Contributors to processing speed deficit in old age: A focus on history of obesity and medical conditions

Melissa E. Pulcini

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Contributors to processing speed deficit in old age:
A focus on history of obesity and medical conditions

by
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Submitted to the Department of Psychology
Eastern Michigan University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY
in
Clinical Psychology

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Abstract

Obesity has been associated with impairment in most cognitive domains, but the nature of this relationship is unclear. Most studies have examined the relationship between cognitive impairment and current obesity and/or history of obesity-related medical conditions. However, a number of “lower-level” obesity factors (e.g., increased adipokines, low grade inflammation, chronic mild hypoventilation) are present even among the otherwise healthy obese population, and it is possible that many of these factors have differential impact on cognition according to magnitude and duration of exposure. Knowledge of a person’s weight history, which may serve as a proxy for a number of lower-level obesity variables that cannot otherwise be measured, may provide additional utility in predicting cognitive functioning. Of the cognitive domains, processing speed is particularly important to study in this context, as its decline plays a large role in driving cognitive aging. Despite this, little is known about the impact of weight history on processing speed in old age. The present study added to the scientific body of literature by using data from the 1999–2000 and 2001–2002 NHANES cycles to examine the relationship between weight history and current processing speed among young-old adults (i.e., adults aged 65–74) using data at three timepoints: young adulthood, late mid-life, and young-old adulthood. A statistically significant relationship between persistent obesity in young adulthood and late middle-age and processing speed in young-old adulthood was identified, but it was found to be fully mediated by vascular health history. Additionally, slow processing speed was associated with the weight trajectory pattern of obesity in late middle-age coupled with the absence of obesity in both young adulthood and young-old adulthood. In regard to study implications, it may be possible that efforts toward prevention of new onset obesity during mid-life, if successful, would protect against slowed processing speed in young-old adulthood.
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Introduction

Statement of the Problem

The prevalence of obesity, a leading cause of preventable death, has nearly tripled among adults in the United States since the late 1970s, and it was estimated that 35.0% and 40.4% of American men and women were obese in 2016, respectively (Sassi, Devaux, Cecchini, & Rusticelli, 2009; Zylke & Bauchner, 2016). At the same time, the percentage of the United States population who are elderly (i.e., 65+ years old) has grown from approximately 9.9% in 1970 to an estimated 14.9% in 2015, with projections to reach 22.1% by 2050 (He, Goodkind, & Kowal, 2016; United States Census Bureau, 2017; United States Department of Health & Human Services, 2014a). Cognitive decline is normative with increasing age, but there is growing evidence that obesity (or obesity-related factors) accelerate this decline (Harada, Natelson Love, & Triebel, 2013; Sabia, Kivimaki, Shipley, Marmot, & Singh-Manoux, 2009; Xu et al., 2011). It follows that America will most likely see an increased number of obese elderly, elderly with a history of obesity, and elderly with greater cognitive decline than what is typically found in normal aging in the coming decades. This has highlighted the importance of understanding the unique cognitive challenges elderly individuals might face as a consequence of obesity or obesity history. It also underscores the importance of understanding the unique value of each obesity index in predicting cognitive functioning in the elderly; this is an especially salient topic given that the most widely used obesity index, body mass index (BMI), underestimates adiposity in the elderly (Heo, Faith, Pietrobelli, & Heymsfield, 2012). Furthermore, it also raises larger questions of (a) whether current and/or history of obesity may be considered independent risks for cognitive dysfunction, and (b) what processes might underlie the relationship between obesity and cognitive dysfunction.
To briefly address the first question, obesity is associated with impairments in attention, processing speed, memory, and executive functioning, although many of the relationships between obesity and cognitive domains appear to vary according to age and sex, and there is conflicting evidence regarding whether these associations are independent or can be sufficiently explained by mediating variables (e.g., hypertension, diabetes). Recently, there has been more focus on lower-level obesity-related factors that may impact cognition (e.g., low grade inflammation, increased circulation of adipocyte hormones, endothelial dysfunction). For example, one recent population-based study of the elderly found that circulating biomarkers of two phenomenon typically seen in obesity (namely, low-grade inflammation and endothelial dysfunction) were associated with impairments in processing speed and executive functioning, and controlling for vascular risk factors only slightly attenuated their relationships (Heringa et al., 2014). It may be that these obesity-related factors that contribute to cognitive decline have an increased effect if the individual is exposed to a greater magnitude (e.g., more hormones released from adipose tissue) and/or over a greater time period (e.g., chronic low-grade inflammation in the chronically obese person, chronic endothelial dysfunction, chronic mild cerebral hypoxia due to chronic mild hypoventilation).

Therefore, rather than studying the relationship between current weight status and cognition, it may be more informative to study long-term weight history and cognition. Indeed, there does appear to be a relationship between weight history and cognitive functioning. For example, obesity during midlife appears to be an independent risk factor for vascular dementia (VaD) and Alzheimer disease (AD) onset in later-life (Xu et al., 2011). Individuals who go on to develop dementia are more likely to have lost a significant amount of weight between midlife and late-life compared with individuals who remain free of dementia (Stewart et al., 2005).
Therefore, the combination of obesity in midlife and weight loss between midlife and late-life, the latter of which is likely to be unintentional, may indicate especially elevated odds of developing dementia.

In addition to those with dementia, many have asked whether body weight history is also related to cognitive functioning both among those without dementia and among the general population. Most of this work has focused on older adults, which is likely due to (a) the idea that older adults will have a greater time period to have experienced impact of weight-related processes on their cognitive functions, and (b) the simple fact that older adults are at greater risk for cognitive decline than any other age group. As expected, preliminary evidence suggests that body weight history is also related to cognitive functioning among those without dementia and in the general population. For example, long-term underweight or obese status during adulthood has been associated with impaired memory and executive functions in late midlife after controlling for sex, age, and education (Sabia et al., 2009). Furthermore, the extent of weight loss or weight gain in middle-aged and older men and women has been associated with poorer performance on visual memory tasks and poorer overall cognitive performance (Brubacher, Monsch, & Stähelin, 2004; Lo, Pachana, Byrne, Sachdev, & Woodman, 2012). However, this area of study is in its infancy, and findings have not been adequately synthesized. There are a myriad of potential mediating and moderating factors that have not yet been accounted for in current research, and very little is known about the potential impact of weight history on processing speed, a domain many consider to be foundational to other cognitive processes (e.g., Vance, 2009).

Processing speed is an especially important cognitive domain in the elderly for many reasons, including the following: (a) In normal cognitive aging, processing speed (along with
spatial ability) declines more rapidly with age than other cognitive abilities (e.g., memory, verbal abilities; Finkel, Reynolds, McArdle, & Pedersen, 2007). Many consider processing speed to be a foundational resource for other cognitive processes, and, according to the processing speed theory of aging, reduced processing speed in old age restricts other cognitive processes to the extent that these cognitive processes rely on processing speed (Finkel et al., 2007; Salthouse, 1996; Vance, 2009). Therefore, processing speed may be a main driver of cognitive aging. (b) Of the cognitive domains, only processing speed appears to be independently associated with longer time to complete everyday tasks in the elderly (Owsley, Sloane, McGwin, & Ball, 2002). (c) Processing speed and spatial abilities, but not memory or other cognitive domains, appear to predict greater life satisfaction prospectively in the very old (Enkvist, Ekström, & Elmståhl, 2013). (d) Greater processing speed has been linked to longer survival time in the elderly, independent of other cognitive impairments and medical conditions (Iwasa et al., 2014). These reasons highlight the need to understand contributors to processing speed in the elderly.

**Study Aims**

The present study added to the body of scientific literature in this area by examining the relationship between weight history (beginning in early adulthood) and current processing speed among men and women aged 65–74, a population typically referred to as the young-old (e.g., Chen, Tsai, Lee, & Lee, 2014; Zizza, Ellison, & Wernette, 2009). The period of early adulthood to young-old adulthood greatly extends the length of weight history in any published study on the relationship between weight history and processing speed. Furthermore, because the present study used data from the 1999–2000 and 2001–2002 cycles of the National Health and Nutrition Examination Survey (NHANES), it was in a unique position to examine the impact of a great number of variables (e.g., current and past medical conditions, blood work, physical activity,
blood pressure, diet, nutrition) that may impact the relationship between weight history and processing speed in a large sample of elderly individuals. While it was hypothesized that weight trajectory would play a role in processing speed in old age, other factors were expected to be very important, and NHANES data provided bountiful opportunity to explore them. The present study made several hypotheses regarding the relationships among NHANES variables and culminated with creation of a model to explain poor processing speed among those with long-term obesity.

It should be noted here that the NHANES is an ongoing study designed to assess the health and nutrition among a sample representative of the United States population, and it involves a number of components, including interviews, laboratory work, and physical examinations. NHANES and other research projects were created by the National Center for Health Statistics (NCHS) in order to collect and provide information to the Centers for Disease Control and Prevention (CDC) for the purposes of guiding public health action and policy (NHANES Plan and Operations, 1999–2010). The 1999–2000 and 2001–2002 NHANES cycles were chosen for the present study due to their inclusion of a processing speed measure, whereas subsequently completed cycles have not.

A secondary aim of the present study was to examine the relationship between various obesity indexes (e.g., body mass index [BMI], percent of total body mass that is comprised of fat as measured by dual energy x-ray absorptiometry [% total fat DEXA], percent of trunk mass that is comprised of fat as measured by DEXA [% trunk fat DEXA], waist circumference [WC], waist-thigh ratio [WTR], waist-height ratio [WHtR]) and processing speed, and determine whether there is an interactive effect of obesity indexes on processing speed. Most studies on the relationship between weight and cognition have relied on BMI to define obesity; however, there
is reason to believe that regional body composition is also important in impacting cognition. In fact, a community study of the elderly found BMI and waist circumference to interact such that high BMI only predicted poor performance on a brief screener for cognitive impairment when abdominal obesity was present (Jeong, Nam, Son, Son, & Cho, 2005). Unfortunately, little more is known due to the paucity of such studies. The present study sought to determine the relationship between processing speed and multiple obesity indexes, as well as determine the best combination of indexes in predicting processing speed.

**Overweight and Obesity Trends and Prevalence**

The prevalence of overweight and obesity in adults aged 20 years or older in 2011–2012 in the United States was estimated with NHANES data using standard World Health Organization (WHO) BMI cut-offs to be 68.5% and 34.9%, respectively (Ogden, Carroll, Kit, & Flegal, 2014). This obesity prevalence represents almost a three-fold increase compared with 12.6% in 1978 (Sassi et al., 2009). A number of other countries, such as Australia, Canada, and England, are nearly as affected by the epidemic, as they have seen their obesity rates more than double in recent decades (Sassi et al., 2009). Although the U.S. may now finally be nearing a stabilization of obesity rates, those countries with historically low rates of obesity (e.g., South Korea, France) are expected to show significant increases in the coming years (Flegal, Carroll, Ogden, & Curtin, 2010; Sassi et al., 2009).

Rates of estimated overweight and obesity vary by age, sex, and race/ethnicity. In the United States, men have higher estimated rates of overweight, but women have higher estimated rates of obesity (Ogden et al., 2014). Overweight rates are also elevated in adults aged 40–59 years (75.3%) and 60+ years (71.6%) compared with adults aged 20–39 years (60.3%; Ogden et al., 2014). Furthermore, Hispanic women and non-Hispanic Black women are estimated to have
higher rates of overweight at each of the above age ranges compared to their non-Hispanic Asian and non-Hispanic White counterparts (Ogden et al., 2014).

Elderly Trends and Prevalence

Similar to obesity, the prevalence of the elderly (adults aged 65+) in the United States has climbed significantly throughout the past century. For example, approximately 8.1%, 9.9%, 12.6%, and 13.0% of the population was elderly in 1950, 1970, 1990, and 2010, respectively (United States Department of Health & Human Services, 2014a). The latest available data indicates that approximately 14.9% of the US population was elderly in 2015 (United States Census Bureau, 2017). Elderly prevalence is expected to climb dramatically in the upcoming decades, partly due to the aging of the baby boomer generation; it has been projected that 22.1% of the U.S. population will be elderly by 2050 (He et al., 2016). Taken together with the aforementioned obesity prevalence data, these data suggest that there will be dramatic increase in the number of obese elderly individuals and elderly individuals with a significant history of obesity in the coming decades in the United States.

Assessing Obesity in the Elderly

To examine the impact of obesity and history of obesity on the elderly, it is first necessary to examine the utility of obesity assessment methods. In doing so, it is also useful to understand how body composition and these indexes typically change with age.

Body mass index. The most commonly used method of assessing obesity among adults is the body mass index (BMI), which is calculated by dividing weight in kilograms (kg) by height in meters squared (m²). The WHO uses BMI as its standard unit for obesity statistics for adults and recommends the following set of international cut-offs for researchers: underweight < 18.50 kg/m²; normal 18.50–24.99 kg/m²; overweight ≥ 25.00 kg/m²; obese ≥ 30.00 kg/m²; obese
class I 30.00–34.99 kg/m²; obese class II 35.00–39.99 kg/m²; and obese class III $\geq 40.00$ kg/m² (WHO, 2010).

Although BMI is the most widely used method for estimating adiposity, there are several known problems with its use. BMI, which relies solely on height and weight, cannot distinguish fat from bone, muscle, and other lean body mass. Given this deficit, it is not surprising that BMI tends to overestimate body fat percentage in those with muscular builds (e.g., athletes) and to underestimate body fat percentage in those who have lost muscle or bone density (e.g., the elderly; NIH, 2010). Indeed, researchers routinely consider types of body fat estimation methods that do not rely solely on anthropometric measurements (e.g., hydrostatic weighing, dual energy X-ray absorptiometry [DEXA]) to be more accurate than BMI (e.g., Duncan, Duncan, & Schofield, 2009; Kupusinac, Stokić, & Doroslovački, 2014). Furthermore, percentage of body fat, when ascertained by these more accurate methods, in individuals with the same BMI value has been shown to vary significantly across age, ethnic, and racial populations (Deurenberg, Yap, & van Staveren, 1998). For example, the elderly have significantly more body fat than young and middle-aged adults at a given BMI (Heo et al., 2012). Moreover, Asians have significantly more body fat than Whites at a given BMI, and White and Hispanic women have significantly more body fat than Black women at a given BMI (Deurenberg, Yap, & Guricci, 2002; Rahman & Berenson, 2010). These findings suggest the potential for underestimation of body fat in Asians and the elderly as well as overestimation of body fat in Black individuals.

Another weakness of BMI is its inability to provide data on body fat distribution or body shape, factors which carry additional information regarding various health risks (Després, 2012). As a result, many researchers continue to advocate for the use of alternative measures of body fat in
research and/or use of BMI cut-offs specific to the population served (Burkhauser & Cawley, 2008; Kagawa, Uenishi, Kuroiwa, Mori, & Binns, 2006).

**Central obesity indexes.** Many other obesity indexes have focused on abdominal adiposity (e.g., waist circumference [WC], waist-to-hip ratio [WHR], waist-thigh ratio [WTR], waist-height ratio [WHtR], % trunk fat DEXA). Interest in these central obesity indexes are related to findings that they predict increased risk for certain obesity-related diseases beyond that conferred by BMI classification and, in fact, are even better predictors of hypertension, dyslipidemia, metabolic syndrome, and type-2 diabetes mellitus (T2DM) than BMI (Guasch-Ferré et al., 2012; Janssen, Katzmarzyk, & Ross, 2002, 2004; Radzevičienė & Ostrauskas, 2013; van Dis, Kromhout, Geleijnse, Boer, & Verschuren, 2009; Yusuf et al., 2004). Reasons for advantages of these central obesity indexes have been theorized to include differences in metabolic activity of visceral and subcutaneous adipose tissues, shared genetic influences between waist circumference and T2DM, and findings that larger hip and thigh circumferences are associated with decreased risk of T2DM (Conway et al., 2011; Mamtani et al., 2014; Power & Schulkin, 2008; Snijder et al., 2003). It should be noted that, although these are called central obesity indexes, WHR, WTR, and WHtR each reflect information about one’s body proportion that goes beyond waist only.

Optimal cutoffs in predicting health risks using the aforementioned central obesity indexes have been found to vary by sex, race/ethnicity, and age (Dobbelsteyn, Joffres, MacLean, & Flowerdew, 2001; Lear, James, Ko, & Kumanyika, 2010). The most common cutoffs for central obesity in men include WC of $\geq 102$ centimeters (cm) and WHR of $\geq 0.95$, whereas the most common cutoffs for women include WC of $\geq 88$cm and WHR of $\geq 0.8$ (Lear et al., 2010). However, these cutoffs are primarily based on studies of Caucasians of European origin, and
there is some evidence to suggest that optimal WC cutoffs for Asians are lower than those of European Caucasians (Lear et al., 2010; Obesity in Asia Collaboration, 2008). There is less conclusive evidence regarding specific central obesity cutoffs for other groups, including African-American, Hispanic, and Middle Eastern populations (Lear et al., 2010). In regard to age, higher cutoff points for WC and WHR appear to be more appropriate for older aged populations up to age 65, at which point the appropriate cutoffs appear to lower slightly (Dobbelsteyn et al., 2001). One study found optimal WC cutoffs in individuals aged 60–74 to be similar to the aforementioned commonly used cutoffs (Gouveia, Marucci, Lebrão, & Duarte, 2014). More research is needed to better understand appropriate central obesity cutoffs for predicting health risks in all age ranges within the elderly populations, particularly in those above 75 years of age.

There is no clear consensus regarding which of the central obesity indexes is most useful in predicting medical outcomes, although one recent systematic review and meta-analysis concluded that WHtR is better in predicting hypertension, T2DM, dyslipidemia, and metabolic syndrome among adults than WC or BMI (Ashwell, Gunn, & Gibson, 2012). Among the elderly, WHtR and WC appear to predict metabolic diseases about equally as well, both surpassing BMI (Guasch-Ferre et al., 2012). WC, but not WHR, is associated with hypertension among the elderly, and WC has been found to predict mortality better than WHR and BMI in this population (de Hollander et al., 2012; Visscher et al., 2001; Woo, Ho, Yu, & Sham, 2002). Relatively less has been published about the value of WTR or % trunk fat DEXA as central obesity indexes, but preliminary data suggest that WTR may be a better predictor of peripheral vascular disease than WC and a better predictor of T2DM in men than WC, WHR, and WHtR (Li, Ford, Zhao, Kahn, & Mokdad, 2010; Lu, Zhou, Waring, Parker, & Eaton, 2010). Taken
together, these results suggest that WTR, WHtR, and WC have great potential as health screening tools. More system comparisons (especially those involving WHtR and WTR) are needed to determine the best index to use to screen for each medical condition.

**Other obesity indexes.** Methods typically considered to be more accurate in estimating adiposity than BMI and the aforementioned central obesity indexes include DEXA, computerized tomography (CT), magnetic resonance imaging (MRI), bioelectrical impedance analysis (BIA), hydrostatic weighing, total body electrical conductivity (TOBEC), and skinfold thickness measurements (Moyad, 2001). These methods tend to be costly, not widely available, and/or necessitate administration by trained technicians, and thus are often not practical to implement in large studies. The NHANES, however, is an ongoing large epidemiological study that does obtain body composition data using one of these methods, namely DEXA. This method uses two x-ray beams of differing wavelengths to analyze body composition. Information on bone mineral content, bone mineral density, and fat-free mass can be yielded with this technique, and estimates of percent body fat can be calculated indirectly from this information (Clasey et al., 1997). Standard DEXA cut-offs for obesity are fat mass ≥ 25% for men and ≥ 35% for women (Donini et al., 2013). Advantages of DEXA include ability to differentiate between fat and lean mass, validity in determining percent body fat within obese and elderly populations, ability to yield regional body composition measurements (e.g., arm, trunk), and good reproducibility in estimates of abdominal fat and lean mass (He, Li, & Kung, 1999; Salamone et al., 2000; Tallroth, Kettunen, & Kujala, 2013). Disadvantages include measurement error introduced by variations in hydration in fat-free mass across individuals and lack of consistency of DEXA scan mode used in research (Clasey et al., 1997; Salamone et al., 2000).
Changes in body composition and obesity indexes with age. Aging is associated with significant changes in body composition, including those involving total adiposity, distribution of adiposity, and fat-free mass, the latter of which includes muscle mass, bone mass, and other nonfat parts of the body (Obisesan et al., 2005; Oldroyd, Stewart, Truscott, Westmacott, & Smith, 1998). Total fat mass and percentage of body fat generally increase with age (Jackson, Janssen, Sui, Church, & Blair, 2012; Kyle, Genton, Slosman, & Pichard, 2001). Some data suggest that total fat mass and body fat percentage stabilizes after about age 80, but other research suggests that they continue to increase well into the 90s in healthy individuals (Jackson et al., 2012; Kyle et al., 2001). Subcutaneous fat (e.g., on arms and legs) decreases begin in late midlife and continues until at least one’s 80s, whereas fat in the viscera and other areas (e.g., organs, muscles) increase during midlife (Oldroyd et al., 1998; WHO Expert Consultation, 2008). Declines in fat-free mass (FFM) and fat-free mass index (FFMI) typically begin during one’s 50s and become significant by ages 65–69 in Black men, 70–74 in Black women and White men, and 75–79 in White women (Obisesan et al., 2005). Bone loss begins even sooner at approximately 30 years of age and is accelerated in the early post-menopausal period in women (Ahlborg et al., 2001; Nuti, Martini, & Gennari, 1995). Furthermore, significantly more lean mass is lost during weight loss in the elderly than is gained during weight gain in this population (Newman et al., 2005). These body composition changes explain why the elderly are prone to both sarcopenia, an age-related loss of muscle tissue, and sarcopenic obesity, the combination of sarcopenia and high fat mass (Evans & Campbell, 1993).

Obesity indexes also tend to vary with age. The obesity indexes of BMI, WHR, and WC increase up to age 64; in the decade thereafter, BMI declines in both sexes, WC increases slightly for men but declines slightly among women, and WHR shows no significant change.
(Dobbelsteyn et al., 2001). Currently, there appear to be no published studies specifically on changes in WHtR or WTR throughout adulthood into old age. It should be cautioned that changes in obesity indexes are not necessarily consistent with body composition changes in the elderly. For example, BMI typically declines in old age, but total fat mass does not appear to do so. Likewise, WC decreases slightly among women after age 64, but visceral fat mass is actually thought to increase in this population. For these reasons, care should be taken when selecting obesity indexes to assess adiposity or related health risks in the elderly. In regard to the present study, it was hypothesized that age would be positively associated with percent body fat estimated by DEXA but would show a slight negative correlation with BMI. It was also hypothesized that WC would show little change with age, but visceral adiposity estimated by % trunk fat DEXA would increase with age.

**Obesity Comorbidity/Mortality**

Obesity is associated with reduced quality of life, financial burden, and increased risk for many medical and psychological disorders, certain types of cognitive decline, and mortality. The present section summarizes the relationships between obesity and these comorbidities, focusing on relationships within the elderly population when data are available.

**Medical.** Overweight/obesity has been named one of the five leading global risks for mortality by the WHO and is associated with three of the other four identified risks: hypertension, high blood glucose levels, and physical inactivity (WHO, 2009). Also a risk factor for hypercholesterolemia and raised triglyceride levels, obesity is associated with increased prevalence of cardiovascular diseases (CVDs), the worldwide leading cause of death (Mendis, 2010; WHO, 2003). Obesity is also a primary risk factor for T2DM, as excess adipose tissue can have a contributory role in increased insulin resistance, resulting in increased blood glucose
levels (Amini et al., 1997). Other potentially life-threatening events or conditions with well-established links to obesity include several types of cancers, chronic kidney disease, obstructive sleep apnea, gallstones, asthma, micronutrient deficiencies, and complications following certain types of surgical procedures (Arif, Rohrer, & Delclos, 2005; Dowsey, Liew, Stoney, & Choong, 2010; Must et al., 1999; Whaley-Connell, Pavey, Afroze, & Bakris, 2006; Xanthakos, 2009). Moreover, obesity is associated with many non-life threatening medical conditions, including osteoarthritis, stress incontinence, gout, gastroesophageal reflux disease, and polycystic ovary syndrome, all of which have been shown to negatively impact health-related quality of life (Jeong, 2008; Roddy, Zhang, & Doherty, 2007; Tincello et al., 2010; Yildiz et al., 2010).

Given this, it is not surprising that obesity has been repeatedly linked to impaired health-related quality of life and disability (e.g., Alvarez-Blasco, Luque-Ramírez & Escobar-Morreale, 2010; Corica et al., 2006; Strain et al., 2010). Those with class III obesity appear to suffer greater health-related limitations in performing physical activities (e.g., walking one mile, walking up steps) than those with class I–II obesity (Casters, Folope, Dechelotte, Tourny-Chollet, & Lemaitre, 2010). Furthermore, there is a well-documented association between obesity and chronic pain in individuals of diverse ages, ranging from children to the elderly (McCarthy, Bigal, Katz, Derby, & Lipton, 2009; Wilson, Samuelson, & Palermo, 2010). Obesity has also been found to have a negative mediating effect on pain outcomes of various procedures, including knee arthroscopy, knee arthroplasty, and hip arthroplasty (Gandhi, Razak, Davey, & Mahomed, 2010; Harrison, Morrell, & Hopman, 2004; Núñez et al., 2009).

Obesity in midlife has been linked to shorter life span, which is consistent with its association with a number of life-threatening conditions (Peeters et al., 2003). In contrast, obesity among the elderly, when measured by BMI, has been associated with survival (Auyeung
et al., 2010; Lee et al., 2014). The origins of these discrepant findings are unclear but are theorized to be related to health risks and conditions in normal weight elderly, including illness, smoking, and normal weight obesity, the latter of which is a condition marked by a normal BMI but a high level of body fat (Richman & Stampfer, 2010). More specifically, a variety of clinical or subclinical illnesses (or related medical treatments) that are more common in the aging population, such as dementia and cancers, often directly or indirectly lead to weight loss (Stewart et al., 2005; Tisdale, 2003; Wannamethee, Shaper, Whincup, & Walker, 2000). The extent of weight loss is associated with worse prognosis in many of these illnesses, and weight loss amongst the elderly is predictive of mortality (Bamia et al., 2010; Martin et al., 2013; Thivat et al., 2010). Therefore, an elderly population sampled at a particular time point will include many who have recently lost weight unintentionally and may have subclinical or clinical illness that put them at greater risk for mortality. Furthermore, elderly individuals who smoke, a behavior which carries a well-documented mortality risk, tend to have a lower BMI and a lower risk of obesity than the elderly who do not smoke (Sulander, Rahkonen, Nissinen, & Uutela, 2007; United States Department of Health & Human Services, 2014d; Wilson, Habib, & Philpot, 2002). Finally, the elderly demonstrate increased cases of normal weight obesity, which is associated with cardiovascular mortality independent of BMI and central fat distribution in the elderly (Batsis et al., 2013). It has been hypothesized that although normal BMI predicts greater mortality in the elderly, the aforementioned factors associated with normal BMI in the elderly, rather than the normal BMI itself, are likely to cause mortality (Richman & Stampfer, 2010). At present, it continues to be debated as to whether there are any true benefits of obesity in old age, or whether this idea is simply an artifact of bias in our research due to reverse causation (Flegal,
Graubard, Williamson, & Cooper, 2011; Richman & Stampfer, 2010). More research is needed to better answer these questions.

**Psychopathology.** Obesity is associated with psychopathology, including depressive disorders, social phobia, panic attacks, agoraphobia, binge eating disorder, attention deficit hyperactivity disorder, and history of alcohol use disorders (Barry & Petry, 2009; Herpertz et al., 2006; Mather, Cox, Enns, & Sareen, 2009; Pagoto et al., 2009). These associations vary according to a host of factors, including age and gender. Generally, women and younger adults evidence greater associations between BMI and psychiatric disorders than men and older adults, respectively (Mather et al., 2009; McCrea, Berger, & King, 2012). Age and gender may also interact. For example, one study found that the probability of a young woman having a common psychiatric disorder (e.g., depressive disorders, anxiety disorders) increases between approximately BMI 20–30 kg/m² with a relative stabilization thereafter (McCrea et al., 2012). In contrast, the association between BMI and common psychiatric disorders takes a “U shaped” pattern in young men, such that both underweight and obesity increases the probability of a common psychiatric disorder (McCrea et al., 2012). The relationship between BMI and common psychiatric disorders attenuates significantly by age 60 in both men and women (McCrea et al., 2012).

**Financial burden.** Economic costs of obesity have been conceptualized on the following three basic levels: individual (e.g., lost opportunities), employer (e.g., lost productivity, higher insurance premiums), and government (e.g., Medicare and Medicaid spending; Runge, 2007). Obesity-related medical costs, which are shared by all three of these levels, are estimated to be approximately $147 billion per year, accounting for 9.1% of the nation’s total medical spending (Finkelstein, Trogdon, Cohen, & Dietz, 2009). Obese
individuals tend to use more health care resources, which may be due to increased prevalence of conditions for which obesity is a risk factor, such as T2DM and asthma, as well as other factors including reduced physical activity, lower quality of life, increased depressive symptoms, and increased risks and costs of surgery (Ahn, Smith, Matthew Lee Dickerson, & Ory, 2012; Kirk, Kuhle, Ohinmaa, Colman, & Veugelers, 2012; Rosemann, Grol, Herman, Wensing, & Szecsenyi, 2008; Trakas, Lawrence, & Shear, 1999). Little has been published on the financial impact of obesity on the elderly, but one study used simultaneous equation system modeling to estimate that individuals who are overweight or obese at age 65 have 6–17% greater health care expenditures during the rest of their lifetimes than those who are normal weight at age 65 (Yang & Hall, 2008).

Cognition. There is growing evidence that obesity is associated with impaired cognition and may even have a contributory role in its development in some cases. Associations have been found between obesity and impairments in attention, processing speed, memory, and executive functions, as detailed below.

Attention. Attention is fundamental to virtually all cognitive tasks, and research suggests obese adults have specific deficits in both automatic and controlled processing within this domain. More specifically, obese adults have been found to have reduced capacity in perceiving or attending to negative facial expressions compared to healthy-weight controls (Cserjési, Vermeulen, Lénárd, & Luminet, 2011). Additionally, Gunstad et al. (2007) found significant negative correlations between body mass index (BMI) and performances on tests requiring attentional processing, including those of working memory, choice reaction, and visual memory span. Higher BMI has also been associated with poorer selective attention and greater rate of decline in selective attention abilities among middle-aged women; however, the same
relationship was not found among men (Cournot et al., 2006). Most recently, Stanek et al. (2013) reported an independent association between elevated BMI and poor performance on a composite of tasks designed to assess attention and processing speed among both men and women.

**Processing speed.** Middle-aged obese adults demonstrate impaired performance on tests of processing speed. In addition to the aforementioned findings by Stanek et al. (2013), another recent study reported higher BMI to be independently associated with poorer performance on the Digit Symbol Substitution Test (DSST), a traditional measure of processing speed, among middle-aged adults without dementia after adjusting for a number of potentially confounding variables (Cournot et al., 2006). Furthermore, Sanz and colleagues (2013) found higher BMI to predict worse performance on the DSST after adjusting for age, sex, education, occupational status, income, smoking, alcohol use, physical activity, psychotropic drugs, and metabolic syndrome variables (i.e., hypertension, dyslipidemia, vascular disease, C-reactive protein) among middle-aged individuals. In contrast to these findings among middle-aged adults, Kuo et al. (2006) reported healthy elderly obese individuals to perform similarly to their normal-weight counterparts on the DSST and to have better performance on the Useful Field of View (UFOV), which relies more heavily on visuospatial speed of processing and less heavily on motor demands, indicating that the relationship between obesity and reduced processing speed may shift with age. In regard to the present study, which includes both healthy and unhealthy volunteers, DSST scores were not expected to be significantly related to current BMI. The extent to which impairment in fine motor speed, which has been found among obese adults, may impact these findings is unclear, although one study did not find evidence for fine motor speed to be a significant contributor to DSST score (Joy, Fein, & Kaplan, 2003; Stanek et al., 2013).
Graphomotor coordination, which could potentially contribute to DSST score, has not been found to differ between normal-weight and obese children (Mond, Stich, Hay, Kraemer, & Baune, 2007). It is unclear if graphomotor coordination or speed differs among the elderly population according to weight category.

**Memory.** Results of several studies indicate the presence of auditory and visual memory deficits in obese adults (Gunstad et al., 2007; Gunstad, Paul, Cohen, Tate, & Gordon, 2006; Wolf, Beiser, Elias, Vasan, & Seshadri, 2007). There is, however, a lack of clarity regarding whether these memory deficits are independently associated with obesity. For example, Gunstad and colleagues (2006) reported an independent association between higher BMI and a variety of memory deficits (as evidenced by poorer performance on immediate and delayed recall and recognition tasks) among obese adults across the adult lifespan. However, Stanek et al. (2013) failed to find an independent association between BMI and memory functioning in a similar study that controlled for a slightly different set of potentially confounding variables.

It is not clear which variables, if any, significantly affect the relationship between BMI and memory. This relationship has not been found to vary with age, but results of studies investigating whether this relationship varies by sex have been inconsistent (Gunstad et al., 2006; Smith, Hay, Campbell, & Trollor, 2011; Stanek et al., 2013). Two studies found higher BMI to be associated with poorer immediate and delayed recall abilities among men without dementia, independent of educational level, blood pressure, diabetes, and other potential confounds, but only one of these studies found such a relationship among women (Gunstad et al., 2006; Smith, Hay, Campbell, & Trollor, 2011; Stanek et al., 2013). Another study found memory deficits in both obese men and women and reported that the relationship between obesity and memory function did not vary significantly by sex (Gunstad et al., 2006).
Executive functioning. Executive functions are complex capabilities that can be used to initiate, manage, and coordinate the use of other mental processes, and allow for complex goal-oriented thought and behavior (Lichtenberger & Kaufman, 2009). Deficits in executive functioning in obese adults have frequently been reported, with most work being published on young and middle-aged adults (Boeka & Lokken, 2008; Fergenbaum et al., 2009; Gunstad et al., 2007; Lokken, Boeka, Yellumahanthi, Wesley, & Clements, 2010; Smith et al., 2011). Among two comprehensive studies that controlled for a host of potentially confounding variables across the adult lifespan, one found an independent association between higher BMI and impaired executive functioning, but the other failed to do so (Gunstad et al., 2007; Stanek et al., 2013). Interestingly, the study that did not find an independent association between BMI and executive dysfunction reported a significant age by BMI interaction, suggesting that obesity-related executive dysfunction may increase with age (Stanek et al., 2013). The finding that long-term obesity during adulthood is associated with greater executive dysfunction in later midlife is consistent with this idea (Sabia et al., 2009). Regarding older adults, fewer studies have examined the relationship between obesity and executive dysfunction, but the majority of these studies support the existence of this relationship (Benito-León, Mitchell, Hernández-Gallego, & Bermejo-Pareja, 2013; Gunstad et al., 2007; Kuo et al., 2006; Walther, Birdsell, Glisky, & Ryan, 2010).

Weight trajectory and risk of cognitive dysfunction and dementia. In addition to current obesity (as detailed above), dramatic weight change and long-term obese status are also linked to cognitive dysfunction. For example, one study found long-term obesity and the extent of weight gain between early adulthood and late middle-age to be associated with executive dysfunction, though this study did not assess processing speed (Swabia et al., 2009). Another study of elderly
subjects (mean age 69.4 years) found that the extent of weight gain or weight loss over the previous 10-year period was associated with poorer performance on a neuropsychological battery (Brubacher et al., 2004). Regarding the present study, it was hypothesized that similar relationships would be found with processing speed. It should be noted here that although weight changes during specific ages may be linked with cognitive impairment and mortality risk, weight cycling itself has not been conclusively linked to either (Stevens et al., 2012). Stevens and colleagues (2012) point out that most studies on the impact of weight cycling do not evaluate whether weight loss was intentional, which may differentiate between weight loss due to illness and weight loss due to active attempts to improve one’s health or appearance. Regarding the present study, it was hypothesized that individuals endorsing significant past-year unintentional weight loss, which may reflect an underlying disease process, would perform worse on the processing speed measure than those who achieved significant past-year weight loss that was intentional and those who were weight-stable in the past year.

The relationship between dementia and body weight is complex. There is some evidence to suggest that obesity during midlife is an independent risk factor for VaD and AD onset in later-life (Xu et al., 2011). However, individuals who go on to develop dementia are more likely to have lost a significant amount of weight between midlife and late-life compared with individuals who remain free of dementia; this weight loss is likely to be unintentional (Stewart et al., 2005). Therefore, the combination of obesity in midlife and unintentional weight loss between midlife and late-life may indicate especially elevated odds of developing dementia.

**Obesity indexes and cognition.** Little is known about which obesity indexes are most closely associated with cognition in the elderly. Most studies examining the link between obesity and cognition use BMI as their sole obesity index, making comparisons impossible (e.g.,
Kuo et al., 2006; Sabina et al., 2009). It may be the case that other obesity indexes, or combinations of indexes, predict cognition better than BMI among the elderly. For example, a community study of the elderly found BMI and waist circumference to interact such that high BMI only predicted poor performance on a brief screener for cognitive impairment when abdominal obesity was present (Jeong et al., 2005). However, little more is known due to the paucity of such studies. The present study sought to determine the relationship between processing speed and multiple obesity indexes. DSST scores were not expected to be significantly correlated with the overall obesity indexes (i.e., BMI, % DEXA total body fat); however, they were expected to show significant negative correlations with the central obesity indexes (i.e. WC, WTR, WHtR, and % DEXA trunk fat). The theoretical importance of central obesity in predicting cognition is due to the aforementioned differences between metabolic activity in visceral and other fat tissue, as well as the superior ability of central obesity indexes to predict a number of health conditions that may impact cognition (e.g., metabolic syndrome, T2DM) relative to BMI. Furthermore, among those who are centrally obese (defined here as WC ≥ 102 cm for men and 88 cm for women), it was hypothesized that individuals meeting BMI obesity criteria (i.e., BMI ≥ 30 kg/m²) and/or DEXA obesity criteria (fat mass ≥ 25% for men and ≥ 35% for women) would perform worse on the DSST. This hypothesis was based on the aforementioned study by Jeong and colleagues (2005). Finally, the best combination of obesity indexes to predict DSST score was explored. It was expected that the best combination would involve % DEXA trunk fat due to the aforementioned theoretical importance of central obesity, as well as it being a more accurate indicator of visceral fat than the other central obesity indexes in this study.
Hypothesized Origins of Impaired Cognitive Functioning in Obese Adults

Given the findings that obesity is associated with impairment in virtually all cognitive domains and may exacerbate age-related cognitive decline, it may prove beneficial to identify the processes that account for this relationship. This section reviews the relationship between obesity and processes that are thought to contribute to cognitive decline.

Medical etiological factors in impaired cognitive functioning in obese adults.

Disrupted oxygen flow. Obesity and physical inactivity, which is more prevalent in the obese population, adversely impact heart and lung functioning, key organs that are responsible for ensuring an adequate supply of blood and oxygen throughout the body (Chlif, Keochkerian, Mourlhon, Choquet, & Ahmaidi, 2005; Sharp, Henry, Sweany, Meadows, & Pietras, 1964). For example, an increased body mass requires the heart to pump a greater volume of blood, thereby placing additional strain on the heart. Furthermore, breathing can become difficult due to the additional upper body compressing the lungs. If the heart and the lungs cannot fully meet the body’s demands for blood and oxygen circulation, the brain may receive inadequate blood and oxygen supplies, conditions respectively known as cerebral hypoperfusion and hypoxia. These conditions may cause neuronal death and decreased brain metabolism, which may lead to impairments in cognition; this idea is supported by animal model studies of cerebral hypoperfusion (Kim et al., 2012). Decreased blood flow in the prefrontal cortex and temporal pole have been found in otherwise healthy overweight and obese adults, and this decreased blood flow appears to be associated with various cognitive deficits (Willeumier, Taylor, & Amen, 2011). Thus, it could be hypothesized that chronic mild hypoxia could have a deleterious impact on cognition in otherwise healthy obese individuals.
Cerebral hypoperfusion and/or cerebral hypoxia is also thought to be a main contributor to cognitive dysfunction in a number of pathological conditions that are associated with obesity, including heart failure (HF), ischemic stroke, vascular dementia (VaD), and several respiratory diseases (Azagra-Calero, Espinar-Escalona, Barrera-Mora, Llamas-Carreras, & Solano-Reina, 2012; Baena-Diez et al., 2010; Strazzullo et al., 2010). Among adults with HF, cerebral hypoperfusion is associated with poorer performance on tests of attention, memory, and executive functioning (Alosco, Spitznagel, et al., 2012). Interestingly, one recent study concluded that deficits in cognitive functioning associated with cerebral hypoperfusion are exacerbated by elevated BMI (Alosco, Spitznagel, et al., 2012).

In regard to ischemic stroke and VaD, interrupted blood supply to the brain is a hallmark of these conditions and appears to be the result of multiple etiological factors. Among those who experience cognitive impairment after a stroke, the most common areas affected appear to be attention, processing speed, and executive function (Cumming, Marshall, & Lazar, 2013). The occurrence of one or more strokes raises an individual’s risk of developing dementia considerably; for example, one study found that 30% of individuals who did not exhibit dementia prior to suffering a stroke developed dementia within three months (Barba et al., 2000). Changes in white matter, including white matter hyperintensities, lesions, and diffusivity in the frontal and parietal regions, are associated with worse cognitive performance in stroke survivors and may play a role in the progression from cognitive deficits during the acute period following stroke to subsequent progressive cognitive decline and dementia (Dufouil et al., 2009; Rasquin, Verhey, Lousberg, & Lodder, 2005; Williamson et al., 2010). Reductions in grey matter in the thalamus have also been associated with cognitive impairment following ischemic stroke and may contribute to cognitive impairment in that population (Stebbins et al., 2008).
Respiratory diseases associated with obesity that have the potential to adversely impact cognition include obstructive sleep apnea syndrome (OSAS), obesity hypoventilation syndrome (OHS), chronic obstructive pulmonary disease (COPD), and chronic asthma (Guo et al., 2013; Murugan & Sharma, 2008). In regard to OSAS, individuals affected by this condition experience multiple episodes of upper airway obstruction while sleeping and, therefore, intermittent deprivation of oxygen (Carlucci, Smith, & Corbridge, 2013). Obese individuals are more likely to experience sleep apnea, which is thought to be at least partly due to a greater amounts of adipose tissue on the neck and soft palate (Azagra-Calero, Espinar-Escalona, Barrera-Mora, Llamas-Carreras, & Solano-Reina, 2012). Adults diagnosed with OSAS have demonstrated cognitive dysfunction in several areas, most notably executive functioning (Daurat, Huet, & Tiberge, 2010; Gale & Hopkins, 2004). Reduced blood oxygen saturation resulting from the intermittent deprivation of oxygen caused by the upper airway obstructions may represent a significant contributor to the cognitive dysfunction in this population. Indeed, animal models of OSAS, which are created through intermittent deprivation of oxygen, implicate the presence of oxidative stress and neuronal cell death via increased oxygen-derived free radicals known as reactive oxygen species (ROS) (Wang, Zhang, & Gozal, 2010). Furthermore, many OSAS neuroimaging studies have reported reduced hippocampal volume, and there is a significant positive correlation between hippocampal volume and blood oxygen saturation in patients with OSAS (Gale & Hopkins, 2004; Lal, Strange, & Bachman, 2012). It is also worth noting here that daytime sleepiness associated with OSAS can impair performance on cognitive tests, although there appears to be a pattern of impaired executive functioning in individuals with OSAS even after controlling for this variable (Daurat et al., 2010).
Compared to OSAS, much less is known about OHS, an often-misdiagnosed syndrome defined as the combination of obesity, abnormal blood levels of carbon dioxide in the daytime, and sleep-disordered breathing in the absence of a known cause (Basoglu & Tasbakan, 2014; Marik & Desai, 2013). Preliminary evidence suggests that OHS, which often presents with OSAS, high C-reactive protein (CRP) levels, and vitamin D deficiency, may result in multiple organ system dysfunction and can be fatal (Marik & Desai, 2013). Observations of mental deterioration have been noted in cases of OHS, but future research is needed to determine specific cognitive changes that occur as a result of this syndrome (Troester, Palfner, Kovacs, & Olschewski, 2013).

COPD, a progressive disease that adversely impacts airflow, typically involves both chronic bronchitis and emphysema (Poulain et al., 2006). Smoking is the leading cause of this disease (United States Department of Health & Human Services, 2014c). It is unclear if obesity is a risk factor for COPD, but obesity appears to be more prevalent in those with COPD and is thought to exacerbate COPD symptoms (Franssen, O’Donnell, Goossens, Blaak, & Schols, 2008). Although many studies have reported cognitive dysfunction in COPD, a specific cognitive profile has not been consistently identified. Some research has indicated a diffuse pattern of cognitive impairment in this population, whereas as other research has only found impairments in memory (De Carolis et al., 2011; Fioravanti, Nacca, Amati, Buckley, & Bisetti, 1995; Incalzi et al., 1993). It has been hypothesized that COPD contributes to cognitive dysfunction via chronic hypoxia (De Carolis et al., 2011). Furthermore, a recent longitudinal study found COPD and asthma in midlife to be associated with an increased risk of mild cognitive impairment (MCI) and dementia in late life (Rusanen et al., 2013). In regard to the present study, current or history of respiratory disease was expected to contribute to processing
speed impairment. Duration of respiratory disease was also expected to be negatively correlated with processing speed task performance.

**Oxidative stress and nutrition.** Oxidative stress can be described as a disturbance in the balance between free radicals derived from oxygen known as ROS and antioxidant defenses on the cellular level (Betteridge, 2000; Wang et al., 2010). Increased amounts of ROS are thought to contribute to tissue damage and cognitive dysfunction (Betteridge, 2000; Wang et al., 2010).

Oxidative stress has been found to increase after consumption of high fat foods, and chronic consumption of high fat foods has been linked to cognitive impairment (Bloomer & Fisher-Wellman, 2009; Winocur & Greenwood, 2005). Additionally, there is an inverse relationship between oxidative stress and fruit and vegetable consumption, which may be related to the high vitamin and antioxidant-rich carotenoid content of these foods (Vetrani, Costabile, Di Marino, & Rivellese, 2013). Indeed, deficiencies in B vitamins and thiamine have been linked to cognitive impairments and Alzheimer disease (Lu’o’ng & Nguyen, 2011; Selhub, Bagley, Miller, & Rosenberg, 2000).

A number of pathological conditions for which obesity is a risk factor (e.g., OSAS, CVD, various types of cancers) are associated with oxidative stress (Vetrani et al., 2013). Even otherwise healthy obese individuals may be at greater risk for oxidative stress than their normal weight counterparts. This idea is supported by studies that have found significant associations between obesity and the dietary characteristics of lower fruit and vegetable consumption and higher total fat consumption, though it should be noted that these associations have not been consistent across studies (Davis, Hodges, & Gillham, 2006; Tohill, Seymour, Serdula, Kettel-Khan, & Rolls, 2004).
In addition to increasing the risk for oxidative stress, obesity and poor nutrition may also contribute to cognitive dysfunction via an increase in free fatty acid plasma concentration (Dali-Youcef, Mecili, Ricci, & Andres, 2013; Haltia et al., 2007). There are at least two mechanisms by which this impairment may occur. First, free fatty acids may contribute to altered brain fat metabolism and elevated fat accumulation in brain white matter (Haltia et al., 2007). This hypothesis is consistent with the findings of greater white matter volume in several basal brain areas in obese individuals relative to healthy-weight controls (Haltia et al., 2007). Second, free fatty acids may contribute to impaired insulin signaling, which may in turn contribute to cognitive impairment via processes discussed later in this document (Dali-Youcef et al., 2013; Haltia et al., 2007).

**Endothelial dysfunction.** Oxidative stress may also contribute to endothelial dysfunction, which refers to a pathological state of the inner lining of blood and lymphatic vessels, known as the vascular endothelium (Münzel, Sinning, Post, Warnholtz, & Schulz, 2008). Biological markers of endothelial dysfunction have been associated with a number of conditions that may lead to impaired cognition, including hypertension, dyslipidemia, and insulin resistance, and these associations may be bidirectional (Münzel et al., 2008). Interestingly, circulating biomarkers of endothelial dysfunction and low-grade inflammation (as discussed below) were associated with impairments in processing speed and executive functioning in a population-based study of the elderly, and accounting for vascular risk factors only slightly attenuated their relationship (Heringa et al., 2014).

**Chronic low-grade inflammation.** Obesity is characterized by increased number and size of fat cells, known as adipocytes, which secrete proinflammatory (e.g., interleukin 6) and anti-inflammatory (e.g., adiponectin) cell-signaling proteins called cytokines (Alexaki et al.,...
An increase in adipose tissue, visceral adipose tissue in particular, has been suggested to result in a higher ratio of proinflammatory to anti-inflammatory cytokines (Trujillo & Scherer, 2005; Tsatsanis et al., 2006). Reduced production of adiponectin, an anti-inflammatory cytokine, in response to greater adipose tissue, and visceral adipose tissue in particular, may have a large contributory role in this process (Tsatsanis et al., 2006). This proinflammatory cytokine imbalance is thought to lead to peripheral inflammation, and, indeed, waist circumference is positively correlated with peripheral inflammation markers and negatively correlated with adiponectin (Ackermann et al., 2011). Moreover, obese individuals demonstrate elevated levels of CRP, a general marker of peripheral inflammation, independent of other known sources of inflammation, such as health and smoking status (Visser et al., 1999).

Inflammation is a protective process performed by the body in order to clear damaging stimuli and assist with tissue repair (Michaud et al., 2013). The biological benefit of obesity-caused peripheral inflammation appears to be increased energy expenditure, with inflammation thereby acting as an energy balance mechanism (Ye & Keller, 2010). However, there are a number of negative consequences to chronically heightened inflammation that could contribute to the processing speed and executive functioning impairments that are found in this population (Heringa et al., 2014). First, results from animal studies suggest that peripheral inflammation is able to evoke central neuroinflammatory response, and this appears to be especially true in older age animals (Barrientos, Hein, Frank, Watkins, & Maier, 2012; Godbout et al., 2005). Second, inflammation resistance may develop over time, causing a greater build-up of proinflammatory cytokines in the bloodstream (Ye & Keller, 2010). These proinflammatory cytokines may interact with free fatty acids to impair insulin signaling (Dali-Youcef et al., 2013; Haltia et al.,
Conditions involving insulin-resistance (as described below) are strongly linked with cognitive impairment. Finally, there is evidence to suggest that central inflammation (specifically, in the hypothalamus) may be triggered by high fat diet in addition to being triggered by the metabolic consequences of excess adipose tissue (Boitard et al., 2014; Velloso, Araujo, & de Souza, 2008). Regarding the present study, higher levels of chronic peripheral inflammation (as suggested by a history of obesity and high level of CRP) were expected to be associated with cognitive impairment.

**Impaired insulin production or signaling.** Insulin, a hormone primarily produced in the pancreas, is important for regulation of carbohydrate and lipid metabolism, as well as neuronal survival and synaptic plasticity (van der Heide, Ramakers, & Smidt, 2006). Peripheral insulin is generally thought to be able to travel through the blood-brain barrier to the brain, although there is some evidence to suggest that central production may occur (Woods, Seeley, Baskin, & Schwartz, 2003; van der Heide et al., 2006). Obese individuals are more likely to experience peripheral impairments in insulin signaling, which may be due, at least in part, to increased systemic inflammation, oxidative stress, and high fat diet in this population (Dali-Youcef et al., 2013; Greenwood & Winocur, 2005; Henriksen, Diamond-Stanic, & Marchionne, 2011).

Peripheral insulin resistance or insufficient insulin production is a hallmark of T2DM, and post-mortem studies have shown central insulin resistance to be greater in T2DM patients than age-matched controls (Liu, Liu, Grundke-Iqbal, Iqbal, & Gong, 2011). The relationship between T2DM and deficits in processing speed, memory, and executive functioning among older adults have been well-established (Blanco et al., 2012; Ryan & Geckle, 2000; van den Berg et al., 2008, 2009; Yaffe et al., 2012; Yeung, Fischer, & Dixon, 2009). Mechanisms for cognitive dysfunction in T2DM are not well understood, but some evidence suggests the role of
hippocampal neuron damage due to inadequate supply of glucose to the brain, reduced central cholinergic activity, decreased functionality of glutamate receptors, oxidative stress, and disruption of the hypothalamic-pituitary adrenal (HPA) axis, in addition to central insulin resistance (Kodl & Seaquist, 2008; Raber, 1998; Shonesy et al., 2012; Vijayakumar, Sirisha, Begam, & Dhanaraju, 2012). Decreased frontal glucose metabolism and impaired neuronal integrity have also been related to BMI and poorer memory and executive function in adults without T2DM but who may be somewhat insulin-resistant (Gazdzinski et al., 2010; Volkow et al., 2009).

Insulin-resistance may also lead to cognitive dysfunction other ways. For example, insulin-resistance, along with other cardiometabolic syndrome symptoms, has been implicated in the pathogenesis of chronic kidney disease, which, in turn, is associated with impaired psychomotor efficiency and processing speed (Jassal, Roscoe, LeBlanc, Devins, & Rourke, 2008; Whaley-Connell et al., 2006). Insulin-resistance may also cause cognitive impairment via promotion of the build-up of beta amyloid (Aβ) plaques found in AD, and in fact, insulin-resistance has been proposed as the primary precipitating event of this disease (Kodl & Seaquist, 2008; Salkovic-Petrisic & Hoyer, 2007). Indeed, autopsies performed in patients with AD show central insulin resistance, and there is considerable similarity between pathology of experimental inducement of central insulin resistance in animal studies and AD pathology in humans (Liu, Liu, Grundke-Iqbal, Iqbal, & Gong, 2011; Shonesy et al., 2012). Such findings have led to the proposal of the term type 3 diabetes to describe this mechanism of neurodegeneration (Steen et al., 2005).

As per the current literature, the potential contributory role of peripheral insulin resistance in impaired processing speed is unclear. Among middle-aged individuals without
diabetes mellitus, two biological markers of peripheral insulin-resistance (i.e., hyperinsulinemia and homeostasis model assessment of insulin resistance [HOMA-IR]), have been associated with poor performance on tests of processing speed; however, the only study that appears to have controlled for BMI when testing the relationship between insulin resistance and poor processing speed to-date reported that it became insignificant after doing so (Sanz et al., 2013; Young, Mainous, & Carnemolla, 2006). This suggests the possibility that peripheral insulin resistance, itself, may not contribute to processing speed decline in a middle-aged population. The relationship between central insulin resistance and AD pathology, however, raises the question of whether insulin resistance would be associated with processing speed decline among the elderly independent of BMI. The present study investigated this question as part of its exploratory analyses.

*Hyperglycemia/hypoglycemia.* Blood glucose level and peripheral insulin resistance are closely related, but distinct, concepts. Insulin is needed to reduce blood glucose levels, and the pancreas of an individual developing insulin resistance typically produces extra insulin in order to compensate for the insulin resistance. The individual can eventually develop hyperglycemia if this extra insulin is no longer adequate to reduce blood glucose levels to a normal range. Therefore, peripheral insulin resistance onset precedes peripheral hyperglycemia onset (United States Department of Health & Human Services, 2017). Once an individual’s fasting glucose level reaches 100–125 mg/dl or HbA1c, a marker of average glucose level in the past 2–3 months, reaches 5.7% to 6.4%, prediabetes is diagnosed (American Diabetes Association, 2014). When fasting glucose level reaches ≥ 126 mg/dl or HbA1c reaches ≥ 6.5%, diabetes mellitus is diagnosed (American Diabetes Association, 2014).
Hyperglycemia in the diabetic or prediabetic range may have an adverse impact on processing speed. Hyperglycemia has been identified as the major contributor to the relationship between metabolic syndrome and impairment in tasks requiring fast perceptual speed among a sample of elderly individuals (Dik et al., 2007). Furthermore, HbA1c levels in the prediabetic range have been linked to impaired processing speed independent of BMI in middle-aged individuals (Sanz et al., 2013). It is unclear as to how hyperglycemia might contribute to cognitive impairment, although specific biological pathways in the brain have been proposed (Kodl & Seaquist, 2008). More broadly, Dik and colleagues (2007) noted that those with diabetes mellitus also show perceptual speed deficits, and suggested that similar glucose intolerance pathology in fronto-subcortical structures may be present in both those with diabetes and prediabetes. There is also strong evidence that hyperglycemia increases the risk for atherosclerosis, possibly via endothelium damage, oxidative stress, and inflammation (Aronson & Rayfield, 2002).

In regard to the present study, it was hypothesized that participants with fasting glucose or HbA1c levels in the prediabetic range would perform worse on the processing speed task than would those with fasting glucose and HbA1c levels in the normal range; individuals diagnosed with diabetes mellitus or on antidiabetic medication were excluded from the sample investigated by this hypothesis. In addition, it was hypothesized that those with diabetes mellitus would perform worse on the processing speed task than the prediabetic and the non-diabetic groups.

Hypoglycemia has also been hypothesized to contribute to worsening cognition in those with diabetes mellitus (Kodl & Seaquist, 2008). Namely, repeated episodes of severe hypoglycemia have been linked to worse cognition in a variety of domains within this population, although findings are mixed and most work has focused on type 1 diabetes, a
condition for which obesity is not a risk factor (e.g., DCCT/EDIC Study Research Group, 2007; Northam et al., 2001). Hypoglycemia history is not included in the NHANES database; therefore, no hypotheses were made regarding history of this condition.

Adipose tissue hormones. It has been proposed that differential levels of adipose tissue-derived hormones, including adiponectin and leptin, may have a complex role in cognitive dysfunction pathology (Gustafson, 2010). Adiponectin (discussed above) has proinflammatory effects that may contribute to the development of cognitive impairment. Circulating levels of leptin, a neuroprotective hormone which is also thought to assist in the regulation of food intake and body weight by acting on the hypothalamus to signal satiety and increase energy expenditure, tend to be elevated in the obese, and obese individuals are also more likely to show peripheral leptin resistance, central leptin insufficiency, and brain atrophy (Harvey, 2007; Heini et al., 1998; Rajagopalan, Toga, Jack, Weiner, & Thompson, 2013). In addition to the hypothalamus, leptin also has receptor sites in several other areas of the brain, including the cerebellum and hippocampus (Funahashi, 2003; Savioz et al., 1997). It has been proposed that leptin deficiencies and leptin resistance in lean and obese individuals, respectively, are related to cognitive dysfunction (Labad et al., 2012). In line with this argument, rats with dysfunctional leptin receptors were found to perform poorly on spatial memory tasks (Li et al., 2002). Another study found higher levels of leptin to be associated with poorer mental flexibility and executive functioning among a group of primarily obese men with T2DM (Labad et al., 2012).

Hypertension. Over 70% of obese adults suffer from hypertension, a condition that is associated with cognitive dysfunction and is linked to deficits in attention, memory, executive functioning, psychomotor functioning, and motor speed among those with heart failure independent of medication status (Alosco, Brickman, et al., 2012; Bramlage et al., 2004; van den
Hypertension has also been found to be significantly associated with cognitive dysfunction independent of obesity among men, although the same relationship was not found among women (Elias et al., 2003). There is some evidence to suggest that, among the general population, only those with long histories of hypertension and those not on antihypertensive medications evidence these cognitive deficits (Farmer et al., 1990; Power, Tchetgen, Sparrow, & Schwartz, 2013).

Prolonged hypertension may impair cognition through disturbed cerebral blood flow distribution and alterations to small cerebral blood vessels, which may lead to inadequate blood supply to brain tissue, blood-brain barrier alterations, and eventually lesions, white matter changes, silent strokes that do not yield any outward symptoms, stroke, and VaD (Elias, Elias, Sullivan, Wolf, & D’Agostino, 2003; Pantoni & Simoni, 2003). Hypertension has also been associated with exacerbated morphological changes that occur during the natural aging process, particularly in the prefrontal cortex, as well as in the temporal and occipital lobes and underlying white matter (Raz, Rodrigue, & Acker, 2003; Strassburger et al., 1997).

Hypertension in midlife is a risk factor for VaD and AD development (Kivipelto, Laakso, Tuomilehto, Nissinen, & Soininen, 2002; Sharp, Aarsland, Day, Sønnesyn, & Ballard, 2011). Interestingly, among those with midlife hypertension who go on to develop dementia, blood pressure tends to decline near the time cognitive functioning starts to decline (Hajjar, Keown, & Frost, 2005). This may result in many individuals with dementia no longer meeting criteria for hypertension. Nevertheless, if hypertension is present in an individual with dementia, it may accelerate cognitive decline (Hajjar et al., 2005).

Dyslipidemia. Dyslipidemia (e.g., unhealthy levels of total cholesterol, high-density lipoprotein [HDL] cholesterol, low-density lipoprotein [LDL] cholesterol, and/or triglycerides) is
a risk factor for cardiovascular diseases, which in turn are risk factors for cognitive decline, late-life dementia, and AD onset in carriers of the ApoE4 allele (Eriksson, Bennet, Gatz, Dickman, & Pedersen, 2010; Reiner, Muacevic-Katanec, Katanec, & Tedeschi-Reiner, 2011). For example, 60–70 and 70–80-year olds with plasma cholesterol levels of ≥ 8 mmol/L demonstrate a coronary heart disease (CHD) risk that is 2.3 and 1.6 times greater than those with cholesterol levels of < 5 mmol/L, respectively (Iversen, Jensen, Scharling, & Schnohr, 2009). The link between plasma lipids and CHD is thought to be primarily due to atherosclerosis, a thickening of artery walls that limits blood flow (Elwood, Pickering, Bayer, & Gallacher, 2002; Iversen et al., 2009). Atherosclerosis itself has also been associated with slower processing speed in the elderly, which may be due to decreased blood flow to the brain (Vinkers et al., 2005). It has been theorized that plasma lipids, including low HDL cholesterol and high LDL cholesterol, may also contribute to cognitive impairment via the build-up of amyloid plaque deposits in the brain (Reed et al., 2014). Given these theoretical etiological factors, it was hypothesized that dyslipidemia would be related to worse processing speed in the present study.

Some studies have already linked dyslipidemia with cognitive impairment, although findings have been mixed. For example, there is some evidence that high triglycerides are related to executive dysfunction in elderly without dementia after controlling for age, gender, education, LDL cholesterol, ApoE4 allele status, and a rating of clinical dementia (Parthasarathy et al., 2014). Low HDL cholesterol may be independently related to memory dysfunction and decline in middle-aged adults and has been associated with reductions in grey matter volume in regions associated with neurodegenerative disease, such as the parahippocampal region (Singh-Manoux, Gimeno, Kivimaki, Brunner, & Marmot, 2008; Ward et al., 2010). Overall, however, studies of the relationship between dyslipidemia and cognitive functioning have yielded
inconsistent results, which may be related to the common pattern of favorable body weight changes prior to dementia onset (Stewart, White, Xue, & Launer, 2007; van den Berg et al., 2009). Unfortunately, the present study did not include a direct measure of dementia.

**Other factors.** Obesity appears to be a risk factor for alcoholic fatty liver disease and non-alcoholic fatty liver disease, conditions which appear to be causally linked to cognitive impairment (Lee et al., 2006). For example, those with end-stage liver disease can experience hepatic encephalopathy, which is thought to be caused by a build-up of toxins in the bloodstream and may involve inattention, confusion, and disorientation (Rahimi & Rockey, 2014). Cognition appears to return to a normal state after hepatic encephalopathy is treated; however, recent evidence suggests that learning deficits may continue after treatment (Umapathy, Dhiman, Grover, Duseja, & Chawla, 2014). Less severe stages of liver disease may also be linked to impaired cognition in certain domains. For example, one study that compared those with mild liver disease and hepatitis C virus (HCV) to controls demonstrated that the former group had worse concentration and memory speed after controlling for depression and fatigue, although DSST scores were not significantly different (Forton et al., 2002). The authors of this study suggested that an impact of chronic HCV on the central nervous system or preexisting individual differences may account for these findings (Forton et al., 2002, 2005). Others have suggested that substance use history accounts for some of the relationship between HCV and cognitive impairment. For example, Huckans et al. (2009) reported impairments in processing speed, as estimated by the DSST, in a group with HCV and SUD history but not in a group with HCV and no SUD history. Nevertheless, deficits in verbal learning, auditory attention, reasoning, and mental flexibility persisted even in the absence of SUD history in those with HCV. The NHANES database used in the present study contains yes/no questions on history of “any liver
condition” and whether those who endorsed this item still have “any liver condition.” Unfortunately, this did not allow for identification of specific liver conditions nor did it allow for specific hypotheses to be made in the present study. Nonetheless, the relationship between “any liver condition” and current processing speed was investigated as part of the present study’s exploratory analyses. Based on the above information, history of “any liver condition” was not expected to be significantly related to processing speed task performance, though this was not a formal hypothesis.

It should also be noted here that hypothyroidism has been linked to subtle cognitive deficits when left untreated, whereas less evidence is available for an adverse impact of hyperthyroidism (Lillevang-Johansen, Petersen, Christensen, Hegedüs, & Brix, 2014; Samuels, 2008, 2014). Hypothyroidism has been associated with obesity; however, the direction of this relationship is unclear (Verma, Jayaraman, Kumar, & Modi, 2008). The NHANES data used in the present study contains yes/no questions on history of “thyroid disease.” Unfortunately, this did not allow for differentiation between types of thyroid disease. In regard to the present study, thyroid disease was not expected to be significantly linked with impaired processing speed unless it was not treated. That being said, upon implementation of the present study, it was discovered to be impossible to determine whether thyroid disease had been treated, as the NHANES data does not include information on history of many of the treatments for thyroid diseases, such as those of radioiodine and surgery (Abraham & Acharya, 2010).

**Combinations of risk factors.** The above subsections have included information on the potential interactive effects of various health conditions on cognition. Some researchers have also attempted to study the relationship between cognition and clusters of risk factors for diseases/events, most notably stroke and cardiovascular disease. In doing so, most of these
studies use full or modified versions of the Framingham Stroke Risk Profile (FSRP) or the Framingham Risk Score (FRS) for general cardiovascular disease (CVD; e.g., Bangen et al., 2010; Elias et al., 2004; Joosten et al., 2013; Kaffashian et al., 2011; Llewellyn et al., 2008). Both the FSRP and FRS for general CVD were developed using data from the Framingham Study, an ongoing cohort study in Framingham, Massachusetts (Boston Medical Center, 2014).

In regard to the FSRP, the following stroke risk factors were identified based on the incidence of stroke over a 10-year period among participants aged 55–84 without a history of stroke at baseline: age, systolic blood pressure, antihypertensive medication, diabetes, smoking status, atrial fibrillation, left ventricular hypertrophy, and history of CVD (defined as one or more of the following: myocardial infarction, angina pectoris, coronary insufficiency, intermittent claudication, congestive heart failure [CHF]; D'Agostino, Wolf, Belanger, & Kannel, 1994; Wolf, D'Agostino, Belanger, & Kannel, 1991). In regard to the FRS for general CVD, the following CVD risk factors were identified based on the incidence of CVD (defined as one or more of the following: heart failure, coronary insufficiency, myocardial infarction, angina pectoris, ischemic or hemorrhagic stroke, transient ischemic attack, peripheral artery disease, or coronary death) over a 10-year period among participants aged 30–74 without a history of CVD at baseline: age, total cholesterol, HDL cholesterol, systolic blood pressure, antihypertensive medication, smoking, and diabetes (D'Agostino et al., 2008). FSRP and FRS for general CVD scores can be calculated by assigning points to each of these risk factors using sex-specific formulas that can be found within their respective publications (D'Agostino et al., 1994, 2008).

As mentioned above, many studies have used full or modified versions of the FSRP and FRS for general CVD to assess the relationship between these groups of risk factors and cognition. Modified versions appear to be used due to availability of data in a study rather than
theoretical differences. For example, Llewellyn and colleagues (2008) calculated FSRP scores without left ventricular hypertrophy and used a different definition of history of CVD (i.e., CHD, CHF, and peripheral vascular disease [PVD]). Llewellyn and colleagues (2008) found that the modified FSRP was related to worse performance in a number of cognitive domains, including processing speed, in their United Kingdom population sample of individuals aged 50 years and older. Research has also shown high FRS for general CVD scores to be associated with worse cognition in a number of areas, most notably executive functioning (Joosten et al., 2013; Kaffashian et al., 2011). The relationship between FRS for general CVD scores and processing speed has not been reported to date. In regard to the present study, it was hypothesized that scores yielded by modified versions of the FSRP and FRS for general CVD would be inversely associated with processing speed performance. The present study calculated FSRP scores without left ventricular hypertrophy and atrial fibrillation, and it used a different definition of CVD (i.e., CHF, angina pectoris, heart attack). The present study calculated FRS for general CVD scores in the same manner as the full version but used a different definition of CVD (i.e., CHF, angina pectoris, heart attack, stroke).

**Psychological etiological factors in impaired cognitive functioning in obese adults.**

**Depression.** Impaired ability to think, concentrate and make decisions are among the symptoms of major depressive disorder (MDD; American Psychiatric Association, 2013). Not surprisingly, research indicates that MDD is associated with impairment in a variety of cognitive domains, including attention, processing speed, memory, and executive functioning (Luo et al., 2013; Marazziti, Consoli, Picchetti, Carlini, & Faravelli, 2010). Obese adults are more likely to experience depressive disorders compared to their non-obese counterparts, with stronger associations among those with greater obesity severity (Castres, Folope, Dechelotte, Tourny-
Chollet, & Lemaitre, 2010; Mather et al., 2009). The connection between depression and obesity is not fully understood, but longitudinal evidence suggests a bidirectional relationship (Luppino et al., 2010). Body image dissatisfaction, reduced levels of social and physical activity, and use of psychotropic medication appear to mediate this relationship (de Wit et al., 2010; Gavin, Simon, & Ludman, 2010; Smits et al., 2010). Additional factors accounting for the relationship between elevated body weight and depression may include HPA-axis dysregulation, hypercortisolemia, unhealthy diet, emotional eating, carbohydrate craving, binge eating, and social stigmatization (Carels et al., 2010; Gibson, 2012; Hawkins & Stewart, 2012; Ouwens, van Strien, & van Leeuwe, 2009; Peterson, Latendresse, Bartholome, Warren, & Raymond, 2012; Wurtman & Wurtman, 1995). Among the elderly, it has been proposed that physical functioning might be a particularly important mediator between obesity and depression, whereas factors important in explaining this relationship in young adults (e.g., body image) may become less important in old age (McCrea et al., 2012).

**Anxiety.** Anxiety has been strongly linked to attentional bias toward threatening information and increased distractibility, which in turn may contribute to short-term memory and executive dysfunctions in this population (Lapointe & Blanchette, 2013). Elevated rates of past-year and lifetime anxiety disorders and symptoms, particularly social phobia and panic attacks, have been documented in the general obese population (Mather et al., 2009). The nature and direction of the relationship between anxiety and obesity is not well understood, but it has been hypothesized that more frequent stress exposure predisposes obese individuals to anxiety disorders (Pickering, Grant, Chou, & Compton, 2007). Additionally, longitudinal evidence suggests that severe anxiety may predispose one to increases in waist circumference and decreases in HDL cholesterol, both of which are predictive of CVD risk and cognitive
impairment (Bombelli et al., 2013; Reiner et al., 2011; Singh-Manoux et al., 2008; van Reedt Dortland, Giltay, van Veen, Zitman, & Penninx, 2013; Yoon et al., 2012). Other potential factors accounting for the relationship between anxiety and higher BMI include unhealthy diet, HPA-axis dysregulation, hypocortisolemia, and psychotropic medication (Boyer, 2000; Hawkins & Stewart, 2012; Smits et al., 2010).

**Attention-deficit/hyperactivity disorder.** Persistent pattern of inattention, difficulties with organization, and impulsivity are among the symptoms of attention-deficit/hyperactivity disorder (ADHD), and each of the three subtypes of this disorder (i.e., predominantly inattentive, predominantly hyperactive/impulsive, and combined) is associated with executive dysfunction (American Psychiatric Association, 2013; Pagoto et al., 2009). Adults with ADHD also exhibit elevated rates of obesity (Pagoto et al., 2009). The relationship between ADHD and obesity is not well understood, but three main theories have been proposed. First, effects of obesity-related comorbidities (e.g., decreased alertness as a consequence of obstructive sleep apnea syndrome) may be mistaken for ADHD symptoms (Cortese & Vincenzi, 2012). Second, cognitive deficits common to ADHD may interact with environmental factors to predispose individuals with ADHD to overeat or make unhealthy food choices (Davis, 2010). This idea is partly supported by findings that impulsivity and/or impaired inhibitory control are positively correlated with external eating, taste-preference driven food choices, and quantity of ready-to-eat and away-from-home foods consumed (Appelhans et al., 2012; Jasinska et al., 2012). Third, it has been hypothesized that deficits in dopaminergic activity in reward centers of the brain underlie both ADHD and obesity and drive their association (Campbell & Eisenberg, 2007; Liu, Li, Yang, & Wang, 2008). For example, individuals with reduced dopaminergic activity in these reward centers may attempt to compensate via behaviors that promote dopaminergic activity, including
overeating and consumption of unhealthy foods (Davis, 2010; Wang et al., 2001). The finding that binge eating disorder, which may be associated with downregulation of the dopamine receptor D2 in the striatum, partially mediates the association between ADHD and obesity is consistent with this hypothesis (Johnson & Kenny, 2010; Pagoto et al., 2009).

**Intellectual disability.** Intellectual disability (ID) is a neurodevelopmental disorder that involves impairment in both intellectual and adaptive functioning (American Psychiatric Association, 2013). Although there is not a strict IQ criterion for diagnosis, individuals with this disorder typically obtain IQ scores of 65–75 or less (American Psychiatric Association, 2013). Adults with ID demonstrate increased prevalence of obesity and earlier age of obesity onset compared with the general population (de Winter, Bastiaanse, Hilgenkamp, Evenhuis, & Echteld, 2012; Melville, Hamilton, Hankey, Miller, & Boyle, 2007). The nature of the association between ID and obesity is uncertain. One longitudinal study found lower IQ at age 11 to predict weight gain and obesity at age 42, a relationship which was partly mediated by education level and diet quality (Chandola, Deary, Blane, & Batty, 2006). A number of risk factors for obesity within the intellectually disabled population have been identified, including female gender, Down syndrome, and ability to eat, prepare meals, and shop for groceries independently. Obese individuals with ID do not appear to have less nutrition knowledge than lean individuals with ID (Caton et al., 2012; Golden & Hatcher, 1997).

**Future research directions in the obesity-related etiology of cognitive dysfunction.** To summarize, there is conflicting evidence regarding whether associations between obesity and cognitive dysfunctions are independent or can be sufficiently explained by mediating variables (e.g., hypertension, diabetes status). In addition to focusing on medical diagnoses as mediating variables, it may be of equal or greater importance for future research to study the contribution of
lower-level obesity-related factors (e.g., low grade inflammation, increased circulation of adipocyte hormones) to cognition decline. This idea is supported by a recent population-based study of the elderly that found that circulating biomarkers of low-grade inflammation and endothelial dysfunction were associated with impairments in processing speed and executive functioning and that accounting for vascular risk factors only slightly attenuated their relationship (Heringa et al., 2014). It may be further hypothesized that these lower-level obesity-related factors that contribute to cognitive decline have an increased effect if the individual is exposed to a greater magnitude (e.g., more hormones released from adipose tissue that contribute to structural brain changes) and/or over a greater time period (e.g., chronic low-grade inflammation in the chronically obese person). Therefore, it follows that knowledge of a person’s weight history, which may serve as a proxy for a number of lower-level obesity variables, may provide additional utility in predicting cognitive functioning than history of medical diagnoses alone. Indeed, there is some evidence to support the notion that weight history may impact cognition. However, this area of study is in its infancy, and its data has not been adequately synthesized. Future research should work to clarify the impact of weight history on cognition.

**Importance of Processing Speed in the Elderly**

Of the cognitive domains that weight history may impact, processing speed may have some of the worst repercussions among the elderly. First, processing speed is a crucial driving factor in many accounts of cognitive aging, which will be elaborated on in the following section. This suggests that weight history-related cognitive deficits may speed the process of cognitive aging. Second, elderly individuals with faster processing speed appear to have more satisfactory outcomes in a variety of areas involving quality, satisfaction and duration of life, and these
outcomes are typically independent of other cognitive domains. For example, faster processing speed in the elderly has been found to be associated with shorter time to complete everyday tasks and greater survival time independent of medical conditions and performance in other cognitive domains (Iwasa et al., 2014; Owsley et al., 2002). Furthermore, processing speed and spatial abilities, but not memory or other cognitive domains, were found to predict greater life satisfaction prospectively in a large population-based sample of 78–98-year-old men and women (Enkvist et al., 2013). Processing speed training may also protect against health-related quality of life decline; a large randomized controlled trial reported that elderly individuals who underwent processing speed training were significantly less likely to evidence extensive health-related quality of life decline at a two-year follow-up evaluation compared with those who underwent memory training, reasoning training, or no training (Wolinsky et al., 2006). Additionally, performance on the digit symbol substitution test (DSST), a commonly used measure of processing speed, has been shown to be a more useful predictor of driving safety in the elderly than performance on cognitive tasks measuring global functioning, visuospatial perception, working memory, semantic fluency, and selective attention (Lafont et al., 2010). Taken together, these findings suggest the importance of efforts to minimize processing speed decline in the elderly. Research that will allow us to better understand the process of cognitive aging and the contributors to processing speed decline among the elderly is also warranted.

**Cognitive Aging**

Humans experience declines in cognitive functioning as they age. Although normal age-related cognitive decline has been difficult to clearly differentiate from pathological cognitive decline due to difficulty ruling out underlying disease states and accounting for impact of
medical history, there is a consensus that declines in most cognitive domains occur with aging even in the absence of known health problems (e.g., Aine et al., 2011; Harada, et al., 2013).

Determining when age-related cognitive decline begins is complex. Decline onset varies by a variety of factors including cognitive domain and birth cohort (Schaie & Willis, 2010). Generally, it believed that fluid abilities, such as problem solving, begin declining in late adolescence or early adulthood, whereas crystallized abilities, such as vocabulary, are maintained or improve into late adulthood (e.g., Kaufman & Horn, 1996). Recently, attention has been drawn to the impact of study design on our conclusions regarding when age-related decline begins (Rönnlund, Nyberg, Bäckman, & Nilsson, 2005; Salthouse, 2009; Schaie, 2009). Most research has been cross-sectional rather than longitudinal for practical reasons, and cross-sectional research appears to be more likely to show continuous age-related decline throughout the adult lifespan than longitudinal research, which is not likely to show significant decline until approximately age 55 or later (Rönnlund et al., 2005; Salthouse, 2009; Schaie, 2009; Schaie & Willis, 2010). Those who contend that age-related cognitive decline begins in early life argue that longitudinal studies do not evidence decline due to retest effects, whereas those who contend that age-related cognitive decline begins in late life argue against the validity of conclusions that have been drawn on the basis of cross-sectional studies due to cohort effects (Salthouse, 2009; Schaie, 2009).

Processing speed, inhibitory control, and working memory are among the factors most frequently hypothesized to be important in explaining, or even driving, normal age-related cognitive decline (e.g., Hasher, Stoltzfus, Zacks, & Rypma, 1991; Rozas, Juncos-Rabadán, & González, 2008; Vance, 2009). Among these, processing speed may be particularly important, as the effect of age on processing speed may mediate the effect of age on working memory and
inhibition (Rozas et al., 2008). Furthermore, changes in the processing factor are a leading indicator of changes in memory and spatial factors, whereas the inverse relationship does not hold nor are changes in the processing factor a leading indicator of changes in the verbal factor (Finkel et al., 2007). These findings are consistent with the processing speed theory of aging, which holds that reduced processing speed in old age restricts other cognitive processes to the extent that these cognitive processes rely on processing speed (Salthouse, 1996). In other words, these findings suggest that processing speed, which is related to fluid ability more so than crystallized ability, drives fluid ability decline but not crystallized ability decline (Finkel et al., 2007).

In addition to these traditionally studied cognitive components, some researchers have sought to understand age-related cognitive decline via the concept of cognitive control, which Manard, Carabin, Jaspar, and Collette (2014) describe as being “required to adjust and flexibly guide people’s behavior in changing environmental circumstances, especially in situations where distracting information or a predominant response tendency must be ignored in order to successfully act in a goal-oriented manner.” Therefore, cognitive control includes aspects of executive and attentional control, goal maintenance, and response selection and inhibition. A thorough review of cognitive control theories and models is beyond the scope of this document. Briefly, information processing theory, among the earliest cognitive control theories proposed, contended automaticity to be on a continuum based on processing speed and interference effects rather than an all-or-nothing phenomenon (Cohen, Dunbar, & McClelland, 1990). Conflict monitoring theory subsequently built on information processing theory by theorizing that cognitive control processes are initiated when a monitoring system in the anterior cingulate cortex detects conflicts in information processing (Botvinick, Braver, Barch, Carter, & Cohen,
Later work also suggested the dorsolateral prefrontal cortex to have a special role in allowing one to actively maintain task-relevant memory representations, referred to as “context processing,” during times of great interference (Kane & Engel, 2002).

It has been theorized that difficulties with context processing play a role in age-related cognitive decline, an idea which became known as the “context processing theory of cognitive aging” (Braver et al., 2001; Braver, Satpute, Rush, Racine, & Barch, 2005). Results of one study support this theory over the role of processing speed or inhibition deficit alone in explaining age-related cognitive decline, although more research is needed to clarify the relative utility of context processing theory of cognitive aging (Rush, Barch, & Braver, 2006).

Within the context processing theory of cognitive aging, context processing has been divided into reactive control and proactive control (Braver et al., 2005; Braver, 2012). Reactive control, which is sometimes referred to as interference resolution, initiates temporary reminders of context information after a probe stimulus (Bélanger, Belleville, & Gauthier, 2010; Braver et al., 2005). In contrast, proactive control, which is sometimes referred to as goal maintenance, actively updates and maintains context information and communicates with other attention systems to prepare for an upcoming probe stimulus (Bélanger et al., 2010; Braver et al., 2005). For example, a person can use proactive control to stop at the bank on her way home from work by keeping her goal of stopping at the bank in mind as she approaches the intersection in which she must make a left turn to go to the bank. In contrast, a person relying on reactive control would not be keeping the goal of stopping at the bank in her mind as she approaches the intersection, but the sight of the intersection may trigger a reminder of her goal of stopping at the bank.
Proactive control processes appear to decline with age more so than reactive control processes (Bélanger et al., 2010; Braver et al., 2005). Preliminary evidence supports the hypothesis that successful use of proactive control processes in the older population is partly dependent upon amount of available cognitive resources, consisting of processing speed and fluid intelligence (Manard et al., 2014). Indeed, older adults are more vulnerable to interference effects on the Stroop test, which is believed to be partially attributable to slowed processing speed, as well as inhibitory deficits (Bugg, DeLosh, Davalos, & Davis, 2007; Troyer, Leach, & Strauss, 2007). Therefore, although the context processing theory of cognitive aging involves many cognitive components, processing speed clearly remains a crucial concept in this account.

Hypothesized Origins of Processing Speed Decline in the Elderly

**Chronic inflammation.** Aging is associated with low grade chronic inflammation (Michaud et al., 2013). Within the aging process, chronic inflammation is believed to be primarily caused by changes in the immune system and increased secretion of adipokines (Michaud et al., 2013). This state of low grade chronic inflammation may be detrimental for the same reasons explained in regard to obesity-related chronic inflammation.

**Neurobiological factors.** The brain’s morphology, activation patterns, and metabolism change throughout the lifespan. During the aging process, reduced total brain volume, reduced total gray matter volume, reduced total white matter volume, and increased volume of ventricles occur (Fjell & Walhovd, 2010). It has been theorized that reduced grey matter is primarily due to factors such as shrinkage of neurons and synaptic spines, and factors such as resultant widened synaptic gaps may impair neural communication and contribute to slower processing speed (Fjell & Walhovd, 2010). In regard to white matter, it has been hypothesized that breakdown of
myelin and/or shortened internodes due to remyelination result in slowed neural communication and, therefore, reduced processing speed (e.g., Lu et al., 2013; Peters, 2009).

Although changes in total brain volume are characteristic of aging, brain matter volume does not decrease uniformly across brain regions. The volume of frontal cortex (particularly in the lateral prefrontal and orbitofrontal cortices), temporal cortex, thalamus, putamen, caudate nucleus, nucleus accumbens, cerebellum, and hippocampus appear to be especially affected by age (Eckert, 2011; Fjell & Walhovd, 2010; Raz et al., 2003; Van Der Werf et al., 2001). Smaller volume and/or magnitude of atrophy over time of many of these areas negatively correlate with processing speed, leading to the proposal of region-specific neurobiological explanations for age-related processing speed decline (e.g., Nadkarni et al., 2014; Van Der Werf et al., 2001). For example, one explanation focuses on specific areas of age-related grey matter reductions that predict poor processing speed, including the bilateral inferior frontal and superior parietal regions and the lingual and left superior frontal gyri (Chee et al., 2009). Other accounts focus on the role of declines in white matter integrity, and, more specifically, volume of white matter hyperintensities and myelin breakdown (Borghesani, Madhyastha, Aylward, & Reiter, 2014; Lu et al., 2013; Papp et al., 2014). Specific areas of these declines in white matter integrity have been found to be particularly important. For example, it has been found that age-related myelin breakdown is more likely to occur in areas of the brain that form myel in later in life, including the frontal lobe (especially in the prefrontal region; Lu et al., 2013). Myelin breakdown in these late-myelinating areas have been found to mediate the relationship between age and processing speed slowing, whereas early-myelinating brain areas have not (Lu et al., 2013). These findings are consistent with accounts of age-related processing speed decline that focus on the role of the prefrontal cortex, or, more broadly, the frontal lobe (e.g., Eckert, 2011). Despite degradation in
the prefrontal area of the brain, research has shown increased activity in the prefrontal cortex in the elderly during a variety of cognitive tasks, including attention/executive functioning and motor planning, compared with younger adults (Berchicci, Lucci, Pesce, Spinelli, & Di Russo, 2012; Ohsugi, Ohgi, Shigemori, & Schneider, 2013). Increased activity in the prefrontal cortex, however, is actually associated with worse ability in many domains, including processing speed (e.g., Woodward, Duffy, & Karbasforoushan, 2013). It has been theorized the increased activity in the prefrontal cortex of the elderly during these tasks may reflect the brain’s attempt to compensate for adverse age-related brain changes or may be the result of the aging brain’s difficulty in recruiting specialized brain regions (Cabeza & Dennis, 2013).

Age-related change in cellular functioning and brain glucose metabolism are thought to have adverse effects on cognition. On a cellular level, oxidative stress within mitochondria, which is believed to occur with age, may lead to the overproduction of reactive oxygen species, which, in turn, may cause cell damage and death (Bergamini, Gambetti, Dondi, & Cervellati, 2004; Yin, Boveris, & Cadenas, 2014). In regard to brain glucose metabolism, declines with age can be seen in many areas of the frontal cortex, as well as in the caudate nuclei and superior lateral temporal cortex (Chételat et al., 2013). Decreased glucose utilization, which is closely liked to regulation of neuronal death, is thought to reflect cognitive impairments (e.g., Gage, Kelly, & Bjorklund, 1984; Mergenthaler, Lindauer, Dienel, & Meisel, 2013).

Changes in activity of a number of other brain chemicals are also seen in aging, and many of these changes are thought to have adverse effects on cognition. For example, older adults evidence reduced dopamine metabolism due to factors such as reduced dopamine transporters in the striatum and reduced binding potential in the striatum and frontal cortex, and impaired dopamine activity has been linked to declines in glucose metabolism in the frontal and
temporal cortices, anterior cingulated gyrus, and caudate regardless of age (Suhara et al., 1991; Volkow et al., 1996, 2000). Based on these findings, it has been suggested that age-related changes in dopamine metabolism may play a contributory role in decreased glucose metabolism in these brain areas, although it could also be hypothesized that decreased glucose metabolism may contribute to reduced dopamine metabolism, as glucose is needed for the synthesis of neurotransmitters (Mergenthaler et al., 2013; Volkow et al., 2000). The proportion of dopamine relative to acetylcholine has been found to be particularly important in the processing of novel stimuli by neurons in the medial temporal lobe and prefrontal cortex (Eckart & Bunzeck, 2013).

Another endogenous chemical for which the elderly develop a lack of sensitivity toward and may subsequently experience adverse cognition is the neuroprotective hormone, leptin (Al Hazzouri, Stone, Haan, & Yaffe, 2013; Folch et al., 2012). Central leptin resistance may be a contributor to cognitive decline in obesity, as stated earlier in this document, but it has also been found to be linked to aging even after the effects of body weight are accounted for (Gabriely, Ma, Yang, Rossetti, & Barzilai, 2002). Changes in activity of other brain chemicals seen in aging and thought to contribute to processes that impair cognition include thyroid stimulating hormone, estrogen, and androgen (Akishita, 2004; Moon et al., 2004; Peeters, 2008).

**Medical events and conditions.** Many medical events and conditions that are more common among the obese also have increased prevalence among the elderly; some examples include T2DM, hypertension, hypercholesterolemia, heart failure, ischemic stroke, vascular dementia, and many cancers (Centers for Disease Control and Prevention, 2014; Copeland et al., 1999; Moon et al., 2013; National Heart Lung and Blood Institute, 2014). Ways in which these events and conditions may contribute to cognitive decline have already been elaborated in this document with the exception of cancer, which will be addressed in the medical treatments
section below. Furthermore, it should be emphasized here that vascular risk factors (e.g., hypertension, hypercholesterolemia, T2DM, cerebrovascular diseases) have been implicated in the progression of MCI to dementia, both of which are more prevalent in the elderly and the latter for which midlife obesity has been documented as a risk factor (Copeland et al., 1999; Xu et al., 2011). That being said, there are certainly medical events and conditions that are not associated with obesity but which could have an adverse impact on the cognition of affected older individuals, including those of hypotension and type 1 diabetes mellitus (Frier, 2011; Hebert et al., 2004).

Medical treatments with potential adverse cognitive effects. Elderly individuals have an increased risk for medication-induced confusion, which is thought to be due to pharmacokinetics and pharmacodynamics that have been altered as a result of the normal aging process or age-related diseases (Flaherty, 1998). Risk increases significantly with the number of medications taken (Flaherty, 1998). Anticholinergic medications in particular often have adverse consequences for cognition in older individuals (Campbell et al., 2009). Use of these medications is prevalent among the elderly, with the most common types including bladder antimuscarinics, first-generation antihistamines, and tricyclic antidepressants (Gray et al., 2015). Acutely, anticholinergic medication use is associated with confusion and slowed information processing speed (Low, Anstey, & Sachdev, 2008; Nebes, Pollock, Halligan, Houck, & Saxton, 2011). Long-term anticholinergic medication use also seems to be problematic, as recent longitudinal studies have linked persistent use with faster decline in episodic memory and higher cumulative burden with increased risk for dementia (Gray & Hanlon, 2016; Papenberg et al., 2017).
In addition, certain chemotherapy and radiation therapy treatments for cancer have been linked to decline in performance across measures of processing speed and executive functioning in longitudinal studies, as well as self-reported increase in severity of memory and concentration problems (Avila et al., 2015; Kohli et al., 2007). There is, however, little evidence to suggest that many types of cancer are associated with cognitive impairment prior to systemic chemotherapy or radiation therapy localized to the brain (Anstey, Sargent-Cox, Cherbuin, & Sachdev, 2015; Avila et al., 2015; Mandelblatt et al., 2014).

**Medical treatments with potential cognitive benefits.** Among individuals with hypertension, current and past use of antihypertensive medications have each been associated with better cognitive performance than among those who have never taken antihypertensive medications or who are not currently taking antihypertensive medication (Farmer et al., 1990). These medications may protect cognition by avoiding vascular damage to the brain secondary to hypertension (Hajjar et al., 2005). Additionally, it was discovered that certain antihypertensive medications protect against cognitive decline to a greater extent than control of blood pressure alone; these include antihypertensive medications that cross the blood-brain barrier and impact the renin-angiotensin-aldosterone system (RAAS) or intracellular calcium metabolism (Hajjar et al., 2005). In particular, angiotensin-converting-enzyme (ACE) inhibitors are believed to be the most efficacious class of hypertensive medication in preventing cognitive decline (Gard, 2010).

Comparatively less is known about the protective effects of anti-diabetic medication use on cognition. Anti-diabetic medication is generally believed to improve cognition or protect against cognitive decline; however, findings are mixed, and improved glycemic control does not consistently predict quality of cognition (Alagiakrishnan, Sankaralingam, Ghosh, Mereu, & Senior, 2013; Gradman, Laws, Thompson, & Reaven, 1993; Hewer, Mussell, Rist, Kulzer, &
Bergis, 2003). Furthermore, anti-diabetic medication usage has not been reliably shown to protect against development of MCI or AD, conditions for which diabetes is a risk factor (Alagiakrishnan et al., 2013).

In regard to hypothyroidism, adverse cognitive effects are generally believed to be reversible with proper medical treatment (Samuels, 2014). Moreover, individuals with long-term use of thyroid medication do not show cognitive abilities that are significantly different than those without a thyroid disorder (Kramer, von Mühlen, Kritz-Silverstein, & Barrett-Connor, 2009).

**Psychosocial factors.** Several psychosocial factors may also be important in explaining cognitive functioning in the elderly, including gender, race, education, mood, sleep, exercise, smoking, diet, and nutrition factors. There is some evidence to suggest that elderly women may experience faster rate of age-related cognitive decline than elderly men; however, other studies have found no differences between genders (Barnes et al., 2003; Mortensen & Hogh, 2001; Zhang, 2006). Furthermore, there is preliminary evidence to suggest that elderly men may perform worse on tests of processing speed than elderly women (MacDonald, Hultsch, Strauss, & Dixon, 2003). In regard to race, African Americans may be more vulnerable to faster rate of cognitive decline, although this also has not been fully established (Lee et al., 2012; Obidi et al., 2008).

Low level of education has been shown to be associated with lower IQ and greater cognitive impairment among the elderly; however, education does not appear to have a significant relationship with processing speed in this population (Kirton & Dotson, 2016; Ritchie, Bates, Der, Starr, & Deary, 2013; Strandberg, Pitkala, Eerola, Tilvis, & Tienari, 2005; Zahodne et al., 2011). Although many have theorized that high education level may have a protective role against rate of cognitive decline, research findings are mixed (e.g., Muniz-
Terrera, Matthews, Dening, Huppert, & Brayne, 2009; Small, La Rue, Komo, Kaplan, & Mandelkern, 1995; Zahodne et al., 2011). It may be the case that high education level is only protective in certain populations or circumstances. This idea is supported by findings that number of stressful life events predict faster rate of cognitive decline in those with a low level of education, but not in those with a high level of education (Tschanz et al., 2013). Additionally, a longitudinal study of community-dwelling elderly without dementia found that, among carriers of two ApoE4 alleles but not among carriers of only one ApoE4 allele, the magnitude of cognitive decline increased as years of education decreased even after adjustments for age, gender, ethnicity, depression, diabetes, history of ischemic heart disease, and history of cerebrovascular disease were made (Shadlen et al., 2005). More research is needed to understand the potential protective role of education against cognitive decline.

Mood and sleep factors have also been hypothesized to impact cognitive functioning in the elderly. Regarding mood, current depressed mood and long-term history of depressive symptoms among the elderly have been associated with worse current cognitive functioning and greater cognitive decline, respectively, and processing speed is among the cognitive domains found to be affected by depression (Gualtieri, Johnson, & Benedict, 2006; Santos et al., 2013; Singh-Manoux et al., 2010). Interestingly, self-reported frequency of feeling lonely has been found to be associated with slower processing speed independent of depression, social networks, and premorbid IQ (O’Luanaigh et al., 2012). Regarding sleep factors, shorter duration and worse quality of sleep have been associated with both worse performance in several cognitive domains (e.g., working memory, attention, abstract problem solving) and increased risk for cognitive impairment among elderly without dementia (Keage et al., 2012; Miyata et al., 2013; Nebes, Buysse, Halligan, Houck, & Monk, 2009; Potvin et al., 2012). However, preliminary evidence
suggests that processing speed does not appear to be impacted by sleep quality (Nebes et al., 2009). Interestingly, daytime napping among the elderly may be associated with less cognitive decline in this population (Keage et al., 2012).

Lack of exercise may also play a key role in cognitive decline in many elderly individuals. Both aerobic exercise and a combination of aerobic and strength training forms of exercise have been shown to improve processing speed task performance (Nouchi et al. 2014; Tam, 2013). More specifically, these effects have typically been found in regard to two or three weekly sessions of exercise for both short-term (e.g., 4 weeks) and long-term (e.g., 3 years) periods of time (e.g., Nouchi et al. 2014; Rikli & Edwards, 1991; van de Rest et al., 2014). The duration of exercise sessions in studies examining their impact on cognition is typically around 30 minutes, totaling a minimum of two sessions or 60 minutes of exercise per week (e.g., Nouchi et al., 2014; Voss et al., 2013). It is not yet well established if less frequent exercise or shorter exercise duration may also benefit processing speed. Compared with anaerobic exercise, aerobic exercise appears to be more beneficial for executive control processes that are frontally-mediated (e.g., switching between tasks, ability to disregard task-irrelevant stimuli, ability to discontinue a planned action; Kramer et al., 1999). Combination training, which includes both aerobic and anaerobic exercises, appears to be more beneficial than either type of exercise alone regarding overall cognition (Colcombe & Kramer, 2003).

In regard to the present study, it was then hypothesized that the group of elderly individuals who engaged in either a minimum of 60 minutes of aerobic exercise weekly or a minimum of two sessions of strength training sessions weekly would exhibit higher scores on the DSST, a traditional measure of processing speed, than those who did not exercise. Further, those who engaged in only aerobic exercise were expected to perform better on the DSST than those
engaged in only strength training exercise, as the DSST has been shown to activate the frontal lobe and involve elements of executive functioning (Davis & Pierson, 2012; Nakahachi et al., 2008). Finally, it was hypothesized that elderly individuals who engaged in combination training would perform better on the DSST compared to the aerobic only, strength training only, and no exercise groups.

Other lifestyle factors, including smoking, alcohol use, and diet history, may also contribute to cognitive impairment in the elderly. Current smoking has been associated with deficits in a number of cognitive domains, including processing speed (Lo, Woodman, Pachana, Byrne, & Sachdev, 2014). It could be hypothesized that smoking causes a decrease in lung functioning that may lead to mild cerebral hypoxia or that inhaled toxins adversely impact the brain. Smoking may also indirectly lead to cognitive dysfunction such that it is a risk factor for a number of conditions that are thought to be causally related to cognitive decline, including CHD (e.g., Wilson et al., 1998). Alcohol use may also be a salient lifestyle factor that contributes to cognitive impairment in this population. Approximately 8.9% of the elderly meet criteria for alcohol abuse, which is associated with dementia in this population, as well as impairments in recent visuospatial memory, verbal memory, and executive functioning (Hudetz & Warltier, 2007; Thomas & Rockwood, 2001). Length of alcohol abuse history is also relevant for cognition outcomes. For example, years of alcohol abuse has been inversely associated with psychomotor speed and short-term memory (DeFranco, Tarbox, & McLaughlin, 1985).

Although heavy alcohol use is known to impair cognition, some evidence suggests that a history of moderate alcohol use may have a protective influence on cognition (Lo et al., 2014). Given the available variables in the NHANES, it was hypothesized that those who endorsed a likely problem with lifetime history of excess alcohol consumption (i.e., answered yes to “Was there
ever a time or times in your life when you drank 5 or more drinks of any kind of alcoholic beverage almost every day?”) would exhibit worse processing speed task performance.

Likewise, it was hypothesized that those who endorsed a likely problem with past-year excess alcohol consumption (i.e., endorsed consuming 5 or more drinks on half or more of the days during the past year) would exhibit worse processing speed. Finally, it was hypothesized that current smoking status would be associated with worse processing speed. It should be noted that those with current or history of chronic use of other drugs, such as cocaine and heroin, have also been found to have impaired cognition in various domains (Lundqvist, 2005). Unfortunately, NHANES did not assess for these factors among the elderly.

Regarding diet, the most consistent findings in this area involve the association between a Mediterranean-type diet and slower cognitive decline and reduced risk for AD (Cheung, Ho, Chan, Sea, & Woo, 2014; Kuczmarski, Allegro, & Stave, 2014). Characteristics of this type of diet include high consumption of vegetables and fruit and low consumption of processed foods, sugar, and saturated fat. This pattern may have a beneficial impact on cognition for a number of reasons. For example, it has also been hypothesized that regular consumption of certain fruits and vegetables that contain polyphenolic compounds with antioxidant, anti-inflammatory, and neuroprotective properties may protect against cognitive decline (Darvesh, Carroll, Bishayee, Geldenhuys, & Van der Schyf, 2010). It has also been hypothesized that high levels of dietary saturated fat may make clearing beta-amyloid proteins from the brain more difficult (Hanson et al., 2013). Other ways in which diets high in fat may lead to cognitive impairment (e.g., central inflammation, impaired insulin signaling) have already been discussed in this document.

A number of vitamins, nutrients, and related chemicals have also found to be important for healthy cognitive functioning among the elderly, including homocysteine, folate, vitamin B₁₂,
iron, and vitamins C, D, and E. Although these factors are being discussed under the psychosocial/diet section of this document, it should be noted here that abnormal levels of these chemicals can occur not only as a result of diet, but also as a result of certain neurologic, psychiatric, hematologic, or genetic reasons (e.g., Hector & Burton, 1988). Homocysteine, folate, and vitamins B₁₂ will be addressed first due to their interdependent relationship. Namely, vitamin B₁₂, vitamin B₆, and folate are thought to be needed to convert homocysteine to an amino acid called methionine, which is needed to produce a variety of other chemicals (Leishear, Ferrucci, et al., 2012). Therefore, if vitamin B₁₂, vitamin B₆, and/or folate levels are depleted, homocysteine levels may increase (Leishear, Ferrucci, et al., 2012). Likewise, increasing folate and B₁₂ via supplements has been shown to decrease homocysteine levels (Graham et al., 1997).

Levels of homocysteine, an amino acid, tend to increase with age and are typically greater in men (Feng et al., 2013). High homocysteine level has been linked to reduced information processing speed and visuoconstructional ability independent of folate levels, although some have argued that high homocysteine levels are only associated with worse cognition in those with low folate levels (Feng et al., 2013; Feng, Ng, Chuah, Niti, & Kua, 2006; Vidal, Dufouil, Ducros, & Tzourio, 2008). Hyperhomocysteinemia, the condition of having high homocysteine levels, has also been linked to lower global cognition (Di Bonito et al., 2007). The pathways by which high homocysteine levels may negatively impact cognition are not well-established; however, it is thought that high levels of homocysteine damage the vascular endothelium (i.e., interior lining of blood and lymphatic vessels) and increase risk for thrombosis and atherosclerosis (Arnesen et al., 1995; Graham et al., 1997). Therefore, hyperhomocysteinemia could be considered an indicator for endothelial dysfunction (Meigs et al., 2001). These factors could, in turn, lead to cognitive impairment. It has also been proposed
that direct neurotoxic effects might explain the link between high homocysteine levels and cognitive impairment, or that insulin resistance might mediate this relationship (Di Bonito et al., 2007). Indeed, T2DM, the hallmarks of which are insulin resistance and hyperglycemia, is among the strongest predictors of peripheral arterial disease (PAD), a vascular disease marked by atherosclerosis (American Diabetes Association, 2003). Interestingly, lowering homocysteine levels (e.g., via folate or B₁₂ supplements) has not been reliably shown to slow cognitive decline (Vogel, Dali-Youcef, Kaltenbach, & Andrès, 2009). This may suggest a number of possibilities, including hyperhomocysteinemia being an indicator, but not necessarily a cause, of endothelial dysfunction. It may also suggest an inability to recover from previous damage, the strong importance of other factors (e.g., diet, exercise) that likely remain unchanged, or limitations in research methodology.

Low folate levels have been associated with worse episodic memory and language ability, but its association with processing speed is less clear (Feng et al., 2006; Jelicic, Jonker, & Deeg, 2001). Findings on the ability of folic acid supplementation to improve processing speed have been mixed (Durga et al., 2007; Malouf & Evans, 2008; Vogel et al., 2009). In addition, some have suggested that low vitamin B₁₂ levels impact the relationship between folate levels and cognition, but findings on the direction of this effect have been contradictory (Doets et al., 2014; Moore et al., 2014).

Vitamin B₁₂ deficiency (typically defined within the range of ≤ 145–260 pmol/L) is associated with a variety of cognitive impairments (e.g., memory problems, slowed thinking, confusion), and it has been hypothesized that cognitive impairments may also occur among elderly with a low-normal range of this vitamin (Hector & Burton, 1988; Leishear, Ferrucci, et al., 2012; Smith & Refsum, 2009). One recent study also found lower vitamin B₁₂ plasma level
to be associated with greater processing speed decline over a period of six years (Leishear, 2011). Furthermore, lower vitamin B₁₂ plasma levels are related to poor sensory and motor peripheral nerve function (Leishear, Boudreau, et al., 2012).

Iron deficiency has also been associated with lower scores on a screening instrument for cognitive impairment among a sample of elderly hospital patients, although it is not known if iron deficiency is specifically associated with processing speed in the elderly (Yavuz et al., 2012). Among those with iron-deficiency, anemia, a condition that is sometimes caused by deficiencies in iron, folate, or vitamin B₁₂, has been linked to worse global cognition (Murray-Kolb & Beard, 2007). Furthermore, severity of anemia has been found to adversely impact processing speed to a greater extent than other cognitive domains (Murray-Kolb & Beard, 2007).

Low levels of vitamin D are associated with poor processing speed, with this relationship being most salient when 25-hydroxyvitamin D level is below 35 nmol/L (Lee et al., 2009). It may also be possible that vitamin E and vitamin C also impact processing speed. For example, vitamin E intake was shown to predict better performance on a battery of cognitive tests that included a processing speed measure (Morris, Evans, Bienias, Tangney, & Wilson, 2002). Results of another study suggest that vitamin C deficiency, but not necessarily vitamin C level itself, may be associated with greater age-related cognitive decline in the general population (Harrison, 2012).

In regard to the present study, it was hypothesized that individuals with low vitamin D level would perform worse on the processing speed task. Low vitamin D level was operationally defined as 25-hydroxyvitamin D level < 35 nmol/L based on the aforementioned work of Lee and colleagues (2009). Note that the current Merck Manual, Professional Edition states that target 25-hydroxyvitamin D levels are approximately 50 to 60 nmol/L for maximal bone health
but does not provide a specific definition of vitamin D deficiency (Johnson, 2016b). Concerning homocysteine and folate, high homocysteine levels were expected to be related to worse performance independent of folate levels. Folate levels, however, were not expected to be significantly correlated with processing speed independent of homocysteine levels. It was difficult to make further hypotheses with confidence given the complicated nature of homocysteine, folate, vitamin B₁₂, iron, and vitamins C, D, and E, but a number of exploratory hypotheses were made in the hypothesis section of this document. For the purposes of these exploratory analyses, folate deficiency was defined as serum folate < 1.4 ng/mL, as suggested by the 1999–2000 CDC Laboratory Procedure Manual in regard to interpretation of results from the Bio-Rad Laboratories’ “Quantaphase II Folate/Vitamin B₁₂” Radioassay Kit. Iron deficiency was operationally defined as a serum ferritin level of < 22µg/L, as this has been found to be the optimal serum ferritin cutoff point for the diagnosis of iron deficiency within community-dwelling older adults (Choi et al., 2005). Vitamin B₁₂ deficiency was defined as < 145 pmol/L and low-normal vitamin B₁₂ level as 145–260 pmol/L, as per the current Merck Manual, Professional Edition (Johnson, 2016a). Vitamin E deficiency was defined as alpha-tocopherol < 11.6 µmol/L or, for adults with hyperlipidemia, a ratio of serum alpha-tocopherol to total lipids of < 0.8 mg/g (Johnson, 2016c). Alpha-tocopherol was chosen rather than gamma-tocopherol, another form of vitamin E with values also available in the NHANES database, because research has shown low alpha-tocopherol to be associated with cognitive impairment and dementia in community-dwelling older adults (Cherubini et al., 2005). Also note that, although both serum and red cell folate assays were performed as part of the NHANES, all analyses in the present study used the serum assay results due to a number of recent findings indicating its relative

Other correlates. Usual slow gait speed and gait speed variability when fast-walking have been linked to worse global cognition and MCI, respectively (Beauchet, Allali, Launay, Herrmann, & Annweiler, 2013; Deshpande, Metter, Bandinelli, Guralnik, & Ferrucci, 2009). Such gait changes typically precede onset of cognitive symptoms in those who go on to develop MCI or dementia (Buracchio, Dodge, Howieson, Wasserman, & Kaye, 2010). These gait patterns are not causally linked to cognitive dysfunction in these individuals, but they are believed to be a result of the same underlying pathological process. Other factors that may slow an individual’s gait speed include psychomotor slowing secondary to depression and relative difficulty walking secondary to obesity, injury, or disability (Atkinson et al., 2007). In regard to the present study, it was hypothesized that gait speed would remain positively correlated with processing speed task performance after controlling for BMI.

Processing Speed Assessment and the Digit-Symbol Substitution Test

Processing speed can generally be defined as the rate at which information can be processed (Lichtenberger & Kaufman, 2009). However, it is difficult to obtain a pure measure of this construct due to a number of confounds in testing. Processing of visual information, for example, depends on a number of other factors, including the integrity of one’s vision, ability to perceive the visual information properly as a whole, and attention capacity. When the processing speed measure requires a written response, motor control and speed may confound results. Furthermore, certain processing speed tests place more attention on visual scanning and attention to detail than others, and some researchers have distinguished processing speed tests based on such considerations. For example, although both require visual processing in a divided-attention
format, Kuo et al. (2006) refers to the Useful Field of View (UFOV) as a measure of visual processing and the DSST as a measure of motor processing speed, seemingly due to the relatively high visual scanning demands of the former and motor demands of the latter. However, labels applied by researchers to the same processing speed test are often different; for example, the DSST, which is historically among the most used measures of processing speed, has been referred to as a measure of motor processing speed, information processing speed, visuo-attentional psychomotor speed, psychomotor functioning, and general cognitive ability by various researchers (González-Blanch et al., 2011; Kuo et al., 2006; Lafont et al., 2010; Lee et al., 2012; Pieters, Maas, & Hulstijn, 2004). Some researchers also decline to label the DSST, instead providing a description of domains it has been used to assess (e.g., Nakahachi et al., 2008). This raises the question of what the DSST actually measures, the answer to which is especially important given the vast amount of research using this measure.

The DSST is a test in which numbers are paired with symbols in a key at the top of a page, and the participant has 120 seconds to copy symbols to corresponding numbers as quickly and accurately as possible. Individuals must be able to complete the sample items and have no significant visual or motor limitations in order to be administered the test. Scores are based on the number of symbols that were copied correctly. Research indicates that Symbol Copy, an optional measure on the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III) and the Wechsler Adult Intelligence Scale-Revised as a Neuropsychological Instrument (WAIS-R-NI) that simply requires subjects to copy symbols from one box to another box below it, accounts for 35–50% of the DSST score variance (Joy et al., 2003; Joy, Fein, Kaplan, & Freedman, 2000; Kreiner & Ryan, 2001). Symbol Copy has generally been considered to be a measure of “motor skill” or “speed” (Joy et al., 2003; Kreiner & Ryan, 2001). Joy and colleagues (2003) further
broke down this variable by assessing for graphomotor speed in a name-writing task. They concluded that the Symbol Copy variable likely contains both graphomotor and perceptual speed components, with the graphomotor component accounting for approximately half of the DSST score variance that is explained by Symbol Copy. Visual scanning efficiency is also very important in the DSST, as Joy and colleagues (2003) found 34% of the DSST score variance to be explained by performance on a visual scanning measure. Memory/learning, although still statistically significant, appear to be less important in explaining DSST scores, accounting for only 4–5% of the variance (Joy et al., 2000, 2003; Kreiner & Ryan, 2001). One study even failed to find a statistically significant association between DSST performance and paired associative learning in older adults (Stephens & Kaufman, 2009). These findings imply that subjects may not benefit from memorizing number-symbol pairs on the DSST, which Joy and colleagues (2003) attempt to explain by hypothesizing that accessing memory to retrieve a symbol may actually take longer than looking at the key to retrieve the symbol, especially as the number of memorized symbols increases. Recently, it has been proposed that the DSST also taps executive functioning on the basis that DSST scores correlate with the Letter-Number Sequencing subtest of the Delis-Kaplan Executive Functions System (D-KEFS) Trail-Making Test to a greater extent than the other subtests (Davis & Pierson, 2012). Finally, it has been hypothesized that fine motor speed and manipulative dexterity may also contribute to DSST scores (Joy et al., 2003). Their roles have not been established, but gait speed has been positively associated with DSST scores (Killane et al., 2014). To summarize, DSST scores appear to primarily reflect graphomotor speed, perceptual speed, visual scanning ability, and executive functioning, although other areas such as learning and memory may play a smaller, yet
still significant, role. It should be noted here that there are a number of DSSTs, including the WAIS-III Digit Symbol—Coding subtest (CD) that is used in the NHANES.

The multifaceted nature of the DSST makes interpreting its scores with regard to one specific cognitive domain difficult; however, this characteristic may also allow for its clinical utility in screening for cognitive dysfunction arising from a variety of sources, and especially those arising from generalized processes (González-Blanch et al., 2011; Joy, Kaplan, & Fein, 2004). For example, the DSST is particularly sensitive to cognitive impairment in multiple sclerosis and schizophrenia, and is a predictor of stroke and heart disease independent of known vascular risk factors (Elkins, Knopman, Yaffe, & Johnston, 2005). The latter suggests the possible utility of DSST scores as an early indicator of poor health prognosis as a function of a premorbid disease state. The DSST is also highly sensitive to aging and age-related changes in brain morphology, and is useful in predicting incident disability, decline in basic and high levels of functional capacity in daily activities, AD, and mortality (Iwasa et al., 2008, 2014; Mosley et al., 2005; Rapp & Reischies, 2005; Salthouse, 1992).

**Justification for the Present Study and Structure of NHANES Database**

Obesity has been associated with cognitive impairment in nearly all cognitive domains. The exact etiological processes that explain this relationship have not been fully elucidated. For example, it is unclear whether the association between obesity and cognitive impairment is independent or can be sufficiently explained by mediating variables (e.g., T2DM, hypertension). In addition to focusing on medical diagnoses as mediating variables (as the majority of research in this area does), it is important to consider the contribution of lower-level obesity-related factors (e.g., low grade inflammation, increased circulation of adipocyte hormones, endothelial dysfunction, insulin resistance, leptin resistance, hypoventilation) that may underlie a number of
obesity-related disorders, as well as be present among obese individuals without obesity-related disorders. Furthermore, it may be the case that lower-level obesity-related factors that contribute to cognitive decline have an increased effect if the individual is exposed to a greater magnitude (e.g., more hormones released from adipose tissue) and/or over a greater time period (e.g., chronic low-grade inflammation in the chronically obese person). Therefore, it follows that knowledge of a person’s weight history, which may serve as a proxy for a number of lower-level obesity variables, may provide additional utility in predicting cognitive functioning than history of medical diagnoses alone. There has been some evidence to support the notion that weight history may impact cognition; however, this area of study is in its infancy, and its data have not been adequately synthesized.

The present study adds to the body of scientific literature in this area by examining the relationship between weight history (beginning in early adulthood) and current processing speed among the young-old (i.e., ages 65–74). The period of early adulthood to age 65–74 greatly extends the length of weight history in any published study on the relationship between weight history and processing speed. The young-old population and the domain of processing speed were chosen in the present study for a number of reasons, including: (a) the number of elderly with significant history of obesity is growing in the United States; (b) processing speed may be foundational to other cognitive processes and drive cognitive aging (Finkel et al., 2007; Salthouse, 1996; Vance, 2009); (c) processing speed in the elderly is predictive of a number of outcomes, including time to complete everyday tasks, life satisfaction, and longevity, to an equal or greater extent than other cognitive domains (Enkvist et al., 2013; Owsley et al., 2002).

Furthermore, it should be noted here that the young-old population was selected for the present study due to consideration of available NHANES variables (e.g., weight “ten years
ago”), consideration of age ranges studied in extant literature in this area (in order to inform this study’s hypotheses), and consideration of the utility of limiting the study to a relatively small age range due to the sensitivity of a number of the relationships of interest to age. Furthermore, it was noted that the large sample size of NHANES allow for the narrowing of age range without sacrificing the necessary statistical power for the present study’s analyses.

The 1999–2000 and 2001–2002 NHANES cycles were chosen for the present study due to their inclusion of a processing speed measure, whereas subsequently completed cycles have not. The variables of these cycles that are relevant to the present study are included in Appendixes A–L and in the methods section of this document. The present study makes a number of hypotheses regarding the relationships among NHANES variables and culminates with creation of a model to explain poor processing speed among those with long-term obesity.
Research Hypotheses

Basic Relationships

The following hypotheses or groups of hypotheses involve basic relationships that would have either replicated those previously reported in the literature or have been very similar to those already reported in the literature:

(1) Age and DSST performance:

There would be a strong negative correlation between age and processing speed task performance (DSST score).

(2) Age and obesity indexes:

(a) Overall indexes: There would be a weak, non-significant negative correlation between age and BMI but a significant positive correlation between age and % total body fat measured by DEXA.

(b) Central indexes: There would be no significant correlation between age and WC but a significant positive correlation between age and % trunk fat measured by DEXA.

(3) Substance use and DSST performance:

(a) Those with probable lifetime history of excess alcohol consumption (i.e., answered yes to “Was there ever a time or times in your life when you drank 5 or more drinks of any kind of alcoholic beverage almost every day?”) would exhibit worse processing speed task performance.
(b) Those with probable past-year excess alcohol consumption (i.e., endorsed consuming 5 or more drinks on half or more of the days during the past year) would exhibit worse processing speed task performance.

(c) Those who currently smoke cigarettes would perform worse on the DSST than those who do not currently smoke cigarettes.

(4) Exercise and DSST performance:

For the purposes of the following hypotheses, the following groups are defined:

**Aerobic-only group**: reported at least 60 minutes of moderate or vigorous aerobic exercise per week but no instances of past-month strength training

**Strength training-only group**: reported at least 8 instances of past-month strength training but no moderate or vigorous aerobic past-month exercise

**Combination training group**: reported at least 60 minutes of moderate or vigorous aerobic exercise per week and at least 8 instances of past-month strength training

**No exercise group**: denied past-month vigorous exercise, moderate exercise, and strength training

(a) The no exercise group would perform worse on the DSST than the aerobic-only, strength training-only, and combination training groups.

(b) The aerobic-only group would perform better on the DSST than the strength training-only group.

(c) The combination training group would perform better on the DSST compared to the aerobic-only, strength training-only, and no exercise groups.
(5) Diabetes status and DSST performance:

For the purposes of these hypotheses, the following groups were operationally defined:

**Diabetes group:** Those with diagnosed history of diabetes or with fasting glucose or HbA\textsubscript{1c} levels in the diabetic range.

**Prediabetes group:** Those without diagnosed history of diabetes who are not currently taking antidiabetic medication and have fasting glucose or HbA\textsubscript{1c} levels in the prediabetic range.

**No diabetes group:** Those without diagnosed history of diabetes who are not currently taking antidiabetic medication and have fasting glucose and HbA\textsubscript{1c} levels in the normal range.

(a) The diabetes group would perform worse on the DSST than the prediabetes and no diabetes groups.

(b) The prediabetes group would perform worse on the DSST than the no diabetes group.

**Main Hypotheses**

The following hypotheses or groups of hypotheses involve relationships that have either not been investigated to-date or have not been reported in the literature with consistency:

(6) Nutritional biochemistry and DSST performance:

(a) Homocysteine levels would be negatively correlated with processing speed independent of serum folate levels.
(b) Serum folate levels would not be significantly correlated with processing speed independent of homocysteine levels.

(c) Those with low 25-hydroxyvitamin D levels (< 35 nmol/l) would perform worse on the processing speed measure than those with healthy vitamin D levels.

**Exploratory (less support from the literature):**

(d) Those with iron deficiency would perform worse on the processing speed task than those without iron deficiency.

(e) Vitamin E levels would be positively correlated with the processing speed measure performance.

(f) Total number of nutrient deficiencies (i.e., vitamin B\textsubscript{12}, vitamin D, vitamin E, folate, iron) would be negatively correlated with processing speed task performance.

(7) Obesity indexes and DSST performance:

(a) DSST scores would not be significantly correlated with the overall obesity indexes (i.e., BMI, % DEXA total body fat).

(b) DSST scores would be significantly negatively correlated with the central obesity indexes (i.e. WC, WTR, WHtR, and % DEXA trunk fat).

(c) Among those who are centrally obese (defined here as WC ≥ 102 cm for men and 88 cm for women):

(1) Individuals meeting BMI obesity criteria (i.e., BMI ≥ 30 kg/m\textsuperscript{2}) would perform worse on the DSST.

(2) Individuals meeting DEXA obesity criteria (fat mass ≥ 25% for men and ≥ 35% for women) would perform worse on the DSST.
**Exploratory (less support from the literature):**

(d) The best combination of obesity indexes to predict DSST score is unknown; however, it was hypothesized that the combination would involve % DEXA trunk fat.

(8) **Weight trajectory and DSST performance:**

The groups in Hypotheses 8a-8c are defined in Table 1. Note that individuals who were underweight (i.e., BMI < 18.5 kg/m²) at one or more of the three timepoints were excluded from these analyses.

(a) Groups 1 and 2 would perform the worst on the DSST.
(b) Group 8 would perform the best on the DSST.
(c) Groups 4, 6, and 7 would perform better than Groups 1 and 2.
(d) Percent of weight gained between early adulthood (age 25) and late middle-age (10 years ago, which would be ages 55–64 in this study) would be associated with worse performance on the DSST.
(e) Absolute value of percent of weight change over the previous 10-year period would be associated with worse performance on the DSST.
(f) Individuals endorsing significant past-year unintentional weight loss would perform worse on the DSST than those who achieved significant past-year weight loss that was intentional and those who were past-year weight-stable.
Table 1

**Hypotheses 8a–8c Groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Obese at age 25</th>
<th>Obese 10 years ago</th>
<th>Obese currently</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Group 2</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Group 3</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Group 4</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Group 5</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Group 6</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Group 7</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Group 8</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>
(9) Peripheral inflammation and DSST performance:

There would be a significant negative correlation between a marker of peripheral inflammation (i.e., CRP level) and processing speed performance, which would remain significant after controlling for health condition and smoking confounds.

(10) Medical history and DSST performance:

(a) Those who endorsed one or more of the following conditions would perform worse on the DSST than those who did not endorse any: problems of blood flow to the heart typically leading to or involving heart muscle damage (i.e., congestive heart failure, coronary heart disease, heart attack), stroke, diabetes, weak/failing kidneys, chronic respiratory disease (i.e., chronic bronchitis or emphysema), and thyroid disease (if untreated).

(b) Duration of respiratory disease would be negatively correlated with processing speed task performance.

(11) Dyslipidemia and DSST performance:

Those with dyslipidemia (i.e., unhealthy levels of total cholesterol, HDL cholesterol, LDL cholesterol, and/or triglycerides) would demonstrate worse processing speed task performance.

(12) Framingham risk scores and DSST performance:
(a) Risk of first stroke, as indicated by score on the modified version of the FSRP, would be inversely associated with processing speed. Note that the modified version of the FSRP, as defined previously in this document, includes age, systolic blood pressure, antihypertensive medication, diabetes, smoking status, CHD, and congestive heart failure.

(b) Risk of onset of CVD, as indicated by FRS for general CVD scores, would be inversely associated with processing speed task performance.

(13) Gait speed and DSST performance:

There would be a significant positive correlation between speed of usual gait and processing speed task performance, which would remain significant after controlling for BMI.

**Final Model**

Finally, the present study used structural equation modeling (SEM) to develop a model of the relationship between weight trajectory and DSST performance. Specifications of the model depended on observed relationships between study variables, which were hypothesized to be consistent with theoretical relationships addressed in the literature review and tested by many of the aforementioned hypotheses. A theoretical mapping of relationships based on the literature review is shown in Figure 1, although this mapping was modified extensively based on the results of tests of relevant hypotheses and practical limitations. In regard to Figure 1, it should be noted that potential causes of processing speed decline that underlie a number of variables on this map (e.g., oxidative stress, endothelial dysfunction, central inflammation) can be causes of a number of factors, while also contributing to the development or persistence of these factors.
Due to their complicated interactions and the lack of biological markers for many of these variables in the NHANES database, they were omitted from the theoretical mapping of relationships in Figure 1, although they did influence reasoning behind many of the hypothesized relationships in the theoretical mapping.
Figure 1. Theoretical model of relationship between persistent obesity and DSST score. Error terms are not shown.
Method

Participants

The present study’s sample consists of the young-old men and women aged 65–74 (n = 1,381) who completed the National Health and Nutrition Examination Survey (NHANES) during the years 1999–2002. NHANES participants were chosen to be representative of the United States population; however, individuals aged 12–19 and over 70 years, as well as certain racial/ethnic/socioeconomic groups (i.e., Non-Hispanic Black, Mexican American, and low-income Caucasian individuals), were oversampled due to being “of particular public health interest” (NHANES Plan and Operations, 1999–2010). NHANES participants were drawn from urban, suburban, and rural locations across the United States, and are of diverse education backgrounds. The aforementioned number of participants aged 65–74 who completed the NHANES during the years 1999–2002 was found to be sufficient for the present study’s secondary analyses based on an a priori power analysis using an expected medium effect size \( f = .25 \) and power = 0.8, which yielded a minimum total sample size for a one-way analysis of variance (ANOVA) with eight groups to be 240 for a 95% confidence interval. See Table 2 for participant characteristics.
Table 2

*Participant Characteristics*

<table>
<thead>
<tr>
<th>Demographic variable</th>
<th>All participants (n = 1,381)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>69.3 (2.9); 65–74</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>28.5 (5.8); 10.8-56.3</td>
</tr>
<tr>
<td>BMI category</td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>1.2</td>
</tr>
<tr>
<td>Normal weight</td>
<td>26.1</td>
</tr>
<tr>
<td>Overweight</td>
<td>38.5</td>
</tr>
<tr>
<td>Obese</td>
<td>34.2</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>50.5</td>
</tr>
<tr>
<td>Female</td>
<td>49.5</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>50.6</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>19.0</td>
</tr>
<tr>
<td>Mexican American</td>
<td>24.0</td>
</tr>
<tr>
<td>Other Hispanic</td>
<td>4.5</td>
</tr>
<tr>
<td>Other Race—including Multiracial</td>
<td>1.9</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Less Than 9th Grade</td>
<td>28.2</td>
</tr>
<tr>
<td>9-11th Grade (Includes 12th grade with no diploma)</td>
<td>17.8</td>
</tr>
<tr>
<td>High School Grad/GED or Equivalent</td>
<td>21.8</td>
</tr>
<tr>
<td>Some College or AA degree</td>
<td>18.3</td>
</tr>
<tr>
<td>College Graduate or above</td>
<td>13.8</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Married/Living with Partner</td>
<td>64.2</td>
</tr>
<tr>
<td>Divorced/Separated</td>
<td>12.4</td>
</tr>
<tr>
<td>Widowed</td>
<td>18.9</td>
</tr>
<tr>
<td>Never married</td>
<td>4.3</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
</tr>
<tr>
<td>Not employed</td>
<td>81.1</td>
</tr>
<tr>
<td>Employed full-time</td>
<td>10.2</td>
</tr>
<tr>
<td>Employed part-time</td>
<td>8.7</td>
</tr>
<tr>
<td>Annual household income</td>
<td></td>
</tr>
<tr>
<td>&lt; $10,000</td>
<td>12.8</td>
</tr>
<tr>
<td>$10,000-$19,999</td>
<td>23.8</td>
</tr>
<tr>
<td>$20,000-$34,999</td>
<td>24.8</td>
</tr>
<tr>
<td>$35,000-$54,999</td>
<td>17.5</td>
</tr>
<tr>
<td>$55,000-$75,000</td>
<td>8.4</td>
</tr>
<tr>
<td>&gt; $75,000</td>
<td>10.9</td>
</tr>
</tbody>
</table>

*Note.* Data are presented as percentages for all categorical variables, and as *M* (SD); range for Age and BMI.

\(^a\)\(n = 1,381\) except for BMI and BMI category (\(n = 1,373\)), education (\(n = 1,374\)), marital status (\(n = 1,317\)), employment status (\(n = 1,379\)), and annual household income (\(n = 1,133\)).
Measures

It should be noted here that, due to the length and number of interviews in the NHANES, only questions from the interviews that are theoretically relevant to the present study are included in the appendices. These questions remain in the order in which they were asked. It should also be noted here that the NHANES “questionnaires” in the appendices are actually personal interviews conducted by NHANES staff or computerized questionnaires completed with the assistance of NHANES staff. Questions were directed toward the sampled person, but a proxy was used if the sampled person (abbreviated SP in the appendixes) needed assistance.

Socio-demographics. Socio-demographic information was collected in the Demographics Questionnaire (Appendix A) and Occupation Questionnaire (Appendix B), which included gender, age, race/ethnicity, education, marital status, number of people living in the household, household income, and employment status.

Anthropometric measures. Current height and weight were measured with a stadiometer and digital scale, respectively (NHANES Anthropometry Procedures Manual, 2000). Using the Weight History Questionnaires, which is a personal interview conducted by NHANES staff, participants were also asked to self-report their current weight and height, as well as recall their weight at 1-year ago and 10-years ago, and weight and height at age 25 (Appendix C). Self-reported highest and lowest adult weight (excluding times of pregnancy) and corresponding ages were also collected. Height and weight allow body mass index (BMI) to be calculated at each of these timepoints. Current waist circumference (WC) and current thigh circumference were determined using measuring tape at a standard position, which allows current waist-thigh ratio (WTR) to be calculated. Additionally, current WC and height allow current waist-height ratio (WHtR) to be calculated.
Dual energy x-ray absorptiometry (DEXA) was conducted with a Hologic Densitometer QDR4500A, allowing the following to be measured or estimated: total mass, fat mass, bone mineral content (BMC), lean mass excluding BMC, lean mass including BMC, percent body fat, and trunk fat (NHANES Body Composition Procedures Manual, 2000). DEXA has good psychometric properties regarding measuring total fat and trunk fat. For example, total body fat measured by DEXA shows strong correlations with total body fat measured by computerized tomography (CT) and magnetic resonance imaging (MRI) -based T-1 mapping (Kullberg et al., 2009). Furthermore, trunk fat measured by DEXA has been shown to strongly correlate with trunk fat measured by CT scan among the elderly ($r = 0.87$ to $0.98$ depending on gender and race/ethnicity), indicating good convergent validity in this population (Snijder et al., 2002).

**Wechsler Adult Intelligence Scale, Third Edition (WAIS-III) Digit Symbol—Coding subtest.** The WAIS-III Digit Symbol—Coding subtest (CD) is a digit symbol substitution test (DSST). It is broadly intended to measure processing speed, and is one of two subtests of the Processing Speed Index (PSI) of the WAIS-III. In the CD, numbers are paired with symbols in a key at the top of the page, and the subject has 120 seconds to copy the symbols to corresponding numbers below the key as quickly and accurately as possible. Individuals who cannot complete the sample items or have significant visual or motor limitations are excluded from taking this test. The CD score is the number of symbols that were copied correctly. There are 133 total items, and therefore, scores range from 0–133, with higher scores indicating better performance. Broadly, the CD is a measure of processing speed; however, more specifically, as reported in detail previously in this document, DSST scores appear to primarily reflect graphomotor speed, perceptual speed, and visual scanning ability, although other areas such as executive functioning and learning/memory may play a smaller, yet still significant, role.
The WAIS-III Digit Symbol—Coding subtest (CD) has acceptable test-retest reliability among 65–74-year olds, which is the age range of the population in the present study ($r = .86$; The Psychological Corporation, 1997). Acceptable reliability is also indicated by a standard error of measurement of 1.12 among 65–74-year olds (The Psychological Corporation, 1997). The CD also shows acceptable criterion validity, as evidenced by a correlation of .77 between WAIS-III and Wechsler Adult Intelligence Scale-Revised (WAIS-R) versions of this subtest among a sample of 16–74-year olds, as well as a correlation of .77 between WAIS-III and WISC-III versions of this subtest among a sample of 16-year-olds (The Psychological Corporation, 1997). Discriminant validity of the CD is reflected by a weak correlation ($r = .25$) with the Raven’s Standard Progressive Matrices (SPM), an untimed test of reasoning. Convergent validity is indicated by a strong negative correlation ($r = -.46$) between scores on the WAIS-R version of the CD (which is very similar to the WAIS-III version of the CD) and the Useful Field of View Test (UFOV), a test of visual processing speed in which higher scores indicate worse performance (Lunsman et al., 2008).

Memory impairment. Participants are asked if they are limited in any way due to difficulty remembering or periods of confusion. They may answer yes, no, don’t know, or refuse to answer.

Medical conditions. Information regarding medical conditions was collected using a number of interviews, including the Blood Pressure Questionnaire (Appendix D), the Diabetes Questionnaire (Appendix E), the Medical Conditions Questionnaire (Appendix F), and the Kidney Conditions Questionnaire (Appendix G). More specifically, participants were asked whether they had ever been diagnosed with certain medical conditions, as well as age at first diagnosis. Diagnoses relevant to this study include asthma, cancer, congestive heart failure,
coronary heart disease, diabetes, hypercholesterolemia, hypertension, kidney failure, stroke, emphysema, thyroid disease, and chronic bronchitis. If endorsed, participants were asked to identify type(s) of cancer as well as whether they still had thyroid disease or chronic bronchitis, whether they had an asthma attack in the past-year, and whether they’d been to the emergency room or urgent care for asthma in the past year. If endorsed, they were also asked whether they took insulin for diabetes (and for how long), whether they took pills for diabetes, and whether they took prescription drugs for hypertension or hypercholesterolemia. Participants were asked if they had been treated for anemia in the past three months, although they were not asked if they had anemia. Finally, participants were asked whether any family members had Alzheimer disease (AD) and, if so, to identify the family member’s relationship to them (e.g., mother, father).

**Physical activity.** Information regarding physical activity was collected using the Physical Activity Questionnaire (Appendix H) and the Physical Activity Individual Activities File (Appendix I). Participants were asked to rate their average level of daily physical activity out of four options. The interviewer then defined moderate and vigorous activities, gave examples for the participant, and then asked if the participant had engaged in any moderate or vigorous activities lasting at least ten minutes in the past month. If moderate or vigorous activities were endorsed, the type of activity, past-month frequency, and duration was collected. Frequency of any strength training exercises was then collected. Participants were asked to report any strength training exercises even if they had included them in the moderate or vigorous activity report.

There is no psychometric data available regarding this particular set of questions. For the purposes of the present study, minutes of aerobic exercise per week was calculated using items
PAD200 and PAD320 of the Physical Activity Questionnaire (Appendix H) and items PADACTIV, PADTIMES, and PADDURAT of the Physical Activity Individual Activities File (Appendix I). Likewise, number of sessions of strength training per week was calculated using items PAD440 and PAD460 of the Physical Activity Questionnaire (Appendix H).

Generally, there is little agreement on how to best assess physical activity in the elderly (Kowalski, Rhodes, Naylor, Tuokko, & MacDonald, 2012). The only systematic review and meta-analysis of validity of indirect measures of physical activity in older adults to-date found that self-reported physical activity in the elderly showed a moderate correlation with direct measures of physical activity (Kowalski et al., 2012). However, it should be noted that the validity of many direct measures of physical activity that are developed primarily on middle-aged samples are questionable among the elderly population due to metabolic or physical activity characteristics. For example, accelerometers are generally less accurate recording lower intensity level activities, which elderly individuals are more likely to do (Garatachea, Luque, & Gallego, 2010; Kowalski et al., 2012). Therefore, there currently appears to be no clear “gold standard” for assessing physical activity in the elderly.

**Diet.** Information regarding diet was collected using the Diet Behavior and Nutrition Questionnaire and the Dietary Interview. In regard to the former, participants were asked to estimate the number of fruits/fruit juices and vegetables they typically consume per day (see Appendix J). In regard to the latter, participants were asked to recall all food and beverage consumed during the previous day (i.e., midnight to midnight). To improve accuracy of recall, participants were asked time, occasion, and place of consumption of each food and beverage they recalled and were shown a list of foods that individuals tend to forget to report. Participants were then asked about specific details of each food and beverage consumed, including amount.
Finally, all reported foods and beverages were repeated to the participant in chronological order for confirmation or correction. Additional information regarding the Dietary Interview can be found in the NHANES Dietary Interview Manual (NHANES Dietary Interview Manual, 1999–2000). Previous day total fat and total saturated fat are estimated using the Dietary Interview data. There are no psychometric data available on the Diet Behavior and Nutrition Questionnaire or the Dietary Interview.

**Blood pressure.** NHANES blood pressure protocol was based on recommendations of the American Heart Association. More specifically, blood pressure was taken by a physician or health technologist using a mercury sphygmomanometer. Three to four trials were obtained. In order to calculate a final blood pressure score, the first blood pressure reading was dropped and the other readings were averaged. For participants who only completed one blood pressure trial, the first blood pressure score was used for the final blood pressure score. Any diastolic readings that were zero were dropped from computing the average unless there were only zero readings. A zero reading likely indicates that the diastolic pressure was not measurable on that trial.

**Cholesterol, triglycerides, C-reactive protein, glucose, and insulin.** Total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, C-reactive protein (CRP), fasting glucose, and fasting insulin were measured using blood samples. Low-density lipoprotein (LDL) cholesterol was calculated from total cholesterol, HDL cholesterol, and triglycerides. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated from fasting glucose and fasting insulin.

**Nutritional biochemistries.** Measurements of vitamin D, vitamin E, folate (serum and red cell assays), vitamin B₁₂, homocysteine, and iron were obtained via blood tests.
**Substance use history.** Information regarding current smoking and smoking history was collected using the Smoking Questionnaire (Appendix K). Information regarding current and past alcohol use was collected using the Alcohol Use Questionnaire (Appendix L). There are no psychometric data available on these questionnaires.

**20-foot-walk test.** The 20-foot-walk test is a frequently used measure of gait speed (e.g., Atkinson et al., 2007; Okoro et al., 2006). In this test, participants are asked to walk down a 20-foot unobstructed hallway or track. Instructions to the participant vary according to the study. Typically, participants are either told to walk at their usual pace or walk at a fast pace. The present study used the 20-foot-walk test to assess usual pace of walking. Assistive devices (e.g., canes, walkers) were allowed if typically used. Time was measured using a hand-held stopwatch.

Despite the frequency of use of this test, little has been published on its psychometric properties. It has shown to produce reliable ratings of gait speed relative to the 8-foot-walk test (ICC 0.912; Newton, Kilma, & Cromwell, 2006). Some concerns have been raised regarding test-retest reliability in similar tests, namely the 10-meter-walk and 20-meter-walk tests. In these tests, the first trial appears to be significantly slower than subsequent trials (Green, Forster, & Young, 2002; Motyl, Driban, McAdams, Price, & McAlindon, 2013). Information on the test-retest reliability of the 20-foot-walk test has not been published to-date.

**Medical treatments.** Participants were asked to list all prescription medications that they are currently taking, as well as number of times each medication was taken in the past 30 days. They were also asked to show the prescription bottles to NHANES staff. Additionally, participants were asked whether they had received cancer chemotherapy in the past 4 weeks or planned to receive cancer chemotherapy in the next 4 weeks. Although this question on
chemotherapy was asked to determine eligibility for venipuncture, it can be used to more inclusively describe medical treatments.

**Procedures**

The present study involved analysis of data from the National Health and Nutrition Examination Survey (NHANES) collected throughout the country between 1999 and 2002. The NHANES created by the National Center for Health Statistics (NCHS) in order to collect health and nutrition data on individuals of all ages living in the United States to provide to the Centers for Disease Control and Prevention (CDC) for the purposes of guiding public health action and policy (NHANES Plan and Operations, 1999–2010). The NHANES protocol received approval from the NCHS Research Ethical Review Board and was reviewed annually. The present study used publically-available NHANES data. No additional permissions were required, and exemption status from the Eastern Michigan University’s Institutional Review Board was obtained in April 2015 (see Appendix M).

NHANES procedures are explained elsewhere (NHANES Plan and Operations, 1999–2010). Briefly, identification of potential participants was accomplished via a multistage probability sampling design aimed at enrolling a sample that is representative of the United States civilian noninstitutionalized household population, although certain populations (individuals aged 12–19, those aged over 70 years, Non-Hispanic black, Mexican American, and low-income Caucasian individuals) were oversampled due to being “of particular public health interest” (NHANES Plan and Operations, 1999–2010). Counties or groups of nearby small counties were divided into neighborhoods, which were selected at random. Residences within each selected neighborhood were then selected at random. The residence was then visited by an NHANES researcher, who determined the eligibility of each resident using a screening
questionnaire that solicited basic demographic data (e.g., age, gender, race). The researcher entered this information into an electronic device that reported whether each participant was eligible, which was based on match with the latest census data. Those identified as eligible were provided information about the study and asked if they would be willing to participate. For each of the two phases of NHANES participation, the home interview and the health examination, documented written consent among adults and parents of participating children, as well as documented assent of participants aged 7–17, was required. The informed consent process and personal interview were typically conducted in English or Spanish, but interpreters for those more comfortable with other languages were used, as needed. The English version of the consent form is included in Appendix N. Remuneration, as detailed below, was only provided after completion of the health examination, which is the second phase of NHANES participation.

Individuals who were eligible and consented/assented then completed the personal interview. This interview took place in the participant’s home unless the participant strongly preferred to complete the interview elsewhere. The personal interview consisted of a series of “questionnaires” about a variety of topics, such as health history, weight history, and alcohol use. Most questionnaires were verbally administered by NHANES staff, whereas the others were completed on a computer with the assistance of NHANES staff. If an individual needed assistance in answering questions, a proxy (e.g., family member) was consulted. During the personal interview, individuals were also administered the WAIS-III Digit Symbol—Coding subtest. Prior to the start of the Coding subtest, participants were asked to put on any glasses that they usually use to read. Those who could not take the Coding subtest without distraction in the home and those who could not complete the sample items on the subtest (e.g., due to physical or cognitive limitations) were not administered the test.
At the end of the personal interview, participants were asked to schedule an appointment for their health examination at a nearby Mobile Examination Center (MEC) during a randomized portion of the day (i.e., morning, afternoon, or evening). Participants were asked to attend during these assigned appointment times, but were allowed to attend during alternate times, if needed. These MEC appointments were made approximately two weeks from the time of the personal interview. A postal letter was sent to participants one week before their scheduled MEC appointment, which included health exam location information, approximate duration of appointment, and remuneration amount. Duration of MEC appointment ranged from 40 minutes to 4 hours depending on the tests administered (which was based on participant age, gender, and health conditions). The amount of the cash remuneration varied from $30 to $100 according to a number of characteristics, including survey year, participant age, and type of appointment attended (i.e., assigned vs. alternate). Namely, adult participants were offered more money than child participants. Adult participants were also offered additional money as an incentive to attend their assigned health examination appointment. To improve attendance, a reminder phone call was also made two days prior to this appointment.

Those who attended the MEC appointment underwent a variety of tests, including those of vision, hearing, blood pressure, walking pace, body composition (i.e., DEXA) and blood (e.g., glucose, iron, CRP). At the end of the health examination, participants were provided their cash remuneration, as well as reimbursement for any incurred travel expense. Approximately 3-4 months after the MEC appointment, participants were mailed a report of results of several of the health tests (e.g., vision, hearing, blood). Individuals with results outside of healthy ranges were recommended to consult a doctor.
For each of the 2-year NHANES cycles in the present study (i.e., 1999–2000 and 2001–2002), approximately 30 counties were sampled and 12,000 individuals were invited to participate. During the 1999–2000 cycle, 9,965 individuals completed the personal interview and, of those, 9,282 completed the health examination (NHANES Plan and Operations, 1999–2010). During the 2000–2001 cycle, 11,309 individuals completed the personal interview and, of those, 10,477 completed the health examination (NHANES Plan and Operations, 1999–2010). Exact response rates of these two cycles have not been reported.

Design

The present study analyzed data collected as part of NHANES during the years 1999–2002. NHANES uses a multistage probability sampling design aimed at enrolling a sample that is representative of the United States civilian noninstitutionalized household population (NHANES Plan and Operations, 1999–2010). As explained above, counties or groups of small counties were divided into neighborhoods, which were selected at random. Residences within each selected neighborhood were then selected at random. Occupants of those residences were then screened to determine study eligibility.

This was a cross-sectional study, as tests were conducted but no interventions were made. Participants were assessed on two occasions: the personal interview and the health exam. The personal interview occurred first, at which time the health exam was scheduled for a date approximately two weeks later. Because these data were collected so close together and do not include repeated measures, the present study used them as the same timepoint. This study also used retrospective pretests (e.g., self-report history of weight and alcohol use).

Analysis
For hypotheses 1–13, data were analyzed using IBM SPSS version 21. All data were screened using frequency distributions and descriptive statistics, and checked for outliers. Relevant data were then assessed for the multivariate statistical testing assumptions of normality, linearity, and homoscedasticity. More specifically, visual inspection of a histogram and normal Q-Q plot for each variable of interest was used to assess univariate normality. Significance of skewness and kurtosis was evaluated at an alpha level of .01. Bivariate scatterplots for all subsets of variables were also examined; roughly elliptical patterns supported the assumption of multivariate normality and linearity. Homoscedasticity was assessed through a visual inspection of bivariate scatterplots and Levene’s Test for Equality of Variances.

Inferential statistical procedures also assume simple random sampling. This assumption was technically not met, as all noninstitutionalized civilians living in the United States did not have equal chance of being selected due to oversampling of certain groups of interest. However, the assumption of independence in independent samples t-tests and Analysis of Variance (ANOVA) was met because participant responses did not influence one another.

The minimum sample size needed within each group in order to run a two-tailed t-test or chi-square test (1 df) using an alpha level of .05 was set at 26, as per results of an a priori power analysis using an expected large effect size ($d = .8$) and power = 0.8. Unless otherwise specified, all statistical analyses excluded underweight participants and used a two-tailed test of significance at alpha level .05.

**Analysis for Hypothesis 1.** It was hypothesized that there would be a strong negative correlation between age and DSST score. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for age and DSST score, and its significance was tested using a two-tailed test of significance at alpha level .05.
Analysis for Hypotheses 2a and 2b. Hypotheses 2a and 2b are concerned the relationship between age and overall and central obesity indexes, respectively. More specifically, it was hypothesized that there would be a weak, non-significant negative correlation between age and BMI but a significant positive correlation between age and % total body fat measured by DEXA. In addition, it was hypothesized that there would be no significant correlation between age and WC but a significant positive correlation between age and % trunk fat measured by DEXA. To test these hypotheses, four Pearson product-moment correlation coefficients were calculated, and significance of these correlations were tested using two-tailed tests of significance at alpha level .05.

Analysis for hypotheses 3a and 3b. It was hypothesized that participants with probable lifetime history of excess alcohol consumption (i.e., answered yes to “Was there ever a time or times in your life when you drank 5 or more drinks of any kind of alcoholic beverage almost every day?”) would exhibit worse processing speed. To test this hypothesis while controlling for gender as a potential confound, a two-way between-subjects ANOVA using a test of significance at alpha level .05 was conducted with gender and probable lifetime history of excess alcohol consumption as the independent variables and DSST score as the dependent variable.

Likewise, it was hypothesized that participants with probable past-year excess alcohol consumption (i.e., endorsed consuming five or more drinks on half or more of the days during the past year) would exhibit worse processing speed. An independent samples t-test using a two-tailed test of significance at alpha level .05 was planned to compare those with and without probable past-year history of excess alcohol consumption on DSST score; however, this analysis could not be conducted as planned due to the probable past-year excess alcohol consumption
group having fewer participants than the minimum group size of 26 determined by the *a priori* power analysis.

**Analysis for Hypothesis 3c.** It was hypothesized that individuals who currently smoke would perform worse on the DSST than those who do not currently smoke. To test this hypothesis, those who endorsed currently smoking tobacco via cigarettes, cigars, and/or pipe were defined as current smokers, whereas those who denied currently smoking tobacco via cigarettes, cigars, or pipe were defined as current non-smokers. An independent samples *t*-test using a two-tailed test of significance at alpha level .05 was conducted to compare those who do and do not currently smoke on DSST score.

**Analysis for Hypothesis 4.** Hypotheses 4a–4c stated the following: The no exercise group would perform worse on the DSST than the aerobic-only, strength training-only, and combination training groups. The aerobic-only group would perform better on the DSST than the strength training-only group. The combination training group would perform better on the DSST compared to the aerobic-only, strength training-only, and no exercise groups. To test these hypotheses, a one-way ANOVA at alpha level .05 was run with exercise group as the independent variable and DSST score as the dependent variable, followed by Tukey’s HSD post-hoc test.

**Analysis for Hypothesis 5.** It was hypothesized that the diabetes group would perform worse on the DSST than the prediabetes and no diabetes groups. It was also hypothesized that the prediabetes group would perform worse on the DSST than the no diabetes group. To test these hypotheses, a one-way ANOVA at alpha level .05 was run with diabetes group as the independent variable and DSST score as the dependent variable, followed by Tukey’s HSD post-hoc test.
**Analysis for Hypothesis 6a.** It was hypothesized that homocysteine levels would be negatively correlated with processing speed independent of serum folate levels. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for homocysteine level and DSST score, and significance of this correlation was tested using a two-tailed test of significance at alpha level .05. A partial correlation calculated for homocysteine level and DSST score while controlling for folate level was then conducted using a two-tailed test of significance at alpha level .05.

**Analysis for Hypothesis 6b.** It was hypothesized that folate levels would not be significantly correlated with processing speed independent of homocysteine levels. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for folate level and DSST score, and significance of this correlation was tested using a two-tailed test of significance at alpha level .05. Given the significant bivariate correlation, a partial correlation controlling for homocysteine level was then conducted using a two-tailed test of significance at alpha level .05.

**Analysis for Hypothesis 6c.** It was hypothesized that those with low vitamin D levels (< 35 nmol/l) would perform worse on the processing speed measure than those with healthy vitamin D levels. To test this hypothesis, an independent samples t-test using a two-tailed test of significance at alpha level .05 was conducted to compare those with and without low vitamin D levels on DSST score.

**Analysis for Hypothesis 6d (exploratory).** It was hypothesized that participants suffering from an iron deficiency (serum ferritin level of < 22µg/L) would perform worse on the processing speed task than participants without an iron deficiency. An independent samples t-test using a two-tailed test of significance at alpha level .05 was conducted to compare participants with and without iron deficiency on DSST score.
Analysis for Hypothesis 6e (exploratory). It was hypothesized that vitamin E level (i.e., alpha-tocopherol) would be positively correlated with processing speed performance. As an additional exploratory analysis, gamma-tocopherol, another type of Vitamin E, was also investigated. For each of the forms of vitamin E included in the NHANES dataset (i.e., alpha-tocopherol and gamma-tocopherol), a Pearson product-moment correlation coefficient was calculated for vitamin E level and DSST score, and significance of this correlation was tested using a two-tailed test of significance at alpha level .05. The Bonferroni post-hoc test was then applied to prevent alpha inflation.

Analysis for Hypothesis 6f (exploratory). It was hypothesized that the total number of nutrient deficiencies (i.e., vitamin B₁₂, vitamin D, vitamin E, folate, iron) would be negatively correlated with processing speed task performance. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for number of nutrient deficiencies and DSST score, and significance of this correlation was tested using a two-tailed test of significance at alpha level .05. Prior to running this analysis, cutoffs for defining nutrient deficiency statuses were reviewed, and relationships between single nutrient deficiencies and processing speed task performance were assessed to determine which nutrients should be included in the analysis.

Analysis for Hypotheses 7a and 7b. It was hypothesized that DSST scores would not be significantly correlated with the overall obesity indexes (i.e., BMI, % DEXA total body fat) but that they would be significantly negatively correlated with the central obesity indexes (i.e. WC, WTR, WHtR, and % DEXA trunk fat). A bivariate correlation matrix was computed, and significance of these correlations was tested using a two-tailed test of significance at alpha level .05.
Analysis for Hypothesis 7c. It was hypothesized that, among those who are centrally obese (WC ≥ 102 cm for men and 88 cm for women), (a) individuals meeting BMI obesity criteria (BMI ≥ 30 kg/m²) would perform worse on the DSST and (b) individuals meeting DEXA obesity criteria (fat mass ≥ 25% for men and ≥ 35% for women) would perform worse on the DSST. To test the first part of the hypothesis, an independent samples $t$-test using a two-tailed test of significance at alpha level .05 was conducted to compare those with central obesity and BMI obesity to those with central obesity but no BMI obesity. Likewise, to test the second part of the hypothesis, an independent samples $t$-test using a two-tailed test of significance at alpha level .05 was conducted to compare those with central obesity and DEXA obesity to those with central obesity but no DEXA obesity.

Analysis for Hypothesis 7d (exploratory). A stepwise multiple regression using backward elimination was run to determine which obesity indices make meaningful contributions to the overall prediction of DSST scores.

Analyses for BMI category by gender interaction on DSST score (exploratory). A series of 2x3 ANOVAs were conducted to investigate main and interaction effects of BMI weight category (i.e., normal weight, overweight, obese) and gender on current DSST score for each of three timepoints (i.e., current, 10 years ago, and age 25), followed by Fischer’s LSD post-hoc tests.

Analysis for Hypotheses 8a–8c. Hypotheses 8a–8c concerned the relationship between weight trajectory and DSST score. Eight groups were created based on whether participants were obese or not obese at age 25, 10 years ago (ages 55–64), and currently (ages 65–74). It was hypothesized that those who were obese at age 25 and 10 years ago would perform the worst on the DSST, whereas those with no history of obesity would perform best on the DSST. It was
also hypothesized that those who were obese at only one timepoint would perform better than those who were obese at age 25 and 10 years ago. To test this hypothesis, a one-way ANOVA with eight groups at alpha level .05 was planned with weight trajectory group as the independent variable and DSST score as the dependent variable, followed by Tukey’s HSD post-hoc test. However, the decision was made to remove three groups from this analysis after it was discovered that each contained a very low number of participants. After removal of these three groups from the analysis, five groups remained. To test this hypothesis using the new groups, a one-way ANOVA with five groups at alpha level .05 with weight trajectory group as the independent variable and DSST score as the dependent variable was conducted, followed by Tukey’s HSD post-hoc test.

**Analysis for Hypothesis 8d.** It was hypothesized that percent of weight gained between early adulthood (age 25) and late middle-age (10 years ago, which is ages 55-64 in the present study) would be associated with worse performance on the DSST. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for percent of weight gained and DSST score, and significance of this correlation was tested using a two-tailed test of significance at alpha level .05. As planned, individuals who were underweight in early adulthood were excluded from this analysis. Additionally, since the question addressed the percent of weight gained between early adulthood and late middle-age, individuals who did not gain weight between these two timepoints were excluded from this analysis.

**Analysis for Hypothesis 8e.** It was hypothesized that the absolute value of the percent of weight change over the previous 10-year period would be associated with worse performance on the DSST. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for absolute value of percent of weight change and DSST score, and significance of
this correlation was tested using a two-tailed test of significance at alpha level .05. As planned, individuals who were underweight 10 years ago (during their “late middle-age” period) were excluded from this analysis, as well as the Hypothesis 8e exploratory analyses.

**Analysis for Hypothesis 8f.** It was hypothesized that individuals endorsing significant past-year unintentional weight loss would perform worse on the DSST than those who achieved significant past-year weight loss that was intentional and those who were past-year weight-stable. No specific hypotheses were made regarding how participants with significant past-year weight gain would perform on the DSST relative to the other three groups.

For the purposes of this hypothesis, “significant past-year weight loss” was defined as having a current body weight that is less than or equal to 95% of the body weight reported one year ago, representing a 5% or greater decrease in body weight. Likewise, “significant past-year weight gain” was defined as having a current body weight that is greater than or equal to 105% of the body weight reported one year ago, representing a 5% or greater increase in body weight. Finally, “past-year weight-stable” was defined as having a weight that was greater than 95% of the body weight reported one year ago but less than 105% of the body weight reported one year ago, representing less than a 5% change in body weight.

To test this hypothesis, a one-way ANOVA at alpha level .05 was run with past-year weight group as the independent variable (four levels: unintentional significant past-year weight loss, intentional significant past-year weight loss, significant past-year weight gain, and past-year weight stable) and DSST score as the dependent variable. The Tukey-Kramer modification of Tukey’s HSD test, which was chosen due to the presence of unequal group sizes, was then used to make post-hoc comparisons of means.
Analysis for Hypothesis 9. It was hypothesized that there would be a significant negative correlation between a marker of peripheral inflammation (i.e., CRP level) and DSST score, which would remain significant after controlling for health condition and smoking confounds. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for CRP level and DSST score, and significance of this correlation was tested using a two-tailed test of significance at alpha level .05. Given that the bivariate correlation was not significant, there was no need to conduct a partial correlation controlling for health conditions and smoking, as planned.

Analysis for Hypothesis 10a. It was hypothesized that participants who endorsed one or more of the following conditions would perform worse on the DSST than those who did not endorse any: problems of blood flow to the heart typically leading to or involving heart muscle damage (i.e., congestive heart failure, coronary heart disease, heart attack), stroke, diabetes, weak/failing kidneys, chronic respiratory disease (i.e., chronic bronchitis or emphysema), and thyroid disease (if untreated). As previously explained, upon implementation of the present study, it was discovered not to be possible to determine whether thyroid disease had been treated; therefore, hypothyroidism was not included in this analysis as planned. To test the hypothesis, an independent samples t-test followed by a two-tailed test of significance at alpha level .05 was conducted to compare DSST scores of those with none of these health conditions and those with ≥ 1 of these health conditions.

Analysis for Hypothesis 10b. It was hypothesized that duration of respiratory disease would be negatively correlated with DSST score. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for duration of respiratory disease and DSST score, followed by a two-tailed test of significance at alpha level .05.
Analysis for Hypothesis 11. It was hypothesized that participants with dyslipidemia (i.e., unhealthy levels of total cholesterol, HDL cholesterol, LDL cholesterol, and/or triglycerides) would demonstrate worse processing speed task performance. To test this hypothesis, an independent samples t-test followed by a two-tailed test of significance at alpha level .05 was conducted to compare DSST scores of participants with and without dyslipidemia.

Analysis for Hypothesis 12a. It was hypothesized that risk of first stroke, as indicated by score on the modified version of the FSRP, would be inversely associated with processing speed. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for modified FSRP score and DSST score, and significance of this correlation was tested using a two-tailed test of significance at alpha level .05. Individuals with a history of stroke were excluded from this analysis, as planned.

Analysis for Hypothesis 12b. It was hypothesized that risk of onset of CVD, as indicated by modified FRS for general CVD scores, would be inversely associated with processing speed task performance. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for modified FRS for general CVD score and DSST score, and significance of this correlation was tested using a two-tailed test of significance at alpha level .05. Individuals with a history of CVD (defined as one or more of the following: CHF, angina pectoris, heart attack, stroke) were excluded from this analysis, as planned.

Analysis for Hypothesis 13. It was hypothesized that there would be a significant positive correlation between speed of usual gait and DSST score, which would remain significant after controlling for BMI. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for gait speed and DSST score, and significance of this correlation was tested using a two-tailed test of significance at alpha level .05. Given that the bivariate
correlation was significant, a partial correlation controlling for BMI was then conducted using a two-tailed test of significance at alpha level .05.

**Final model.** Mplus 6.1 was used for the final structural equation model (Muthén & Muthén, 2008). Missing data was treated with weighted least squares with mean and variance adjustment (WLSMV) due to the use of categorical data. A theoretical model of the relationship between persistent obesity and DSST score, as outlined in Figure 1, was extensively revised prior to testing due to practical limitations, results of the previously described analyses, and theoretical considerations. Confirmatory modeling was used, with an absolute fit index cut-off of root mean square error of approximation (RMSEA) ≤ 0.06 and an incremental index cut-off of comparative fit index (CFI) ≥ 0.95 (Bentler, 1990; Hu & Bentler, 1999). Additionally, chi-square statistics were examined for significance, with nonsignificant results suggestive of acceptable fit. Further, standardized factor loadings of > .35 were required for indicators to be retained in the measurement model (Brown, 2006).
Results

Prior to each parametric analysis, data were assessed with respect to all assumptions relevant to the planned statistical tests. Namely, group data for relevant variables were checked for normality using visual inspection of a histogram and Q-Q plot, significance of skewness and kurtosis was evaluated at an alpha level of .01, bivariate scatterplots for all subsets of variables were examined for roughly elliptical patterns to support the assumptions of multivariate normality and linearity, and homoscedasticity was assessed through a visual inspection of bivariate scatterplots and Levene’s Test for Equality of Variances. Nonparametric tests were used to analyze data that were not normally distributed and could not achieve normality with the appropriate transformation.

Of the total 1,381 participants in the study sample, 1,143 had a recorded DSST score, and 238 did not have a recorded DSST score. Common reasons for lack of DSST score included decision not to attempt the DSST or its sample exercise due to distractions in the home environment (n = 90), refusal to complete the DSST sample exercise (n = 33), and inability to complete the DSST sample exercise due to cognitive (n = 26) or physical (n = 25) limitations. Independent samples t-tests failed to reveal a statistically significant difference in mean age, $t(1379) = -0.705, p = .481$, or mean BMI, $t(1371) = -0.372, p = .710$, between the group with recorded DSST scores and the group without recorded DSST scores. See Table 2 for participant characteristics. Of note, gender was identified as a potential covariate for analyses involving DSST score. Namely, men were found to have significantly lower DSST scores ($M = 40.3, SD = 18.2$) compared to women ($M = 44.2, SD = 18.6$), $t(1141) = -3.643, p < .001$. Therefore, gender was considered as a potential covariate in relevant analyses.
Hypothesis 1 Results

It was hypothesized that there would be a strong negative correlation between age and processing speed task performance, as indicated by DSST score. A Pearson product-moment correlation coefficient calculated for age and DSST score revealed a very weak, but statistically significant, negative relationship between age and DSST score, $r_{(1141)} = -.084, p = .005$.

Hypothesis 2a Results

It was hypothesized that there would be a negative correlation between age and BMI that would not reach statistical significance. A Pearson product-moment correlation coefficient calculated for age and BMI yielded a very weak, but statistically significant, negative correlation, $r_{(1371)} = -.071, p = .008$.

In contrast, it was hypothesized that there would be a significant positive correlation between age and % total body fat measured by DEXA. Given that the NHANES database contained multiply imputed data for DEXA measurements, a Pearson product-moment correlation coefficient was calculated for each of the five versions of completed data, and these estimates were then pooled by calculating their mean. Results were not statistically significant, $r_{(1239)} = .003, p = .916$.

Hypothesis 2b Results

It was hypothesized that there would be no significant correlation between age and WC. Consistent with this hypothesis, the correlation between age and WC was not statistically significant, $r_{(1210)} = -.006, p = .835$.

In contrast, it was hypothesized that there would be a significant positive correlation between age and % trunk fat measured by DEXA. A Pearson product-moment correlation coefficient was calculated for each of the five versions of completed data. Results of these
estimates were then pooled, failing to reveal a significant relationship between age and % total trunk fat measured by DEXA, $r(1239) = -0.009, p = .752$.

**Hypothesis 3a Results**

It was hypothesized that those with probable lifetime history of excess alcohol consumption (i.e., answered “yes” to “Was there ever a time or times in your life when you drank 5 or more drinks of any kind of alcoholic beverage almost every day?”) would exhibit worse processing speed task performance than those without probable lifetime history of excess alcohol consumption (i.e., answered “no” to this question). In order to control for gender as a potential confound in this analysis, a two-way between-subjects ANOVA was run with gender and probable lifetime history of excess alcohol consumption as the independent variables and DSST score as the dependent variable. Results revealed a main effect for probable lifetime history of excess alcohol consumption on DSST score, $F(1, 1039) = 5.742, p = .017$, but failed to reveal a significant main effect for gender on DSST score or a significant interaction effect between the two independent variables. More specifically, participants with probable lifetime history of excess alcohol consumption scored significantly lower on the DSST ($M = 36.5, SD = 16.3$) than those without probable lifetime history of excess alcohol consumption ($M = 43.7, SD = 18.7$), indicating worse processing speed task performance.

**Hypothesis 3b Results**

Hypothesis 3b concerned the survey question “In the past 12 months, on how many days did you have 5 or more drinks of any alcoholic beverage?” It was predicted that those with probable past-year excess alcohol consumption (i.e., endorsed consuming five or more drinks on half or more of the days during the past year) would exhibit slower processing speed than those without probable past-year excess alcohol consumption (i.e., reported consuming five or more
drinks on fewer than half of the days during the past year). Due to the number of participants in the probable past-year excess alcohol consumption group (n = 14) being less than the minimum group size of 26 determined by the \textit{a priori} power analysis, an independent samples \textit{t}-test could not be conducted as planned.

**Hypothesis 3c Results**

It was hypothesized that individuals who currently smoke would perform worse on the DSST than those who do not currently smoke. As expected, individuals who reported that they currently smoke cigarettes, cigars, and/or pipes scored significantly lower on the DSST ($M = 37.0$, $SD = 17.0$) than those who reported that they do not currently smoke ($M = 43.4$, $SD = 18.1$), indicating worse processing speed task performance, $t(624) = -3.989$, $p < .001$.

In exploratory analyses, the relationship between current smoking frequency and DSST score was investigated. A one-way between subjects ANOVA was performed to compare the effect of smoking frequency on DSST score in the “not at all,” “some days,” and “everyday” conditions. There was a statistically significant effect of smoking frequency on DSST score for the three groups, $F(2, 623) = 8.661$, $p < .001$. A post hoc Tukey’s HSD test revealed that the “not at all” group ($M = 43.4$, $SD = 18.1$) scored significantly higher on the DSST than the “everyday” group ($M = 36.3$, $SD = 17.1$), whereas the “some days” group ($M = 40.3$; $SD = 16.4$) did not differ significantly from either group. Results indicate that nonsmokers performed significantly better on the processing speed task than everyday smokers, whereas individuals who smoked only “some days” of the week performed in a manner that was not statistically different from the nonsmokers or the everyday smokers.
Hypothesis 4 Results

Using the operational definitions for no exercise, aerobic-only, strength training-only, and combination training specified in the hypotheses section of this document, it was hypothesized that (a) the no exercise group would perform worse on the DSST than the aerobic-only, strength training-only, and combination training groups; (b) the aerobic-only group would perform better on the DSST than the strength training-only group; and (c) the combination training group would perform better on the DSST compared to the aerobic-only, strength training-only, and no exercise groups. A one-way ANOVA conducted with exercise group as the independent variable and DSST score as the dependent variable revealed a statistically significant effect of exercise group on DSST score, $F(3, 959) = 31.697, p < .001$. Post hoc Tukey’s HSD tests were then performed, revealing that the combination training group ($M = 53.4, SD = 15.1$) scored significantly higher on the DSST than the aerobic-only ($M = 47.3, SD = 17.5; p = .017$), strength training-only ($M = 41.9, SD = 17.9; p = .009$), and no exercise groups ($M = 37.8, SD = 18.1; p < .001$). It also revealed that the aerobic-only group scored significantly higher on the DSST than the no-exercise group, $p < .001$. No other group differences were statistically significant.

Hypothesis 5 Results

Using the operational definitions for diabetes, prediabetes, and no diabetes specified in the Hypotheses section of this document, it was predicted that the diabetes group would perform worse on the DSST than the prediabetes and no diabetes groups. It was also expected that the prediabetes group would perform worse on the DSST than the no diabetes group. To test these hypotheses, a one-way ANOVA at alpha level .05 was run with diabetes status as the independent variable (three levels) and DSST score as the dependent variable, revealing a
significant effect of diabetes status on DSST score \([F (2, 758) = 14.04, p < .001]\). Post hoc comparisons using the Tukey HSD test indicated that the mean DSST score of the diabetes group \((M = 36.5, SD = 17.0)\) was significantly lower than both the prediabetes group \((M = 43.9, SD = 18.3; p < .001)\) and the no diabetes group \((M = 43.7, SD = 19.8; p < .001)\). The difference between the prediabetes group and the no diabetes group was not statistically significant, \(p = .992\).

In exploratory analyses, the potential impact of past-month blood glucose regulator medication on DSST was investigated among participants with diabetes, using the same operational definition for this condition as above. An independent samples \(t\) test failed to find a statistically significant difference in mean DSST scores between participants with diabetes who reported past-month use of blood glucose regulator medication and participants with diabetes who denied past-month use of blood glucose regulator medication, \(t (273) = .519, p = .604\).

Next, the relationship between fasting blood glucose and DSST score was investigated. Individuals were divided into the following groups based on their fasting blood glucose levels: diabetic range \((> 125 \text{ mg/dl})\), prediabetic range \((100–125 \text{ mg/dl})\), normal range \((70–99 \text{ mg/dl})\), and hypoglycemic range \((< 70 \text{ mg/dl})\). Only one individual was found to have tested within the hypoglycemic range; therefore, this category was excluded from subsequent analyses. A one-way ANOVA with fasting blood glucose group as the independent variable (three levels) and DSST score as the dependent variable failed to find a significant effect of fasting blood glucose on DSST score \([F (2, 465) = 2.39, p = .093]\).

The relationship between HbA\(_{1c}\) and DSST score was then investigated. Individuals were divided into the following groups based on their HbA\(_{1c}\) values: diabetic range \((\geq 6.5\%)\), prediabetic range \((5.7\% \text{ to } 6.4\%)\), and normal range \((< 5.7\%)\). A one-way ANOVA with HbA\(_{1c}\)
group as the independent variable (three levels) and DSST score as the dependent variable revealed a significant effect of HbA1c group on DSST score \( F (2, 1042) = 18.22, p < .001 \). Post hoc comparisons using the Tukey HSD test indicated that the mean DSST score of the diabetic range group \( (M = 36.0, SD = 17.0) \) was significantly lower than both the prediabetic range group \( (M = 41.3, SD = 18.3; p = .007) \) and the normal range group \( (M = 45.3, SD = 18.6; p < .001) \). In addition, the prediabetic range group scored significantly lower than the normal range group, \( p = .007 \).

Finally, the relationship between HOMA-IR and DSST score was investigated. HOMA-IR was calculated by multiplying fasting insulin (U/l) by fasting blood glucose (mg/dl) and dividing by 405, as described by Matthews and colleagues (1985). Individuals taking insulin were excluded from this analysis. Peripheral insulin resistance was operationally defined as a HOMA-IR value of greater than the 75th percentile; this criterion was chosen in accordance with the practice of a number of other studies (e.g., Lee et al., 2006; Nasution, Setiati, Trisnohadi, & Oemardi, 2006; Wilson et al., 2007). An independent samples t-test conducted to compare DSST scores of participants with peripheral insulin resistance \( (M = 38.7, SD = 18.3) \) and without peripheral insulin resistance \( (M = 43.6, SD = 17.6) \) revealed a statistically significant difference between groups, \( t (389) = -2.311, p = .021 \). The same analysis among only participants without diabetes was attempted, but it could not be completed due to the number of participants in the peripheral insulin resistance group \( (n = 6) \) being lower than the minimum sample size of 26 determined by the a priori power analysis.

**Hypothesis 6a Results**

It was hypothesized that homocysteine levels would be negatively correlated with processing speed task performance independent of folate levels. First, a Pearson product-
moment correlation between homocysteine level and DSST score was calculated, which revealed a statistically significant weak negative relationship between these two variables, \( r (1039) = -0.108, p < .001 \). Next, a partial correlation was run to determine the relationship between these two variables while controlling for folate level. There was a statistically significant very weak negative partial correlation between homocysteine level and DSST score while controlling for folate level, \( r (1038) = -0.084, p = .007 \). A comparison of the zero-order correlation and partial correlation suggests that folate had relatively little influence in controlling for the relationship between homocysteine level and processing speed task performance. Results indicate that higher homocysteine levels are very weakly associated with worse processing speed task performance independent of folate levels.

In an exploratory analysis, participants with and without hyperhomocysteinemia were compared on DSST score. Hyperhomocysteinemia was defined as \( \geq 12 \mu\text{mol/L} \) based on the work of Castañon, Lauricella, Kordich, and Quintana (2007). An independent samples \( t \)-test revealed that participants with hyperhomocysteinemia scored significantly lower on the DSST \((M = 37.2, SD = 18.0)\) than participants without hyperhomocysteinemia \((M = 44.0, SD = 18.5)\), indicating worse processing speed task performance, \( t (1041) = -4.764, p < .001 \). Cohen’s effect size \((d = .37)\) suggested weak-to-moderate practical significance.

**Hypothesis 6b Results**

It was hypothesized that folate levels would not be significantly correlated with processing speed independent of homocysteine levels. A Pearson product-moment correlation between folate level and DSST score revealed a statistically significant weak positive association between these two variables, \( r (1039) = .204, p < .001 \). In addition, there was a statistically significant weak positive partial correlation between folate level and DSST score while
controlling for homocysteine level, \( r (1038) = .193, p < .001 \). A comparison of the zero-order correlation and partial correlation suggests that homocysteine level had very little influence in the relationship between folate level and processing speed task performance. Results indicate that higher folate levels are weakly associated with better processing speed task performance regardless of homocysteine levels.

No participants in the present study met folate deficiency criteria (i.e., serum folate < 1.4 ng/mL). Given the lack of consensus on the lower limit of serum folate reference values in the literature and the results from the present study’s previous correlation analyses that showed folate to be positively associated with processing speed independent of homocysteine levels, it was deemed acceptable to include a folate variable in this analysis that would capture folate depletion rather than folate deficiency. A serum folate value < 8 ng/mL was chosen for a cutoff for “folate depletion” based on the results of De Bruyn and colleagues (2014). An independent samples \( t \)-test conducted to compare those with and without folate depletion on DSST score showed that participants with folate depletion scored significantly lower on the DSST (\( M = 35.0, SD = 18.5 \)) than participants without folate depletion (\( M = 43.6, SD = 18.3 \)), indicating worse processing speed task performance, \( t (1026) = -4.406, p < .001 \). Cohen’s effect size (\( d = .47 \)) suggested moderate practical significance.

Next, a two-way ANOVA conducted to investigate interaction effects between hyperhomocysteinemia and folate depletion on DSST score failed to show a statistically significant interaction, \( F (1, 1022) = .797, p = .372 \). See Figure 2. Note that results of main effects for this analysis are identical to the previously reported \( t \)-test results.
Figure 2. DSST scores by folate depletion and hyperhomocysteinemia status. Significant main effects for hyperhomocysteinemia, $p < .001$, and folate depletion, $p < .001$, on DSST score. Non-significant interaction effect between hyperhomocysteinemia and folate depletion on DSST score, $p = .372$. 
Hypothesis 6c Results

It was hypothesized that participants with low 25-hydroxyvitamin D levels (< 35 nmol/L) would perform worse on the processing speed task than those with healthy vitamin D levels. Results of an independent samples $t$-test conducted to compare those with low vitamin D levels and those without low vitamin D levels on DSST score showed that participants with low vitamin D levels scored significantly lower on the DSST ($M = 39.2$, $SD = 17.9$) than participants without low vitamin D levels ($M = 46.0$, $SD = 16.8$), indicating worse processing speed task performance, $t (516) = -2.855$, $p = .004$.

Exploratory analyses were used to investigate possible interaction effects between individual obesity variables, gender, and 25-hydroxyvitamin D level on DSST score. First, a 2x2x2 factorial ANOVA was conducted to investigate interaction effects of current obesity status (two levels: obese, non-obese), gender (two levels: male, female), and 25-hydroxyvitamin D status (two levels: low vitamin D, adequate vitamin D) on DSST score. The interaction effect between vitamin D status and gender trended toward significance, $F (1, 518) = 2.957$, $p = .086$, such that men’s DSST scores tended to be more negatively impacted by low vitamin D status than women’s DSST scores. No other interaction effects were significant.

Second, a 2x2x2 factorial ANOVA was conducted to investigate potential interaction effects between late middle-age obesity history, gender, and current 25-hydroxyvitamin D level on DSST score. The interaction effect between late middle-age obesity history and vitamin D status was statistically significant, $F (1, 504) = 5.116$, $p = .024$, such that low vitamin D status appeared to have little impact DSST score in those with history of late middle-age obesity but did appear to have significant impact on DSST score in those without history of late middle-age obesity. More specifically, among those without late middle-age obesity, those with current low
vitamin D level had lower DSST scores ($M = 37.5, SD = 18.2$) than those without current low vitamin D level ($M = 48.2, SD = 16.1$). See Figure 3 for more information. No other interaction effects were significant.
Figure 3. Interaction effects between gender, current vitamin D status, and obesity status on DSST score for current obesity status and obesity status ten years ago. Significant interaction effect between obesity status ten years ago (i.e., late middle-age obesity history) and vitamin D status on DSST score, $p = .024$. Interaction effect between vitamin D status and gender on DSST score trended toward significance, $p = .086$, when data was analyzed by current obesity status. All other interaction effects were non-significant.
Hypothesis 6d Results (exploratory)

It was hypothesized that participants with iron deficiency (serum ferritin level < 22µg/L) would perform worse on the processing speed task than participants without iron deficiency. An independent samples \( t \)-test was conducted to compare participants with iron deficiency to participants without iron deficiency on DSST score. The iron deficient group scored lower on the DSST \((M = 39.3, SD = 18.0)\) compared to the non-iron deficient group \((M = 43.0, SD = 18.5)\), but this difference was not statistically significant, \( t (1026) = -1.391, p = .165 \).

Hypothesis 6e Results (exploratory)

It was hypothesized that vitamin E level (i.e., alpha-tocopherol) would be positively correlated with processing speed task performance. A Pearson product-moment correlation coefficient calculated for alpha-tocopherol (µmol/L) and DSST score using a two-tailed test of significance at alpha level .05 revealed a statistically significant weak-to-moderate positive relationship between these two variables, \( r (490) = .258, p < .001 \), indicating that higher alpha-tocopherol levels are associated with better processing speed task performance.

A set of exploratory analyses were conducted to investigate the relationship between gamma-tocopherol and DSST score. In contrast to the findings involving alpha-tocopherol, a Pearson product-moment correlation coefficient calculated for gamma-tocopherol and DSST score revealed a statistically significant weak inverse relationship between these two variables, \( r (417) = -.140, p = .004 \), indicating that higher gamma-tocopherol levels are associated with worse processing speed task performance. Next, a correlation was calculated for alpha-tocopherol and gamma-tocopherol, which revealed a moderate inverse relationship, \( r (497) = -.395, p < .001 \). Finally, a partial correlation between gamma-tocopherol level and DSST score while controlling for alpha-tocopherol level was run, which failed to indicate a significant
relationship, $r(409) = -0.012, p = .804$. Results suggest that higher gamma-tocopherol levels are not associated with worse processing speed task performance after alpha-tocopherol levels are controlled.

Another exploratory analysis was attempted in order to assess the relationship between vitamin E deficiency status and DSST score. It was discovered that only 2 of the 492 participants with both an alpha-tocopherol value and DSST score met vitamin E deficiency criteria (i.e., alpha-tocopherol < 11.6 µmol/L or, for adults with hyperlipidemia, a ratio of serum alpha-tocopherol to total lipids of < 0.8 mg/g). Therefore, the relationship between vitamin E deficiency status and DSST score could not be assessed.

**Hypothesis 6f Results (exploratory)**

It was hypothesized that the total number of nutrient deficiencies (i.e., vitamin D, iron, vitamin B₁₂, vitamin E, folate) would show a negative correlation with processing speed task performance. Prior to running this analysis, cutoffs for defining nutrient deficiency statuses were reviewed, and relationships between single nutrient deficiencies and processing speed task performance were assessed. Low vitamin D level (25-hydroxyvitamin D < 35 nmol/L), folate depletion (serum folate < 8 ng/mL), iron deficiency (serum ferritin level < 22µg/L), and low vitamin E level (alpha-tocopherol < 11.6 µmol/L or, for adults with hyperlipidemia, a ratio of serum alpha-tocopherol to total lipids of < 0.8 mg/g) have already been addressed in hypotheses 6b-e. In regard to vitamin B₁₂, a one-way ANOVA run at alpha level .05 with vitamin B₁₂ group as the independent variable (three levels: deficient [< 145 pmol/L], low-normal range [145–260 pmol/L], normal range [> 260 pmol/L]) and DSST score as the dependent variable failed to reveal a significant effect of vitamin B₁₂ group on DSST score [$F(2, 1025) = .132, p = .876]$. 
Based on the above analyses, the following nutrient deficiencies/depletions were chosen to be included in the main analysis for this hypothesis: 25-hydroxyvitamin D level (< 35 nmol/L), serum ferritin level (< 22 µg/L), and serum folate depletion (< 8 ng/mL). A Pearson product-moment correlation coefficient calculated for total number of these nutrient deficiencies/depletions and DSST score using a two-tailed test of significance at alpha level .05 revealed a statistically significant weak negative relationship between these two variables, $r(1141) = -.111, p < .001$, indicating that greater number of nutrient deficiencies/depletions is associated with worse processing speed task performance.

In an exploratory analysis, a one-way ANOVA was run with methylmalonic acid quartile as the independent variable and DSST score as the dependent variable, revealing a significant effect of methylmalonic acid quartile on DSST score [$F(3, 1036) = 5.104, p = .002$]. Post hoc comparisons using the Tukey-HSD test indicated that the highest methylmalonic acid quartile scored significantly lower on the DSST ($M = 38.7, SD = 18.9$) than the second highest quartile ($M = 44.0, SD = 17.9$), third highest quartile ($M = 43.9, SD = 18.4$), and bottom quartile ($M = 43.8, SD = 18.6$). No other group differences were statistically significant.

**Results of Exploratory Analyses on Self-Reported Dietary Habits**

The relationship between self-reported dietary habits and processing speed task performance was explored. Results of vegetables and fruits/fruit juices are presented first, as these were the only self-reported eating habit variables for which exploratory analyses were planned. Note that these analyses were only possible for participants examined during the 1999–2000 data collection cycle due to subsequent changes in the NHANES Diet Behavior and Nutrition questionnaire.
A Pearson product-moment correlation coefficient calculated for self-reported number of helpings of vegetables consumed per day and DSST score revealed a statistically significant weak-to-moderate positive relationship between these two variables, \( r(556) = .231, p < .001 \), indicating that greater self-reported number of helpings of vegetables consumed per day is associated with better processing speed task performance. A Pearson product-moment correlation coefficient calculated for self-reported number of helpings of fruits/fruit juices consumed per day and DSST score revealed a statistically significant weak positive relationship between these two variables, \( r(555) = .137, p < .001 \), indicating that greater self-reported number of helpings of fruits/fruit juices consumed per day is associated with better processing speed task performance. Self-reported numbers of helpings of vegetables and fruits/fruit juices consumed per day were found to have a moderate positive relationship with one another, \( r(708) = .344, p < .001 \).

A stepwise multiple regression was then run to determine whether daily number of fruits/fruit juices made a meaningful contribution to the overall prediction of DSST score above and beyond that of daily number of helpings of vegetables. Note that the statistical assumptions of stepwise multiple regression, including the lack of multicollinearity, were met prior to running this analysis. A significant regression equation was found, \( F(2,554) = 16.725, p < .001 \) with an R² of .053 with the predictor daily number of helpings of vegetables, but daily number of helpings of fruits/fruit juices did not meaningfully contribute to the model.

Relationship between DSST score and self-reported number of helpings of each of the following types of foods were investigated in additional exploratory analyses: breads/grain foods, milk/dairy foods, and protein foods. None of the Pearson product-moment correlation coefficients calculated for these variables and DSST score reached statistical significance.
Hypotheses 7a and 7b Results

It was hypothesized that DSST scores would not be significantly correlated with the overall obesity indexes (i.e., BMI, % DEXA total body fat) but would show significant negative correlations with the central obesity indexes (i.e., WC, WTR, WHtR, and % DEXA trunk fat).

First, bivariate correlations were calculated to analyze the relationship between DSST score and each of the obesity indexes that were not derived from DEXA (i.e., BMI, WC, WTR, and WHtR). Results are displayed in Table 3. As hypothesized, these analyses revealed statistically significant inverse relationships between DSST score and each of the central obesity indexes (i.e., WC, WTR, WHtR) but no statistically significant relationship between DSST score and the overall obesity index (i.e., BMI).

Next, the relationship between DSST score and each DEXA variable (i.e., % DEXA total body fat and % DEXA trunk fat) was analyzed using multiply imputed data. For each DEXA variable, bivariate correlations between DSST score and each of its five versions of completed data were calculated, and results of these estimates were pooled. In contrast to what was hypothesized, a very weak but statistically significant positive correlation between DSST score and % total body fat measured by DEXA was found. Further, results failed to show a statistically significant correlation between DSST score and % trunk fat measured by DEXA. See Table 3 for more information.
Table 3

*Summary of Correlations between DSST Score and Obesity Indexes*

<table>
<thead>
<tr>
<th></th>
<th>DSST score</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall obesity indexes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>-.046</td>
<td>.121</td>
</tr>
<tr>
<td>DEXA % total body fat</td>
<td>.076(^a)</td>
<td>.013</td>
</tr>
<tr>
<td><strong>Central obesity indexes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WC</td>
<td>-.072</td>
<td>.019</td>
</tr>
<tr>
<td>WHtR</td>
<td>-.135</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>WTR</td>
<td>-.154</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>DEXA % trunk fat</td>
<td>.050(^a)</td>
<td>.103</td>
</tr>
</tbody>
</table>

*Note.* BMI = body mass index; WC = waist circumference; WHtR = waist-height ratio; WTR = waist-thigh ratio; DEXA = dual energy x-ray absorptiometry.

\(^a\)Pooled estimates using multiply imputed data.
Hypothesis 7c Results

It was hypothesized that, among participants who met WC central obesity criteria, those who also met BMI obesity criteria would perform worse on the DSST than those who did not.

An independent samples t-test conducted to compare centrally obese individuals with BMI obesity ($M = 40.9$, $SD = 18.0$) and without BMI obesity ($M = 44.3$, $SD = 18.3$) on DSST score revealed a statistically significant difference between groups, $t (667) = -2.448$, $p = .015$.

Similarly, it was hypothesized that, among participants who met WC central obesity criteria, those who also met DEXA obesity criteria would perform worse on the DSST than those who did not. An independent samples t-test to compare centrally obese individuals with and without DEXA obesity on DSST score was run for each of the five versions of the completed DEXA data. Results of these estimates were then pooled. In contrast to what was hypothesized, results failed to show a statistically significant difference between centrally obese individuals with and without DEXA obesity on DSST score, $t (660) = .642$, $p = .521$.

Hypothesis 7d Results (exploratory)

The question of which obesity indexes make meaningful contributions to the overall prediction of DSST scores was explored. Note that, for Hypothesis 7d exploratory analyses, single imputation of missing DEXA data was used rather than multiple imputation to allow for multiple regression analysis. Also note that correlations between the dependent variable and the predictor variables as shown in Table 3 are weaker than ideal for multiple regression analysis; however, the decision was made to continue given the exploratory nature of this analysis.

While testing the present data against statistical assumptions of stepwise multiple regression, the problem of multicollinearity was identified on the basis of a bivariate correlation
matrix of the obesity indices using a cut-off value of .7, as shown in Table 4. It was further confirmed by examining the tolerance and variance inflation factor for each predictor variable.
<table>
<thead>
<tr>
<th></th>
<th>BMI</th>
<th>WC</th>
<th>WHtR</th>
<th>WTR</th>
<th>DEXA % total body fat</th>
<th>DEXA % trunk fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WC</td>
<td>.859</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHtR</td>
<td>.902</td>
<td>.896</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>WTR</td>
<td>.126</td>
<td>.468</td>
<td>.422</td>
<td>1.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DEXA % total body fat</td>
<td>.595</td>
<td>.362</td>
<td>.589</td>
<td>-.086</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>DEXA % trunk fat</td>
<td>.674</td>
<td>.514</td>
<td>.701</td>
<td>.100</td>
<td>.949</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*Note. BMI = body mass index; WC = waist circumference; WHtR = waist-height ratio; WTR = waist-thigh ratio; DEXA = dual energy x-ray absorptiometry. All correlations significant at p < .01.*
Based on this data, the following obesity indices were excluded from the multiple regression analysis: BMI, WC, and DEXA % trunk fat. A stepwise multiple regression using backward elimination was then run to determine which of the remaining obesity indices (i.e., WHtR, WTR, DEXA % total body fat) make meaningful contributions to the overall prediction of DSST scores. A significant regression equation was found (F(2, 1025) = 29.188, p < .001) with an R^2 of .054 with the predictors WHtR and DEXA % total body fat, which indicates that 5.4% of variance in DSST score is explained by movement in WHtR and DEXA % total body fat. WTR did not meaningfully contribute to the model. Results are further detailed in Table 5.
### Table 5

**Summary of Multiple Regression Analyses for Obesity Index Variables Predicting DSST Score**

<table>
<thead>
<tr>
<th>Model 1</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Part value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b</td>
<td>SE b</td>
<td>β</td>
<td>T</td>
<td>p</td>
</tr>
<tr>
<td>Constant</td>
<td>63.738</td>
<td>6.098</td>
<td>10.452</td>
<td>&lt; .001</td>
<td></td>
</tr>
<tr>
<td>WHtR</td>
<td>-55.845</td>
<td>10.330</td>
<td>-251</td>
<td>-5.406</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>WTR</td>
<td>-2.625</td>
<td>3.307</td>
<td>-030</td>
<td>-7.94</td>
<td>.427</td>
</tr>
<tr>
<td>DEXA % total body fat</td>
<td>.489</td>
<td>.095</td>
<td>.218</td>
<td>5.170</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 2</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Part value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b</td>
<td>SE b</td>
<td>β</td>
<td>T</td>
<td>p</td>
</tr>
<tr>
<td>Constant</td>
<td>60.203</td>
<td>4.166</td>
<td>14.452</td>
<td>&lt; .001</td>
<td></td>
</tr>
<tr>
<td>WHtR</td>
<td>-60.654</td>
<td>8.366</td>
<td>-273</td>
<td>-7.250</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>DEXA % total body fat</td>
<td>.523</td>
<td>.084</td>
<td>.234</td>
<td>6.217</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

*Note. WHtR = waist-height ratio; WTR = waist-thigh ratio; DEXA = dual energy x-ray absorptiometry.*
Results of Exploratory Analyses on BMI Category by Gender Interaction on DSST Score

In exploratory analyses, a series of 2x3 ANOVAs were conducted to investigate main and interaction effects of BMI weight category (i.e., normal weight, overweight, obese) and gender on current DSST score for each of the following three timepoints: current, 10 years ago, and age 25. These are described below.

First, regarding the current timepoint, results revealed a significant main effect for gender, $F (1, 1120) = 20.880, p < .001$ and a trend toward a significant main effect for current weight category, $F (2, 1120) = 2.919, p = .054$. More specifically, men scored significantly lower on the DSST ($M = 40.4, SD = 18.2$) than women ($M = 44.4, SD = 18.6$). Additionally, the currently obese group tended to score lower on the DSST ($M = 40.7, SD = 18.0$) than the currently overweight ($M = 43.4, SD = 18.1$) and currently normal weight ($M = 43.0, SD = 19.7$) groups, though these differences are not assumed to be significant, as $p$ values were not calculated for these group differences. The interaction effect between gender and current weight category was statistically significant, $F (2, 1120) = 9.753, p < .001$. More specifically, there was a statistically significant simple effect of gender within the normal weight group, $F (1, 1114) = 33.039, p < .001$, but not within the overweight or obese groups. Fischer’s LSD post hoc tests revealed that currently normal weight females scored significantly higher on the DSST ($M = 49.3, SD = 18.2$) than currently normal weight males ($M = 37.1, SD = 18.8$). Further, as Figure 4a reveals, the mean DSST score of the female group decreased when the weight category increased from normal weight to overweight, whereas the mean DSST score of the male group increased during that interval.
Figure 4a. DSST scores by current BMI category and gender. Significant interaction effect between gender and current weight category on DSST score, $p < .001$. Additionally, there is a significant main effect for gender, $p < .001$, and a trend toward significance for current weight category, $p = .054$. 
Second, regarding the late middle age timepoint (i.e., 10 years ago), results revealed significant main effects for gender, $F(1, 1098) = 13.740, p < .001$ and late middle age weight category, $F(2, 1098) = 11.415, p < .001$. More specifically, men scored significantly lower on the DSST ($M = 40.8, SD = 18.1$) than women ($M = 44.8, SD = 18.3$). Additionally, Fischer’s LSD post-hoc tests revealed that the late middle age obese group scored significantly lower on the DSST ($M = 38.2, SD = 17.7$) than the late middle age overweight ($M = 43.2, SD = 17.7$) and the late middle age normal weight ($M = 45.5, SD = 18.3$) groups. The interaction effect between gender and late middle age weight category was statistically significant, $F(2, 1098) = 6.207, p = .002$. There was a statistically significant simple effect of gender within the normal weight group, $F(1, 1092) = 24.328, p < .001$, but not within the overweight or obese groups. Fischer’s LSD post hoc tests revealed that females who were normal weight in late middle age scored significantly higher on the DSST ($M = 49.8, SD = 18.3$) than males who were normal weight in late middle age ($M = 40.3, SD = 18.4$). Moreover, as Figure 4b reveals, the mean DSST score of the female group decreased when the weight category increased from normal weight to overweight, whereas the mean DSST score of the male group increased during that interval.
Figure 4b. DSST scores by late middle-age BMI category and gender. Significant interaction effect between gender and late middle-age BMI category (i.e., BMI category 10 years ago) on current DSST score, $p = .002$. Additionally, there are significant main effects for gender, $p < .001$, and late middle-age weight category, $p < .001$, on current DSST score.
Finally, regarding the age 25 timepoint, results revealed significant main effects for gender, $F(1, 999) = 4.255, p = .039$ and age 25 weight category, $F(2, 999) = 5.782, p = .003$. More specifically, men scored significantly lower on the DSST ($M = 41.2, SD = 17.9$) than women ($M = 45.4, SD = 17.6$). Additionally, Fischer’s LSD post-hoc tests revealed that the age 25 normal weight group scored significantly higher on the DSST ($M = 44.2, SD = 17.6$) than the age 25 overweight ($M = 40.8, SD = 18.2$) and the age 25 obese ($M = 35.6, SD = 17.8$) groups. No other group differences were statistically significant. See Figure 4c.
Figure 4c. DSST scores by young adult BMI category and gender. Non-significant interaction effect between gender and young adult BMI category (i.e., BMI category at age 25) on current DSST score. Significant main effects for gender, $p = .039$, and young adulthood weight category, $p = .003$, on current DSST score.
Hypothesis 8a–8c Results

Eight groups were created based on whether participants were obese at age 25, 10 years ago (ages 55–64), and currently (ages 65–74), as depicted in Table 6. It was hypothesized that participants who were obese at age 25 and 10 years ago would perform the worst on the DSST, whereas those with no history of obesity would perform best on the DSST. It was also hypothesized that those who were obese at only one timepoint would perform better than those who were obese at age 25 and 10 years ago.

To test these hypotheses, a one-way ANOVA with eight groups at alpha level .05 with weight trajectory group as the independent variable and DSST score as the dependent variable was planned. Prior to this analysis, however, it was discovered that three of the eight groups contained very few participants, as shown in Table 6. The decision was made to remove these groups from this analysis rather than combine them with similar groups because it was unclear as to which other group, if any, was most similar to each of the three groups in question. For example, the mean DSST score of Group 4 was extremely low and may suggest that the individuals in this group are relatively unique, perhaps due to illness, and could not be appropriately combined into another group for this analysis. After removal of these groups, five groups remained. Means and standard deviations for each of the new and original groups are included in Table 6.
Table 6

*Means and Standard Deviations of DSST Score by Weight Trajectory Group*

<table>
<thead>
<tr>
<th>Hypothesis 8 Group Original</th>
<th>New</th>
<th>Obese at age 25</th>
<th>Obese 10 years ago</th>
<th>Obese currently</th>
<th>n</th>
<th>DSST score</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>29</td>
<td>37.2</td>
<td>18.0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>_</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>7</td>
<td>34.1</td>
<td>18.6</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>_</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>2</td>
<td>39.5</td>
<td>31.8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>_</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>5</td>
<td>26.6</td>
<td>12.7</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>B</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>152</td>
<td>41.9</td>
<td>16.6</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>C</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>54</td>
<td>32.8</td>
<td>16.7</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>D</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>163</td>
<td>43.7</td>
<td>17.3</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>E</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>558</td>
<td>45.4</td>
<td>17.9</td>
<td></td>
</tr>
</tbody>
</table>

*Note.* Groups removed from Hypothesis 8 analyses due to low sample size are shaded in grey.
Given the results of preliminary analyses that showed a statistically significant relationship between gender and DSST score, conducting an ANCOVA rather than an ANOVA was considered. However, the relationship between the covariate (i.e., gender) and predictor variable (i.e., weight trajectory group) would have violated the ANCOVA assumption of independence of the covariate and treatment effect (Miller & Chapman, 2001). Therefore, the decision was then made to conduct the one-way ANOVA as planned, with the addition of an exploratory analysis to assess for interaction effects between gender and weight trajectory group on DSST score.

A one-way ANOVA with five groups with weight trajectory group as the independent variable and DSST score as the dependent variable was conducted. Results showed a significant effect of weight trajectory group on DSST score, $F(4, 951) = 7.851, p < .001$. Post hoc comparisons using the Tukey-HSD test revealed that Group C scored significantly lower on the DSST than Groups B, D, and E. No other group differences were statistically significant, though a slight trend toward significance for Group A scoring lower than Group E was noted, $p = .102$. In an exploratory analysis, a two-way ANOVA conducted to investigate interaction effects between gender and weight trajectory group on DSST score failed to reveal a statistically significant interaction, $F(4, 946) = .577, p = .679$.

Group differences in mean processing speed between participants with history of persistent obesity (i.e., obesity in both early adulthood and late middle-age) and participants with history of persistent non-obesity (i.e., obesity in neither early adulthood nor late middle-age) were also investigated in exploratory analyses. The persistent obesity group consisted of a combination of the original Groups 1 and 2, whereas the persistent non-obesity group consisted of a combination of the original Groups 7 and 8. Results of an independent samples $t$-test
conducted to compare mean DSST scores of those with persistent obesity ($M = 36.6, SD = 17.9$) to those with persistent non-obesity ($M = 45.0, SD = 17.8$) revealed a statistically significant difference between groups, $t(755) = -2.770, p = .006$. Other exploratory analyses showed that persistently obese males ($M = 33.1, SD = 17.5$) had significantly lower DSST scores than persistently non-obese males ($M = 42.9, SD = 18.1$), $t(409) = -2.423, p = .006$. No statistically significant difference in DSST score between persistently obese females ($M = 41.4, SD = 18.0$) and persistently non-obese females ($M = 47.4, SD = 17.1$) was found, $t(344) = -1.326, p = .186$; however, caution was taken when interpreting results of this analysis, as the number of participants in the persistently obese female group ($n = 15$) was lower than the minimum group size of 26 needed to run a two-tailed $t$-test at alpha level .05 determined by an a priori power analysis.

**Hypothesis 8d Results**

It was hypothesized that the percent of weight gained between early adulthood (age 25) and late middle-age (age 55–64) would be associated with worse performance on the DSST. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for DSST score and percent weight gain between early adulthood and late middle-age. Results of this analysis uncovered a statistically significant weak negative correlation between DSST score and percent weight gain between early adulthood and late middle-age, $r(805) = -.14, p < .001$.

In exploratory analyses, the relationship between performance on the DSST and extent of weight gain (i.e., absolute weight gain in pounds) between early adulthood and late middle-age was assessed. Results of a Pearson product-moment correlation coefficient revealed a statistically significant weak negative relationship between DSST score and extent of weight gain between early adulthood and late middle-age, $r(805) = -.14, p < .001$. Next, the
relationship between performance on the DSST and extent of weight loss (i.e., absolute weight loss in pounds) between early adulthood and late middle-age was assessed. The correlation between DSST score and extent of weight loss between early adulthood and late middle-age was not significant, \( r(83) = .03, p = .80 \).

**Hypothesis 8c Results**

It was hypothesized that the absolute value of the percent of weight change over the previous 10-year period (i.e., from late middle-age to young-old) would be associated with worse performance on the DSST. To test this hypothesis, a Pearson product-moment correlation coefficient was calculated for DSST score and the absolute value of percent of weight change over the previous 10-year period, revealing a statistically significant weak negative relationship, \( r(1096) = -.11, p < .001 \).

In exploratory analyses, a Pearson product-moment correlation coefficient was calculated for DSST score and the extent of weight change over the previous 10 year period (i.e., absolute value of weight change in pounds), revealing a statistically significant weak negative correlation between these two variables, \( r(1096) = -.13, p < .001 \). Exploratory analyses also showed statistically significant weak inverse relationships between performance on the DSST and the extent of weight loss (i.e., absolute value of weight loss in pounds) over the previous 10 year period, \( r(409) = -.20, p < .001 \), as well as between performance on the DSST and the extent of weight gain (i.e., absolute value of weight gain in pounds) over the previous 10 year period, \( r(685) = -.13, p < .001 \).

**Hypothesis 8f Results**

It was hypothesized that individuals with unintentional significant past-year weight loss would perform worse on the DSST than those who achieved intentional significant past-year
weight loss and those who were past-year weight-stable. No specific hypotheses were made regarding how participants with significant past-year weight gain would perform on the DSST relative to the other three groups. A one-way ANOVA was run with past-year weight group as the independent variable (four levels) and DSST score as the dependent variable, revealing a significant effect of past-year weight group on DSST score \( F(3, 1022) = 12.53, p < .001 \). Post hoc comparisons using the Tukey-HSD test indicated that the unintentional significant past-year weight loss group scored significantly lower on the DSST (\( n = 65, M = 31.0, SD = 17.1 \)) than the intentional significant past-year weight loss group (\( n = 83, M = 41.0, SD = 17.9 \)), the significant past-year weight gain group (\( n = 187, M = 42.1, SD = 18.8 \)), and the past-year weight-stable group (\( n = 691, M = 44.8, SD = 17.6 \)). No other group differences were statistically significant.

**Hypothesis 9 Results**

It was hypothesized that there would be a significant negative correlation between CRP level and DSST score and that this correlation would remain significant after controlling for health and smoking confounds. In contrast to the predicted outcome, a Pearson product-moment correlation coefficient calculated for CRP level and DSST score failed to reveal a statistically significant relationship between these two variables, \( r(1027) = -.045, p = .153 \).

**Hypothesis 10a Results**

It was hypothesized that individuals who endorsed one or more of the following conditions would perform worse on the DSST than those who did not: problems of blood flow to the heart typically leading to or involving heart muscle damage (i.e., congestive heart failure [CHF], coronary heart disease [CHD], or heart attack), stroke, diabetes, weak/failing kidneys, chronic respiratory disease (i.e., chronic bronchitis or emphysema), and thyroid disease (if untreated). As previously explained, upon implementation of the present study, it was
discovered not to be possible to determine whether thyroid disease had been treated; therefore, thyroid disease was not included in this analysis. Results of an independent samples $t$-test conducted to compare mean DSST scores of those with none of these health conditions ($M = 44.8, SD = 18.9$) to those with $\geq 1$ of these health conditions ($M = 38.4, SD = 17.3$) showed a statistically significant difference between groups, $t (1113) = -5.642, p < .001$.

In exploratory analyses, a series of $t$-tests were conducted in order to investigate the relationship between individual self-reported medical conditions and DSST score. Results of these analyses are listed in Table 7. In addition, a one-way ANOVA was run with cardiac diagnostic group as the independent variable (four levels: no history of CHF, CHD, or heart attack; history positive for CHF; history positive for only CHD; history positive for only heart attack) and DSST score as the dependent variable, revealing a significant effect of cardiac diagnostic group on DSST score [$F (3, 1090) = 5.91, p = .001$]. Post hoc comparisons using Tukey’s HSD test indicated that the group without history of any of these cardiac diagnoses scored significantly higher on the DSST ($M = 42.9, SD = 18.7$) than the group with history of CHF ($M = 35.6, SD = 17.1; p = .013$) and the group with history positive for only heart attack ($M = 33.2, SD = 15.5; p = .014$). No other group differences were statistically significant.
Table 7

Results of t-tests Comparing Groups on DSST Score by Self-reported History of Medical Condition

<table>
<thead>
<tr>
<th>Condition</th>
<th>M</th>
<th>SD</th>
<th>df</th>
<th>T</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>34.5</td>
<td>16.7</td>
<td>1137</td>
<td>-3.555</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>No</td>
<td>42.7</td>
<td>18.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>36.0</td>
<td>16.5</td>
<td>1113</td>
<td>-5.308</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>No</td>
<td>43.6</td>
<td>18.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39.6</td>
<td>17.8</td>
<td>1136</td>
<td>-4.452</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>No</td>
<td>44.5</td>
<td>18.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weak or failing kidneys</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>35.6</td>
<td>16.0</td>
<td>1136</td>
<td>-2.746</td>
<td>.006</td>
</tr>
<tr>
<td>No</td>
<td>42.6</td>
<td>18.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39.3</td>
<td>17.0</td>
<td>1129</td>
<td>-2.349</td>
<td>.019*</td>
</tr>
<tr>
<td>No</td>
<td>42.9</td>
<td>18.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic respiratory disease</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39.5</td>
<td>17.0</td>
<td>1138</td>
<td>-1.638</td>
<td>.102</td>
</tr>
<tr>
<td>No</td>
<td>42.5</td>
<td>18.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any liver condition</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>44.3</td>
<td>17.0</td>
<td>1136</td>
<td>.670</td>
<td>.503</td>
</tr>
<tr>
<td>No</td>
<td>42.2</td>
<td>18.6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. *Did not remain statistically significant after Bonferroni correction for alpha inflation. Cardiac = self-reported history of congestive heart failure, coronary heart disease, and/or heart attack. Chronic respiratory disease = chronic emphysema and/or chronic bronchitis.
**Hypothesis 10b Results**

It was hypothesized that duration of respiratory disease would be negatively correlated with processing speed task performance. In contrast to the predicted outcome, a Pearson product-moment correlation coefficient calculated for duration of respiratory disease and DSST score revealed a nonsignificant positive relationship between these two variables, $r (85) = .178$, $p = .104$.

**Hypothesis 11 Results**

It was hypothesized that individuals with dyslipidemia (i.e., high levels of total cholesterol, low levels of HDL cholesterol, high levels of LDL cholesterol, and/or high levels of triglycerides) would demonstrate worse processing speed. To test this hypothesis, an independent samples $t$-test was conducted to compare DSST scores of those with dyslipidemia ($M = 42.2$, $SD = 18.4$) and without dyslipidemia ($M = 44.4$, $SD = 18.4$), which failed to reveal a statistically significant difference between groups, $t (543) = -1.306$, $p = .192$.

In exploratory analyses, the relationship between each of the above types of dyslipidemia (i.e., unhealthy levels of total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides) and DSST score was investigated. The relationship between DSST and high levels of non-HDL cholesterol was also examined. A series of independent samples $t$-tests using a two-tailed test of significance at alpha level .05 was conducted to compare participants with and without each dyslipidemia type on DSST score. Results showed significantly lower DSST scores in those with low HDL cholesterol ($M = 39.9$, $SD = 18.5$) compared to those without low HDL cholesterol ($M = 44.4$, $SD = 18.2$), $t (1018) = -3.699$, $p < .001$. Significantly lower DSST scores were also found among those with high non-HDL cholesterol ($M = 40.6$, $SD = 18.8$) compared to those without high non-HDL cholesterol ($M = 43.5$, $SD = 18.4$), $t (1018) = -2.045$, $p = .041$. 
Additionally, results showed a trend toward significance for lower DSST scores in those with high LDL cholesterol ($M = 39.7, SD = 19.1$) compared to those without high LDL cholesterol ($M = 43.9, SD = 18.1$), $t(1018) = -1.859, p = .064$. In contrast to what would have been expected, results showed significantly higher DSST scores in those with high triglycerides ($M = 46.8, SD = 16.8$) compared to those without high triglycerides ($M = 42.1, SD = 18.6$), $t(459) = 2.332, p = .020$. Further, results failed to show a significant difference between DSST scores in those with high total cholesterol compared to those without high total cholesterol, $t(1018) = -.585, p = .559$. After the Bonferroni correction was applied to prevent alpha inflation, mean group DSST scores only remained significantly different between participants with and without low HDL cholesterol.

Additional analyses were later used to explore whether the above relationships differed by sex. Results showed sex-specific relationships between DSST score and two types of dyslipidemia: high non-HDL cholesterol and high triglycerides. Namely, men with high non-HDL cholesterol scored significantly lower on the DSST ($M = 36.8, SD = 17.2$) than men without high non-HDL cholesterol ($M = 41.9, SD = 18.4$), $t(517) = -2.442, p = .015$, but the same relationship was not found among women, $t(499) = -1.013, p = .312$. Moreover, women with high triglycerides scored significantly higher on the DSST ($M = 51.0, SD = 17.2$) than women without high triglycerides ($M = 43.3, SD = 18.3$), $t(227) = 2.725, p = .007$, but the same relationship was not found among men, $t(230) = .486, p = .628$.

**Hypothesis 12a Results**

It was hypothesized that risk of first stroke, as indicated by score on a modified version of the FSRP, would be inversely associated with processing speed task performance. A Pearson product-moment correlation coefficient calculated for modified FSRP score and DSST score
revealed a statistically significant weak negative correlation between these two variables, $r (216) = -.136, p = .045.$

**Hypothesis 12b Results**

It was hypothesized that risk of onset of CVD, as indicated by score on a modified version of the FRS for general CVD, would be inversely associated with processing speed task performance. A Pearson product-moment correlation coefficient calculated for modified FRS for general CVD score and DSST score revealed a statistically significant weak negative correlation between these two variables, $r (171) = -.205, p = .007.$

**Hypothesis 13 Results**

It was hypothesized that there would be a significant positive correlation between speed of usual gait and processing speed and that this correlation would remain significant after controlling for BMI. Speed of usual gate (ft/s) was calculated using results from the 20-foot-walk test. A Pearson product-moment correlation coefficient calculated for gait speed and DSST score revealed a statistically significant moderate positive correlation between these two variables, $r (999) = .369, p < .001.$ Next, a partial correlation was run to determine the relationship between gait speed and DSST score while controlling for BMI. A statistically significant moderate positive correlation between gait speed and DSST score remained after controlling for BMI, $r (998) = .366, p < .001.$ A comparison of the zero-order correlation and partial correlation suggests that BMI had very little influence in controlling for the relationship between gait speed and DSST score. Results indicate that faster usual gait speed is moderately associated with faster processing speed regardless of BMI.
Final Model

The originally proposed theoretical model of the relationship between persistent obesity and DSST score, as depicted in Figure 1, required extensive revision prior to testing due to practical limitations, results of the previously described analyses, and theoretical considerations. Most notably, it was deemed inappropriate to hypothesize that persistent obesity (which refers to the span of time from young adulthood to late middle-age in the present study) would have a bidirectional relationship with current habits and characteristics (e.g., diet, physical activity, cholesterol levels), as there was a 10-year gap between late middle-age and the time of data collection (i.e., young adulthood); therefore, these observed variables were removed from the original model. Additionally, a number of proposed latent constructs (i.e., depression, physical inactivity history, diet/nutrient history) were removed from the model due to lack of available indicators to represent them. In other words, this information was not collected as part of the NHANES cycles under analysis. Likewise, one proposed indicator of “brain oxygen flow disruption/insufficiency” (i.e., chronic hypoventilation during sleep or awake periods) was removed due to this data not having been collected. Furthermore, some observed variables (i.e., chronic respiratory disease, peripheral inflammation) were removed from the model due to the lack of significant relationship with DSST score found in earlier analyses. The remaining variables were then examined for theoretical considerations. It was noted that each of the remaining variables were vascular risk factors that conceivably could have a) been partially “caused” by a history of persistent obesity and b) contributed to a decline in processing speed. Another consideration relating to the decision to proceed with a model that focused on vascular health history was the understanding that vascular risk factors are more theoretically relevant to a decline in processing speed than risk factors associated with only Alzheimer disease (AD), as
deficits of processing speed and executive functioning are typical of a vascular pattern of cognitive impairment whereas deficits in memory and language are typical of cognitive impairment seen in AD, particularly in this age group when AD is less likely to be advanced stages in which additional domains tend to become impaired (American Psychiatric Association, 2013; Gasecki, Kwarciany, Nyka, & Narkiewicz, 2013; Lezak, Howieson, Bigler, & Tranel, 2012). As a result of the above considerations, a measurement model of vascular health history was hypothesized using the remaining variables as indicators, as depicted in Figure 5. Additionally, a structural model in which vascular health history partially mediates the relationship between persistent obesity and DSST score was hypothesized, as shown in Figure 6. Note that cardiac history in Figure 5 refers to a binary variable that reflects the presence or absence of self-reported CHD, CHF, and/or heart attack, which is consistent with its use in previous analyses in the present study.
Figure 5. Hypothesized measurement model of vascular health history. Error terms not shown.
Figure 6. Revised hypothesized structural model of DSST score. Error terms not shown.
The hypothesized measurement model for vascular health history was tested using confirmatory factor analysis (CFA) prior to assessment of the hypothesized structural model. The hypothesized measurement model included one latent variable (i.e., vascular health history) and four observed indicators (i.e., self reported history of hypertension, stroke, diabetes, and cardiac event/condition). Results of the CFA for vascular health history revealed an acceptable fit between the measurement model and the present study’s data [$\chi^2$ (2, 1380) = 1.404, $p = .496$; CFI = 1.000; RMSEA = .000 (90% CI = .000–.048)]. Further, the standardized factor loadings for each of the four indicators exceeded the cut-off criterion of >.35 and, therefore, were retained in the measurement model. See Table 8 for complete information on factor loadings.
Table 8

*Confirmatory Factor Analysis for Vascular Health History*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Estimate</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>0.57</td>
<td>0.08</td>
<td>0.000</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.66</td>
<td>0.07</td>
<td>0.000</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.45</td>
<td>0.06</td>
<td>0.000</td>
</tr>
<tr>
<td>Cardiac</td>
<td>0.44</td>
<td>0.06</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*Note.* Standardized regression weights and two-tailed *p* values are reported.
Next, the revised hypothesized structural model of DSST score, as previously depicted in Figure 6, was tested, revealing inadequate fit with the present study’s data \( \chi^2 (8, 874) = 15.409, p = .052; \) CFI = 0.949; RMSEA = 0.033 (90% CI = .000–.057). See Figure 7 and Table 9 for results regarding individual factor loadings of the revised hypothesized structural model.
Figure 7. Revised hypothesized structural model of DSST score with standardized regression weights. Error terms not shown. **p < .001.
Table 9

*Factor Loading Summary of Revised Hypothesized Structural Model of DSST Score*

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>SE</th>
<th>Estimate/SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DSST score on:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular health history</td>
<td>10.27 (0.35)</td>
<td>2.50</td>
<td>4.11</td>
<td>0.000</td>
</tr>
<tr>
<td>Persistent obesity</td>
<td>0.05 (0.00)</td>
<td>3.91</td>
<td>0.01</td>
<td>0.990</td>
</tr>
<tr>
<td><strong>Vascular health history on:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent obesity</td>
<td>0.82 (0.29)</td>
<td>0.17</td>
<td>4.81</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*Note.* Standardized estimates are in parentheses. Two-tailed $p$ values are reported.
Modification indices and factor loadings were then examined to determine if an adjustment to the structural model could be made to improve model fit in the event that the adjustment made theoretical sense. In doing so, the direct path between persistent obesity and DSST score was removed. The resulting structural model, as depicted in Figure 8, was then tested, revealing adequate fit with the present study’s data [$\chi^2 (9, 874) = 14.661, p = .101; \text{CFI} = 0.961; \text{RMSEA} = 0.027 (90\% \text{ CI} = .000–.051)$]. See Figure 9 and Table 10 for results regarding individual factor loadings of the final model.
Figure 8. Final structural model of DSST score. Error terms not shown.
**Figure 9.** Final structural model of DSST score with standardized regression weights. Error terms not shown. **p < .001.**
Table 10

*Factor Loading Summary of Final Structural Model of DSST Score*

<table>
<thead>
<tr>
<th>DSST score on:</th>
<th>Estimate</th>
<th>SE</th>
<th>Estimate/SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular health history</td>
<td>10.93 (0.37)</td>
<td>2.34</td>
<td>4.68</td>
<td>0.000</td>
</tr>
<tr>
<td>Vascular health history on:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent obesity</td>
<td>0.81 (0.29)</td>
<td>0.16</td>
<td>5.03</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*Note.* Standardized estimates are in parentheses. Two-tailed p values are reported.
Discussion

Hypothesis 1 Discussion

It was hypothesized that there would be a strong negative correlation between age and processing speed task performance, as indicated by Digit Symbol Substitution Test (DSST) score. This hypothesis was based on the consensus that declines in most cognitive domains occur with aging even in the absence of known health problems as well as research that supports the notion that processing speed is among the most important factors in explaining normal age-related cognitive decline (e.g., Aine et al., 2011; Harada et al., 2013; Hasher et al., 1991; Rozas et al., 2008; Vance, 2009).

This hypothesis was partly supported by the data. Age was found to have a significant inverse relationship with DSST score, which suggests that processing speed task performance declines as age increases within the young-old age category. This finding is consistent with previous research on other tests of processing speed within this age category, including the Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV) Processing Speed Index (PSI) subtests Coding and Symbol Search (Wisdom, Mignogna, & Collins, 2012).

The strength of the relationship between age and DSST score in the present study was weak, whereas it was predicted to be strong. This finding may be related to the cross-sectional nature of the present study, as longitudinal effects have been shown to be larger than cross-sectional effects for the Wechsler Adult Intelligence Scale-Revised (WAIS-R) DSST and a variety of other cognitive measures among a sample of older adults aged 66–92 at baseline who were followed for up to five 18-month intervals (Sliwinski & Buschke, 1999). In other words, cross-sectional age differences in processing speed may be less obvious than longitudinally-measured age-related changes in this population (Sliwinski & Buschke, 1999).
Additionally, evidence of increased intragroup variability on tests of processing speed as age increases, as captured by Wisdom, Mignogna, and Collins (2012) with the use of the coefficient of variation (CV), should be considered when interpreting these results. The CV, which is calculated by dividing the standard deviation by the mean and multiplying by 100, has utility as a measure of score dispersion above and beyond that of standard deviation, the latter of which has been shown to vary relatively little on the WAIS-IV PSI subtests for participants within this age category (Wisdom et al., 2012). In other words, in regard to a variable whose mean decreases with age but whose standard deviation remains stable with age (similar to the DSST variable in the present study), the variable will show increased score dispersion with age, which would then yield a weaker correlation between that variable and age.

On the other hand, it is possible that the relationship between age and processing speed would be stronger in a population older than the present study’s sample of 65–74-year olds. Salthouse (2012) presented data suggestive of stability in rate of decline in processing speed in adults up to age 75, but future research is needed to understand whether this rate of decline remains stable, or perhaps accelerates, beyond age 75. Finally, the finding that age was only weakly correlated with DSST score in the present study highlights the importance of other contributors to processing speed task performance in this age group.

**Hypothesis 2 Discussion**

It was hypothesized that age would show a significant positive association with % body fat as measured by dual energy x-ray absorptiometry (DEXA) but would show a slight, negative, statistically insignificant correlation with body mass index (BMI). Likewise, it was hypothesized that visceral adiposity estimated by % trunk fat DEXA would increase significantly with age but waist circumference (WC) would not be significantly correlated with age. These hypotheses
were based on a number of interrelated findings that highlight the changing body composition with age as well as the discrepancy between this group’s body composition markers and obesity indexes. The hypotheses involving anthropometrically derived obesity indexes (i.e., BMI, WC) were largely supported by the data, whereas those involving DEXA-derived obesity indexes (i.e., % body fat DEXA, % trunk fat DEXA) were not.

The hypothesis that % total fat DEXA would increase with age had been informed by a study that showed increase in bioelectrical impedance analysis (BIA)-derived percentage of total body fat with age across the adult lifespan (Kyle, et al., 2001). The present study, however, did not find a statistically significant relationship between age and % total fat DEXA among its young-old participants. The absence of this finding may be related to the specific age decade under investigation (ages 65–74) and the timing of the onset of significant age-related decline in fat-free mass. Namely, Obisesan and colleagues (2005) found that declines in fat-free mass typically began during one’s 50s but did not become significant until ages 65–69 in Black men, 70–74 in Black women and White men, and 75–79 in White women. It may be the case that many participants in the present study had not yet experienced significant decline in fat-free mass, a change in body composition that would have contributed to increased % total fat DEXA values. Another possible explanation for the apparent discrepancy between the results of Kyle and colleagues (2001) and the present study pertains to the health of their respective participants, as the former attempted to exclude individuals with acute or chronic diseases (a number of which are known risk factors for dementia). Because dementia risk increases with age and individuals who go on to develop dementia are more likely to have lost a significant amount of weight between midlife and late-life compared to individuals who remain free of dementia, it may be the
case that the present study contained more individuals at relatively higher ages with recently reduced body weights (Stewart et al., 2005).

The hypothesis that % trunk fat DEXA would increase with age in the young-old population had been informed by results of a cross-sectional study reported by Oldroyd and colleagues (1998), which showed increased % trunk fat DEXA in males over the age of 50 ($M = 59.2$ years) and postmenopausal women ($M = 61.6$ years) relative to males below the age of 50 ($M = 37.5$ years) and premenopausal women ($M = 37.2$ years), respectively. Results of the present study suggest that the increase in abdominal fat that appears to occur between approximately midlife and late midlife may not continue to occur during the young-old portion of the lifespan (i.e., 65–74 years of age). This idea is supported by findings from a recent cross-sectional study of women using BIA, which found statistically significant increases in visceral fat area during the third, fourth, and fifth decades of life but statistically insignificant increases in visceral fat area in the sixth decade of life and beyond (Gába & Přidalová, 2014).

**Hypothesis 3 Discussion**

The hypothesis that participants with probable lifetime history of excess alcohol consumption would exhibit worse processing speed task performance than participants without this history was supported by the data. This finding is not surprising given that individuals with a history of chronic alcohol use are at risk for alcohol-induced neurocognitive disorders. In addition, there is evidence of impaired cognition during periods of abstinence subsequent to chronic alcohol use, mostly with regard to tasks dependent on the hippocampus and/or prefrontal cortex (e.g., working memory and executive functioning; Staples & Mandyam, 2016). Further, history of chronic alcohol use is associated with other lifestyle variables that may be independently linked to worsened processing speed task performance, such as those of smoking.
The present study adds information to the current body of literature on associations between history of chronic excess alcohol use and processing speed task performance in a nationally representative sample of young-old adults.

The hypothesis that participants who currently smoke would perform worse on the DSST than those who do not currently smoke was supported by the data. Moreover, exploratory analyses showed that everyday smokers performed worse on the DSST than nonsmokers, whereas occasional smokers did not differ significantly from either group. Results indicate that smoking everyday is associated with worsened processing speed in adults aged 65–74 compared to not smoking. This finding was expected, as smoking has been hypothesized to lead to impaired cognition through the initiation of atherogenesis and subsequent development of atherosclerosis, which can lead to cardiovascular and/or cerebrovascular diseases that negatively impact cognition (Messner & Bernhard, 2014). It is also possible that daily smoking may decrease lung functioning, which in turn may discourage individuals from participation in regular aerobic exercise, which itself is linked with improved cognitive outcomes and decreased risk of cardiovascular and cerebrovascular diseases. Previous research has found that, among women aged 40–79, current smokers and previous smokers scored lower on the WAIS-III PSI than never-smokers (Lo et al., 2014). The present study’s findings add information to the current body of literature on associations between frequency of current smoking behavior and processing speed task performance in a nationally representative sample of young-old adults.

**Hypothesis 4 Discussion**

Participants were divided into the following groups for this set of hypotheses: participants who did not engage in regular exercise (no exercise group); participants who engaged in both regular aerobic exercise and regular strength training exercise (combination training group);
participants who engaged in regular aerobic exercise only (aerobic-only group); and participants who engaged in regular strength training exercise only (strength training-only group). Among these groups, it was hypothesized that the no exercise group would perform worst on the DSST, whereas the combination training group would perform the best and the aerobic-only group would outperform the strength training-only group.

These hypotheses were based on results of experimental studies showing the benefit of immediate and regular aerobic exercise on processing speed and other aspects of cognition (e.g., Nouchi et al. 2014; Tam, 2013). Additionally, they were informed by an experimental study that found evidence for a program of aerobic exercise to selectively improve performance of executive control processes supported by the frontal and prefrontal regions of the brain (e.g., switching between tasks, ability to disregard task-irrelevant stimuli, ability to discontinue a planned action), which is relevant to the present study given that the DSST involves elements of executive functioning and has been shown to activate the frontal lobe (Davis & Pierson, 2012; Nakahachi et al., 2008). Further, these hypotheses were informed by results of a meta-analysis on the effects of exercise on the cognitive functioning of older adults that yielded the finding that those in combination training programs demonstrated improvements in cognitive outcomes to a greater degree than those in aerobic training groups (Colcombe & Kramer, 2003).

This group of hypotheses was partially supported by the results of the present study. As predicted, the present study found that, in regard to the DSST, the combination training group outperformed each of the other three exercise groups, and the aerobic-only group outperformed the no-exercise group. However, in contrast to what was hypothesized, the strength training-only group did not perform in a significantly different manner on the DSST than the aerobic-only group or the no exercise group. Results suggest that, in this nationally representative sample of
adults aged 65–74, regular strength training may have an additive effect on regular aerobic exercise with regard to its association with improved processing speed task performance but that regular strength training alone does not have a significant association with processing speed task performance relative to that of no exercise. Interestingly, results from two recent 24-week, randomized, double-blind, placebo-controlled trials that tested the effect of strength training (vs. no exercise training) with or without protein supplementation in older adults found that strength training with protein supplementation improved information processing speed relative to no exercise with protein supplementation, but the same benefits of strength training were not found among participants who did not receive protein supplementation (van de Rest et al., 2014). This suggests the possibility of diet having a moderating role with regard to the impact of strength training exercises on information processing speed outcomes. Indeed, many tasks created to measure processing speed have a strong motor component, and it would seem that increased muscle strength (which requires adequate dietary protein to achieve) could have a beneficial impact on motor speed; however, efforts taken by van de Rest and colleagues (2014) to control for motor speed on performance outcomes suggest that the benefits of strength training on information processing speed in those who received protein supplementation is not simply due to increased motor speed secondary to strengthened muscles. Future research is needed to clarify the role of diet and nutrition in regard to cognitive outcomes of exercise programs for older adults.

Hypothesis 5 Discussion

Using the operational definitions for diabetes, prediabetes, and no diabetes specified in the Hypotheses section, participants with diabetes were expected to perform worse on the DSST than participants with prediabetes and participants without diabetes. In addition, participants
with prediabetes were expected to perform worse on the DSST than those without diabetes. These hypotheses were informed by studies that have shown processing speed impairment in those with type-2 diabetes mellitus (T2DM), as well as findings of similar impairment in those with metabolic syndrome, suggesting that cognitive decline may develop in the early stages of T2DM (e.g., van den Berg et al., 2008). The present study’s hypotheses were partially supported by the results. Namely, the mean DSST score of the diabetes group was significantly lower than both the prediabetes group and the no diabetes group; however, the mean DSST score of the prediabetes group did not differ significantly from the no diabetes group.

Exploratory analyses were used to investigate the relationship between individual markers of diabetes status and processing speed task performance. Concerning fasting blood glucose group (i.e., diabetic range, prediabetic range, normal range), group membership did not have a statistically significant effect on DSST score. Regarding HbA1c group (i.e., diabetic range, prediabetic range, normal range), those in the diabetic range performed worst on the DSST, those in the normal range performed best, and those in the prediabetic range performed better than those in the diabetic range but worse than those in the normal range; each of these group differences was statistically significant.

These results showed that individuals with diabetes demonstrated worse processing speed task performance relative to individuals free of diabetes when HbA1c level was used to define diabetes status but not when fasting blood glucose level was used to define diabetes status. It may be the case that chronic hyperglycemia, as represented by HbA1c diabetic range, is involved in the etiology of impaired processing speed in young-old adults or otherwise associated with this impairment, whereas current hyperglycemia status itself is less relevant. Alternatively, it is possible that measurements of HbA1c, a non-fasting test, were more accurate than measurements
of fasting blood glucose given that the latter would have been vulnerable to human error in recall (e.g., inaccurate report of hours of fasting status).

Further, the finding that participants in the HbA1c prediabetic range performed better than those in the HbA1c diabetic range but worse than those in the HbA1c normal range supports the theory that diabetes-associated cognitive decline may begin developing in the early stages of the disease (van den Berg et al., 2008). The present study’s finding that young-old adults with prediabetic HbA1c levels demonstrate impaired processing speed relative to same aged peers with normal HbA1c are consistent with previous research that has found this relationship among middle-aged adults and adds to the current literature (Sanz et al., 2013; Young, Mainous, & Carnemolla, 2006).

Exploratory analyses were also used to investigate the relationship between peripheral insulin resistance and processing speed task performance. Participants with peripheral insulin resistance, operationally defined as a homeostasis model assessment of insulin resistance (HOMA-IR) score above the 75th percentile, performed significantly worse on the DSST than participants without peripheral insulin resistance. This could be taken to support the theory that cognitive decline develops in the early stages of T2DM, as peripheral insulin resistance proceeds the onset of hyperglycemia in the development of T2DM; however, in the present study, the majority of individuals with peripheral insulin resistance also had diabetes mellitus. This is not surprising because average onset of T2DM during the years 1999 to 2002 ranged from 52 to 53 years of age, whereas the participants in the present study were aged 65–74 (Centers for Disease Control and Prevention, 2017). The low number of participants who had peripheral insulin resistance but were free of diabetes prevented investigation of the potential impact of peripheral insulin resistance on processing speed task performance among non-diabetic young-old adults.
Hypothesis 6 Discussion

**Homocysteine.** Folate and vitamin B\textsubscript{12} are needed to convert homocysteine to methionine; therefore, homocysteine levels may increase when levels of folate or vitamin B\textsubscript{12} are depleted (Leishear, Ferrucci, et al., 2012). Vitamin B\textsubscript{12} level and DSST score were not significantly associated in the present study. It was, therefore, unnecessary to control for vitamin B\textsubscript{12} level in either the homocysteine or folate analyses. The discussion that follows focuses on the relationship between homocysteine and processing speed as it relates to the potential impact of folate.

Some research has found high homocysteine levels to be associated with reduced information processing speed independent of folate levels, but results of other studies suggest that high homocysteine levels are only associated with worse cognition in those with low folate levels (Feng et al., 2013; Feng et al., 2006; Vidal et al., 2008). Results from the present study indicate that, among a nationally representative sample of adults aged 65–74, homocysteine level has a weak inverse relationship with processing speed and a very weak inverse relationship with processing speed after controlling for folate level.

Although the above results were statistically significant, their practical value is low. In contrast, hyperhomocysteinemia, defined as homocysteine level $\geq 12$ μmol/L, showed a moderate relationship to DSST score and may be of greater practical significance than homocysteine level. This relationship was independent of folate status, as no statistically significant interaction between hyperhomocysteinemia and folate depletion was found.

Results support the hypothesis that higher homocysteine level, and hyperhomocysteinemia in particular, is associated with worse processing speed independent of folate and vitamin B\textsubscript{12} levels in young-old adults. In other words, reduced processing speed in
young-old adults with hyperhomocysteinemia is not simply a consequence of low folate or vitamin B\textsubscript{12} levels.

Results from the present study are consistent with findings from a recent study showing that, among adults aged 65–80 with normal serum levels of folate and vitamin B\textsubscript{12}, DSST scores of those with hyperhomocysteinemia were significantly lower than those without hyperhomocysteinemia; the same relationship was not found among adults aged 50–64 in that study, indicating that this relationship may be sensitive to age (Hsu et al., 2016). Moreover, hyperhomocysteinemia was not significantly associated with performance in any other neuropsychological domain, which adds to the body of literature that supports the idea that reduced processing speed is the type of cognitive impairment most associated with hyperhomocysteinemia (Hsu et al., 2016; Feng et al., 2006; Feng et al., 2013).

Whether hyperhomocysteinemia causes cognitive dysfunction or is a marker of this dysfunction is uncertain. Hyperhomocysteinemia has been theorized to be a common risk factor for many dementia subtypes (including Alzheimer disease [AD] and vascular dementia [VaD]) via disrupted cerebrovascular homeostasis (Kamut, Vacek, Kalani, & Tyagi, 2015). Specific mechanisms of action suggested by research include, but are not limited to, facilitation of oxidative distress, direct neurotoxic effects, increased risk for atherosclerosis and thrombosis via damage to the vascular endothelium, and disruption of the blood-brain barrier leading to microvascular degeneration and accumulation of toxic substances (Arnesen et al., 1995; Di Bonito et al., 2007; Graham et al., 1997; Kamut et al., 2015).

**Folate.** There is a lack of consensus on the lower limit of serum folate reference values in the literature. The 1999–2000 CDC Laboratory Procedure Manual defined folate deficiency as serum folate < 1.4 ng/mL with regard to interpretation of results from the particular radioassay
kit that was used (CDC Laboratory Procedure Manual). In contrast, the current Merck Manual states that folate deficiency is likely if serum folate is $< 3$ ng/mL (Johnson, 2016d). Further, according to the World Health Organization (WHO), serum folate level that is $< 3$ ng/mL indicates folate deficiency, whereas the 3 ng/mL to 5.9 ng/mL range indicates “possible folate deficiency” (WHO, 2015). These criteria are generally consistent with results of an early experimental study of the development of folate deficiency through a low folate diet that was conducted by a physician on himself, which concluded that a persistent serum folate level of less than 3 ng/mL led to folate deficiency, as evidenced by megaloblastic changes in his blood cells (Herbert, 1962). More recently, the use of a higher cut-off value has also been argued, as some metabolic changes associated with folate deficiency can be observed prior to changes in blood cells (Green et al., 2008; De Bruyn, Gulbis, & Cotton, 2014).

The present study had selected an operational definition of folate deficiency to be serum folate $< 1.4$ ng/mL in order to be consistent with the 1999–2000 CDC Laboratory Procedure Manual. However, none of the participants in the present study met that criterion. Given that folate and DSST score were found to have a statistically significant positive relationship independent of homocysteine level in a previous analysis in the present study, the utility of an alternate folate cut-off value was explored. Namely, a cutoff value of $< 8$ ng/mL was selected for the present study’s operational definition of folate depletion on the basis of recent research, with 9.5% of the present study’s sample meeting this criterion (De Bruyn, Gulbis, & Cotton, 2014). Those with folate depletion performed significantly worse on the processing speed task than those without folate depletion independent of hyperhomocysteinemia status. Therefore, based on results of the present study, folate depletion is of greater practical significance than folate level in regard to its relationship to processing speed among young-old adults.
Results of the present study are not consistent with results of an earlier study of adults aged 55–85 living in the Netherlands that failed to find a statistically significant difference in processing speed task performance between participants with and without low folate level (Jelicic et al., 2001). Relative to the present study, Jelicic and colleagues (2001) used a similar folate cutoff (i.e., 7 ng/mL) and processing speed task (i.e., a letter substitution task). This discrepancy highlights the need for additional research to clarify this relationship, as it is not yet known whether low folate level has a causal or contributory relationship to slowed processing speed in young-old adults and/or whether low folate level is a marker of another condition that explains this association.

Folate is believed to be important to cognitive and emotional functioning. Symptoms of folate deficiency can include depression and confusion (Johnson, 2016d; Reynolds, 2002). Furthermore, some have speculated that low folate level contributes to an increased risk for dementia (e.g., Reynolds, 2002). There is some evidence to support this idea. For example, one large prospective study of older adults over a 2.4-year period found that baseline folate level, but not baseline B₁₂ or homocysteine levels, predicted incident dementia (Kim et al., 2008). During the follow-up period of that study, those with incident dementia showed an accelerated decline in folate and a steeper increase in homocysteine compared to those who did not develop dementia. Moreover, one recent study using amyloid positron emission tomography (PET) scans found that those whose imaging was positive for amyloid plaques had lower folate levels than those who tested negative (Yoshinaga, Nishimata, Kajiya, & Yokoyama, 2017). Of course, these studies are not experimental in nature and cannot show evidence for a causal role of folate in the development of dementia.
Folate is also important to physical functioning, and a chronic low level of this vitamin can cause medical problems that lead to cognitive and/or emotional dysfunction (Reynolds, 2002). For example, chronic alcohol use can impair intestinal absorption of folate, leading to folate deficiency and subsequent development of alcoholic liver disease and its associated cognitive impairments (Medici & Halsted, 2013). Additionally, folate assists in proper deoxyribonucleic acid (DNA) methylation, without which cancer and other diseases are more likely to develop (Crider, Yang, Berry, & Bailey, 2012; Duthie, 2011). Though most types of cancers themselves are not believed to impair cognition, cancer treatments of systemic chemotherapy and radiation localized to the brain may negatively impact processing speed and executive functioning (Anstey et al., 2015; Avila et al., 2015; Mandelblatt et al., 2014).

**Vitamin D.** The hypothesis that participants with low 25-hydroxyvitamin D levels would perform worse on the processing speed task than those with healthy vitamin D levels was supported by the data. This finding is consistent with previous research among adults of various ages (Karakis et al., 2016; Lee et al., 2009). The present study contributes to the literature by reporting this relationship specifically within a nationally representative sample of young-old adults. Findings that suggest that, among young-old adults, men’s processing speed tends to be more negatively impacted by low vitamin D status than women’s processing speed are also noteworthy.

It is unclear if, and to what extent, low 25-hydroxyvitamin D level contributes to slowed processing speed or whether it is primarily a biomarker for one or more other conditions. This question is complicated by the dual functioning of vitamin D through both endocrine (e.g., regulation of calcium and phosphate absorption) and intracellular (e.g., regulation of target gene expression) signaling mechanisms (Vanherwegen, Gysemans, & Mathieu, 2017). Moreover, the
vitamin D receptor (VDR) and the enzyme needed for conversion of vitamin D to its active form are both present in the human brain, as well as multiple other tissues throughout the human body (Eyles, Smith, Kinobe, Hewison, & McGrath, 2005; Feldman & Malloy, 2014). Given this, vitamin D functioning is likely to have a variety of bodily effects. Consistent with this idea is empirical evidence that implicates vitamin D in skeletal, immune functioning, cardiovascular health, and cancer outcomes (Wilson, Tripkovic, Hart, & Lanham-New, 2017).

There are, therefore, several possible explanations for the present study’s finding that young-old adults with low vitamin D levels evidenced slower processing speed than young-old adults with healthy vitamin D levels. Select possibilities relevant to the present study are briefly discussed here. First, it may be the case that a certain level of 25-hydroxyvitamin D is needed in order to support good vascular health, as low 25-hydroxyvitamin D has been associated with endothelial dysfunction and arterial stiffness (Mheid et al., 2011). There is also evidence to suggest that 25-hydroxyvitamin D may contribute to impaired glucose metabolism (Binkley, Ramamurthy, & Krueger, 2010). These findings are consistent with the associations between low 25-hydroxyvitamin D level and the two cognitive domains most likely to be impacted by cerebrovascular damage: processing speed and executive functioning (Karakis et al., 2016).

Second, there may be a more direct impact of 25-hydroxyvitamin D on the brain. Empirical studies have suggested a role for 25-hydroxyvitamin D in protecting neuronal integrity via detoxification pathways and synthesis of proteins necessary for neuronal survival (Buell & Dawson-Hughes, 2008). Third, research suggests that 25-hydroxyvitamin D may be protective against depression, a disorder that often includes slowed cognitive and psychomotor speed (Marazziti et al., 2010). Mechanisms by which 25-hydroxyvitamin D may be protective against depression are not well-established, but one hypothesis is that 25-hydroxyvitamin D reduces the
increased neuronal levels of calcium ions that drive depression (Berridge, 2017). Fourth, lower 25-hydroxyvitamin D has been associated with the presence of obesity, a condition that has also been associated with slowed processing speed (Mai, Chen, Camargo, & Langhammer, 2012). Per the current literature, it is not clear whether obesity promotes low serum 25-hydroxyvitamin D levels, low serum 25-hydroxyvitamin D promotes obesity, they are related through other common variables (e.g., diet), or some combination thereof (Mai, et al., 2012). In any case, results of the present study indicate that history of persistent obesity in young adulthood and late middle-age does not account for the relationship between low 25-hydroxyvitamin D level and slow processing speed in young-old adults once vascular health history is controlled.

The present study’s finding that current low vitamin D level significantly and negatively impacts DSST score in the absence of late middle-age obesity history (but not in the presence of late middle-age obesity history) in young-old adults is interesting, though its meaning is unclear. Perhaps reasons for low vitamin D tend to differ between young-old adults with and without history of late middle-age obesity. It could be hypothesized that reasons for low vitamin D in young-old adults without history of late middle-age obesity tend to contribute to slowed processing speed whereas reasons for low vitamin D in young-old adults with history of late middle-age obesity tend not to contribute as much to slowed processing speed.

**Iron deficiency.** Research on the relationship between iron deficiency and processing speed has primarily focused on infants and children (e.g., Hamid, Amal, Rohani, & Norimah, 2010). Little has been reported on this relationship among adults, and what has been reported is mostly limited to women of childbearing age (e.g., Murray-Kolb & Beard, 2007; Scott & Murray-Kolb, 2016). Findings from that body of research suggest that severity of anemia may adversely impact processing speed to a greater extent than other cognitive domains, whereas
severity of iron deficiency may be associated with a broader pattern of cognitive dysfunction (Murray-Kolb & Beard, 2007). Regarding older adults, one study reported an association between iron deficiency and lower scores on a cognitive impairment screening measure (Yavuz et al., 2012). The present study adds to the literature by reporting that young-old adults with iron deficiency do not have significantly slower processing speed than young-old adults without iron deficiency, though it should be emphasized that this finding does not imply that these two groups have equivalent processing speed abilities. More research is needed to better understand the relationship between iron deficiency and processing speed in young-old adults.

**Vitamin E.** There are multiple forms of vitamin E, including tocopherols, tocotrienols, and stereoisomers (Johnson, 2016c). Of these, alpha-tocopheral is the most biologically active, whereas gamma-tocopherol is the most abundant in the typical American diet (Brigelius-Flohe & Traber, 1999; Camara et al., 2014; Johnson, 2016c). Vitamin E is believed to be important in preventing diseases caused by oxidative stress through its antioxidant properties, though additional mechanisms for health promotion are also likely (Brigelius-Flohe & Traber, 1999; Niki, 2015).

Results from the present study indicate that higher alpha-tocopherol levels are associated with better processing speed task performance in young-old adults. This finding is consistent with a study of community-dwelling older adults that reported that those with alpha-tocopherol levels in the highest tertile were significantly less likely to be suffering from cognitive impairment or dementia than those in the lowest tertile (Cherubini et al., 2005). These results, though they do not imply a causal role of vitamin E on health outcomes, are consistent with the idea that vitamin E may aid in the prevention and/or treatment of diseases driven by oxidative stress. Clinical trials testing this theory have been inconsistent and somewhat disappointing thus
far, though there is growing evidence that d-l-alpha-tocopherol supplementation can slow functional decline in AD (Dysken et al., 2014; Niki, 2015).

Only 2 of the 492 participants with both an alpha-tocopherol value and DSST score in the present study met vitamin E deficiency criteria; therefore, the relationship between vitamin E deficiency and processing speed could not be assessed as planned. Results suggest that vitamin E deficiency is rare in young-old adults in the United States and that a study of greater sample size would be needed to properly assess this relationship. Of note, the low percentage of participants meeting criteria for vitamin E deficiency in the present study is similar to results from a study of European adults aged 55–87 that used a similar vitamin E deficiency criterion (Polito et al., 2005). These findings are consistent with the assertion that vitamin E deficiency is uncommon in developed countries (Johnson, 2016c).

Surprisingly, exploratory analyses revealed higher levels of gamma-tocopherol to be associated with worse cognitive functioning in young-old adults, though this relationship nearly vanished once the effect of alpha-tocopherol level was controlled. There is a paucity of published information on the relationship between gamma-tocopherol and cognition in the literature to date. When literature in areas outside of cognition is consulted for context, a few important differences between alpha-tocopherol and gamma-tocopherol emerge. First, recent research has shown that tocopherols regulate signaling pathways in the inflammatory process; namely, during allergic inflammation, alpha-tocopherol is anti-inflammatory, whereas gamma-tocopherol is pro-inflammatory (Abdala-Valencia, Berdnikovs, & Cook-Mills, 2013; Berdnikovs et al., 2009). Second, there is some difference in associations between health outcomes and serum levels of these two tocopherols. A recent meta-analysis, for example, concluded that serum alpha-tocopherol level, but not serum gamma-tocopherol level, was inversely associated
with the risk of prostate cancer (Cui, Liu, & Xu, 2014). Results of the present study, as well as the studies described above, suggest that the role of gamma-tocopherol should be more closely studied. If better physical and cognitive outcomes are seen for alpha-tocopherol than gamma-tocopherol, it may be advisable to consider efforts to increase alpha-tocopherol in the typical American diet.

**Vitamin B<sub>12</sub>**. Vitamin B<sub>12</sub> status, which was defined based on serum vitamin B<sub>12</sub> level, was not found to have a significant relationship with DSST score in the present study. Results are in contrast to a population-based study of older adults in the Netherlands that found that those with low serum vitamin B<sub>12</sub> levels performed significantly worse on a letter substitution task designed to measure processing speed (Jelicic et al., 2001). Reasons for this discrepancy are unclear, and there does not appear to be any other published studies that have assessed this particular relationship.

One limitation in research on the relationship between vitamin B<sub>12</sub> and cognition has been the considerable difficulty in accurately assessing the former. Vitamin B<sub>12</sub> is often assessed using serum B<sub>12</sub> levels, as was done in the present study. Some, however, have expressed concern that this method may not accurately reflect intracellular vitamin B<sub>12</sub> levels (e.g., Hin et al., 2006). Instead, other potential indicators of low vitamin B<sub>12</sub> status (i.e., high methylmalonic acid and high total homocysteine) have been suggested for use either alone or in combination with serum B<sub>12</sub> level (Clarke et al., 2003; Hin et al., 2006; Smith & Refsum, 2009). Of those two potential indicators, high methylmalonic acid has been described as a more specific marker of vitamin B<sub>12</sub> deficiency (Tangney, Tang, Evans, & Morris, 2009).

Interestingly, exploratory analyses in the present study indicated that individuals in the highest quartile for methylmalonic acid had significantly slower processing speed than
individuals in each of the other quartiles. These results are consistent with a community-based study of older adults in England that found that participants in the top two quartiles of methylmalonic acid level had a 3.7-fold risk for cognitive impairment, as operationally defined as a Mini-Mental State Examination (MMSE) score of < 22/30, compared to those in the bottom two quartiles (Hin et al., 2006). It is difficult to conclude that low vitamin B\textsubscript{12} is associated with slower processing speed in young-old adults on the basis of the present study, as there is still some uncertainty regarding whether methylmalonic acid accurately reflects intracellular vitamin B\textsubscript{12} (Miller, 2006). In any case, high methylmalonic acid is associated with slowed processing speed in young-old adults.

**Hypothesis 7 Discussion**

**Individual obesity indexes.** The present study sought to determine the relationship between processing speed and various obesity indexes in young-old adults. There was no statistically significant relationship between BMI and DSST score. This was expected because individuals with midlife obesity have an increased risk for developing dementia, and individuals who go on to develop dementia are more likely to have lost a significant amount of weight between midlife and late-life (Xu et al., 2011; Stewart et al., 2005). Furthermore, those who are obese during midlife may develop dementia earlier; a recent study found overweight and obese BMI at age 50 to be associated with earlier onset of AD compared to normal BMI, with each unit increase in BMI at age 50 predicting earlier onset by 6.7 months (Chuang et al., 2016).

The present study found statistically significant inverse relationships between DSST and each of the following central obesity indexes: WC, waist-height ratio (WHiR), and waist-thigh ratio (WTR). This was expected due to the greater utility of central obesity indexes in predicting a number of health conditions that have associated cognitive decline relative to BMI, which is in
part believed to be due to differences between metabolic activity in visceral and other fat tissue. Of these relationships, results of the present study suggest that those involving WHtR and WTR have greater practical value than WC in regard to their relationship with processing speed in young-old adults. It is possible that these findings reflect these indexes’ abilities to predict the presence of relevant medical conditions (i.e., those associated with cognitive decline) within the young-old adult population. For example, WHtR and WC were found to predict diabetes mellitus, hyperglycemia, atherogenic dyslipidemia, and metabolic syndrome better than BMI in a large cohort of Mediterranean adults aged 55–80 at high cardiovascular risk (Guasch-Ferre et al., 2012).

The present study found a very weak, statistically significant positive correlation between DSST score and % total body fat DEXA. These results were not as predicted and suggest that greater adiposity is related to better processing speed in young-old adults. It should, however, be noted that the magnitude of this finding suggests low practical value. Nevertheless, it may be the case that young-old adults with greater adiposity performed better on the cognitive task since they may have been less likely to be in the early stages of development of AD or other type of dementia process (Xu et al., 2001). Results of the present study are generally consistent with a recent community-based study of adults aged 74–94 that found that individuals in the lowest tertile of DEXA body fat evidenced poorer executive functioning compared to those in the middle tertile for men and the middle and highest tertiles for women (Smith et al., 2014).

The present study failed to find a statistically significant correlation between DSST score and % trunk fat measured by DEXA. This finding is in contrast to the statistically significant inverse relationships between DSST and the other central obesity indexes included in this study (i.e., WC, WHtR, and WTR). It may be the case that central adiposity itself (i.e., % trunk fat
measured by DEXA) is not predictive of medical conditions associated with cognitive decline among young-old adults as was previously hypothesized. Rather, it may be the case that an increase in waist circumference (resulting in increased WC, WHtR, and WTR) occurs as a result of complications from medical conditions associated with cognitive decline. For example, gastroparesis, a disorder in which gastric emptying is delayed in the absence of physical obstruction, is a common complication of uncontrolled diabetes and often includes the symptom of bloating (Dickman et al., 2013; Koch & Calles-Escandón, 2015). Results of the present study highlight the importance of factors other than trunk adiposity in the relationship between anthropometrically derived central obesity indexes and processing speed in young-old adults.

**Combinations of obesity indexes.** The hypothesis that, among participants who met WC central obesity criteria, those who also met BMI obesity criteria would perform worse on the DSST was supported by the data. Results suggest that BMI obesity adds some value in predicting poor processing speed task performance beyond WC alone among a nationally representative sample of young-old U.S. adults. The reason this may be the case, however, is unclear. This hypothesis was based on findings from a community study of elderly individuals in Korea that found obese BMI (defined as ≥ 25 kg/m² per modified WHO guidelines) predicted a positive result on a brief screener for dementia using an empirically supported cut-point only when abdominal obesity was also present (Jeong et al., 2004; Jeong et al., 2005).

The related hypothesis that, among participants who met WC central obesity criteria, those who also met DEXA obesity criteria would perform worse on the DSST was not supported by the data. Results suggest that BMI adds greater value than a more accurate estimate of current adiposity in this population. It is unclear as to why this may be the case, but, as
hypothesized above, BMI may somehow better take into account other factors important in this population. Future research is needed to better understand this relationship.

Finally, an attempt was made to find which combination of obesity indexes made the most meaningful contribution to the prediction of DSST score among young-old adults. Given the weak to very weak relationships between individual obesity indexes and DSST score uncovered in prior analyses in the present study, it was not expected that findings of good practical significance would be made in this planned analysis. After excluding a number of indexes from a stepwise multiple regression based on issues of multicollinearity (i.e., BMI, WC, DEXA % trunk fat), WHtR, DEXA % total body fat, and WTR remained. Results indicated that WHtR and DEXA % total body fat accounted for 5.4% of variance in DSST score, and that WTR did not meaningfully contribute to the model. Although results suggest WHtR and DEXA % total body fat did make significant contributions to the overall prediction of DSST scores, the low $R^2$ value indicates that this model was not a good fit. This suggests that current obesity indexes may not be particularly valuable in the prediction of processing speed in young-old adults. Indeed, based on these findings as well as on the literature previously discussed, it would appear that midlife obesity indexes are of greater predictive value on cognition in young-old adults than are current obesity indexes.

**BMI category.** The present study found that young-old adults who were obese in young adulthood have slower processing speed than young-old adults who had normal range BMI in young adulthood. Additionally, young-old adults who were obese in late middle age were found to have slower processing speed than young-old adults who were overweight in late middle age as well as young-old adults who had normal range BMI in late middle age. These results are generally consistent with the theory that history of persistent obesity, which is operationally
defined in this study as obesity throughout young adulthood and late middle age, is associated with slower processing speed in young-old adults.

**BMI category and gender interaction.** The present study found that young-old males had slower processing speed than young-old females. When potential interactions with BMI were assessed, it was found that this relationship was mostly limited to individuals with normal range BMI. More specifically, findings from the present study suggest that normal range BMI is associated with slower processing speed in males aged 65–74 (i.e., young-old males) compared to their female counterparts. The same relationship was found between BMI and current processing speed when BMIs at various time points were used. These time points included current BMI (i.e., young-old BMI), BMI 10 years ago (i.e., late middle age BMI), and BMI at age 25 (i.e., young adult BMI). In contrast, no significant differences in processing speed between males and females in the other BMI categories studied (i.e., obese, overweight) were found at any of the time points, with the exception of a trend toward men who were obese in young adulthood having slower processing speed than women who were obese at that time.

It is unclear as to why this relationship would be almost entirely limited to those with normal range BMI. One possible explanation is that men in the normal range BMI category may tend to have a greater number of, or more severe, medical problems that can adversely impact processing speed over time than do women in the normal range BMI category. Another possible explanation is that women may tend to have faster processing speed than men under “normal conditions” (i.e., normal range BMI) but are, perhaps, more sensitive to the cognitive effects of some of the comorbidities of overweight and obesity that can contribute to slowed processing speed over time.

**Hypothesis 8 Discussion**
**Pattern of obesity.** Participants were divided into eight groups based on all possible combinations of obesity status (yes/no) at age 25, 10 years ago, and the present, as depicted in Table 5. It was hypothesized that participants who were obese at age 25 (i.e., young adulthood) and 10 years ago (i.e., late middle age) would perform the worst on the DSST. In addition, it was hypothesized that participants with no history of obesity would perform best on the DSST. Further, it was hypothesized that those who were obese at only one timepoint would perform better than those who were obese at age 25 and 10 years ago.

The analyses could not be run as originally planned due to three of the eight groups containing very few participants. Each of these three groups shared the characteristic of obesity at age 25. In retrospect, it seems likely that the small numbers of participants in these groups is due to a lower prevalence of obesity in the past relative to the current day. Namely, in the present study, data from participants aged 65–74 was collected during the years 1999–2002, which means that self-reported young adult weight (i.e., age 25) referred to the participants’ weights during the years 1950–1962. The prevalence of obesity in U.S. adults aged 20–29 during the years 1960–1962, however, was estimated to be only 7.6% (Flegal, Carroll, Kuczmarski, & Johnson, 1998). Obesity rates rose dramatically in the United States and many other developed countries between approximately 1976 and 1994 (Flegal et al., 1998). Consistent with this increase, the present study evidenced an adequate number of participants with self-reported late middle age (i.e., age 55–64) weight, which referred to the participants’ weights during the years 1989–1992, in the obese range.

After removal of the three groups containing very few participants from the planned analysis, five groups remained; they are shown in Table 6. Results revealed that Group C (defined as those who were obese at late mid-life but not during young adulthood or the present)
scored significantly lower on the DSST than Groups B, D, and E. No other group differences were statistically significant, though a slight trend toward significance for Group A (defined as those who were obese at each of the three time points) scoring lower than Group E (defined as those who were not obese at any of the three time points) was noted.

The finding that Group C (defined as those who were obese at late mid-life but not during young adulthood or the present) scored significantly lower on the DSST than Groups B, D, and E suggests that, of the young-old adults who were not obese at age 25, the pattern of the presence of obesity in late middle age and the absence of obesity at the present is associated with significantly slower processing speed than any other possible pattern of obesity status at those two time points (i.e., presence of obesity at late middle age and at the present; absence of obesity at late middle age and the present; absence of obesity at late middle age and presence of obesity at the present).

More specifically, when comparing Groups B and C, both groups gained significant weight by late middle age and were possibly facing similar obesity-related health risks at that time. It may be the case that Group B (those who remained obese at the present) outperformed Group C because Group C represents those individuals who lost between late middle age and the present secondary to physical illness (obesity-related or otherwise) or preclinical dementia. Further, it is possible that Group E outperformed Group C because those in Group E did not gain as much weight by late middle age or reach the obesity category, at which point risk for many diseases is known to increase. Finally, it is possible that Group D outperformed Group C because becoming obese in young-old adulthood is less of a health risk than becoming obese in middle age. Generally, results suggest that slowed processing speed in young-old adults may be more related to the timing of their obesity status rather than number of time points for which they
can be categorized as obese, though some caution is taken with regard to this conclusion due to inability to compare each of the eight groups as planned.

In any case, exploratory analyses were then conducted to better understand the relationship between persistent obesity (i.e., obesity during young adulthood and late middle-age) and processing speed in young-old adults. Young-old adults with a history of persistent obesity were found to have slower processing speed than young-old adults with a history of persistent non-obesity (i.e., obesity neither during young adulthood nor during late middle-age). These findings are consistent with the hypothesis that long-term obesity in adulthood is associated with slower processing speed in older adults.

**Extent of weight gain between early adulthood and late middle-age.** The hypothesis that the extent of weight gain between early adulthood (i.e., age 25) and late middle-age (i.e., age 55–64) would be associated with slower processing speed was supported by the data. Results are consistent with Sabia and colleagues (2009), who reported the extent of weight gain between early adulthood and late middle-age among a large sample of London-based office staff to be associated with executive dysfunction. Further, findings from an exploratory analysis in the present study suggest that there is no significant relationship between processing speed in young-old adults and the extent of weight loss between early adulthood and late middle-age. Taken together, results suggest that weight gain, but not weight loss, between early adulthood and late middle-age is associated with slower processing speed in young-old adulthood. It may be the case that weight gain during this time is detrimental to processing speed via onset of weight-related diseases or disorders that also impact processing speed over time. Alternatively, it may be the case that onset of new diseases or disorders during this time led to both weight gain and slower processing speed, or that slow processing speed in early adulthood led to weight gain over
time. Overall, however, results are generally consistent with the contraindication of gaining a great amount of weight between early adulthood and late middle-age and suggest that amount of weight lost between these two timepoints, assuming that one is not underweight at either time point, is not detrimental to processing speed in young-old adulthood.

**Extent of weight change between late middle-age and young-old adulthood.** The hypothesis that the extent of weight change over the previous 10-year period (i.e., from late middle-age to young-old) would be associated with worse performance on the DSST was supported by the data. Likewise, exploratory analyses uncovered inverse relationships between processing speed and the extent of weight loss over the previous 10-year period as well as between processing speed and the extent of weight gain over the same time period. These findings are consistent with a previous study that have found that the extent of weight change during a 10-year period between late middle-age (mean age 59) and early young adulthood (mean age 69) was associated with poorer overall cognitive performance (Brubacher et al., 2004). The present study adds to the literature by reporting this relationship to also be true of processing speed among a nationally-representative sample of young-old adults. The findings of the present study and that of Brubacher and colleagues (2004) may be related to the pattern of significant weight loss between midlife and late-life prior to onset of dementia (Stewart et al., 2005). However, because the present study did not include a baseline processing speed measure, it is not possible to rule out the possibility that slower baseline processing speed led to, or contributed to, significant weight change during the 10-year period in question.

**Past-year weight change.** The present study found that young-old adults with unintentional significant past-year weight loss performed worse on the DSST than participants who experienced significant intentional past-year weight loss, significant past-year weight gain,
or past-year weight stability. This finding is consistent with the tendency for unintentional weight loss to be associated with an underlying illness, which may or may not also be impacting cognition. Results may have implications for the utility of conducting brief cognitive screenings of young-old adults who present to their physicians with past-year unintentional weight loss.

**Hypothesis 9 Discussion**

Peripheral inflammation is a metabolic consequence of excess adipose tissue, and obese individuals tend to evidence higher levels of peripheral inflammation markers independent of other known sources of inflammation (Visser et al., 1999). Obesity creates a state of chronic low-grade peripheral inflammation, and research suggests that this state may lead to cognitive impairment through mechanisms such as invocation of central neuroinflammatory response, development of inflammation resistance, accumulation of proinflammatory cytokines in the bloodstream, and interaction of these cytokines with free fatty acids to impair insulin signaling (Dali-Youcef et al., 2013; Ye & Keller, 2010).

The present study’s hypothesis that C-reactive protein (CRP), a marker of peripheral inflammation, would have a statistically significant inverse association with processing speed among young-old adults was not supported by the data; their association was in the expected direction but did not reach statistical significance. The few other extant studies that have reported on the relationship between CRP and processing speed in older adult populations have yielded mixed findings (Tegeler et al., 2016; Trollor et al., 2012).

There are a number of possible explanations for the lack of a clear relationship between CRP and processing speed in older adult populations. First, CRP is only one of several markers of peripheral inflammation, which also include interleukins-1β, -6, -8, -10, -12, plasminogen activator inhibitor, serum amyloid A, tumour necrosis factor-α, and vascular adhesion molecule-
It may be the case that some of these other markers of peripheral inflammation are more closely associated with processing speed in young-old adults. Of these, interleukins -6 and -12 may be of particular importance (Palta et al., 2015; Rafnsson et al., 2007; Trollor et al., 2012). Second, it is possible that CRP does not have a significant relationship to processing speed but does have a significant relationship to one or more other cognitive domains among young-old adults. There is, in fact, some evidence to suggest an association between CRP and executive functioning in this age group (Schram et al., 2007; Sweat et al., 2008; Tegeler et al., 2016). Third, it is possible that a history of elevated CRP level in midlife is more relevant to processing speed performance in older adult populations than current CRP level. No published study has reported on this to-date; however, high CRP in midlife has been found to be associated with decline in inductive reasoning ability ten years later (Gimeno, Marmot, & Singh-Manoux, 2008).

**Hypothesis 10 Discussion**

The hypothesis that individuals who endorsed history of one or more of the following conditions would perform worse on the DSST was supported by the data: cardiac (i.e., congestive heart failure [CHF], coronary heart disease [CHD], or heart attack), stroke, diabetes, weak/failing kidneys, and chronic respiratory disease (i.e., chronic bronchitis or emphysema). Potential mechanisms for cognitive decline with regard to these diseases and conditions have already been discussed.

Exploratory analyses were used to investigate group differences in processing speed with respect to the presence or absence of each of the aforementioned conditions, as well as hypertension and any liver condition. Among the conditions tested, all but chronic respiratory disease, any liver condition, and CHD in the absence of other cardiac conditions were
significantly linked to slower processing speed. Furthermore, length of chronic respiratory
disease was not significantly correlated with processing speed task performance. Results suggest
that history of any liver condition, history of chronic respiratory disease, length of chronic
respiratory disease, and history of CHD in the absence of other cardiac conditions may not be
relevant factors with regard to current processing speed in young-old adults.

**Hypothesis 11 Discussion**

The hypothesis that participants with one or more types of dyslipidemia, as determined
by blood tests, would demonstrate worse processing speed was not supported by the data. This
finding suggests that overall lipid health status, as operationally defined as the presence or
absence of one or more types of dyslipidemia, may not be important with regard to current
processing speed in young-old adults. Results of exploratory analyses, however, indicate that
three individual types of dyslipidemia are salient to this relationship: low high-density
lipoprotein [HDL] cholesterol, high non-HDL cholesterol, and high triglycerides, the latter two
of which are sex-specific. Each of these three is discussed below.

**Low HDL cholesterol.** Among both men and women in the present study, young-old
adults with low HDL cholesterol had worse DSST performance than those without low HDL
cholesterol. Because young-old adults are in the age range that is particularly susceptible to a
preclinical stage of dementia, the present study’s finding is consistent with results of large
prospective studies that show HDL cholesterol to have an inverse relationship with risk of all-
cause dementia (Koch & Jensen, 2016; Reitz et al., 2010). The present study’s finding is also
consistent with research that shows low HDL cholesterol to be independently associated with
memory dysfunction and decline in middle-aged adults and linked to structural brain changes in
regions associated with AD (Singh-Manoux et al., 2008; Ward et al., 2010). How low HDL
cholesterol, in particular, may contribute to the development of cognitive impairment and dementia is not well established, but indirect pathways are believed to include atherosclerosis, which may lead to decreased cerebral blood flow, as well as increased risk for other vascular events and diseases that in turn can cause cognitive impairment and dementia (Ancelin et al., 2013; Vinkers et al., 2005). There also appears to be a relationship between low HDL and build-up of amyloid plaque deposits in the brain, though the nature of this relationship is unclear (Reed et al., 2014). In addition to low levels of HDL cholesterol, emerging evidence suggests that other aspects of HDL cholesterol may be problematic for some individuals with cognitive impairment or dementia. Namely, one recent study reported decreased efficiency of HDL cholesterol among those with AD (Camponova et al., 2017).

**High non-HDL cholesterol.** Among men only, those with high non-HDL cholesterol evidenced significantly slower processing speed than those without high non-HDL cholesterol. The relationship between processing speed and low-density lipoprotein [LDL] cholesterol, on the other hand, did not reach statistical significance for either gender.

Non-HDL cholesterol is calculated by subtracting HDL cholesterol from total cholesterol, which yields an estimate of cholesterol concentration among all atherogenic lipoproteins: LDL cholesterol, very-low density lipoprotein (VLDL) cholesterol, intermediate-density lipoprotein (IDL) cholesterol, and lipoprotein (a) [Lp(a)] cholesterol (Virani, 2011). Therefore, non-HDL cholesterol is a more comprehensive measure of atherogenic lipoproteins than LDL cholesterol.

Although LDL cholesterol is the current primary target for treatment of dyslipidemia, many doctors have argued for the use of non-HDL cholesterol in place of, or in addition to, LDL cholesterol in clinical practice on the basis that it is more predictive of cardiovascular risk than LDL cholesterol or, at the least, adds additional value (Rana, Boekholdt, Kastelein, & Shah,
Nevertheless, LDL cholesterol continues to receive greater attention than non-HDL cholesterol in the empirical literature, and, not surprisingly, there are numerous published studies that include information on the relationship between LDL cholesterol and cognition but very few, if any, that address the relationship between non-HDL cholesterol and cognition. Results from the present study provide support to the value of studying non-HDL cholesterol.

Because LDL cholesterol comprises a large portion of non-HDL cholesterol, empirical findings regarding the relationship between LDL cholesterol and cognition are briefly described here. Concerning the present study, mean difference in DSST score between groups with and without high LDL cholesterol was not statistically significant but did show a trend toward significance, suggesting lower processing speed in those with high LDL cholesterol. This relationship was stronger among men than women but, again, did not reach statistical significance when analyses were limited to men. In regard to the literature to date, the relationship between processing speed and LDL cholesterol level in older adults is not well established, but one recent study of older adults found that greater variability in LDL cholesterol readings across study visits was associated with worse processing speed and other aspects of cognition, as well as lower cerebral blood flow and greater white matter hyperintensity (WMH) load (Smit et al., 2016). The findings on the relationship between LDL cholesterol and other cognitive domains have been mixed. For example, one recent study of older adults with cardiovascular risk factors found higher LDL cholesterol to be related to worse performance on a working memory task, whereas another recent study of healthy middle-aged and older aged adults found LDL cholesterol to be associated with better episodic memory (Leritz, McGlinchey, Salat, Milberg, 2016; Meusel et al., 2017).
**High triglycerides.** Among women only, those with high triglycerides evidenced significantly faster processing speed than those without high triglycerides. This relationship was surprising, as high triglyceride level is considered to be a biomarker of cardiovascular disease (CVD) risk, though it should be noted that triglyceride itself is not directly atherogenic (Miller et al., 2011). There have been few published studies on the relationship between current triglyceride levels and processing speed in older adults to date. One such study failed to find a statistically significant relationship between processing speed and triglycerides, but this study did not report on sex-specific relationships (van den Kommer, Dik, Comijs, Jonker, & Deeg, 2012). More research is needed in this area to determine whether this is a stable finding and, if so, to explore the nature of this relationship. Reasons for such a relationship are unclear, though the authors of a prospective study that found a relationship between high triglyceride levels and decreased risk of AD in women hypothesized that this finding may reflect a survival bias (Ancelin et al., 2013). Findings on the relationship between triglycerides and other cognitive domains among older adults have been mixed (Parthasarathy et al., 2014; van den Kommer et al., 2012).

**Hypothesis 12 Discussion**

The hypotheses that risk of first stroke, as indicated by score on a modified version of the Framingham Stroke Risk Profile (FSRP), and risk of CVD onset, as indicated by score on a modified version of the Framingham Risk Score (FRS) for general CVD, would each be inversely associated with DSST score was supported by the data. Scores reflecting risk of first stroke and risk of CVD onset each showed a statistically significant weak inverse relationship with DSST score. Findings indicate that, among this nationally representative cross-sectional sample of young-old adults, processing speed tends to decrease as risk of first stroke or risk of
CVD onset increases. Although only weak relationships were found, results suggest the potential impact of stroke and CVD risk factors on processing speed in young-old adults without history of stroke or CVD. They also suggest the possibility that some cognitive decline or impairment may be present in these individuals prior to first stroke or CVD onset.

Of course, because these equations were designed to predict risk for first stroke or onset of CVD rather than processing speed or other aspects of cognition, some of their components may not be optimal when the goal is to predict current processing speed in young-old adults. FRS for general CVD, for example, takes total cholesterol into account, whereas the present study did not support the utility of total cholesterol in predicting processing speed in the young-old adult population.

**Hypothesis 13 Discussion**

The hypothesis that there would be a significant positive correlation between usual gait speed and processing speed after controlling for BMI was supported by the data. Therefore, although walking speed has been found to be slower among obese older adults compared to their normal weight counterparts, BMI does not explain the association between slower walking speed and slower processing speed in young-old adults (Xu, Houston, Gropper, & Zizza, 2009). Results from the present study are consistent with those from another recent study that found lower processing speed to be a major contributor to slower gait speed after controlling for other cognitive domains, age, BMI, and other potential confounds in late-middle aged and older adults (Killane et al., 2014).

The finding that gait speed decelerates faster in the years preceding mild cognitive impairment (MCI) diagnosis in affected individuals compared to the normal cognitive aging population suggests the role of shared pathological processes of organic etiology in the
relationship between slowed gait speed and cognitive decline (Albers et al., 2015; Buracchio, Dodge, Howieson, Wasserman, & Kaye, 2010; Kikkert, Vuillerme, van Campen, Hortobagyi, & Lamoth, 2016). For example, cerebral white matter hyperintensities (WMHs), which are areas of abnormal change in white matter found on head computerized tomography (CT) and brain magnetic resonance imaging (MRI) scans that reflect changes in interstitial fluid mobility and water content, demyelination, and/or axonal damage, are increasingly common with age and are associated with vascular risk factors, stroke, and dementia (Wardlaw, Valdés Hernández, & Muñoz-Maniega, 2015). WMHs are believed to be causally related to slowed gait speed and reductions in the cognitive domains of processing speed and executive functioning in affected individuals depending on their size, location, and total volume (Wakefield et al., 2010). It has been hypothesized that WMHs can impact gait speed directly through disrupting mobility-related pathways or indirectly through disrupting pathways important for executive functions (Bolandzadeh et al., 2014). Likewise, it can be hypothesized that slower processing of visuospatial information may contribute to slower gait speed. The finding from a recent study that performance on the DSST significantly mediates the relationship between WMHs and gait speed supports these hypotheses, as the DSST is a measure of processing speed that has also been shown to reflect visual scanning ability and executive functioning (Bolandzadeh et al., 2014; Davis & Pierson, 2012; Joy et al., 2003).

**Final Model Discussion**

It had been reasoned that bodily states caused by obesity that tend to be present even among otherwise healthy obese individuals (e.g., increased adipokines, low grade inflammation) might contribute to worsened processing speed above and beyond that of diagnosed diseases, disorders, and medical events for which obesity has been shown to often have a contributory role
(e.g., T2DM, stroke). Additionally, it was thought that these obesity-related bodily states (e.g., increased adipokines, low grade inflammation) might have a differential impact on cognition according to magnitude and duration of exposure. Persistent obesity was conceptualized as a way of identifying long duration of exposure to these bodily states.

Results of the present study’s final model suggest that vascular health history mediates the relationship between persistent obesity and processing speed among adults aged 65–74; however, no evidence for the direct contribution of persistent obesity to current processing speed was found. Likewise, results of Hypothesis 7 analyses did not provide evidence for persistent obesity being related to processing speed to a greater extent than obesity in late middle-age. Taken together, results of the present study do not provide support for the cumulative impact of obesity during young adulthood and late middle-age on processing speed in young-old adults. One possible explanation for this finding may be that the brain is more vulnerable to the effects of obesity-related bodily states (e.g., increased adipokines, low grade inflammation) during late middle-age than during young adulthood. Additionally, the recent finding that the low grade systemic inflammation associated with obesity tends to impair the blood brain barrier only in those with already diseased brains would also support the lack of importance of obesity in young adulthood relative to obesity in late middle-age (Elwood, Lim, Naveed, & Galea, 2017).

Consistent with this idea, it may be the case that those who are obese when preclinical dementia begins experience more rapid decline.

**Limitations of the Present Study**

The present study had several limitations. As a non-experimental, cross-sectional study, causality of processing speed cannot be inferred. Longitudinal data would have provided many advantages, including the opportunity for collection and analysis of repeated cognitive tests and
biochemistry data. The use of retrospective pretests (e.g., self-report of weight ten years ago, self-report of weight at age 25) did allow for investigation of associations between weight trajectory and other variables, but reliance on these retrospective pretests may have been problematic with regard to their accuracy. For example, one recent study of older adults found that 20 year retrospectively recalled weights tend to underestimate both 20-year prior assessed weights and 20 year prior self-reported weights by an average of 4.2 ± 13.0 and 1.2 ± 11.5 pounds, respectively (Dahl & Reynolds, 2013). Another limitation of the present study was the use of only one measure of processing speed. Cognitive tests are rarely able to measure one domain in isolation. Given that the DSST primarily reflects graphomotor speed, perceptual speed, visual scanning ability, and executive functioning, results need to be interpreted within this specific context. Moreover, the present study was limited by the low number of participants in some of the weight trajectory groups, which prevented some planned analyses from being run. Finally, the present study would have benefitted from the inclusion of weight data at time points between young adulthood and late middle-age. More specifically, the present study assumed that the combined presence of obesity in young adulthood and late middle-age was generally consistent with a state of “persistent obesity” throughout that time; however, this assumption may not be fair, as weight can fluctuate considerably over time.

**Conclusions and Recommendations for Future Research**

The present study did not provide evidence for the cumulative impact of obesity during young adulthood and late middle-age on processing speed in young-old adults. In contrast, it highlighted the link between slower processing speed and the weight trajectory pattern of obesity in late middle-age coupled with the absence of obesity in both young adulthood and young-old adulthood. That being said, results should be interpreted with caution due to study limitations,
especially because the low number of participants in some of the weight trajectory groups prevented the processing speed outcomes of those groups from being investigated. Future studies that use similarly large sample sizes but analyze more recent data would be less likely to encounter the same problem given the history of obesity prevalence trends in the United States.

An indirect effect of persistent obesity during young adulthood and late middle-age on processing speed in young-old adults through vascular health history was identified by the present study, but there was no evidence for a direct effect. It may be the case that persistent obesity does not have a direct effect on processing speed in young adulthood; however, limitations in the present study prevent this conclusion from being drawn. Future research should include weight data at time points between young adulthood and late middle-age in order to more accurately classify individuals as persistently obese throughout that time period. In addition, future studies should strive to use measured weights rather than self-reported weights, as this would improve the accuracy of the collected weight data and, by extension, would likely improve the accuracy of weight category classification. Moreover, future studies should include a measure of processing speed at baseline to investigate the relationship between weight trajectory and change in processing speed as well as to investigate the possibility that slower baseline processing speed predicts subsequent weight patterns.
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Appendix A: Demographics Questionnaire

RIAGENDR – Gender

RIDAGEYR - Age at Screening

RIDRETH1 - Race/Ethnicity – Recode
Mexican American
Other Hispanic
Non-Hispanic White
Non-Hispanic Black
Other Race - Including Multi-Racial

DMDEDUC2 - Education Level - Adults 20+
Less Than 9th Grade
9-11th Grade (Includes 12th grade with no diploma)
High School Grad/GED or Equivalent
Some College or AA degree
College Graduate or above

DMDMARTL - Marital Status
Married
Widowed
Divorced
Separated
Never married
Living with partner

DMDHHSIZ - Total number of people in the Household

INDHHINC - Annual Household Income
$ 0 to $ 4,999
$ 5,000 to $ 9,999
$10,000 to $14,999
$15,000 to $19,999
$20,000 to $24,999
$25,000 to $34,999
$35,000 to $44,999
$45,000 to $54,999
$55,000 to $64,999
$65,000 to $74,999
$75,000 and Over
Over $20,000
Under $20,000
Appendix B: Occupation Questionnaire

OCQ150 - Type of work done last week

English Text:
(SP Interview Version) In this part of the survey I will ask you questions about {your/SP's} work experience. Which of the following {were you/was SP} doing last week . . .
Working at a job or business,
With a job or business but not at work,
Looking for work, or
Not working at a job or business?

OCQ180 - Hours worked last week at all jobs

English Text:
How many hours did {you/SP} work last week at all jobs or businesses?

OCQ210 - Usually work 35 or more hours per week

English Text:
{Do you/Does SP} usually work 35 hours or more per week in total at all jobs or businesses?
Appendix C: Weight History Questionnaire

WHD010 - Current self-reported height (inches)
English Text:
These next questions ask about {your/SP's} height and weight at different times in {your/his/her} life. How tall {are you/is SP} without shoes?

WHD020 - Current self-reported weight (pounds)
English Text:
How much {do you/does SP} weigh without clothes or shoes?

WHQ030 - How do you consider your weight
English Text:
{Do you/Does SP} consider {your/his/her}self now to be . . .
Overweight,
Underweight, or
About the right weight?
Refused
Don't know

WHD040 - Like to weigh more, less or same
English Text:
Would {you/SP} like to weigh . . .
More,
Less, or
Stay about the same?
Refused
Don't know

WHD050 - Self-reported weight-1 yr ago (pounds)
English Text:
How much did {you/SP} weigh a year ago?

WHD060 - Weight change intentional
English Text:
Was the change between {your/SP's} current weight and {your/his/her} weight a year ago intentional?

**WHQ070 - Tried to lose weight in past year**

English Text:
During the past 12 months, {have you/has SP} tried to lose weight?

**WHQ090 - Tried not to gain weight in past year**

English Text:
During the past 12 months, {have you/has SP} done anything to keep from gaining weight?

**WHD110 - Self-reported weight-10 yrs ago (pounds)**

English Text:
How much did {you/SP} weigh 10 years ago? [If you don't know {your/his/her} exact weight, please make your best guess.]

English Instructions:
ENTER WEIGHT IN POUNDS OR KILOGRAMS. IF PREGNANT, ASK FOR WEIGHT BEFORE PREGNANCY.

**WHD120 - Self-reported weight - age 25 (pounds)**

English Text:
How much did {you/SP} weigh at age 25? [If you don't know {your/his/her} exact weight, please make your best guess.]

English Instructions:
IF PREGNANT, ASK FOR WEIGHT BEFORE PREGNANCY.

**WHD130 - Self-reported height - age 25 (inches)**

English Text:
How tall {were you/was SP} at age 25? [If you don't know {your/his/her} exact height, please make your best guess.]

**WHD140 - Self-reported greatest weight (pounds)**

English Text:
Up to the present time, what is the most {you have/SP has} ever weighed?

**WHD150 - Age when heaviest weight**

English Text:
How old {were you/was SP} then? [If you don't know {your/his/her} exact age, please make your best guess.]

**WHD160 - Least self-reported weight since 18(lbs)**

English Text:

What is the least {you/SP} ever weighed since {you were/s/he was} 18?

English Instructions:

DO NOT INCLUDE WEIGHT DURING PREGNANCY.

**WHD170 - Age when lightest weight**

English Text:

How old {were you/was SP} then? [If you don't know {your/his/her} exact age, please make your best guess.]
Appendix D: Blood Pressure Questionnaire

BPQ020 - Ever told you had high blood pressure
English Text:
  {Have you/Has SP} ever been told by a doctor or other health professional that
  {you/s/he} had hypertension, also called high blood pressure?

BPQ030 - Told had high blood pressure - 2+ times
English Text:
  {Were you/Was SP} told on 2 or more different visits that {you/s/he} had hypertension,
  also called high blood pressure?

BPQ050A - Now taking prescribed medicine (for hypertension)
English Text:
  HELP AVAILABLE (Are you/Is SP) now taking prescribed medicine

BPQ080 - Doctor told you - high cholesterol level
English Text:
  {Have you/Has SP} ever been told by a doctor or other health professional that
  {your/his/her} blood cholesterol level was high?

BPQ100D - Now taking prescribed medicine (for cholesterol)
English Text:
  (Are you/Is SP) now following this advice to take prescribed medicine?
Appendix E: Diabetes Questionnaire

DIQ010 - Doctor told you have diabetes
English Text:
The next questions are about specific medical conditions. {Other than during pregnancy, {have you/has SP}/(Have you/Has SP)} ever been told by a doctor or health professional that {you have/{he/she/SP} has} diabetes or sugar diabetes?

DIQ040Q - Number of years of age
English Text:
How old {was SP/were you} when a doctor or other health professional first told {you/him/her} that {you/he/she} had diabetes or sugar diabetes?

DIQ050 - Taking insulin now
English Text:
{Is SP/Are you} now taking insulin

DIQ060Q - Number of mos/hrs taking insulin
English Text:
For how long {have you/has SP} been taking insulin?

DIQ060U - Unit of measure (month/year)
English Instructions:
ENTER UNIT (months or years)

DIQ070 - Take diabetic pills to lower blood sugar
English Text:
{Is SP/Are you} now taking diabetic pills to lower {{his/her}/your} blood sugar? These are sometimes called oral agents or oral hypoglycemic agents.
Appendix F: Medical Conditions Questionnaire Variables

MCQ010 - Ever been told you have asthma

English Text:
Has a doctor or other health professional ever told {you/SP} that {you have/s/he/SP has} asthma?

Code or Value Value Description
1 Yes
2 No
7 Refused
9 Don't know

MCQ040 - Had asthma attack in past year

English Text:
During the past 12 months, {have you/has SP} had an episode of asthma or an asthma attack?

MCQ050 - Emergency care visit for asthma/past yr

English Text:
[During the past 12 months], {have you/has SP} had to visit an emergency room or urgent care center because of asthma?

MCQ053 - Taking treatment for anemia/past 3 mos

English Text:
During the past 3 months, {have you/has SP} been on treatment for anemia, sometimes called "tired blood" or "low blood"? [Include diet, iron pills, iron shots, transfusions as treatment.]

MCQ160B – MCQ160L

English Text:
Has a doctor or other health professional ever told {you/SP} that {you/s/he} . . .had {condition}?

MCQ160B - Ever told had congestive heart failure
MCQ160C - Ever told you had coronary heart disease
MCQ160D - Ever told you had angina/angina pectoris
MCQ160E - Ever told you had heart attack  
MCQ160F - Ever told you had a stroke  
MCQ160G - Ever told you had emphysema  
MCQ160I - Ever told you had thyroid disease  
MCQ160K - Ever told you had chronic bronchitis  
MCQ160L - Ever told you had any liver condition

MCQ170I - Do you still have thyroid disease  
English Text:  
{Do you/Does SP} still . . . have another thyroid disease?

<table>
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<th>Value Description</th>
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</thead>
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<tr>
<td>2</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>Refused</td>
</tr>
<tr>
<td>9</td>
<td>Don't know</td>
</tr>
</tbody>
</table>

MCQ170K - Do you still have chronic bronchitis  
English Text:  
{Do you/Does SP} still . . . have chronic bronchitis?

MCQ170L - Do you still have a liver condition  
English Text:  
{Do you/Does SP} still . . . have any kind of liver condition?

MCQ180B - MCQ180L – Age when first told had {condition}  
English Text:  
How old {were you/was SP} when {you were/s/he was} first told {you/s/he} . . .had {condition}?  
MCQ180B - Age when told you had heart failure  
MCQ180C - Age when told had coronary heart disease  
MCQ180D - Age when told you had angina pectoris  
MCQ180E - Age when told you had heart attack  
MCQ180F - Age when told you had a stroke  
MCQ180G - Age when told you had emphysema  
MCQ180I - Age when told you had thyroid disease  
MCQ180K - Age when told you had chronic bronchitis  
MCQ180L - Age when told you had a liver condition
MCQ220 - Ever told you had cancer or malignancy

English Text:
{Have you/Has SP} ever been told by a doctor or other health professional that {you/s/he} had cancer or a malignancy of any kind?

MCQ230A- MCQ230C - What kind of cancer

English Text:
What kind of cancer was it?

English Instructions:
ENTER UP TO 3 KINDS.

MCQ240A –MCQ240DD - Age cancer diagnosed

English Text:
How old {were you/was SP} when {TYPE OF CANCER/cancer} was first diagnosed?

MCQ250B - Blood relatives have Alzheimer's

English Text:
Including living and deceased, were any of {SP's/ your} biological that is, blood relatives including grandparents, parents, brothers, sisters ever told by a health professional that they had . . .Alzheimer's disease?

MCQ260BA- MCQ260BF – Which Blood relatives have Alzheimer's

English Text:
Which biological [blood] family member?

English Instructions:
CODE ALL THAT APPLY

   MCQ260BA - Blood relative-Alzheimer's-mother*
   MCQ260BB - Blood relative-Alzheimer's-father*
   MCQ260BC - Blood relative-Alzheimer's-mom's mother*
   MCQ260BD - Blood relative-Alzheimer's-mom's father*
   MCQ260BE - Blood relative-Alzheimer's-dad's mother*
   MCQ260BF - Blood relative-Alzheimer's-dad's father*

*Categories are either endorsed or missing
Appendix G: Kidney Conditions Questionnaire

KIQ020 - Ever told you had weak/failing kidneys

English Text:

{Have you/Has SP} ever been told by a doctor or other health professional that {you/s/he} had weak or failing kidneys? Do not include kidney stones, bladder infections, or incontinence.
Appendix H: Physical Activity Questionnaire

PAQ180 - Avg level of physical activity each day

English Text:

Please tell me which of these four sentences best describes {your/SP's} usual daily activities? [Daily activities may include {your/his/her} work, housework if {you are/s/he is} a homemaker, going to and attending classes if {you are/s/he is} a student, and what {you/s/he} normally {do/does} throughout a typical day if {you are/he/she is} a retiree or unemployed.] . . .

{you sit/he/she sits} during the day and {do/does} not walk about very much.
{you stand or walk/he/she stands or walks} about a lot during the day, but {do/does}not have to carry or lift things very often
{you/he/she} lift(s) light load or {have/has} to climb stairs or hills often.
{you/he/she} {do/does} heavy work or {carry/carries} heavy loads.

PAD200 - Vigorous activity over past 30 days

The next questions are about physical activities including exercise, sports, and physically active hobbies that {you/SP} may have done in {your/his/her} leisure time or at school over the past 30 days. First I will ask you about vigorous activities that cause heavy sweating or large increases in breathing or heart rate. Then I will ask you about moderate activities that cause only light sweating or a slight to moderate increase in breathing or heart rate. Over the past 30 days, did {you/SP} do any vigorous activities for at least 10 minutes that caused heavy sweating, or large increases in breathing or heart rate? Some examples are running, lap swimming, aerobics classes or fast bicycling.

Yes
No
Unable to do activity

PAD320 - Moderate activity over past 30 days

[Over the past 30 days], did {you/SP} do moderate activities for at least 10 minutes that cause only light sweating or a slight to moderate increase in breathing or heart rate? Some examples are brisk walking, bicycling for pleasure, golf, and dancing.

Yes
No
Unable to do activity
**PAD440 - Muscle strengthening activities**

Over the past 30 days, did {you/SP} do any physical activities specifically designed to strengthen {your/his/her} muscles such as lifting weights, push-ups or sit-ups? Include all such activities even if you have mentioned them before.

**PAD460 - Number of times past 30 days**

[Over the past 30 days], how often did {you/SP} do these physical activities? [Activities designed to strengthen {your/his/her} muscles such as lifting weights, push-ups or sit-ups.]

**PAQ500 - Activity comparison last mo - last yr**

How does the amount of activity that you reported {for SP} for the past 30 days compare with {your/his/her} physical activity for the past 12 months? Over the past 30 days, {were you/was he/she} . . .

more active
less active, or
About the same?

**PAQ540 - Compare activity with 10 years ago**

Compared with {yourself/himself/herself} 10 years ago, would you say that {you are/SP is} . . .

More active now,
Less active now, or
About the same?
Appendix I: Physical Activity Individual Activities File

PADACTIV - Leisure time activity

English Text:
[Over the past 30 days], what {vigorous/moderate} activities did {you/SP} do?

English Instructions:
CODE ALL THAT APPLY.

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<td>DANCE</td>
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<td>FISHING</td>
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<td>FOOTBALL</td>
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<td>STAIR CLIMBING</td>
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<td>37</td>
<td>STRETCHING</td>
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Code or Value | Value Description
---|---
39 | TENNIS
40 | TREADMILL
41 | VOLLEYBALL
42 | WALKING
43 | WEIGHT LIFTING
44 | YARD WORK
50 | BOXING
51 | FRISBEE
52 | HORSEBACK RIDING
53 | MARTIAL ARTS
54 | WRESTLING
55 | YOGA
56 | CHEERLEADING AND GYMNASICS
57 | CHILDREN'S GAMES (E.G. DODGEBALL, KICKBALL)
58 | ROPE JUMPING
59 | SKATEBOARDING
60 | SURFING
61 | TRAMPOLINE JUMPING
71 | OTHER

For each of the above that are coded, the following questions are asked:

PADLEVEL - Activity level

English Text:
    Reported intensity level of activity

Code or Value | Value Description
---|---
1 | MODERATE
2 | VIGOROUS

PADTIMES - # of times did activity in past 30 days

English Text:
    [Over the past 30 day], how often did {you/SP} do {activity}? 

PADDURAT - Average duration of activity (minutes)

English Text:
[Over the past 30 days], on average about how long did {you/SP} do {activity} each time?

**PADMETS - MET score for activity (calculated from above information)**

**English Text:**

Metabolic equivalent (MET) intensity level for activity.
Appendix J: Diet Behavior and Nutrition

**DBD270c - Helping of fruit/fruit juices eaten/day**

English Text:
On an average day, how many helpings of the following kinds of foods {do you/does SP}eat? Fruits or fruit juices.

English Instructions:
RESPONDENT SHOULD DEFINE 'HELPING'.

**DBD270d - Helping of vegetables eaten/day**

English Text:
On an average day, how many helpings of the following kinds of foods {do you/does SP}eat? Vegetables, including vegetable salads.

English Instructions:
RESPONDENT SHOULD DEFINE 'HELPING'.
Appendix K: Smoking Questionnaire

SMQ020 - Smoked at least 100 cigarettes in life
English Text:
These next questions are about cigarette smoking and other tobacco use. {Have you/Has SP} smoked at least 100 cigarettes in {your/his/her} entire life?

SMD030 - Age started smoking cigarettes regularly
English Text:
How old {were you/was SP} when {you/s/he} first started to smoke cigarettes fairly regularly?

SMQ040 - Do you now smoke cigarettes
English Text:
{Do you/Does SP} now smoke cigarettes . .
Every day,
Some days, or
Not at all?

SMQ050Q - How long since quit smoking cigarettes (if do not smoke currently)
English Text:
How long has it been since {you/SP} quit smoking cigarettes?

SMQ050U - Unit of measure (day/week/month/year)
Weeks
Months
Years

SMD055 - Age last smoked cigarettes regularly
English Text:
How old {were you/was SP} when {you/s/he} last smoked cigarettes {fairly regularly}?

SMD057 - # cigarettes smoked per day when quit
English Text:
At that time, about how many cigarettes did {you/SP} usually smoke per day?
SMD070 - # cigarettes smoked per day now
English Text:
   On average, how many cigarettes {do you/does SP} now smoke per day?

SMD075 - How many years smoked this amount
English Text:
   For about how many years {have you/has SP} smoked this amount?

SMD080 - # days smoked cigs during past 30 days
English Text:
   On how many of the past 30 days did {you/SP} smoke a cigarette?

SMD090 - Avg # cigarettes/day during past 30 days
English Text:
   During the past 30 days, on the days that {you/SP} smoked, about how many cigarettes did {you/s/he} smoke per day?
Appendix L: Alcohol Use History Questionnaire

**ALQ100 - Had at least 12 alcohol drinks/1 yr?**

English Text:

The next questions are about drinking alcoholic beverages. Included are liquor (such as whiskey or gin), beer, wine, wine coolers, and any other type of alcoholic beverage. In any one year, \{have you/has SP\} had at least 12 drinks of any type of alcoholic beverage? By a drink, I mean a 12 oz. beer, a 4 oz. glass of wine, or an ounce of liquor.

**ALQ110 - Had at least 12 alcohol drinks/lifetime?**

English Text:

In \{your/SP's\} entire life, \{have you/has he/ has she\} had at least 12 drinks of any type of alcoholic beverage?

**ALQ120Q - How often drink alcohol over past 12 mos**

English Text:

In the past 12 months, how often did \{you/SP\} drink any type of alcoholic beverage? PROBE: How many days per week, per month, or per year did \{you/SP\} drink?

**ALQ130 - Avg # alcoholic drinks/day -past 12 mos**

English Text:

In the past 12 months, on those days that \{you/SP\} drank alcoholic beverages, on the average, how many drinks did \{you/he/she\} have?

**ALQ140Q - #days have 5 or more drinks/past 12 mos**

English Text:

In the past 12 months, on how many days did \{you/SP\} have 5 or more drinks of any alcoholic beverage? PROBE: How many days per week, per month, or per year did \{you/SP\} have 5 or more drinks in a single day?

**ALQ150 - Ever have 5 or more drinks every day?**

English Text:

Was there ever a time or times in \{your/SP's\} life when \{you/he/she\} drank 5 or more drinks of any kind of alcoholic beverage almost every day?
Appendix M: IRB Exempt Letter

RESEARCH @ EMU

UHSRC Determination: EXEMPT

DATE: April 6, 2015

TO: Melissa Pulcini, M.S.
    Eastern Michigan University

Re: UHSRC: # 741791-1
    Category: Exempt category 4
    Approval Date: April 6, 2015

Title: Contributors to processing speed deficit in old age: A focus on history of obesity and medical conditions

Your research project, entitled Contributors to processing speed deficit in old age: A focus on history of obesity and medical conditions, has been determined Exempt in accordance with federal regulation 45 CFR 46.102. UHSRC policy states that you, as the Principal Investigator, are responsible for protecting the rights and welfare of your research subjects and conducting your research as described in your protocol.

Renewals: Exempt protocols do not need to be renewed. When the project is completed, please submit the Human Subjects Study Completion Form (access through IRBNet on the UHSRC website).

Modifications: You may make minor changes (e.g., study staff changes, sample size changes, contact information changes, etc.) without submitting for review. However, if you plan to make changes that alter study design or any study instruments, you must submit a Human Subjects Approval Request Form and obtain approval prior to implementation. The form is available through IRBNet on the UHSRC website.

Problems: All major deviations from the reviewed protocol, unanticipated problems, adverse events, subject complaints, or other problems that may increase the risk to human subjects or change the category of review must be reported to the UHSRC via an Event Report form, available through IRBNet on the UHSRC website.

Follow-up: If your Exempt project is not completed and closed after three years, the UHSRC office will contact you regarding the status of the project.

Please use the UHSRC number listed above on any forms submitted that relate to this project, or on any correspondence with the UHSRC office.

Good luck in your research. If we can be of further assistance, please contact us at 734-487-3090 or via e-mail at human.subjects@emich.edu. Thank you for your cooperation.

Sincerely,

Jennifer Kellman-Fritz
Chair
University Human Subjects Review Committee
Appendix N: Consent Form

National Health and Nutrition Examination Survey (NHANES)

The attached brochure gives the facts about NHANES. The survey is one in a series conducted by the National Center for Health Statistics (NCHS). These surveys tell us about the health and nutrition of people in this country. They combine an interview with a physical exam. The exams are done in mobile units. Each year of the survey, we will examine about 5,000 people in 15 different towns and cities across the country.

In the mobile exam center, our medical team will collect health data by examining you, doing lab testing, and asking questions about your health. As in any other exam like this, some procedures may give slight discomfort. Examples are collecting a blood sample or doing the dental exam. The exam may take from 2-1/2 to 4 hours. The time depends on your age, since some procedures are done only for certain ages.

The survey exam is not a substitute for regular health care. However, if we discover urgent health conditions, we will refer you for immediate treatment. You will receive a report on many exam results if you choose. NHANES does not cover the cost of any health care you may decide to seek after the exam. You may be contacted in the future for further research.

We will use information collected in the survey only for research and statistical reports. All health data and samples that we collect in NHANES will be kept strictly private. Unless you agree, our staff is not allowed to discuss that you are part of this survey under penalty of Federal law: Section 308(d) of the Public Health Service Act (42 USC 242m) and the Privacy Act of 1974 (5 USC 552A). However, we will refer clear signs of physical abuse of a child to the State agency that looks into child abuse and neglect.

You may participate in the survey or not. That is your choice. No penalties or loss of benefits will come from refusing to take part. If you choose to take part, you may refuse any part of the exam and are free to drop out anytime. Also, during the interviews you may choose not to answer any question.

To discuss any aspect of the survey, you can make a free call to Dr. Kathryn Porter at the U.S. Public Health Service office at 1-800-452-6115, Monday-Friday, 9 AM-6 PM EST. If you have questions about your rights as a survey participant, call Dr. Lester R. Curtin at 1-800-223-8118.

For the Survey Participant who is 18 Years Old or Older (and emancipated minors):

I have read the information above and in the attached brochure, which explains the nature and purpose of NHANES. I freely choose to take part in the survey. I understand that data about me will be released only as described.

__________________________  __________________________
Signature of participant    Date

☐ I do not want a written report of my exam results.

__________________________  __________________________  __________________________
Signature of staff member    Date    Witness (if required)    Date

__________________________  __________________________  __________________________  __________________________  __________________________
Print name of participant    First    Middle    Last    SP ID

Public reporting burden of this collection of information is estimated to average 6.6 hours per response for total participation, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to CDC/ATS/DR Reports Clearance Officer; 1600 Clifton Road, MS D-24, Atlanta, GA 30333. ATTN: PRA (0920-0237).