study, data from the following time points will be used: screening, baseline, visits 1 through visit 10 with the exception of visit 5. Cognitive measures were not administered during visit 5, therefore that visit will not be included in the analyses. The use of this data was approved by the University of Massachusetts Institutional Review Board.

2.3 Measures

2.3.1 Hypertension, Diabetes, and Smoking

Hypertension risk was measured by average systolic blood pressure. An average blood pressure value was created based on an average of the measures at baseline and visits 1-3. Diabetes risk was measured by fasting blood glucose. Fasting blood glucose was measured at baseline, visit 1, and visit 3 and these scores were averaged. Smoking was measured by a self-report of current smoking, answered by "yes" or "no".

2.3.2 Depressive Symptoms

Participants were administered the Center for Epidemiological Studies-Depression Scale (CES-D), a 20-item measure assessing depressive symptoms. Depressive symptom totals at baseline and visits 1- 3 were averaged to create a depressive symptoms score. Depressive symptoms assessed included loss of appetite, depressed mood, psychomotor retardation, feelings of helplessness and hopelessness, sleep disturbances and feelings of guilt and worthlessness (Radloff, 1977). The questionnaire asked participants to indicate how often they experienced the symptoms in the past week. Items were rated on a 4-point scale ranging from 0 (Rarely or none of the time, less than 1 day) to 3 (Most or all of the time, 5-7 days).

Higher scores on the CES-D are indicative of more depressive symptomatology. The total score range is 0-60 with scores at 16 or more indicative of a risk for clinical depression. The CES-D has had high internal consistency in general and clinical populations (coefficient $\alpha = .80$ and $\alpha = .90$, respectively) (Radloff, 1977). The measure has also been established to have criterion validity in the original measure sample (Radloff, 1977).

2.3.3 East Boston Naming Test

The East Boston Memory Test (EBMT) is a measure of verbal episodic memory (Gfeller & Horn, 1996). Participants are read a paragraph length story and then are asked to immediately recall story elements. After an approximately 10 minute delay, the participant is asked to again recall story elements. Key words of the story are marked absent or present. Scores range between 0 -12 points. The EBMT is also correlated with another measure of episodic memory, Logical Memory, a subtest of the Wechsler Memory Scale-Revised (WMS-R; Wechsler, 1987). The immediate EBMT is correlated with Logical Memory I ($r = .42$) and the delayed EBMT is correlated with Logical Memory II ($r = .61$).

2.3.4 Symbol Digit Modalities Test

The Symbol Digit Modalities Test (SDMT) measures processing speed (Smith, 1982). Participants were timed on how quickly they could match numbers with symbols. Time to complete the task was 90 seconds. Scores range from 0-110 points and the score is the number of items correctly completed within 90 seconds. The SDMT is highly correlated with the Digit Symbol subtest of the Wechsler Adult Intelligence Scale- Fourth Edition (WAIS-IV; r = .80; Sheridan et al., 2006; Wechsler, Coalson, & Raiford, 2008).

2.3.5 Digit Span Backwards

The Digit Span Backwards (DSB) measures working memory. The DSB is a section of the Digit Span subtest from the WAIS-IV (Wechsler et al., 2008). Participants are asked to repeat a series of numbers backwards. The series of numbers range from two numbers to seven numbers. For each series of numbers, there are two trials. After answering incorrectly to two trials of the same span the measure is discontinued. Total scores range from 0-12 points. Reliability was calculated using split-half and Cronbach's coefficient alpha. Reliability coefficients for the sample age groups ranged from: (r = .82-.86). The DSB has good validity with each WAIS subtest and across different clinical populations.

2.4 Data Analyses

Descriptive statistics were examined to characterize the sample and to evaluate the data for normal distribution and outliers. We also examined baseline differences on our predictors and cognitive outcomes between racial groups. Hierarchical linear modeling (HLM) was used to test all hypotheses given its ability to account for dependency in the data due to repeated measures over time (Raudenbush, Bryk, & Congdon, 2013). Specifically, we fit a two-level growth curve model within person change over time at level 1 and between person differences at level 2. HLM also uses maximum likelihood estimation, so it provides model-based estimates for participants with some missing outcome data. Thus, analyses included all participants who completed at least one measurement occasion of a given outcome variable. Effect size was calculated by evaluating the additional percent variance explained with the addition of predictors (pseudo r^2) for significant associations. Control variables included age (grand mean centered), family income at baseline, and education attainment level.

Primary continuous predictor variables (i.e., average depressive symptoms, average blood pressure, and average glucose) were also centered around the grand mean. Smoking at baseline, a categorical variable, remained uncentered. Race was dummy coded such that European Americans were used as the reference group for all analyses. Interaction terms were created using the centered continuous variables and the un-centered dummy coded racial groups. Time was centered at visit 10. Thus, the model intercept represents the level of the relevant outcome at the final visit. This allowed us to examine the long-term effects of our predictors, which were measured early in midlife, on cognitive function at the end of midlife.

CHAPTER 3

RESULTS

3.1 Preliminary Analyses

Prior to testing my primary hypotheses, I first determined the best models to characterize trajectories of change over time for each of my outcome variables. Specifically, I compared the fit of unconditional linear and quadratic models for each of the cognitive outcomes (i.e., episodic memory, processing speed, and working memory). The quadratic model was not a significantly better model than the linear model for episodic memory ($\chi^2 = 5.93874$, $df = 4$, $p = 0.203$); thus, the linear model was used to test hypotheses for this cognitive domain. However, the quadratic model was a significantly better model than the linear model for processing speed ($\chi^2 = 70.67857$, $df = 4$, $p < 0.001$) and working memory ($\chi^2 = 33.37686$, $df = 4$, $p < 0.001$) and was used in subsequent analyses for these cognitive domains.

3.2 Equations

3.2.1 Research Question One: Smoking, Diabetes, Depressive Symptoms, and Hypertension Predicting Cognitive Decline

The model equation used to test if smoking, depressive symptoms, blood pressure, and diabetes predict SMDT and DSB is as follows:

Level-1 Model:

$$Cognitive\ Outcome_{ij} = \beta_{0j} + \beta_{1j}*(YEAR10_{ij}) + \beta_{2j}*(YEARQ_{ij})[1] + r_{ij}$$

Level-2 Model:

[1] For the model with EBMT (i.e., episodic memory) as an outcome, a linear model was the best fit and thus $YEARQ_{ij}$ was not included.

$$\beta_{0j} = \gamma_{00} + \gamma_{01}*(AGE0_j) + \gamma_{02}*(PREDICTOR_j) + \gamma_{03}*(EDUCATION_j) + \gamma_{04}*(INCOME_j) + u_{0j}$$

$$\beta_{1j} = \gamma_{10} + \gamma_{11}*(AGE0_j) + \gamma_{12}*(PREDICTOR_j) + \gamma_{13}*(EDUCATION_j) + \gamma_{14}*(INCOME_j) + u_{1j}$$

$$\beta_{2j} = \gamma_{20} + \gamma_{21}*(AGE0_j) + \gamma_{22}*(PREDICTOR_j) + \gamma_{23}*(EDUCATION_j) + \gamma_{24}*(INCOME_j) + u_{2j}$$

At level 1 (person-level), cognitive outcome at time *i* for participant *j* was predicted from the level of the relevant outcome at visit 10 (β_{0j}), rate of change at visit 10 (β_{1j}), and yearly change in rate of change (β_{2j}) for participant *j*. At level 2, these coefficients dropped down to become the outcomes. The level of the cognitive outcome at visit 10 (β_{0j}) was predicted by the intercept (γ_{00}), age (γ_{01}), relevant predictor (γ_{02}), education (γ_{03}), and income (γ_{04}). The rate of change in the cognitive outcome at visit 10 (β_{1j}) was predicted by the intercept (γ_{10}), age (γ_{11}), relevant predictor (γ_{12}), education (γ_{13}), and income (γ_{14}). The change in the rate of change in the cognitive outcome (i.e., acceleration/deceleration; β_{2j}) was predicted by the intercept (γ_{20}), age (γ_{21}), relevant predictor (γ_{22}), education (γ_{23}), and income (γ_{24}).

Random effects (u_{0j}, u_{1j}, u_{2j}) were included for scores at visit 10, rate of change at visit 10, and yearly change in rate of change (i.e., acceleration/deceleration) to allow each participant to deviate from the sample averages.

3.2.2 Research Question Two: Race Predicting Cognitive Decline

The model equation for race predicting cognitive outcome is as follows:

Level-1 Model:

$$Cognitive\ Outcome = \beta_{0j} + \beta_{1j}*(YEAR10_{ij}) + \beta_{2j}*(YEARQ_{ij})^{2} + r_{ij}$$

Level-2 Model:

$$\beta_{0j} = \gamma_{00} + \gamma_{01}*(AGE0_j) + \gamma_{02}*(AfAM_j) + \gamma_{03}*(ASIAN_j) + \gamma_{04}*(EDUCATION_j) + \gamma_{05}*(INCOME_j) + u_{0j}$$

$$\beta_{1j} = \gamma_{10} + \gamma_{11}*(AGE0_j) + \gamma_{12}*(AfAM_j) + \gamma_{13}*(ASIAN_j) + \gamma_{14}*(EDUCATION_j) + \gamma_{15}*(INCOME_j) + u_{1j}$$

$$\beta_{2j} = \gamma_{20} + \gamma_{21}*(AGE0_j) + \gamma_{22}*(AfAM_j) + \gamma_{23}*(ASIAN_j) + \gamma_{24}*(EDUCATION_j) + \gamma_{25}*(INCOME_j) + u_{2j}$$

At level 1 (person-level), cognitive outcome at time *i* for participant *j* was predicted from participant *j* at visit 10 (β_{0j}), rate of change (β_{1j}) and yearly change in rate of change (β_{2j}). At level 2, we were interested in average gap in scores at visit 10 between African Americans and European Americans (γ_{02}), the average gap in the rate of change in scores between African Americans and European Americans (γ_{12}), the gap in yearly change in rate of change between the two groups (γ_{22}), the average gap in scores at visit 10 between East Asians and European Americans (γ_{03}), the average gap in the rate of change for East Asians (γ_{13}), the average gap in yearly change in rate of change between those two groups (γ_{23}). As with my first research question, these associations were estimated controlling for age, education, and income.

[2] For the model with EBMT (i.e., episodic memory) as an outcome, a linear model was the best fit and thus $YEARQ_{ij}$ was not included.

Random effects ($u_{0j},\ u_{1j},\ u_{2j}$) were again included for scores at visit 10, the linear rate of change at visit 10, and yearly change in rate of change in order to allow each participant to deviate from the sample averages. Since race was dummy coded, the intercept is interpretable as the value of the relevant outcome for European Americans, the reference group.

3.2.3 Research Question Three: Race Moderating the Association Between Risk Factors and Cognitive Decline

The model equations for race moderating predictors and cognitive outcome is as follow:

Level-1 Model:

$$Cognitive\ Outcome = \beta_{0j} + \beta_{1j}*(YEAR10_{ij}) + \beta_{2j}*(YEARQ_{ij})^{3} + r_{ij}$$

Level-2 Model:

$$\beta_{0j} = \gamma_{00} + \gamma_{01}*(AGE0_j) + \gamma_{02}*(AFAM_j) + \gamma_{03}*(ASIAN_j) + \gamma_{04}*(PREDICTOR_j) + \gamma_{05}*(PREDICTORxAF_j) + \gamma_{06}*(PREDICTORxAS_j) + \gamma_{27}*(EDUCATION_j) + \gamma_{28}*(INCOME_j)\ \ u_{0j}$$

$$\beta_{1j} = \gamma_{00} + \gamma_{11}*(AGE0_j) + \gamma_{12}*(AFAM_j) + \gamma_{13}*(ASIAN_j) + \gamma_{14}*(PREDICTOR_j) + \gamma_{15}*(PREDICTORxAF_j) + \gamma_{16}*(PREDICTORxAS_j) + \gamma_{17}*(EDUCATION_j) + \gamma_{18}*(INCOME_j)\ \ u_{1j}$$

$$\beta_{2j} = \gamma_{20} + \gamma_{21}*(AGE0_j) + \gamma_{22}*(AFAM_j) + \gamma_{23}*(ASIAN_j) + \gamma_{24}*(PREDICTOR_j) + \gamma_{25}*(PREDICTORxAF_j) + \gamma_{26}*(PREDICTORxAS_j) + \gamma_{27}*(EDUCATION_j) + \gamma_{28}*(INCOME_j)\ \ u_{2j}$$

[3] The model with EBMT as the outcome did not include $YEARQ_{ij}$.

At level 1 (person-level), cognitive outcome at time *i* for participant *j* was predicted from participant *j* at visit 10 (β_{0j}), rate of change at visit 10 (β_{1j}), and yearly change in rate of change (β_{2j}). At level 2, the level of the cognitive outcome at visit 10 (β_{0j}) was predicted by the intercept (γ_{00}), the gap in scores at visit 10 between African Americans and European Americans at the mean level of the relevant predictor (γ_{02}), the gap in scores at visit 10 between East Asians and European Americans at the mean level of the relevant predictor (γ_{03}), the gap in scores at visit 10 in the reference group for every additional predictor added (γ_{04}), the gap in cognitive scores between African Americans and European Americans for every additional unit of predictor added (γ_{05}), and the gap in cognitive scores between East Asians and European Americans for every additional unit of predictor added (γ_{06}).

The rate of change in the cognitive outcome at visit 10 (β_{1j}) was predicted by the intercept (γ_{10}), the gap in the rate of change at visit 10 scores between African Americans and European Americans at the mean level of the relevant predictor (γ_{12}), the gap in the rate of change between East Asians and European Americans at the mean level of the relevant predictor (γ_{13}), the gap in the rate of change for the reference group for every additional predictor added (γ_{14}), the gap in the rate of change between Africans Americans and Europeans Americans for every additional predictor added (γ_{15}), and the gap in the rate of change between East Asians and European Americans for every additional predictor added (γ_{16}).

The change in the rate of change in the cognitive outcome (i.e., acceleration/deceleration; β_{2j}) was predicted by the intercept (γ_{20}), the gap in the yearly change in rate of change between African Americans and European Americans at the mean level of the relevant predictor (γ_{22}), the gap in the yearly change in rate of change between East Asians and European Americans at the mean level of the relevant predictor (γ_{23}), the gap in the reference group for yearly change in rate of change for every additional predictor added (γ_{24}), the gap in the yearly change in rate of change between African American and European Americans for every additional predictor added (γ_{25}), and the gap in the yearly change in rate of change between East Asians and European Americans for every additional predictor added (γ_{26}).

Random effects (u_{0j}, u_{1j}, u_{2j}) were included for scores at visit 10, rate of change at visit 10, and yearly change in rate of change to allow each participant to deviate from the sample averages. The interaction terms were added to the model uncentered.

3.3 Participants

Participants (N = 1,953) included European Americans (n = 1,000), African Americans (n = 516), and East Asians (n = 437; Table 4). Chi-square analyses indicated that European Americans had significantly greater education attainment than African Americans and East Asians (χ_2 = .000) as well as significantly greater income than African Americans (χ_2 = .000). A one-way ANOVA indicated that age did not significantly differ between groups (p = .395). Mean and standard deviations for the average value of our risk factors and cognitive outcomes at baseline (i.e., visit 4) are reported (Table 5). Of note, East Asians had the lowest mean levels in all four of the risk factors compared to African Americans who had the highest mean levels across three out of four risk factors (Table 5). Due to missing data, sample sizes included in models to test hypotheses ranged from N = 1,865 to 1,867.

3.4 Preliminary Analyses on Baseline Cognitive Data (Visit 4)

An overarching goal in this study was to determine longitudinal associations between risk factors and cognitive decline in different racial groups. In preliminary analyses – to aid in interpretation of longitudinal analyses – we determined proximal associations between our risk factors (i.e., diabetes, depressive symptoms, hypertension, and smoking) and cognitive measures (i.e., EBMT, SDMT, and DSB) at visit 4 which was the first time at which cognition was assessed. We also determined if the proximal associations between risk factors and cognitive outcomes were moderated by racial group.

Results of these HLM models – with time centered at visit 4 – indicated several significant associations between risk factors and cognition. Depressive symptoms were significantly associated with lower EBMT scores (γ_{02} = - 0.017, SE = 0.005, p = 0.002), SDMT scores (γ_{02} = - 0.11, SE = 0.035, p = 0.002), and DSB scores (γ_{02} = - 0.020, SE = 0.008, p = 0.009). Hypertension was significantly associated with lower EBMT scores (γ_{02} = - 0.009, SE = 0.003, p < 0.001) and DSB scores (γ_{02} = - 0.010, SE = 0.004, p = 0.009). Diabetes was significantly associated with lower SDMT scores (γ_{02} = - 0.022, SE = 0.009, p = 0.019). Smoking was not significantly associated with EBMT, SDMT, or DSB scores.

There were several significant differences in cognition between racial groups at visit 4. Compared to European Americans, African Americans had significantly lower

EBMT scores (γ_{02} = - 0.55, *SE* = 0.09, *p* <0.001), SDMT scores (γ_{02} = - 4.92, *SE* = 0.56, *p* <0.001), and DSB scores (γ_{02} = - 1.21, *SE* = 0.12, *p* <0.001). East Asians participants had significantly lower EBMT scores (γ_{03} = - 0.06, *SE* = 0.02, *p* = 0.005) and DSB scores (γ_{03} = - 0.74, *SE* = 0.13, *p* <0.001) than European Americans, but significantly higher scores in SDMT scores (γ_{03} = 1.14, *SE* = 0.58, *p* = 0.049).

Race significantly moderated the association between depressive symptoms and EBMT scores such that, more depressive symptoms were associated with poorer EBMT scores in African Americans relative to European Americans (γ_{05} = - 0.03, *SE* = 0.01, *p* = 0.007). Race significantly moderated the association between depressive symptoms and SDMT scores such that more depressive symptoms were associated with poorer SDMT scores in African Americans relative to European Americans (γ_{05} = -0.19, *SE* = 0.08, *p* = 0.012). Additionally, the association between smoking and SDMT scores is significantly different between East Asians and European Americans such that smoking for European Americans was associated with poorer SDMT scores relative to East Asian smokers (γ_{06} = 5.03, *SE* = 2.04, *p* = 0.014).

3.5 Primary Analyses

3.5.1 Unexplained Variability Across Models

In all models, unexplained variability was calculated to determine how much of the intercept, linear slope, and quadratic slope were unexplained after accounting for level 2 predictors (i.e. depressive symptoms, diabetes, hypertension, and smoking). There was significant unexplained variability in EBMT, SDMT and DSB scores at visit 10, rate of change at visit 10 and yearly change in rate of change across the study, allowing the addition of between-person predictors.

3.5.2 Risk factors predicting cognitive outcomes

To test aim 1, which was to determine if diabetes, hypertension, smoking, and depressive symptoms predicted longitudinal decline in our cognitive outcomes, we ran two-level HLM models. A surprising finding from the models was that there was little to no evidence of cognitive decline over time; cognition remained stable or increased over time.

Nonetheless, we determine if our predictors were associated with cognitive change – if not *decline* – over time. Partially consistent with our hypotheses, smoking was significantly negatively associated with linear change in EBMT scores (Table 6). EBMT scores remained constant across the study for smokers whereas for non-smokers, EBMT scores improved over time; these slopes were significantly different (Figure 1). Also, smoking was significantly positively associated with the quadratic slope in SDMT scores such that for smokers, the yearly change in rate of change increased for SDMT scores across the study. In comparison, for non-smokers, SDMT scores initially increased than began to decline towards the end of the study (Table 7 and Figure 2). Smoking accounted for 1.23% of the variance in EBMT score rate of change and 2.37% of the variance in SDMT scores yearly change in rate of change.

While not the primary focus of our analyses, we found several of our risk factors were associated with cognitive outcomes at visit 10. Hypertension, smoking, diabetes, and depressive symptoms were significantly associated with lower EBMT scores; as a point of comparison, only depressive symptoms and hypertension were significantly associated with EBMT scores at visit 4. Proportion of variance in EBMT scores explained by our risk factors were as follows: hypertension (1.19%), smoking (1.58%), diabetes (0.87%), and depressive symptoms (1.00%). For SDMT, depressive symptoms, hypertension, and diabetes were significantly associated with lower scores at visit 10; as a comparison, only depressive symptoms and diabetes were significantly associated at visit 4. Proportion of variance in SDMT scores at visit 10 explained by our risk factors were as follows: depressive symptoms (1.74%), diabetes (2.06%), and hypertension (1.39%). Hypertension and diabetes were significantly associated with lower DSB scores at visit 10; at visit 4, depressive symptoms and hypertension were significantly associated with DSB scores (Table 8). Proportion of variance explained in DSB scores at visit 10 explained in this model was 0.49% for hypertension and 0.50% for diabetes.

In summary, the hypothesis that our risk factors would be associated with longitudinal decline was only partially supported. Smoking was the only risk factor to be negatively associated with cognitive function; smokers had lower EBMT and SDMT scores over time compared to non-smokers. Nonetheless, there were more numerous proximal associations between the risk factors and cognition at visit 10 – and as reported earlier – at visit 4 (i.e., at baseline cognitive testing).

3.5.3 Race predicting cognitive outcomes

We next tested aim 2, that cognitive change over time would differ by race. Similar to baseline cognitive data at visit 4, results of the three models indicated that African Americans had significantly lower EBMT scores, lower SDMT scores, and lower DSB scores at visit 10 than European Americans (Table 9). East Asians had significantly lower EBMT scores and DSB scores but significantly higher SDMT scores at visit 10 than European Americans.

Our hypothesis that African American women would exhibit more decline over time in EMBT scores compared to European American was not supported; indeed, as noted earlier, there was little evidence of cognitive decline in the sample. For East Asians, EBMT scores significantly increased compared to European Americans (Figure 3). Race accounted for 7.1% of variance in EBMT scores at the intercept (visit 10) and 6.3% of variance in rate of change in EBMT scores.

Our hypothesis that African American women would exhibit more decline over time in SDMT scores than European Americans was not supported. However, African Americans had significantly different yearly change in rate of change across the study compared to European Americans (Table 9). That is, the shape of change was significantly different between racial groups. African Americans had a linear increase in SDMT scores over time, whereas East Asians and European Americans scores exhibited a downward curvilinear change (Figure 4) indicating African Americans are experiencing a distinct course of cognition compared to East Asians and European Americans. Race accounted for 9.2% of the variance in SDMT scores at visit 10 and 5.3% of the variance in change in rate of change of SDMT scores at visit 10.

The three racial groups did not significantly differ in rate of change and yearly change in rate of change. Race accounted for 6.25% of the variance in DSB scores at the visit 10.

3.5.4 Race as a moderator in the associations between risk factors and cognitive outcomes

The goal of aim 3 was to test if race moderated the associations between risk factors and cognitive outcomes. Twelve HLM models were run to test aim 3 because there are four risk factors crossed with three racial groups. Race significantly moderated the associations between smoking, depressive symptoms, and hypertension with EBMT and SDMT outcomes. These significant interaction models were reviewed below.

The first moderator effect indicated a significant interaction between smoking and racial group such that being a smoker vs. a non-smoker was associated with poorer EBMT scores over time for East Asians more than European Americans. Specifically, East Asian non-smokers experienced a significantly greater *increase* in EBMT over time compared to European American non-smokers, whereas East Asian smokers experienced a greater *decline* in EBMT over time compared to European American smokers (Table 10, Figure 5). This moderator effect was not expected because we hypothesized a significant interaction between smoking and EBMT scores for African Americans. Results of simple slope comparisons indicated that smoking was a significant predictor for rate of change in EBMT scores for East Asians ($\gamma_{ss} = -0.1897$, $SE = 0.0507$, $p < 0.001$), but was not a significant predictor of rate of change for African Americans ($\gamma_{ss} = 0.0003$, $SE = 0.0464$, $p > 0.50$) or for European Americans (Table 10). There was no significant interactions between hypertension, diabetes, and depressive symptoms and race in EBMT scores. The interaction between race and smoking accounted for 0.42% of the variance in EBMT scores for linear slope.

The second moderator effect revealed that race significantly moderated the association between depressive symptoms and SDMT. Specifically, there was a significant interaction between depressive symptoms and East Asians such that depressive symptoms were more strongly associated with poorer SDMT scores for European Americans compared to East Asians. Additional depressive symptoms did not adversely impact SDMT scores at visit 10 for East Asians; whereas for European Americans, additional depressive symptoms decreased SDMT scores (Table 12, Figure 6).

After conducting simple slope comparisons for this interaction between depressive symptoms and SDMT scores, results indicated that depressive symptoms were a significant predictor of SDMT scores at visit 10 for African Americans ($\gamma_{ss} = -0.2866$, $SE = 0.0656$, $p < 0.001$; Figure 6) and European Americans (Table 12) but not for East Asians ($\gamma_{ss} = 0.0018$, $SE = 0.0777$, $p > 0.50$). The interaction between race and smoking accounted for 0.7% of the variance in SDMT scores at visit 10.

For the third significant moderator effect, contrary to expectations, there was a significant interaction between hypertension and race such that every additional unit of hypertension was associated with a better SDMT trajectory for African Americans compared to European Americans. Specifically, African Americans with greater hypertension had significantly *faster* processing speed in yearly change in rate of change across the study compared to European Americans, where year to year change in SDMT scores did not significantly change with greater hypertension for European Americans (Table 14). Further probing indicated that hypertension was a significant predictor of yearly change in rate of change for African Americans ($\gamma_{ss} = 0.0041$, $SE = 0.0019$, $p = 0.03$; Figure 7) but not a significant predictor for European Americans (Table 12) or East Asians ($\gamma_{ss} = -0.0036$, $SE = 0.0026$, $p = 0.17$). The interaction between race and hypertension accounted for 3.6% of the variance in yearly change in rate of change for SDMT scores.

CHAPTER 4

DISCUSSION

Dementia-related cognitive decline may begin in midlife (Sperling et al., 2011). This study was one of the first longitudinal studies of racial group differences in risk factors for poor cognitive outcomes in midlife. Contrary to hypotheses, we determined that not all risk factors associated with cognitive decline in late life (i.e., depressive symptoms, smoking, hypertension, and diabetes) were associated with cognitive *change* during midlife. However, we found several proximal associations between risk factors in midlife and cognitive outcomes. Further, some associations between risk factors and cognitive outcomes varied by racial group.

Results of this study contribute to our understanding of cognitive function during midlife in unanticipated ways. First, contrary to expectations, there was little evidence of cognitive decline in midlife. Cognition either remained stable or improved over time; improvements were likely secondary to practice effects. Second, there were differences in cognitive function between our racial groups. African American women had lower scores in episodic memory, processing speed, and working memory than European American women throughout the study period. These racial group differences have implications for understanding cognition in midlife, as well as risk of dementia for different racial groups. We address these themes in more detail below.

4.1 Stability in Cognition During Midlife

Our finding that cognitive function was *stable* or *improved* across the study was unexpected because we anticipated decline. Whereas our results are consistent with other studies that examined cognitive function during midlife (Fuh, Wang, Lee, Lu, & Juang, 2006; Greendale et al., 2009; Lamar, Resnick, & Zonderman, 2003), they are contrary to previous analyses conducted in the SWAN dataset that found longitudinal cognitive decline in episodic memory and processing speed (Karlamangla, Lachman, Han, Huang, & Greendale, 2017). There are two reasons why our results may have differed from the previous analyses of the SWAN dataset. First, in the previous study, researchers controlled for practice effects and menopause transition by using baseline measures of cognitive function at a later time than in my study (i.e., visit 7). Secondly, researchers included data from follow up visit 12 in their analyses, a time point that was not available for use in the present study.

4.2 Racial Group Differences in Cognition

African American women performed more poorly on episodic memory, processing speed, and working memory scores than European American and East Asian women at the beginning and end of the study period. That is, at baseline, African Americans had lower scores on episodic memory, processing speed, and working memory than European Americans and these differences persisted over time. These are some of the first data about race-based differences in cognitive function at midlife. Indeed our results are consistent with other studies in which African Americans scored lower on cognitive tests than European Americans in older adult (Gupta et al., 2016; Lyketsos et al., 1999; Sachs-Ericsson & Blazer, 2005; Sawyer et al., 2009; Wolinsky et al., 2011) and younger adult samples (i.e. Zahodne, Manly, Seeman, & Lachman, 2017).

There is debate about whether race and ethnicity are a proxy for SES, and if the cognitive differences observed between racial groups in psychological research are due to SES (Kawachi, Daniels, & Robinson, 2005; Manly, 2005). SES has been associated with cognitive outcomes in Hispanics, African Americans, and European American older adults (i.e., Zahodne, Stern, & Manly, 2015). However, in our data, racial group differences in cognition remained after controlling for income and education. Thus, our findings suggest that there are factors that contribute to racial group differences in cognition other than SES.

4.3 Predictors of Cognitive Change in Midlife

Although we expected that depressive symptoms, diabetes, hypertension, and smoking would be associated with cognitive *change*, only our hypothesis about smoking was supported. That is, smokers had poorer processing speed and episodic memory than non-smokers over time and these findings are consistent with other data indicating that smoking is associated with cognitive decline in older adults (Anstey, Von Sanden, Salim, & O'Kearney, 2007; Collins, Sachs-Ericsson, Preacher, Sheffield, & Markides, 2009; Ott et al., 2004; Reitz, Luchsinger, Tang, & Mayeux, 2005) and midlife adults (Anstey, Sargent-Cox, Garde, Cherbuin, & Butterworth, 2014; Richards, Jarvis, Thompson, & Wadsworth, 2003; Sabia et al., 2012).

Despite the fact that depressive symptoms, diabetes, and hypertension were not associated with cognitive *change*, they were significantly associated with cognition in proximal analyses. Indeed, the most reliable predictors of poor episodic memory, working memory, and processing speed were depressive symptoms, diabetes, and hypertension. These findings are largely consistent with other studies in midlife and older adult samples (Anstey, Sargent-Cox, Garde, Cherbuin, & Butterworth, 2014; Bangen et al., 2015; Brewster, Peterson, Roker, Ellis, & Edwards, 2017; Evans, Charness, Dijkstra, & Fitzgibbons, 2019; Gifford et al., 2013; Hamilton et al., 2014; Singh-Manoux et al., 2010; Tarraf et al., 2017; Zahodne et al., 2014). Depressive symptoms, diabetes, and hypertension are associated with poorer cognition at a vital time period (i.e., midlife) when dementia pathology most likely develops.

There is some indication that that were more significant associations between risk factors and cognition later versus earlier in midlife. For example, diabetes earlier in midlife was associated with poorer processing speed but - 8 years later - diabetes was also significantly associated with poorer episodic memory and working memory. The adverse effect of diabetes on cognition may get worst as participants get older.

The adverse effects of hypertension and smoking on cognition also increased with age. Diabetes, hypertension, and smoking are all risk factors for cardiovascular disease and our data – while preliminary – suggest adverse associations between heart health and cognition. Indeed, cardiovascular disease is a risk factor for cognitive impairment, AD, and VaD (Baumgart et al., 2015; Samieri et al., 2018).

4.4 Race as a Moderator between Risk Factors and Cognitive Decline

Our hypothesis that the associations between risk factors and cognitive decline in processing speed, working memory, and episodic memory would be stronger for African American women compared to European American and East Asian women was not supported. However, race was a significant moderator in the associations between smoking and episodic memory, depressive symptoms and processing speed, and hypertension and processing speed,, but contrary to expectations; the findings are discussed in more detail below.

4.4.1 Race, smoking, and episodic memory

Smoking was associated with greater decline in episodic memory for East Asian women compared to European American and African American women. We anticipated that African American smokers, due to being disproportionately affected by disparities that adversely impact health, would experience greater decline than European American or East Asian smokers; but that hypothesis was not supported. Smoking is detrimental to cognitive function (Anstey et al., 2014; Collins et al., 2009; Sabia et al., 2012; Vásquez et al., 2016) and this association may be stronger in East Asians compared to European American and African American midlife women. The adverse effect of smoking on episodic memory for East Asian women may be a long-term consequence of early smoking behavior, because the proximal association between smoking and episodic memory was not significant at the beginning of the study. That is, smoking at baseline was significantly associated with cognition measured seven years later. These results have clinical implications; that is, East Asian midlife smokers are at greater risk for cognitive decline than non-smokers and could be targeted for intervention.

4.4.2 Race, depressive symptoms, and processing speed

Contrary to our hypothesis that depressive symptoms would be a stronger risk factor of poorer cognition for African American compared to European American women, results indicated depressive symptoms were not significantly different as a risk factor for both groups of women. African American and European American women with more depressive symptoms had lower processing speed in midlife compared to those with fewer depressive symptoms; this was not the case for East Asian participants. The significant associations between depressive symptoms and processing speed for European Americans and African Americans are consistent with previous literature in older adults that found depressive symptoms were negatively associated with processing speed in African Americans and European Americans (Bielak, Gerstorf, Kiely, Anstey, & Luszcz, 2011; Hamilton et al., 2014; Köhler et al., 2010; Zahodne et al., 2014). Our findings suggest that processing speed in African Americans and European Americans may be vulnerable to the effects of depressive symptoms; therefore depressive symptoms should be targeted in early intervention and prevention strategies for these two populations.

4.4.3 Race, hypertension, and processing speed

Contrary to predictions, hypertension was associated with significant increases – and not decreases – in processing speed across midlife for African Americans. This curious finding is inconsistent with previous literature that found hypertension detrimentally impacts processing speed (Gottesman et al., 2014; Hajjar et al., 2017; Knopman et al., 2001). In our study, African Americans had a significantly higher average systolic blood pressure compared to European Americans and East Asians (Table 5). Hypertension is operationalized as systolic blood pressure of 130 and higher (Whelton et al., 2018). Based on these guidelines, approximately 32% of African American women had hypertension compared to 9.6% of East Asian women and 8.5% of European American women. Although a third of our African American sample had hypertension, higher hypertension levels were associated with *faster* processing speed in this racial group. It is possible that hypertensive medication use could improve cognition or buffer the effects of hypertension on cognition specifically processing speed. Further research on this anomalous finding is warranted.

4.4.4 Race, diabetes, and cognition

Diabetes was more prevalence in African Americans compared to European Americans, which is consistent with previous findings (Fryar, Ostchega, Hales, Zhang, & Kruszon-Moran, 2017). Contrary to predictions – and previous research (Mayeda et al., 2014; Rajan et al., 2016) – we did not find a significant association diabetes and cognitive decline in African Americans compared to European Americans.

There are a number of reasons why our results may have differed from previous findings. First, the previous studies examined both pre-existing (baseline) and incident (follow-up) diabetes; the pre-existing measures were more strongly associated with cognition that the more proximal measures. In our study, we used an average diabetes score over several years just prior to our cognitive assessments rather than a pre-existing measure, which might account for our null findings. Second, the mean age of participants in previous studies was older [e.g., 60 (Mayeda et al., 2014) and 73 years (Rajan et al., 2016) than in our study (e.g., 46 years). Thus, the adverse effects of diabetes on cognition may not be evident until late-midlife or older adulthood. Third, in previous studies, diabetes was measured multiple ways, whereas we measured diabetes in one manner. Thus, diabetes may have been measured more reliably in past research, allowing for a more accurate assessment of associations with cognition.

4.5 Implications

This study has public health, clinical, and theoretical implications. Racial disparities in cognitive aging is a public health concern, particularly because the U.S. aging population is growing more racially and ethnically diverse. It is important for researchers to determine which risk factors adversely impact cognitive aging and may contribute to these racial disparities. Our study suggests that risk factors hold different relevance for different racial groups (e.g. East Asian smokers had greater episodic memory decline compared to European American and African American smokers). Results of this study could inform clinical practice for clinicians who serve ethnically diverse midlife adults. For example, clinicians should be aware that depressive symptoms may pose a greater risk for poor processing speed in European American and African American female patients relative to Asian Americans. Early intervention for Asian American women who are smokers should be implemented to prevent decline in episodic memory.

There are theoretical implications of the current results. The aims of this study were based on the cumulative disadvantage hypothesis; however our results were not consistent with this theoretical framework but instead supported a different health disparities framework, the persistent inequality theory. The persistent inequality theory theorizes that race-based health disparities are relatively unchangeable across time, in part due to social determinants of health (e.g., SES) that are stable across the lifespan (Ferraro & Farmer, 1996). The allocation and availability of resources (i.e., education, healthcare access, income, and housing) is often determined based on one's racial identity and certain racial groups are persistently disadvantaged across the life course. This theory is supported by our finding that African Americans had lower cognitive outcomes in all three cognitive domains throughout the course of the study compared to East Asians and European Americans. Our study illustrated that inequality in cognition persisted across midlife for African Americans. This study underscores the potential importance of early life social determinants in setting the foundation for cognitive health across the lifespan. Understanding disparities in cognitive aging means examining cognition at all stages of life and how risk factors of cognitive decline contribute to the development and maintenance of these cognitive inequalities.

4.6 Limitations

The sample was comprised of women and thus results may not generalize to men. We do not have the immigration status for our sample, which is particularly relevant for our East Asian women, who are more likely to be first or second generation Americans. Our Asian American sample consisted of persons of Japanese and Chinese descent, therefore results may not generalize to other Asian ethnic groups. Likewise, our results may not generalize to racial or ethnic groups not captured in our sample (e.g., Hispanics). Our finding of relatively stable cognitive function in midlife suggests that our sample may not have been followed long enough to observe cognitive decline.

4.7 Future Research and Conclusions

Hypertension, diabetes, depressive symptoms, and smoking were not associated with longitudinal cognitive decline but exhibited proximal associations with poor cognition. Although our risk factors were not associated with cognition in the manner we anticipated, they are indeed predictive of poorer cognitive performance in midlife women. When investigating longitudinal cognitive decline, future research should investigate other risk factors, aside from the ones addressed in the current study (e.g., psychosocial stress). Racial disparities in cognition are evident in midlife for African American women, illustrated by lower episodic memory, working memory, and processing speed scores in African American women relative to European American and East Asian women. Future research should investigate risk factors or mechanisms that may be responsible for vulnerabilities in cognition across the lifespan for African American women compared to their European American and East Asian counterparts.

Likewise, our study has illustrated that our risk factors hold different relevance for cognition between the three racial groups. Future research should further examine *why* certain risk factors (e.g., smoking, depressive symptoms) may hold different relevance to cognition for specific racial groups. Additionally, future research should examine other risk factors that may be more salient or relevant in some racial groups compared to others. For example, discrimination as a risk factor of poorer cognition may be more relevant to African Americans compared to their European American counterparts. These more relevant or salient risk factors in African Americans could contribute to their lower cognitive performance across the lifespan compared to European Americans. By identifying racial group differences in risk factors of poor cognition, we can develop targeted interventions and/or preventions that can be tailored to the needs of specific racial groups.

APPENDIX A

TABLES

Table 1. Studies Examining Cognitive Decline in Older Adult Samples

	Processing Speed	Working Memory	Episodic Memory	Global Cognition
Diabetes	+ Arvanitakis et al., 2004 + Hassing et al., 2004 + Knopman et al., 2009 + Gregg et al., 2000 - Arvanitakis et al 2010 (cross-sectional) - Bangen et al. 2015	- Arvanitakis et al., 2004 - Hassing et al., 2004 - Espeland et al., 2011 -Arvanitakis et al., 2010 (cross-sectional)	+ Okereke et al., 2008 + Pappas et al., 2017 + Wennberg et al., 2017 + Espeland et al., 2011 - Arvanitakis et al., 2004 - Hassing et al., 2004 - Knopman et al., 2009 - Bangen et al. 2015	- Arvanitakis et al 2010 (cross-sectional) + Okereke et al., 2008 + Crowe et al., 2010 + Gregg et al., 2000 + Mayeda et al., 2016
Hypertension	+ Hajjar et al. 2017 - Knopman et al., 2009	0	- Schneider et al., 2014 - Knopman et al., 2009 + Elias et al, 2010 (cross-sectional)	+ Gifford et al., 2013 (cross-sectional) + Gatto et al, 2008 (cross-sectional) +Obisesan et al., 2008 (cross-sectional)
Current Smoking	0	0	+ Reitz et al., 2005 - Vasquez et al., 2016	+ Collins et al., 2009 + Ott et al., 2004 + Anstey et al., 2007

Depressive Symptoms	+ Bielak et al., 2011 + Kohler, van Boxtel et al., 2010 + Brewster et al, 2017 (cross-sectional) + Hamilton et al, 2014 (cross-sectional)	0	+ Gonzalez et al., 2008 - Ganguli et al., 2006 - Royall et al., 2012 + Kohler van Boxtel et al., 2010 + Panza et al., 2009 + Gallagher et al., 2016 + Brewster et al, 2017 (cross-sectional) + Hamilton et al, 2014 (cross-sectional) + Evans et al. 2019 (cross-sectional)	+ Kohler von Boxtel et al., 2010 + Hazzouri et al., 2014 + Paterniti et al., 2002 + Chodosh et al., 2007 + Dotson et al., 2008 + Wilson et al., 2004 (composite score) + Wilson et al., 2014 (composite score) + Goveas et al 2014 + Baer et al., 2012 +Panza et al., 2009

Note. + = positive finding; - = negative finding

Table 2. Studies Examining Cognitive Decline in Midlife Adult Samples

	Processing Speed	Working Memory	Episodic Memory	Global Cognition
Diabetes	+ Knopman et al., 2001 - Anstey et al., 2014	- Anstey et al., 2014	- Debette et al., 2011 - Anstey et al., 2014 -Knopman et al., 2001	+ Rawlings et al., 2014 (midlife diabetes and cognition examined 20 years later) + Nooyens et al., 2010
Hypertension	+ Knopman et al., 2001 -Anstey et al., 2014 + Tarraf et al. 2017 (cross-sectional)	-Anstey et al., 2014	- Debette et al., 2011 - Anstey et al., 2014 -Knopman et al., 2001 + Singh-Manoux et al., 2005 (cross-sectional) + Tarraf et al., 2017 (cross-sectional)	0
Current Smoking	- Knopman et al., 2001 + Anstey et al., 2014	- Anstey et al., 2014	- Debette et al., 2011 - Anstey et al., 2014 - Knopman et al., 2001 + Richards et al., 2003	+ Sabia et al., 2012
Depressive Symptoms	- Anstey et al, 2014 + Singh-Manoux et al., 2010 (cross-sectional)	- Anstey et al., 2014	-Anstey et al., 2014	+ Singh-Manoux et al., 2010 (cross-sectional)

Note. + = positive finding; - = negative finding

Table 3. Racial Differences Between European Americans and African Americans

	Processing Speed		Episodic Memory		Working Memory	
	EA	AA	EA	AA	EA	AA
Diabetes	- Mayeda et al., 2014 (midlife) * Knopman et al., 2001 (midlife) - Obidi et al., 2008 (cross-sectional; older adults) * Knopman et al 2009 (midlife)	+ Mayeda et al., 2014 (midlife) * Knopman et al., 2001 (midlife) + Obidi et al., 2008 (cross-sectional; older adults) * Knopman et al 2009 (midlife)	- Rajan et al., 2016 (older adults; composite score with executive function and global function) - Dore et al., 2016 (cross-sectional; interaction with poverty status)	+ Rajan et al., 2016 (older adults; composite score with executive function and global function) + Dore et al., 2016 (cross-sectional; interaction with poverty status/below poverty level)	- Dore et al., 2016 (cross-sectional; interaction with poverty status)	+ Dore et al., 2016 (cross-sectional; interaction with poverty status/below poverty level)
Hypertension	+ Gottesman et al., 2014 (midlife) + Knopman et al., 2001 (midlife)	- Gottesman et al., 2014 (midlife) -Knopman et al., 2001 (midlife)	0		0	
Current Smoking	- Knopman et al., 2001 (midlife)	+ Knopman et al., 2001(midlife)	+ Schneider et al., 2014 (older adults)	- Schneider et al., 2014 (older adults)	0	
Depressive Symptoms	* Wilson et al., 2004 (older adults; composite of episodic memory and processing speed) + Zahodne et al., 2014 (older adults; cross-sectional)	* Wilson et at al., 2004 (older adults; composite score of episodic memory and processing speed) - Zahodne et al., 2014 (older adults; cross-sectional)	* Wilson et al., 2004 (older adults; composite of episodic memory and processing speed) - Zahodne et al., 2014 (older adults; cross-sectional)	* Wilson et al., 2004 (older adults; composite of episodic memory and processing speed) + Zahodne et al., 2014 (older adults; cross-sectional)	0	

Note.+ = positive finding; - = negative finding; * = no racial differences; EA = European Americans; AA = African Americans

Table 4. Demographic Characteristics by Racial Group in the Sample

Characteristic	European American (*n* = 1,000)	African American (*n* = 516)	East Asian (*n* = 437)
Mean Age (SD)	45.95 (2.73)	45.88 (2.61)	46.11 (2.58)
Family Income (*n*)			
Less than $19,999	57	100	16
$20,000 to $49,999	306	210	120
$50,000 to $99,999	432	156	179
$100,000 or more	193	29	105
Education Level (*n*)			
Less than High School	12	23	23
High School Graduate	119	102	66
Some College/Technical School	290	200	126
College Graduate	224	82	136
Post Graduate Education	353	102	86

Note. Missingness for family income was as follows: European American (1.2%), African American (4.1%), and East Asian (3.9%). Missingness for education level was as follows: European American (0.2%), African American (1.4%), and East Asians (0%). African Americans had significantly lower educational attainment and family income compared to East Asians and European Americans. East Asians had significantly lower educational attainment compared to European Americans.

Table 5. Average of Risk Factors and Cognitive Outcomes at Visit 4 by Racial Group

Variables	European American (*n* = 1,000)	African American (*n* = 516)	East Asian (*n* = 437)
Risk Factors, *M* (SD)			
Depressive Symptoms	8.43 (6.73)	9.89 (7.57)*	8.08 (6.58)
Hypertension	112.48 (12.27)+	124.14 (15.84)	110.68 (11.90)
Diabetes	93.69 (23.04)	102.08 (33.87)*	93.41 (12.35)
Smoking (# of smokers)	115	104	34
Cognitive Outcomes, *M* (SD)			
Processing Speed (SDMT)	57.86 (9.74)	51.05 (11.91)	58.62 (9.10)
Working Memory (DSB)	7.23 (2.33)	5.86 (2.15)	6.42 (1.98)
Episodic Memory (EBMT)	10.40 (1.52)	9.57 (2.06)	9.77 (1.71)

Notes. * = African Americans had significantly higher values than European Americans and East Asians; + = all racial groups are significantly different; Missingness on SDMT are as follows: African Americans (3.7%), East Asians (4.1%), and European Americans (5.0%). Missingness on DSB are as follows: African Americans (4.8%), East Asians (4.1%), and European Americans (6.3%). Missingness on EBMT are as follows: African Americans (4.5%), East Asians (4.1%), and European Americans (5.1%).

Table 6. Change in EBMT as Predicted by Smoking, Depressive Symptoms, Diabetes, and Hypertension

Measure	Depressive Symptoms Coefficient *(SE)*	Diabetes Coefficient *(SE)*	Hypertension Coefficient *(SE)*	Smoking Coefficient *(SE)*
Fixed effects				
Cognitive Outcome (intercept), γ_{00}	10.37 (0.035)**	10.37 (0.035)**	10.37 (0.035)**	10.42 (0.038)**
Age, γ_{01}	-0.02 (0.013)	-0.014 (0.013)	-0.007 (0.013)	-0.017 (0.013)
Smoking, γ_{02}	---	---	---	-0.39 (0.108)**
Depressive Symptoms, γ_{03}	-0.02 (0.005)*	---	---	---
Hypertension, γ_{04}	---	---	-0.008 (0.003)*	---
Diabetes, γ_{05}	---	-0.004 (0.002)*	---	---
Education, γ_{06}	0.19 (0.033)**	0.19 (0.033)**	0.19 (0.033)**	0.181 (0.033)**
Family Income, γ_{07}	0.17 (0.044)**	0.19 (0.044)**	0.18 (0.043)**	0.182 (0.044)**
Cognitive Change (linear slope), γ_{10}	0.05 (0.008)**	0.05 (0.008)**	0.05 (0.008)**	0.06 (0.008)**
Age, γ_{11}	-0.0004 (0.003)	-0.0004 (0.003)	-0.0007 (0.003)	-0.0008 (0.003)
Smoking, γ_{12}	----	---	---	-0.05 (0.024)*
Depressive Symptoms, γ_{13}	0.0003 (0.001)	---	---	---
Hypertension, γ_{14}	---	---	0.0002 (0.0006)	---
Diabetes, γ_{15}	---	-0.0003 (0.0003)	---	---
Education, γ_{16}	-0.012 (0.007)	-0.012 (0.007)	0.19 (0.033)**	-0.014 (0.007)
Family Income, γ_{17}	0.007 (0.010)	0.006 (0.010)	0.18 (0.044)**	0.004 (0.010)
Random Effects		Variance Components		
Intercept, τ_{00}	0.82**	0.82**	0.82**	0.82**
Linear slope, τ_{11}	0.008*	0.008*	0.008*	0.008*
Level 1, σ_2	1.92	1.92	1.92	1.92
Model Deviance *(df)*	31881.86 (14)	31889.65 (14)	31878.39 (14)	31885.60 (14)

Note. * = $p < 0.05$, ** = $p < 0.001$

Table 7. Change in SDMT as Predicted by Smoking, Depressive Symptoms, Diabetes, and Hypertension

	Depressive Symptoms	Diabetes	Hypertension	Smoking
Measure	Coefficient *(SE)*	Coefficient *(SE)*	Coefficient *(SE)*	Coefficient *(SE)*
Fixed effects				
Cognitive Outcome (intercept), γ_{00}	58.05 (0.245)**	58.05 (0.244)**	58.06 (0.245)**	58.25 (0.264)**
Age, γ_{01}	-0.59 (0.092)**	-0.56 (0.092)**	-0.502 (0.093)**	-0.590 (0.093)**
Smoking, γ_{02}	---	---	---	-1.32 (0.762)
Depressive Symptoms, γ_{03}	-0.186 (0.037)**	---	---	---
Hypertension, γ_{04}	---	---	-0.079 (0.018)**	---
Diabetes, γ_{05}	---	-0.056 (0.010)**	---	---
Education, γ_{06}	0.154 (0.233)**	1.55 (0.233)**	1.53 (0.233)**	1.55 (0.236)**
Family Income, γ_{07}	2.26 (0.314)**	2.43 (0.308)**	2.43 (0.310)**	2.55 (0.310)**
Cognitive Change (linear slope), γ_{10}	0.45 (0.093)*	-0.25 (0.093)*	-0.247 (0.093)*	0.310 (0.010)*
Age, γ_{11}	-0.035 (0.035)	-0.034(0.035)	-0.036 (0.036)	-0.030 (0.0035)
Smoking, γ_{12}	----	---	---	0.546 (0.294)
Depressive Symptoms, γ_{13}	0.0007 (0.014)	---	---	---
Hypertension, γ_{14}	---	---	0.001 (0.007)	---
Diabetes, γ_{15}	---	-0.002 (0.004)	---	---
Education, γ_{16}	-0.016 (0.089)	-0.018 (0.089)	-0.018 (0.089)	0.001 (0.090)
Family Income, γ_{17}	-0.185 (0.120)	-0.172 (0.118)	0.166 (0.119)	-0.148 (0.118)
Cognitive Change (curvature), γ_{20}	-0.09 (0.015)**	-0.094 (0.015)**	-0.093 (0.015)**	-0.108 (0.016)**
Age, γ_{21}	-0.005 (0.006)	-0.006 (0.006)	-0.007 (0.006)	-0.004 (0.006)
Smoking, γ_{22}	---	---	---	0.120 (0.047)*
Depressive Symptoms, γ_{23}	0.0009 (0.002)	---	---	---
Hypertension, γ_{24}	---	---	0.002 (0.001)	--
Diabetes, γ_{25}	---	0.0006 (0.0007)	---	---
Education, γ_{26}	0.002 (0.014)	0.002 (0.014)	0.003 (0.014)	0.006 (0.014)
Family Income, γ_{27}	-0.032 (0.019)	-0.031 (0.019)	-0.030 (0.019)	-0.028 (0.019)
Random Effects		Variance Components		
Intercept, τ_{00}	81.13**	80.86**	81.41**	82.36**
Linear slope, τ_{11}	1.32*	1.28*	1.31*	1.14*
Curvature, τ_{22}	0.05**	0.05**	0.05**	0.05**
Level 1, σ_2	26.32	26.33	26.33	26.32
Model Deviance *(df)*	57367.38 (22)	57359.54 (22)	57368.37 (22)	57382.19 (22)

Note. * = $p < 0.05$, ** = $p < 0.001$

Table 8. Change in DSB as Predicted by Smoking, Depressive Symptoms, Diabetes, and Hypertension

Measure	Depressive Symptoms Coefficient (*SE*)	Diabetes Coefficient (*SE*)	Hypertension Coefficient (*SE*)	Smoking Coefficient (*SE*)
Fixed effects				
Cognitive Outcome (intercept), γ_{00}	6.90 (0.054)**	6.90 (0.054)**	6.90 (0.054)**	6.91 (0.058)**
Age, γ_{01}	-0.026 (0.020)	-0.02 (0.020)	-0.017 (0.021)	-0.026 (0.020)
Smoking, γ_{02}	---	---	---	-0.052 (0.167)
Depressive Symptoms, γ_{03}	-0.012 (0.008)	---	---	---
Hypertension, γ_{04}	---	---	-0.009 (0.004)*	---
Diabetes, γ_{05}	---	-0.006 (0.002)*	---	---
Education, γ_{06}	0.451 (0.051)**	0.45 (0.051)**	0.45 (0.051)**	0.45 (0.052)**
Family Income, γ_{07}	0.146 (0.069)*	0.149 (0.068)*	0.146 (0.068)*	0.166 (0.068)*
Cognitive Change (linear slope), γ_{10}	-0.061 (0.024)*	-0.062 (0.024)*	-0.061 (0.024)*	-0.059 (0.026)*
Age, γ_{11}	-0.0007 (0.009)	-0.0005 (0.009)	-0.001 (0.009)	-0.0006 (0.009)
Smoking, γ_{12}	----	---	---	-0.012 (0.076)
Depressive Symptoms, γ_{13}	-0.003 (0.004)	---	---	---
Hypertension, γ_{14}	---	---	0.003 (0.002)	---
Diabetes, γ_{15}	---	-0.0008 (0.001)	---	---
Education, γ_{16}	-0.036 (0.023)	-0.035 (0.023)	-0.035 (0.023)	-0.035 (0.023)
Family Income, γ_{17}	-0.070 (0.031)*	-0.068 (0.030)*	0.065 (0.031)*	-0.066 (0.030)*
Cognitive Change (curvature), γ_{20}	-0.016 (0.004)**	-0.016 (0.004)**	-0.016 (0.004)**	-0.016 (0.004)**
Age, γ_{21}	-0.0003 (0.001)	-0.0003 (0.001)	-0.0003 (0.001)	-0.0002 (0.001)
Smoking, γ_{22}	---	---	---	0.001 (0.012)
Depressive Symptoms, γ_{23}	-0.0007 (0.0006)	---	---	---
Hypertension, γ_{24}	---	---	0.00005 (0.0003)	--
Diabetes, γ_{25}	---	0.00002 (0.0002)	---	---
Education, γ_{26}	-0.007 (0.004)	-0.006 (0.004)	-0.006 (0.004)	-0.006 (0.004)
Family Income, γ_{27}	-0.013 (0.005)	-0.011 (0.004)*	-0.011 (0.005)*	-0.012 (0.005)*
Random Effects		Variance Components		
Intercept, τ_{00}	3.38**	3.37**	3.37**	3.39**
Linear slope, τ_{11}	0.07**	0.07*	0.07*	0.07*
Curvature, τ_{22}	0.002**	0.002**	0.05**	0.002**
Level 1, σ_2	1.74	1.74	1.74	1.74
Model Deviance (*df*)	32698.05 (22)	32696.93 (22)	32695.57 (22)	32704.45 (22)

Note. * = $p < 0.05$, ** = $p < 0.001$

Table 9. Change in EBMT, SDMT, and DSB as Predicted by Race

Measure	EBMT Coefficient *(SE)*	SDMT Coefficient *(SE)*	DSB Coefficient *(SE)*
Fixed effects			
Cognitive Outcome (intercept), γ_{00}	10.59 (0.048)**	59.18 (0.334)**	7.30 (0.074)**
Age, γ_{01}	-0.01 (0.013)	-0.59 (0.090)**	-0.03 (0.020)
African American, γ_{02}	-0.64 (0.088)**	-5.84 (0.604)**	-1.49 (0.1305)**
East Asian, γ_{03}	-0.24 (0.086)*	1.79 (0.603)*	-0.49 (0.133)**
Education, γ_{04}	0.17 (0.033)**	1.57 (0.229)**	0.04 (0.133)**
Family Income, γ_{05}	0.13 (0.044)*	1.64 (0.310)**	0.05 (0.0689)
Cognitive Change (linear slope), γ_{10}	0.04 (0.0101)**	-0.28 (0.131)*	-0.09 (0.034)*
Age, γ_{11}	-0.0005 (0.003)	-0.03 (0.035)	-0.0009 (0.009)
African American, γ_{12}	-0.02 (0.020)	0.38 (0.240)	0.03 (0.062)
East Asian, γ_{13}	0.06 (0.020)*	-0.25 (0.234)	-0.08 (0.060)
Education, γ_{14}	0.17**	-0.02 (0.090)	-0.30 (0.023)
Family Income, γ_{15}	0.13*	-0.10 (0.122)	-0.07 (0.031)*
Cognitive Change (curvature), γ_{20}	----	-0.10 (0.021)**	-0.02 (0.005)**
Age, γ_{21}	----	-0.005 (0.006)	-0.0003 (0.001)
African American, γ_{22}	----	0.09 (0.038)*	0.004 (0.010)
East Asian, γ_{23}	----	0.06 (0.038)	-0.006 (0.010)
Education, γ_{24}	----	0.001 (0.014)	-0.006 (0.004)
Family Income, γ_{25}	----	-0.02 (0.019)	-0.01 (0.005)*
Random effects		Variance Components	
Intercept, τ_{00}	0.77**	74.99**	3.18**
Linear slope, τ_{11}	0.008*	1.26*	0.07**
Curvature, τ_{22}	----	0.05**	0.002**
Level 1, σ^2	1.92	26.32	1.74
Model Deviance *(df)*	31793.36 (16)	571196.52 (25)	32569.72 (25)

Note. * = $p < 0.05$, ** = $p < 0.001$

Table 10. Race Moderating the Association Between Smoking and EBMT

Measure	EBMT	
	Main Effect Coefficient *(SE)*	Interaction Coefficient *(SE)*
Fixed Effects		
Cognitive Outcome (intercept), γ_{00}	10.63 (0.05)**	10.63 (0.05)**
Age, γ_{01}	-0.02 (0.01)	-0.02 (0.013)
African American, γ_{02}	-0.63 (0.09)**	-0.68 (0.09)**
East Asian, γ_{03}	-0.26 (0.09)*	-0.23 (0.09)*
Smoking, γ_{04}	-0.35 (0.11)**	-0.41 (0.15)*
African American-Smoking, γ_{05}	----	0.33 (0.23)
East Asian- Smoking, γ_{06}	----	-0.33 (0.30)
Education, γ_{07}	0.17 (0.033)**	0.16 (0.033)**
Family Income, γ_{08}	0.12 (0.045)*	0.12 (0.044)*
Cognitive Change (linear slope), γ_{10}	0.05 (0.01)**	0.04 (0.01)
Age, γ_{11}	-0.0007 (0.003)	-0.0009 (0.003)
African American, γ_{12}	-0.013 (0.020)	-0.02 (0.02)
East Asian, γ_{13}	0.05 (0.02)*	0.07 (0.020)**
Smoking, γ_{14}	-0.05 (0.02)	-0.03 (0.03)
African American-Smoking, γ_{15}	----	0.03 (0.05)
East Asian- Smoking, γ_{16}	----	-0.16 (0.07)*
Education, γ_{17}	-0.01 (0.008)	-0.01 (0.008)
Family Income, γ_{18}	-0.002 (0.010)	-0.001 (0.01)
Random Effects	Variance Component	
Intercept, τ_{00}	0.76**	0.76**
Linear slope, τ_{11}	0.008*	0.007*
Level 1, σ_2	1.92	1.92
Model Deviance *(df)*	31782.73 (18)	31773.46 (22)

Note. * = $p < 0.05$, ** = $p < 0.001$

Table 11. Race Moderating the Association Between Depressive Symptoms and EBMT

Measure	EBMT Main Effect Coefficient *(SE)*	EBMT Interaction Coefficient *(SE)*
Fixed effects		
Cognitive Outcome (intercept), γ_{00}	10.59 (0.048) **	10.59 (0.048)**
Age, γ_{01}	-0.01 (0.013)	-0.02 (0.013)
African American, γ_{02}	-0.64 (0.09)**	-0.64 (0.088)**
East Asian, γ_{03}	-0.24 (0.09)*	-0.28 (0.087)*
Depressive Symptoms, γ_{04}	-0.02 (0.005)*	-0.006 (0.007)
African American-Depressive Symptoms, γ_{05}	---	-0.02 (0.012)
East Asian- Depressive Symptoms, γ_{06}	---	-0.021 (0.013)
Education, γ_{07}	0.17 (0.03)**	0.16 (0.033)**
Family Income, γ_{08}	0.13 (0.04)*	0.11 (0.046)*
Cognitive Change (linear slope), γ_{10}	0.04 (0.01)**	-0.04 (0.010)**
Age, γ_{11}	-0.0005	-0.0004 (0.003)
African American, γ_{12}	-0.02 (0.02)	-0.02 (0.020)
East Asian, γ_{13}	0.06 (0.20)*	-0.05 (0.020)*
Depressive Symptoms, γ_{14}	0.0003 (0.001)	-0.0003 (0.002)
African American-Depressive Symptoms, γ_{15}	---	0.003 (0.003)
East Asian- Depressive Symptoms, γ_{16}	---	-0.0005 (0.003)
Education, γ_{17}	-0.01 (0.007)	-0.009 (0.007)
Family Income, γ_{18}	-0.0003 (0.010)	0.0005 (0.010)
Random Effects	Variance Components	
Intercept, τ_{00}	0.77**	0.76**
Linear slope, τ_{11}	0.008*	0.008*
Level 1, σ_2	1.92	1.92
Model Deviance *(df)*	131793.36 (16)	31765.38 (22)

Note. * = $p < 0.05$, ** = $p < 0.001$

Table 12. Race Moderating the Association Between Depressive Symptoms with SDMT and DSB

Measure	SDMT		DSB	
	Main Effect Coefficient *(SE)*	Interaction Coefficient *(SE)*	Main Effect Coefficient *(SE)*	Interaction Coefficient *(SE)*
Fixed effects				
Cognitive Outcome (intercept), γ_{00}	59.16 (0.33)**	59.16 (0.33)**	7.30 (0.07)**	7.31 (0.074)**
Age, γ_{01}	-0.60 (0.089)**	-0.60 (0.089)**	-0.026 (0.02)	-0.03 (0.020)
African American, γ_{02}	-5.81 (0.600)**	-5.71 (0.600)**	-1.15 (0.13)**	-1.13 (0.135)**
East Asian, γ_{03}	1.71 (0.60)*	1.87 (0.602)*	-0.49 (0.13)**	-0.48 (0.134)**
Depressive Symptoms, γ_{04}	-0.18 (0.600)**	-0.18 (0.05)**	-0.016 (0.005)*	-0.007 (0.011)
African American-Depressive Symptom , γ_{05}	----	-0.103 (0.082)	---	-0.027 (0.018)
East Asian- Depressive Symptom, γ_{06}	----	0.19 (0.092)*	---	0.01 (0.020)
Education, γ_{07}	1.51 (0.228)**	1.5 (0.223)**	0.41 (0.05)**	0.40 (0.050)**
Family Income, γ_{08}	1.33 (0.314)**	1.32 (0.314)**	0.05 (0.69)	0.03 (0.070)
Cognitive Change (linear slope), γ_{10}	-0.29 (0.13)*	-0.28 (0.131)*	-0.08 (0.03)*	-0.09 (0.03)*
Age, γ_{11}	-0.03 (0.035)	-0.04 (0.040)	-0.0009 (0.009)	-0.002 (0.009)
African American, γ_{12}	-0.38 (0.24)	-0.41 (0.241)	0.031 (0.06)	0.04 (0.062)
East Asian, γ_{13}	-0.26 (0.23)	-0.24 (0.236)	0.08 (0.06)	0.073 (0.060)
Depressive Symptoms, γ_{14}	-0.009 (0.014)	0.002 (0.020)	0.0003 (0.001)	0.001 (0.005)
African American-Depressive Symptom , γ_{15}	----	-0.04 (0.03)	---	-0.001 (0.005)
East Asian- Depressive Symptom, γ_{16}	----	-0.007 (0.036)	---	-0.01 (0.008)
Education, γ_{17}	-0.02 (0.090)	-0.02 (0.090)	-0.03 (0.02)	-0.03 (0.023)
Family Income, γ_{18}	-0.11 (0.124)	-0.11 (0.124)	-0.07 (0.03)*	-0.07 (0.032)
Cognitive Change (curvature), γ_{20}	-0.10 (0.02)**	-0.10 (0.02)**	-0.02 (0.005)**	-0.02 (0.005)**
Age, γ_{21}	-0.005 (0.006)	-0.006 (0.006)	-0.0003 (0.001)	-0.0004 (0.001)
African American, γ_{12}	0.09 (0.04)*	0.09 (0.04)*	0.004 (0.010)	0.004 (0.010)
East Asian, γ_{23}	-0.06 (0.04)	-0.06 (0.038)	0.006 (0.010)	0.005 (0.010)
Depressive Symptoms, γ_{24}	0.0005 (0.002)	0.004 (0.003)		0.00005 (0.0008)
African American-Depressive Symptom , γ_{25}	----	-0.01 (0.005)	---	-0.0002 (0.001)
East Asian- Depressive Symptom, γ_{26}	----	-0.003 (0.006)	---	-0.0008 (0.001)
Education, γ_{27}	0.002 (0.014)	0.0009 (0.14)	-0.006 (0.004)	-0.006 (0.004)
Family Income, γ_{28}	-0.02 (0.020)	-0.02 (0.020)	-0.01 (0.005)	-0.01 (0.005)*
Random Effects	Variance Components			
Intercept, τ_{00}	73.71**	73.20**	3.18**	3.16**
Linear slope, τ_{11}	1.27*	1.26*	0.07**	0.07**
Curvature, τ_{22}	0.05**	0.05**	0.002**	0.002**
Level 1, σ_2	26.31	26.32	1.74	1.74
Model Deviance *(df)*	57169.57(28)	57154.22 (34)	32569.72 (25)	32556.48 (34)

Note. * = $p < 0.05$, ** = $p < 0.001$

Table 13. Race Moderating Hypertension with EBMT and DSB

Measure	EBMT		DSB	
	Main Effect Coefficient *(SE)*	Interaction Coefficient *(SE)*	Main Effect Coefficient *(SE)*	Interaction Coefficient *(SE)*
Fixed Effects				
Cognitive Outcome (intercept), γ_{00}	10.59 (0.048)**	10.58 (0.049)**	7.30 (0.074)**	7.30 (0.076)**
Age, γ_{01}	-0.015 (0.01)	-0.01 (0.013)	-0.03 (0.02)	-0.03 (0.020)
African American, γ_{02}	-0.64 (0.09)**	-0.60 (0.096)**	-1.15 (0.13)**	-1.16 (0.150)**
East Asian, γ_{03}	-0.24 (0.09)*	-0.24 (0.090)*	-0.49 (0.13)**	-0.48 (0.139)**
Hypertension, γ_{04}	-0.008 (0.003)*	-0.003 (0.004)	-0.009 (0.004)*	-0.001 (0.006)
African American-Hypertension, γ_{05}	---	-0.0008 (0.006)	---	0.003 (0.009)
East Asian- Hypertension, γ_{06}	---	0.003 (0.007)	---	0.003 (0.011)
Education, γ_{07}	0.17 (0.03)**	0.17 (0.033)**	0.41 (0.05)**	0.41 (0.051)**
Family Income, γ_{08}	0.13 (0.04)*	0.13 (0.45)*	0.05 (0.07)	0.05 (0.069)
Cognitive Change (slope), γ_{10}	0.041 (0.01)**	-0.04 (0.01)**	-0.09 (0.03)*	-0.09 (0.03)*
Age, γ_{11}	-0.0005 (0.003)	-0.001 (0.003)	-0.0009 (0.009)	0.001 (0.009)
African American, γ_{12}	-0.02 (0.02)	-0.03 (0.021)	0.030 (0.06)	0.02 (0.067)
East Asian, γ_{13}	0.06 (0.02)*	0.06 (0.020)*	0.08 (0.06)	0.085 (0.063)
Hypertension, γ_{14}	0.0002 (0.0006)	0.0004 (0.0009)	0.0003 (0.002)	-0.001 (0.003)
African American-Hypertension, γ_{15}	---	0.008 (0.001)	---	0.003 (0.005)
East Asian- Hypertension, γ_{16}	---	0.00005 (0.002)	---	0.003 (0.005)
Education, γ_{17}	-0.010 (0.007)	-0.009 (0.007)	-0.03 (0.02)	-0.03 (0.023)
Family Income, γ_{18}	-0.0003 (0.10)	0.0002 (0.010)	-0.07 (0.03)*	-0.067 (0.031)*
Cognitive Change (curvature), γ_{20}	----	----	-0.02 (0.005)**	-0.019 (0.005)**
Age, γ_{21}	----	----	-0.0003 (0.001)	-0.0003 (0.001)
African American, γ_{12}	----	----	0.004 (0.010)	0.01 (0.011)
East Asian, γ_{23}	----	----	0.006 (0.010)	0.007 (0.010)
Hypertension, γ_{24}	----	----		-0.0002 (0.0004)
African American-Hypertension, γ_{25}	----	----	---	-0.0006 (0.0006)
East Asian-Hypertension, γ_{26}	----	----	---	-0.0004 (0.004)
Education, γ_{27}	----	----	-0.006 (0.004)	-0.006 (0.004)
Family Income, γ_{28}	----	----	-0.01 (0.005)*	-0.01 (0.005)*
Random Effects		Variance Components		
Intercept, τ_{00}	0.77**	0.77**	3.18**	3.17**
Linear slope, τ_{11}	0.008*	0.008*	0.07**	0.07**
Curvature, τ_{22}	---	---	0.002**	0.002**
Level 1, σ_2	1.92	1.92	1.74	1.74
Model Deviance *(df)*	31793.36 (16)	31784.73 (22)	32569.72 (25)	32568.08 (34)

Note. * = $p < 0.05$, ** = $p < 0.001$

Table 14. Race Moderating Hypertension with SDMT

Measure	SDMT	
	Main Effect Coefficient *(SE)*	Interaction Coefficient *(SE)*
Fixed Effects		
Cognitive Outcome (intercept), γ_{00}	59.16 (0.35)**	59.19 (0.342)**
Age, γ_{01}	-0.58 (0.09)**	-0.58 (0.09)**
African American, γ_{02}	-5.75 (0.64)**	-5.60 (0.66)**
East Asian, γ_{03}	1.78 (0.60)*	1.75 (0.63)*
Hypertension, γ_{04}	-0.009 (0.018)	0.006 (0.027)
African American-Hypertension, γ_{05}	----	-0.04 (0.04)
East Asian- Hypertension, γ_{06}	----	-0.01 (0.05)
Education, γ_{07}	1.56 (0.230)**	1.57 (0.23)**
Family Income, γ_{08}	1.64 (0.310)**	1.63 (0.31)**
Cognitive Change (slope), γ_{10}	-0.30 (0.13)*	-0.31 (0.13)*
Age, γ_{11}	-0.03 (0.036)	-0.003 (0.036)
African American, γ_{12}	0.43 (0.252)	0.29 (0.260)
East Asian, γ_{13}	-0.26 (0.234)	-0.33 (0.244)
Hypertension, γ_{14}	-0.004 (0.007)	-0.01 (0.010)
African American-Hypertension, γ_{15}	----	0.025 (0.016)
East Asian- Hypertension, γ_{16}	----	-0.014 (0.020)
Education, γ_{17}	-0.02 (0.90)	-0.02 (0.90)
Family Income, γ_{18}	-0.10 (0.122)	-0.10 (0.122)
Cognitive Change (curvature), γ_{20}	-0.10 (0.02)1**	-0.01 (0.02)**
Age, γ_{21}	-0.006 (0.006)	-0.005 (0.006)
African American, γ_{12}	0.08 (0.04)*	0.06 (0.041)
East Asian, γ_{23}	-0.06 (0.04)	-0.072 (0.039)
Hypertension, γ_{24}	-0.0004 (0.001)	-0.001 (0.0002)
African American-Hypertension, γ_{25}	----	0.005 (0.003)*
East Asian-Hypertension, γ_{26}	----	-0.003 (0.003)
Education, γ_{27}	0.001 (0.014)	0.001 (0.014)
Family Income, γ_{28}	-0.02 (0.019)	-0.02 (0.019)
Random Effects	Variance Components	
Intercept, τ_{00}	74.93**	74.89**
Linear slope, τ_{11}	1.26*	1.22*
Curvature, τ_{22}	0.046**	0.044**
Level 1, σ_2	26.33	26.33
Model Deviance *(df)*	57188.84 (28)	57178.96 (34)

Note. * = $p < 0.05$, ** = $p < 0.001$

Table 15. Race Moderating Diabetes with EBMT, SDMT, and DSB

Measure	EBMT Coefficient *(SE)*	SDMT Coefficient *(SE)*	DSB Coefficient *(SE)*
Fixed Effects			
Cognitive Outcome (intercept), γ_{00}	10.58 (0.048)**	59.08 (0.33)**	7.29 (0.074)**
Age, γ_{01}	-0.01 (0.013)	-0.58 (0.089)**	-0.02 (0.020)
African American, γ_{02}	-0.63 (0.088)**	-5.68 (0.604)**	-1.14 (0.135)**
East Asian, γ_{03}	-0.25 (0.088)*	1.63 (0.608)*	-0.51 (0.135)**
Diabetes, γ_{04}	-0.003 (0.002)*	-0.06 (0.021)	-0.007 (0.003)*
African American-Diabetes, γ_{05}	-0.0004 (0.003)	0.03 (0.021)	0.007 (0.005)
East Asian- Diabetes, γ_{06}	0.002 (0.006)	-0.06 (0.042)	-0.005 (0.009)
Education, γ_{07}	0.17 (0.33)**	1.52 (0.228)**	0.40 (0.051)**
Family Income, γ_{08}	0.13 (0.45)*	1.55 (0.309)**	0.04 (0.069)
Cognitive Change (slope), γ_{10}	-0.04 (0.01)**	-0.31 (0.131)*	-0.10 (0.03)*
Age, γ_{11}	-0.0005 (0.003)	-0.03 (0.035)	0.0008 (0.009)
African American, γ_{12}	-0.01 (0.020)	0.37 (0.240)	0.03 (0.062)
East Asian, γ_{13}	0.05 (0.020)*	-0.28 (0.237)	0.07 (0.060)
Diabetes, γ_{14}	-0.0003 (0.0005)	-0.008 (0.006)	-0.002 (0.002)
African American-Diabetes, γ_{15}	-0.0002 (0.0007)	0.02 (0.009)	0.003 (0.002)
East Asian-Diabetes , γ_{16}	-0.0007 (0.007)	-0.01 (0.016)	-0.0001 (0.023)
Education, γ_{17}	-0.01 (0.007)	-0.02 (0.090)	-0.03 (0.023)
Family Income, γ_{18}	-0.0005 (0.010)	-0.09 (0.122)	-0.07 (0.031)*
Cognitive Change (curvature), γ_{20}	----	-0.10 (0.02)**	-0.02 (0.005)**
Age, γ_{21}	----	-0.006 (0.006)	-0.0003 (0.001)
African American, γ_{12}	----	0.8 (0.04)*	0.003 (0.010)
East Asian, γ_{23}	----	-0.07 (0.04)	0.003 (0.010)
Diabetes, γ_{24}	----	-0.0001 (0.0009)	-0.005 (0.010)
African American-Diabetes, γ_{25}	----	0.002 (0.001)	-0.0003 (0.0003)
East Asian- Diabetes, γ_{26}	----	-0.003 (0.002)	-0.00007 (0.0007)
Education, γ_{27}	----	0.001 (0.014)	-0.006 (0.004)
Family Income, γ_{28}	----	-0.01 (0.019)	-0.01 (0.005)*
Random Effects		Variance Components	
Intercept, τ_{00}	0.77**	73.68**	3.16**
Linear slope, τ_{11}	0.008*	1.18*	0.06**
Curvature, τ_{22}		0.04**	0.002**
Level 1, σ^2	1.92	26.34	1.74
Model Deviance *(df)*	31787.435 (22)	57162.55 (34)	32560.03 (34)

Note. * = $p < 0.05$, ** = $p < 0.001$

APPENDIX B

FIGURES

Figure 1. Smoking Predicts EBMT

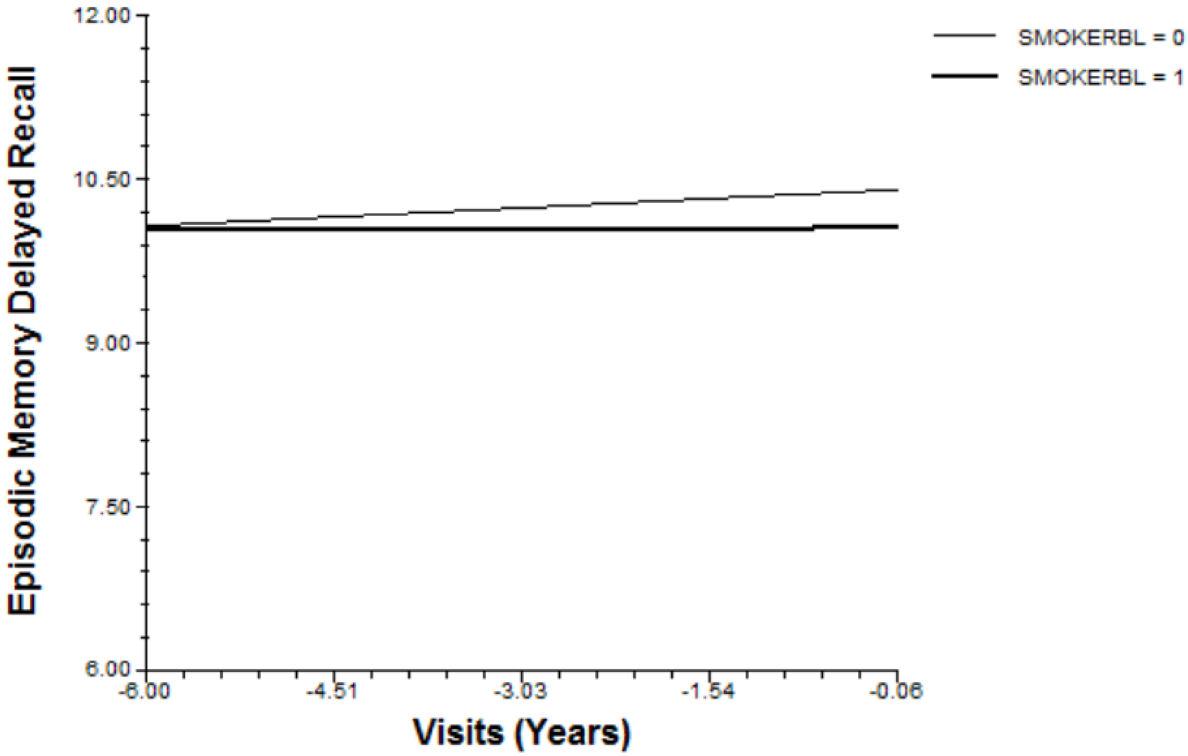


Figure 2. Smoking Predicts SDMT

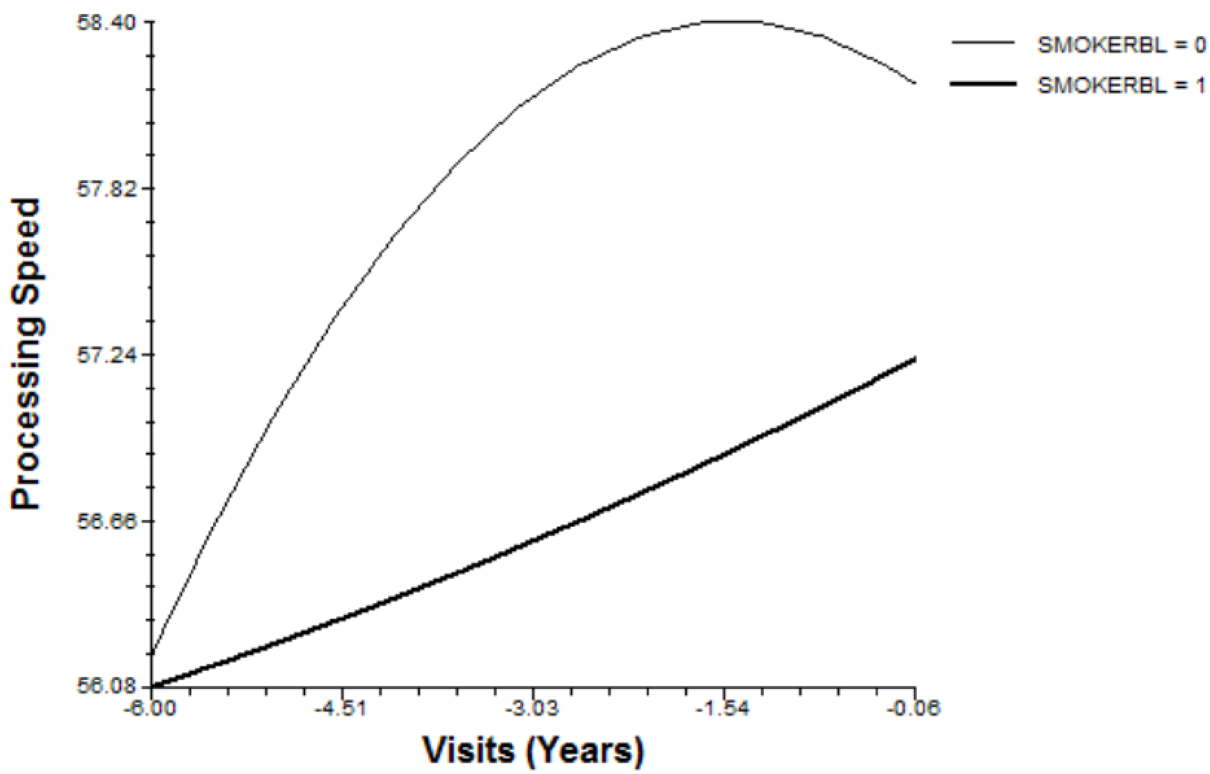


Figure 3. Race Predicts EBMT

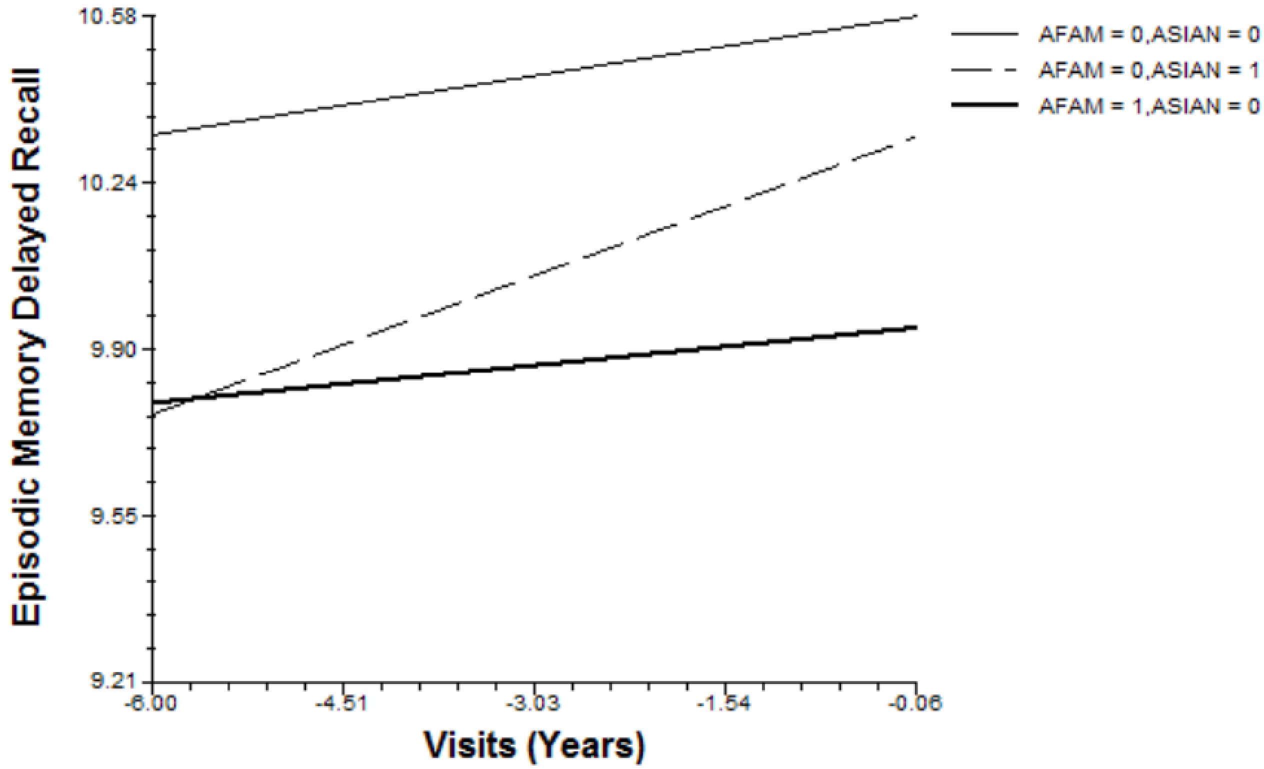


Figure 4. Race Predicts SDMT

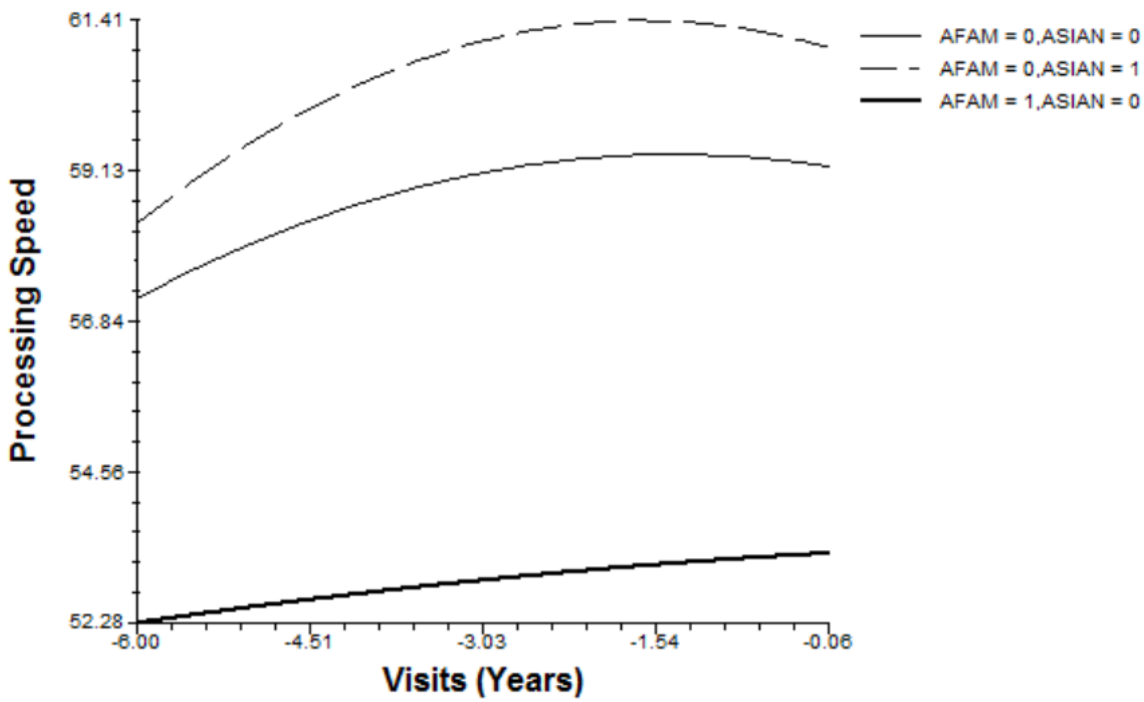


Figure 5. Race-Smoking Interaction on EBMT

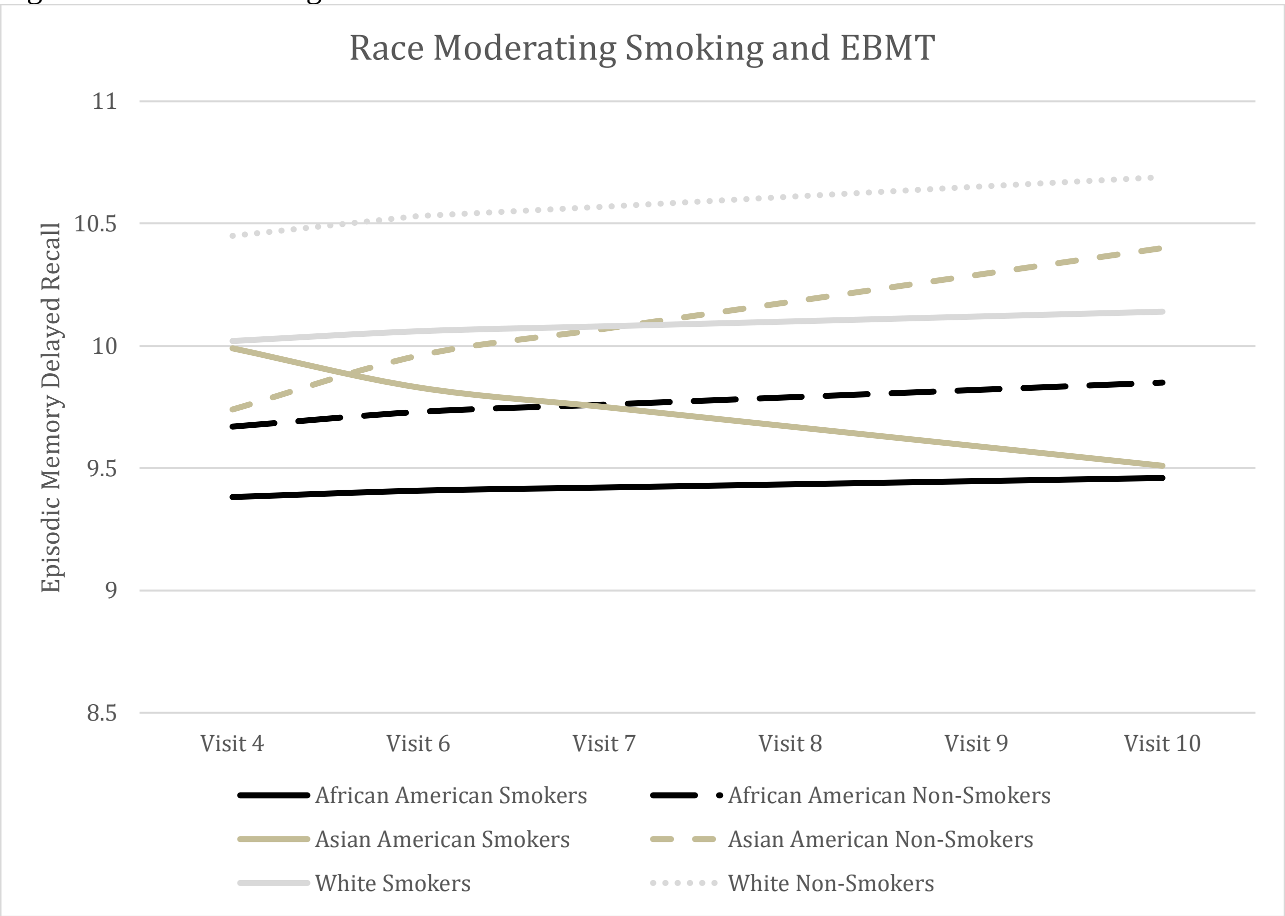


Figure 6. Race-Depressive Symptoms Interaction on SDMT

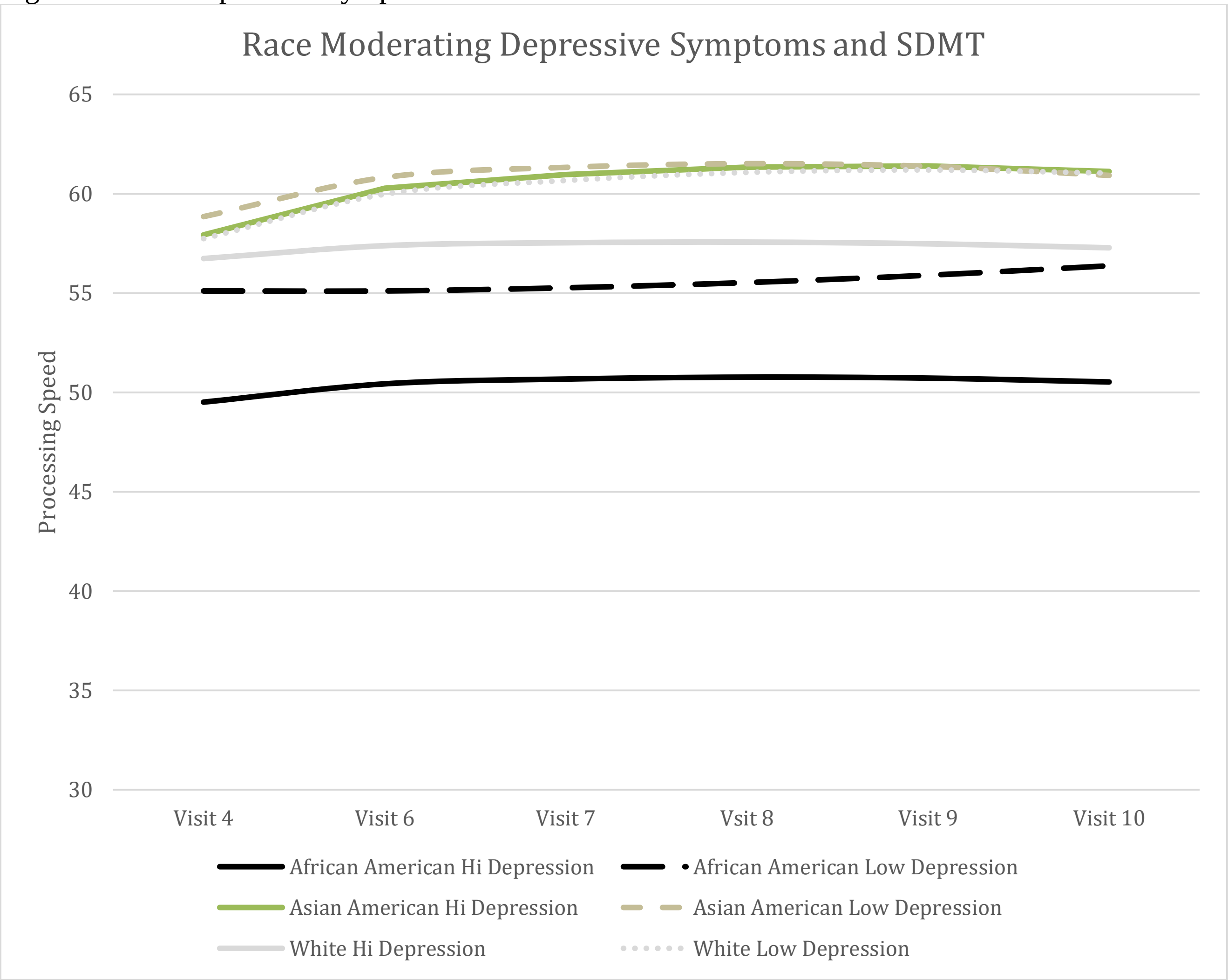
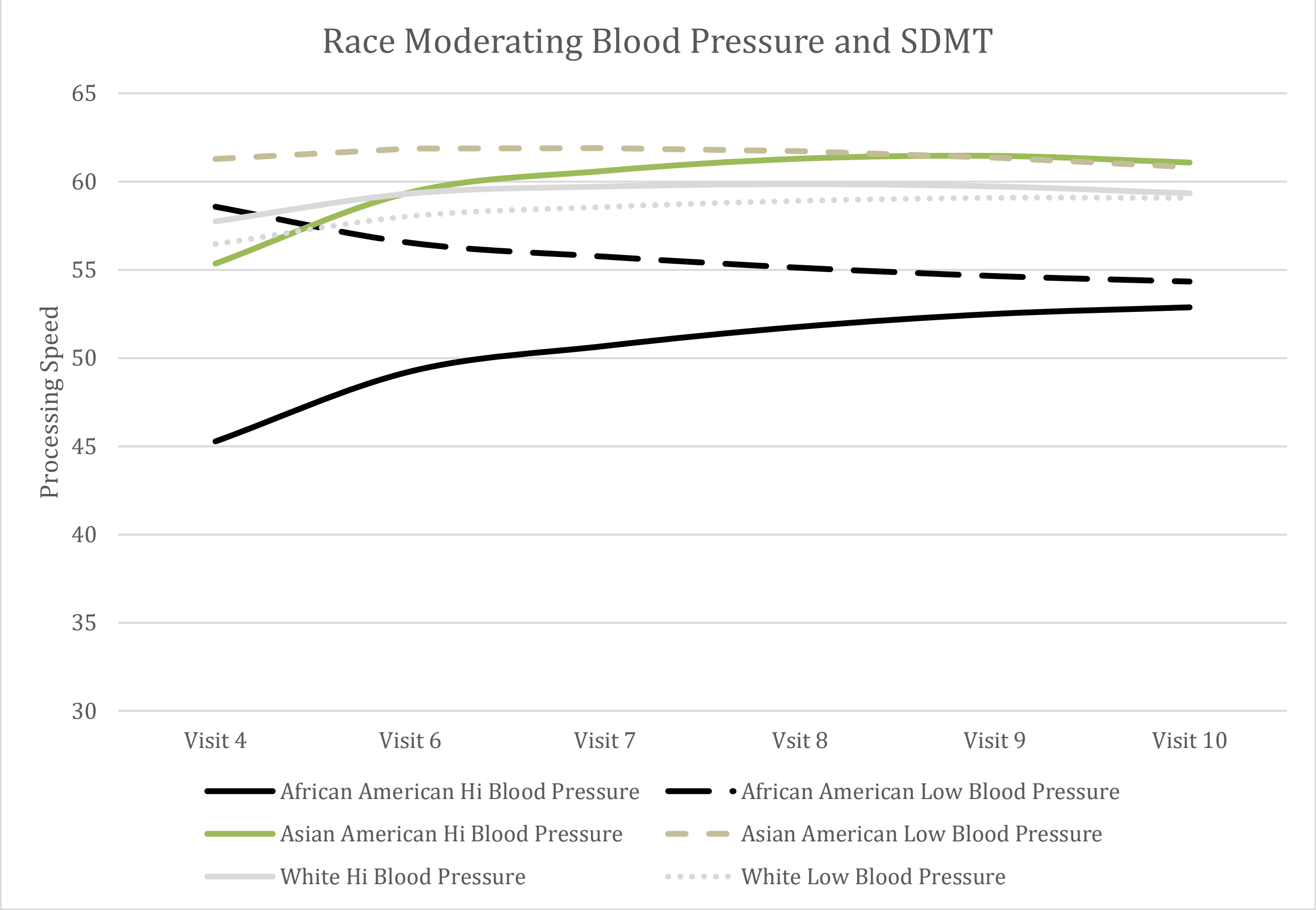


Figure 7. Race-Hypertension Interaction on SDMT



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