Change in BMI and Cognition in Middle-Aged and Older Adults: the Seattle Longitudinal Study

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Abstract

Prior literature on the relationship between Body Mass Index (BMI) and cognition has been inconsistent. Thus, these relationships were examined in 1,023 participants (54.5%female) from the 1998 and 2005 waves of the Seattle Longitudinal Study (SLS). Participants were divided into two groups for the purpose of comparison, a middle-aged group (n=587; Age Range=40-64 years) and an older adult group (n=436; Age Range=65-93 years). The SLS records cognitive data in six abilities. Health variables included BMI, hypertension and smoking. Hierarchical multivariate regression analyses were used to examine relationships amongst change in BMI, cognition, hypertension, and smoking at both time points. Mean BMI for the study sample did not significantly change over time, but had a significant impact on predicting change in cognitive factor scores. A reduction in performance for change in verbal memory was identified with increased change in BMI for middle-aged adults, and an improvement in performance with change in verbal memory and change in spatial orientation with decreased change in BMI for older adults were found. Hypertension was not a significant mediator of the BMI-cognition relationships. However, smoking status was found to be a full mediator of the BMI-cognition relationship. Previous smoking at some time in the past explained the association between change in verbal memory and BMI over a seven-year period. The implications of this study yield new contributions to how increased BMI can negatively influence change in cognitive function in midlife adults, and how this association may change in older adulthood.
Keywords: Body mass index, cognition, middle-aged and older adults, smoking status, hypertension status

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Review of the Literature

The number of adults in the U.S. that are overweight or obese, as measured by body mass index (BMI), has grown to a critical state and drastic measures are needed to overcome this serious issue (Dahl, Hassing, Fransson, Reynolds, & Pedersen, 2013). The prevalence of high BMI is a cause for particular concern when regarding health due to the fact that obesity is one of the leading causes of preventable death in the United States (Gunstad, Lhotsky, Wendell, Ferrucci, & Zonderman, 2010; Kaufman, Auguston, & Patrick, 2012). The relationship between cognitive function and BMI has been at the center of investigations in recent years, but has yielded inconsistent results such as positive (Gunstad et al., 2010), detrimental (Dahl et al., 2013), and no relationships (Albanese, Hardy, Wills, Kuh, Guralnik, & Richards, 2012). For example, positive associations have suggested that being overweight or obese was associated with increased attention and reasoning abilities (Gunstad et al., 2010; Kuo, Jones, Milberg, Tennstedt, Talbot, Morris, & Lipstz, 2006). In contrast, negative associations suggested that being overweight or obese was associated with decreased global cognitive function, psychomotor speed and memory (Benito-Leon, Mitchell, Hernandez-Gallego, & Bermejo-Pareja, 2013). Particular methods, such as study design, analyses and cognitive abilities examined, may account for mixed results in the BMI-cognition relationship.

Influence of Age

The importance of age factors may be a factor when investigation the BMI-cognition relationship, as differential relationships may emerge across the adult lifespan. An investigation of BMI and global cognitive function in adults aged 70 years an older revealed that lower levels of global cognition and higher BMI were important predictors of mortality (Gustafson, Mazzuco, Ongaro, Antuono, Forloni, Albani, & Gallucci, 2012). The average BMI was lower among those with a low MMSE (≤24), than older adults with an MMSE >24 (23.7 kg/m^2 versus 25.3 kg/m^2, $p<.001$; Gustafson et al., 2012). This indicated that higher BMI in old age might serve as a protective factor to global cognition. Dahl and colleagues (2013) examined BMI and cognitive functioning across midlife. They identified a negative effect of being overweight or obese in midlife on cognitive abilities in late life (Dahl et al., 2013). This was observed for participants in across midlife and the cognitive abilities that were influenced by changes in BMI in this investigation were verbal, spatial, memory and perceptual speed. The implications of this study suggested that increases in BMI in midlife could have negative consequences on cognitive performance in late life. Similar findings were observed in a study of BMI and cognitive performance across the adult lifespan (Stanek, Strain, Devlin, Cohen, Paul, Crosby & Gunstad, 2013). Increased BMI was independently associated with decreased attention, processing speed, and fine motor speed. The results from these studies suggest that it is important to consider age factors when examining the BMI-cognition relationship.

Influence of Demographic Factors

Socioeconomic status may be an important factor to account for when investigating the BMI-cognition relationship. Pavlik and colleagues suggested that a significant proportion of variation in cognition may be accounted for by demographic variables such as age, gender, ethnicity, and measures of socioeconomic status (SES) and thus, should be controlled for when studying cognitive function (Pavlik, Hyman, & Doody, 2005).

Gender differences may be an important factor to account for when investigating the BMI-cognition relationship In a longitudinal study by Elias, Elias, Sullivan, Wolf, and D'Agostino (2003), adverse effects of obesity and hypertension were associated with poorer performances on immediate and delayed memory recall and word fluency in men only. Obese and hypertensive men performed more poorly than men classified as either obese or hypertensive. Participants who were non-obese and non-hypertensive had the best memory performance of all the groups (Elias et al., 2003). Reasons for these gender differences in the BMI-cognition relationship may result from different methods, analyses and measures, and reveal the importance of examining gender in investigations.

Influence of Health Factors

Some of the health factors that may be influential to the BMI-cognition association include presence of hypertension and smoking. Hypertension has been consistently associated with obesity in the general public and has been linked to cognitive deficits in normal functioning, independent-living adults (Crichton, Elias, Davey, & Alkerwi, 2014; Elias et al., 2003; Pavlik et al., 2005). Hypertension, along with greater levels of obesity, negatively affected executive function (Waldstein & Katzel, 2006), fluid intelligence (Yu, Ryan, Schaie, Willis, & Kolanoski, 2009), global cognitive functioning (Frewen, Finucane, Savva, Boyle, & Kenny, 2013), and significantly increased the pace of decline in logical reasoning performances (Kuo et al., 2006).

In addition, smoking is another health risk factor implicated in the BMI-cognition relationship. Smoking has been found to be independently associated with reduced global cognitive functioning (Crichton et al., 2014). Further, smoking is well known to be a health hazard to the cardiovascular system and research suggests that smoking negatively impacts cognition. Cherbuin, Reglade-Meslin, Kumar, Jacomb, Easteal, Christensen, & Anstey (2009) examined lifestyle predictors that could lead to MCI. They found that past smoking increased the risk of transitioning to MCI two-three times more than in participants who did not smoke (Cherbuin et al., 2009). Furthermore, smoking has been linked to BMI (Menon, Jahn, Mauer, & O'Bryant, 2013). For instance, Kaufman and colleagues (2012) found that participants who currently smoke were less likely to be obese than never and former smokers and had a lower mean BMI. Former smokers were more likely to be obese and had the highest mean BMI (Kaufman et al., 2012). Multiple hypotheses were suggested to explain this relationship, which included sedentary behavior and nicotine's effect as an appetite suppressant (Kaufman et al., 2012). In addition, Akbartabartoori, Lean, and Hankey (2005) found smoking status was negatively associated with BMI. Nonsmokers and former smokers were more likely to be overweight and current smokers were more likely to have lower BMI, but within the normal weight range (Akbartabartoori et al., 2005). These investigations suggest that smoking is detrimental to cognitive health and associated with lower BMI when compared to non-smokers.

BMI, MCI and Dementia

Additional studies of the BMI-cognition relationship have included individuals with either mild cognitive impairment (MCI) or dementia-like diseases, such as Alzheimer's Disease (AD) or Parkinson's Disease (PD). Weight change in midlife and later life has been associated with MCI and dementia prevalence (Cronk, Johnson, & Burns, 2010; Hughes, Borenstein, Schofield, Wu, & Larson, 2009).

Many studies have investigated the relationship between BMI and MCI (Cherbuin et al., 2009; Chu, Tam, Lee, Yik, Song, Cheung, & Lam, 2009; Cronk et al., 2010; Ho, Raji, Becker, Lopez, Kuller, Hua, & Thompson, 2010), Alzheimer's Disease (Bedard, Molloy, Bell, & Lever, 2000; Chu et al. 2009; Ewers, Schmitz, Hansson, Walsh, Fitzpatrick, Bennet, & Hampel, 2012; Ho et al., 2010; Spaccavento, Prete, Craca, & Fiore, 2009), dementia (Creavin, Gallacher, Pickering, Fehily, Ebrahim, & Ben-Shlomo, 2012; Gao, Nguyen, Hendrie, Unverzagt, Hake, Smith-Gamble, & Hall, 2011; Hughes et al., 2009; Ogunniyi, Gao, Unverzagt, Baiyewu, Gureje, Nguyen, & Hendrie, 2011), Parkinson's Disease (Kim, Oh, Lee, Moon, Oh, Shin, & Lee, 2012), and vascular dementia (Doruk, Naharci, Bozoglu, Isik, & Kilic, 2010). The majority of these studies reached a consensus that lower BMI, such as from obese/overweight to normal weight/under weight in late life was a likely indicator of MCI, AD, PD, or dementia. This has been observed over time and in cross-sectional studies as well. However, a few studies concluded that being overweight and/or obese may be a protective factor and suggest that low BMI may be an indicator of declining health (Cronk et al., 2010; Ewers et al., 2012; Hughes et al., 2009; Spaccavento et al., 2009). There does not seem to be a significant difference between overweight and obese participants in regards to risk for dementia (Hughes et al., 2009); however, being overweight and/or obese may act as a protective factor for participants with MCI (Cronk et al., 2010) and possibly AD (Spaccavento et al., 2009). Investigating weight status and change in weight at different times in the adult life span may be an important role for suggesting how overweight and/or obesity may be a protective factor (Hughes et al., 2009). Investigation of whether

BMI has a more robust relationship with certain cognitive abilities in a sample of normal cognitive functioning adults may be of interest to clinicians.

Summary and Conclusions

Due to the growing presence of overweight or obese adults in the U. S., recent investigations have examined the BMI-cognition relationship, but none have yielded consistent implications of that relationship (Albanese et al., 2012; Dahl et al., 2013; Gunstad et al., 2010). BMI and cognition may have an intricate relationship with each other that can help understand how physical and cognitive health interact as people age. Further, prior research has not thoroughly examined the influence hypertension and smoking have on the BMI-cognition relationship. Longitudinal data has yielded inconsistent findings that included a negative effect on perceptual speed in relation to being overweight/obese (Dahl et al., 2013), and a positive effect on attention and reasoning in relation to being obese (Gunstad et al., 2010). It is important to account for age and demographic factors along with health factors, such as hypertension and smoking status, when analyzing the BMI-cognitive function relationship because these variables are known to be influential in prior literature.

The purpose of this thesis was to examine change in cognitive function and BMI in a community dwelling sample of adult participants from the Seattle Longitudinal Study (SLS). In addition, another objective was to investigate how hypertension and smoking mediate the BMI-cognition relationship. Investigation of these variables occurred at two fixed time points. Examining the influence of these factors on the BMI-cognition relationship can yield important contributions to previous literature by highlighting relationships between BMI and cognitive function in middle-aged and older adults with common health issues and behaviors. Furthermore, it can address inconsistencies found in previous research, and provide practical implications regarding the relationships between health, cognition, and aging.

Expected outcomes of this investigation included: increase in BMI will be positively associated with change in inductive reasoning and negatively associated with change in perceptual speed, spatial orientation, number skills, verbal ability, and verbal memory factor scores; increased change in BMI will be associated with lower cognitive function for middle-aged adults and higher cognitive functioning for older adults. Hypertension presence will be expected to fully mediate the BMI-cognition relationship and explain the association of change in BMI and change in cognition. Moreover, smoking status will also serve a full mediator and explain the association of change in BMI and change in cognition in both midlife and old age.

Methods

Participants

This study was a secondary retrospective analysis from the Seattle Longitudinal Study (SLS). The participants analyzed in this study were from the SLS 1998 and 2005 data waves. The SLS is a successive cohort design, with the first cohort recruited in 1956 from a health maintenance organization (HMO) based in the Pacific Northwest (Schaie, 2012). Follow-ups occurred every 7 years and new samples were added at each follow-up. Participants were assessed at each wave by trained research staff in small groups and individually with a series of surveys and cognitive tests. Participants were also given a set of surveys to complete on their own and mail back when finished (Schaie, 2012).

Participants from the SLS that were included in the current study had to be at least 40 years of age and completed two waves of data collection, in 1998 and 2005. Participants were excluded if they were diagnosed with dementia before the investigation, and if any information on their BMI and cognitive factor scores were missing. Only an ID number identified participant data obtained. The Youngstown State University's Institutional Review Board and the SLS research committee approved the use of these data.

A total of 1,023 participants (54.5% female) from the SLS were included in the analyses from both the 1998 and 2005 waves. Average age of the sample in 1998 was 61.43 years (SD = 12.32; Range = 40-93). Participants were divided into two groups for the purpose of comparison, a middle-aged group (n = 587; Age Range = 40-64 years) and an older adult group (n = 436; Age Range = 65-93 years). White, not Hispanic, (94.4%) represented the majority ethnicity of the population. The average reported years of education received was 15.70 (SD = 16.00; Range = 7-20), and the two most frequent years of education received in the sample were 16 years of education (20.3%) and 12 years of education (15.2%).

Measures

Gender and years of education attainment were the demographic variables of interest and were obtained from the Life Complexity Inventory from the SLS (Schaie, 2012). Years of education attainment was measured as a continuous variable and gender and ethnicity were categorical. Demographics can be found at Table 1.

Other measures of interest in this investigation included cognitive and health variables. The test battery included psychometric ability and rigidity-flexibility measures that have been collected since the beginning of the SLS, as well as additional markers for the ability factors that were added to the basic battery (Schaie, 2012).

Cognitive Variables

The SLS records cognitive data on 6 abilities that were calculated into factor scores. Those abilities included: inductive reasoning, spatial orientation, number skills, verbal ability, verbal memory, and perceptual speed (Schaie, 2012). These separate cognitive assessments were condensed into a factor scores for each participant.

The inductive reasoning task was used to measure the ability to recognize and understand novel concepts and involves the solution of logical problems. This was done by the primary mental ability (PMA) reasoning task, the ADEPT Letter Series (Blieszner, Willis, & Baltes, 1981), Word Series and Number Series (Thurstone, 1962).

The PMA spatial orientation assessment, Object Rotation (Quayhagen, 1979; Schaie, 1985), Alphanumeric Rotation (Willis & Schaie, 1983), and Cube Comparison (Ekstrom, French, Harman, & Dermen, 1976) measured the ability to visualize and mentally manipulate spatial configurations in two or three dimensions, to maintain orientation with respect to spatial objects, and to perceive relationships among objects in space.

The PMA number skills task, Addition task (Ekstrom et al., 1976), and Subtraction and Multiplication task (Ekstrom et al., 1976) were used to measure the ability to understand numerical relationships and to solve simple quantitative problems rapidly and accurately.

The PMA verbal ability task (Hertzog, 1989; Schaie, Willis, Jay, & Chipuer, 1989), Educational Testing Service (ETS) Vocabulary V-2, and ETS Vocabulary V-4 tasks (Ekstrom et al., 1976) were used to understand ideas expressed in words. This assessment indicated the range of a participant's passive vocabulary used in activities where information was obtained by reading or listening.

The PMA perceptual speed task, Identical Pictures task (Ekstrom et al., 1976), Number Comparison task (Ekstrom et al., 1976), and Finding A's tasks (Ekstrom et al., 1976) were incorporated to measure the ability to find figures, make comparisons and carry out other simple tasks involving visual perception with speed and accuracy.

The PMA verbal memory task was used to measure the ability that involves the memorization and recall of meaningful language units. An immediate recall and delayed recall task was used to assess these abilities (Zelinski, Gilewski, & Schaie, 1993).

Changes in these cognitive factors were determined by subtracting time 1 from time 2 and were then analyzed as continuous variables.

Health Variables

The health variables of BMI, presence of hypertension, and smoking were included from the Health Behavior Questionnaire of the SLS (Schaie, 2012). Values in the normal weight range were from 18.5 to 24.9, overweight ranged from 25.0-29.9 and obese ranged from 30 and greater. In the 1998 cohort, 38.2% of the sample were categorized as normal weight, 36.8% were categorized as overweight and 24.3% were obese. In 2005, 36.9% were normal weight, 38.2% were overweight, and 24.0% were obese. To investigate change in BMI, a change score was created taking into account the difference in BMI between times 2 (2005) and 1 (1998).

Hypertension. In terms of reported hypertension, in 1998, 117 (14.6%) participants positively endorsed having hypertension, while 686 (85.4%) reported no hypertension. In 2005, 249 (30.9%) participants endorsed having hypertension, and 556 (69.1%) reported no hypertension. A detailed age-based breakdown of reported hypertension in 1998 and 2005 can be found in Table 3. Change in hypertension status was assessed by examining whether hypertension status changed over time, and creating the following groups: hypertension at both time points, hypertension endorsement at one time point, no hypertension at either time point.

Smoking. In terms of reported smoking, out of 1017 participants, 51 (5.0%) reported yes in 1998, 446 (43.9%) reported not now but in the past and 520 (51.1%) reported never. In 2005, 40 (3.9%) of participants reported yes to smoking, 449 (44.0%) to smoked in the past but not currently, and 532 (52.1%) reported never smoking. A detailed age-based breakdown of reported smoking in 1998 and 2005 can be found in Table 3. Change in smoking status was assessed by examining change in status over time, resulting in the following groups: current smoking at both times, previous smoking or current smoking at either time point, previous smoking, but not current smoking at both time points, previous smoking or never smoked at either time point, and never smoked at both time points.

Analyses

Proposed statistical analyses were performed in SPSS version 22. Hierarchical multivariate regression analyses were used to examine change (from 1998 to 2005) in BMI, cognition, hypertension, and smoking. Gender and educational attainment were covariates in the models. Criteria to investigate and determine mediation was guided from the method developed by Baron and Kenny (1986). Up to four-step hierarchical regression analyses were conducted to examine if hypertension and smoking mediated the BMI-cognition relationship. The first step included the multivariate regression of change in BMI predicting change in cognitive abilities, adjusted for gender and education attainment. The second step investigated whether change in BMI could predict the mediator variables (hypertension and smoking status were the mediator variables of interest at this step, in separate models). The third step investigated relationship between the mediator variables and change in cognition as the dependent variable. The final step integrated change in BMI, the mediator, and the covariates to observe the effect on change in cognition. If the mediator was did not retain a significant relationship in any of the steps 1-3, then the process was stopped. Moreover, hierarchical models were separated by age group.

Results

Mean baseline cognitive scores in each domain are reported in table 2. The average BMI of the 1998 cohort was 27.35 (SD = 5.60) and the average BMI of the 2005 cohort was 27.34 (SD = 5.67). The mean change in BMI from time 1 to time 2 was -.01 (SD = 2.59; p = .919). The BMIs for the two age groups were as follows: a mean BMI of 27.87 (SD = 6.34) for middle-aged participants and 26.65 (SD = 4.33) for older adult participants in 1998 (time 1); and a mean BMI of 28.18 (SD = 6.43) for middle-aged participants and 26.21 (SD = 4.21) for older adult participants in 2005 (time 2). Overall, adults in midlife increased their BMI over time, while older adults decreased their BMI during the seven-year follow-up interval but these changes were significant (t = 2.77, p = .006 for midlife; t = -3.97, $p < .001$ for older adults).

The mean change from time 1 to time 2 in cognitive factor scores in middle-aged adults were as follows: change in verbal memory was -.64 (SD = 5.86), change in number skills was -1.71 (SD = 3.00), change in inductive reasoning was -.53 (SD = 3.27), change in spatial orientation was .05 (SD = 4.72), change in perceptual speed was -.69 (SD = 3.35), and change in verbal ability was .19 (SD = 2.84). The average change in cognitive factor scores from time 1 to time 2 for older adults were as follows: change in verbal memory was -2.89 (SD = 6.89), change in number skills was -4.58 (SD = 4.68), change in inductive reasoning was -3.44 (SD = 4.10), change in spatial orientation was -3.45 (SD = 5.30), change in perceptual speed was -3.96 (SD = 4.56), and change in verbal ability was -1.44 (SD = 3.66).

Change in BMI and Cognition

Step one of the hierarchical regression analysis was to examine change in BMI and cognition over the seven-year period for middle-aged and older adult participants. Results for middle-aged participants revealed change in BMI was not a significant predictor of inductive reasoning change, $F(1, 583) = 2.39$, $p = .123$, change in number skills, $F(1, 583) = 1.53$, $p = .217$, verbal ability change, $F(1, 568) = 2.08$, $p = .150$, or change in spatial orientation, $F(1, 583) = 0.86$, $p = .355$. The overall model of change in BMI was a significant predictor of change in verbal memory, $F(1, 583) = 4.36$, $p = .037$ and revealed a trend for change in perceptual speed, $F(1, 583) = 3.38$, $p = .067$. Change in BMI as a predictor denoted a negative association with verbal memory scores, which indicated a reduction in change of verbal memory as BMI increased, over the seven-year period for middle-aged participants. Education was a significant covariate for only change in verbal memory, $F(1, 583) = 4.27$, $p = .039$, and indicated that fewer years of education was associated with more detrimental change in verbal memory in midlife, and gender did not demonstrate any significant associations.

Analysis of older adults' change in BMI and cognition over the seven year period identified a significant model of change in BMI predicting change in verbal memory, $F(1, 432) = 9.00$, $p = .003$, and change in spatial orientation, $F(1, 432) = 7.16$, $p = .008$. The results indicated that negative change in BMI resulted in greater positive change verbal memory and spatial orientation scores on the cognitive battery for older adults. There were not any significant relationships between change in BMI and change in cognition for number skills $F(1, 432) = 1.12$, $p = .291$, inductive reasoning, $F(1, 432) = 2.39$, $p = .123$, perceptual speed, $F(1, 432) = 0.24$, $p = .495$, and verbal ability $F(1, 432) = 0.50$, $p = .823$. Education revealed a significant association for change in inductive reasoning, $F(1, 432) = 4.94$, $p = .027$ and identified a trend for change in verbal memory, $F(1, 432) = 3.50$, $p = .062$. Gender was not a significant covariate.

See Tables 4 and 5 for additional details of the analyses investigating change in BMI as a predictor of change in cognition for both age groups, respectfully. It should be noted that for both middle-aged and older adult sub-samples, the percentage of variance accounted for by change in BMI was relatively low (ranging from .004 to .015 for midlife adults, and .003 to .030 for older adults), suggesting that other variables in addition to change in BMI may better account for variation cognitive change.

Hypertension As a Mediator

Results of step two of the hierarchical regression with hypertension serving as a mediator of the BMI-cognition relationship in midlife demonstrated a lack of significance. Change in BMI was not a significant predictor of absence of hypertension at both time points ($p = .598$) or absence of hypertension at either time point ($p = .650$). This suggests that hypertension status was not a significant mediator of the BMI-cognition relationship in midlife. Subsequent steps to test the mediation relationship were not conducted due to insignificance at this step.

As for the older adult participants, hypertension was not found to be a significant mediator when analyzed at step two of the hierarchical regression. Change in BMI was not a significant predictor of absence of hypertension at both time points or hypertension at either time point, $p = .207$ and $p = .514$, respectfully. This suggests that hypertension status was not a significant mediator of the BMI-cognition relationship in old age. Again, subsequent steps to test the mediation relationship were not conducted due to insignificance of hypertension at this step.

Smoking As a Mediator

The second model of the hierarchical regression analysis was to examine smoking status as a mediator of the BMI-cognition relationship. Change in BMI was a significant predictor of smoking status for middle-aged adults. Change in BMI was a significant predictor for previous smoking or current smoking at either time point ($p = .003$), for previous smoking both time points ($p = .035$), and no smoking at both time points ($p = .026$). At step three of the mediation analysis, previous smoking or current smoking at either time point was a significant predictor of change in verbal memory ($p = .006$). In the final step of the mediation analysis, prior smoking or current smoking at either time 1 or 2 remained significant ($p = .006$) and change in BMI was not significant ($p = .058$) for change in verbal memory, indicating that this particular smoking variable was a significant full mediator to the BMI-verbal memory relationship and accounted for the positive increase in verbal memory as BMI increased. Education attainment was the only significant covariate ($p = .038$).

For older adults, change in BMI was not a significant predictor of smoking status at step two of the hierarchical regression for previous smoking or current smoking at either time point ($p = .795$), previous smoking at both time points ($p = .926$), previous smoking or no smoking at either time point ($p = .627$), or no smoking at both time points ($p = .982$). These findings suggested that smoking status was not a significant mediator of the BMI-cognition relationship in older adults, thus additional steps to further test mediation were not conducted for older adults.

See Tables 6, 7, and 8 for additional details of the steps 2, 3, and 4 of the analyses investigating smoking status as a mediator for the BMI-cognition relationship for midlife. It should be noted that the percentage of variance accounted for by change in BMI was relatively low (ranging from .012 to .037 for midlife) for middle-aged sub-samples, suggesting that other variables in addition to smoking status may better account for variation cognitive change.

Discussion

The results of the current study revealed many influences in regards to the BMI-cognition relationship over a period of 7 years in middle-aged and older adult adults. First, this is extends findings to similar studies that investigated age group differences, particularly middle-aged and older adults in a longitudinal setting (Akbartabartoori et al., 2005; Nilsson & Nilsson, 2009; Stanek et al., 2013). Mean BMI for the study sample did not exhibit a significant change over the seven-year period, but had a significant influence on predicting change in cognitive factor scores. Change in BMI was a significant predictor of detrimental change in cognition for middle-aged adults in verbal memory and revealed a trend for perceptual speed. As change in BMI increased by one unit, change in both verbal memory and perceptual speed decreased (Table 4).

Change in BMI in older adults revealed significant positive associations and predicted increased positive change in verbal memory and in spatial orientation as BMI decreased. The cognitive associations for both age groups directional change were not expected in this investigation as previous literature expressed a negative association between these two variables. This may be due to the range of the cognitive data from the SLS, and other factors that were not controlled for, such as leisure activities and social interactions with family members or friends. The contrasting age associations found for the BMI-cognition relationships were expected (Dahl et al., 2013; Nilsson & Nilsson, 2009; Stanek et al., 2013). These findings support and extend previous research showing high BMI is associated with poor cognitive performance in middle-aged adults. However, in this study low BMI was associated with increased positive change cognition in older adults. This was an unexpected finding based on previous literature and could be due to higher education attainment in this sample, testing bias, or other measures that were not controlled for in this study. In addition, the finding of change in BMI predicting change in verbal memory for both age groups may suggest that BMI and verbal memory may have a complex age-based relationship that warrants further investigation. The association of BMI and verbal memory could represent an inverse linear relationship, where higher BMI in midlife could exhibit detrimental effects on verbal memory, but change in older adulthood with higher BMI demonstrating a positive effect on verbal memory change (Dahl, et al., 2013). However, due to low variance accounted for in the hierarchical regression models, and the fact that only two time points were investigated in the current study, further investigation to identify specific pathways of how change in BMI relates with change in verbal memory is necessary.

The influence of hypertension as a mediator for either age group was not significant. This was an unexpected finding due to previous literature that has observed the presence of hypertension to demonstrate a negative association with cognitive functioning in middle-aged adults (Crichton et al., 2014; Kuo et al., 2005; Pavlik et al., 2004). Examples of prior literature have found associations of hypertension with lower cognitive functioning (Crichton et al., 2014).

Previous smoking at a time in the past mediated the relationship between change in BMI and change in verbal memory in middle-aged adults. The effect was positive, thus indicating that a history of smoking coupled with current smoking explained the increased performance in verbal memory. Behavior characteristics, such as leisure activities or social interaction may account for this positive association. This was not an expected outcome as prior literature has explained negative influences of smoking on BMI and cognition, including verbal memory (Cherbuin et al., 2009; Crichton et al., 2014; Richards, Jarvis, Thompson, & Wadsworth, 2003). No association of smoking as a mediator was identified for older adults. This may be due to the small number of older adults who reported currently smoking at the time of data collection, or total years since having quit smoking may be longer than that of middle-aged adults. Moreover, other activities, such as exercise or leisure activities, may be influencing the results found in this investigation.

Limitations

Some strengths of this study included its longitudinal design, range of cognitive data, and large sample size; these are some of the factors of interest that the SLS was to observe, normative change in healthy adults over long periods of time. However, this study was limited by several factors. First, the sample was well educated, healthy, and not ethnically diverse, which limits generalizability beyond similar samples. Moreover, hypertension, smoking, and BMI were based on self-reports. In addition, for the purpose of analysis, BMI change was calculated as a continuous variable (which can be viewed as a strength due to higher accuracy of the BMI metric), rather than investigating changes in weight status categories (such as change from normal to overweight, or normal to underweight). Further, it was unknown whether change in weight was intentional for health purposes or unintentional; changes in weight category membership may lead to more substantial differences in cognitive functioning over time, or further clarify the BMI-cognition relationship. Further, in regards to the smoking variable, developing a different way to measure this variable, such as taking into account years smoking, or how many times per day one smokes may differentially impact the results.

Another limitation is lack of consideration of medications to manage hypertension. Additionally, to further investigate mediation relationships, structural equation modeling should be used in the future to better disentangle partial versus full mediation. Investigating cognitive performance at each time point, rather than creating change scores should also be considered. All of these concerns limit the generalizability of these findings; however, the current study is still helpful when making comparisons to prior research on healthy aging.

Future Directions

Future studies should analyze more ethnically diverse samples, and investigate the BMI-cognition relationship for a period greater than 7 years. The latter option may help view long-term changes that can predict health and cognition in older adults from young age and middle age. Waist circumference and exercise frequency and duration are some other areas of health that can be investigated in terms of the BMI-cognition relationship. Additional health research topics to explore could be examining the role diet has on the BMI-cognition relationship or taking into account total years since smoking cessation. Other areas of interest in terms of cognitive performance with the SLS cognitive factor scores, may be participants who transition from normal cognitive functioning to MCI or AD.

Conclusion

The results of this study extended prior findings about associations of how change in cognition can be predicted by change in BMI. A novel finding of the relationship of change in verbal memory and BMI may vary as a function of age, and it is currently unclear whether it is due to a cohort difference or a developmental change. History of smoking coupled with current smoking was a positive mediator of the BMI-cognition relationship in terms of change in verbal memory in midlife. This was unexpected and warrants further investigation. The results of the current study should help guide future research on the relationship between BMI and cognition across adulthood.

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Table 1. Demographics

	Percentage of sample (frequency)
Gender (n= 1023)	
Female	54.5% (558)
Male	45.5% (465)
Age (n= 1023)	
Middle-Aged (40-64)	57.4 % (587)
Older Adults (65+)	42.6 % (436)
Race (n=1008)	
White (not Hispanic)	95.8% (966)
Other	4.2% (42)
Midlife Education Attainment (n=587)	
Mean (SD) 16.12 (2.42)	
Older Adult Education Attainment (n=436)	
Mean (SD) 15.13 (2.78)	

Table 2. Descriptive Variables for Cognitive Factor Scores in 1998 and 2005

Age Group	Cognitive Factor	1998 (Time 1)	2005 (Time 2)
Midlife Adults (n=587)	Inductive Reasoning	54.72 (6.82)	54.20 (7.20)
	Spatial Orientation	53.97 (7.05)	54.02 (7.14)
	Number Skills	50.87 (8.88)	49.15 (8.87)
	Verbal Ability	52.30 (7.40)	52.49 (7.18)
	Verbal Memory	53.48 (8.17)	52.84 (8.32)
	Perceptual Speed	53.59 (5.77)	52.90 (6.12)
Older Adults (n=436)	Inductive Reasoning	47.06 (6.95)	43.62 (7.10)
	Spatial Orientation	46.56 (7.28)	43.11 (7.61)
	Number Skills	48.25 (8.34)	43.67 (8.40)
	Verbal Ability	50.94 (8.19)	49.50 (8.30)
	Verbal Memory	45.87 (8.86)	42.98 (9.87)
	Perceptual Speed	46.58 (5.70)	42.63 (7.18)

Table 3. Change in Descriptive Health Variables from 1998 to 2005

		Time 1 (1998)	Time 2 (2005)
Midlife Adults (n=587)			
BMI Status	Below 18.5	4 (0.7%)	5 (0.9%)
	18.5-24.9	216 (36.8%)	200 (34.1%)
	25.0-29.9	211 (35.9%)	211 (35.9%)
	30.0 and Above	156 (26.6%)	171 (29.1%)
Hypertension Status	Yes	31 (7.3%)	92 (21.7%)
	No	392 (92.7%)	332 (78.3%)
Smoking Status	Yes	37 (6.3%)	30 (5.1%)
	Not Now, But in the Past	236 (40.5%)	243 (41.6%)
	No, Never	310 (53.2%)	312 (53.3%)
Older Adults (n=436)			
BMI Status	Below 18.5	3 (0.7%)	4 (0.9%)
	18.5-24.9	175 (40.1%)	177 (40.6%)
	25.0-29.9	165 (37.8%)	180 (41.3%)
	30.0 and Above	93 (21.3%)	75 (17.2%)
Hypertension Status	Yes	86 (22.6%)	157 (41.2%)
	No	294 (77.4%)	224 (58.8%)
Smoking Status	Yes	14 (27.5%)	10 (2.3%)
	Not Now, But in the Past	210 (48.4%)	206 (47.2%)
	No Never	210 (48.4%)	220 (50.5%)

Table 4. Multivariate Regression Analysis of Change in BMI and Cognition in Midlife Adults

Dependent Variable	Parameter	B	SE B	t
Inductive Reasoning Change[a]	BMI Change	-0.08	0.05	-1.54
	Male	-0.10	0.28	-0.37
	Education	0.04	0.06	0.61
Spatial Orientation Change[b]	BMI Change	0.07	0.07	0.93
	Male	0.01	0.40	0.34
	Education	0.04	0.06	0.54
Number Skills Change[c]	BMI Change	-0.06	0.05	-1.24
	Male	0.14	0.25	0.54
	Education	0.08	0.05	1.60
Verbal Memory Change[d]	BMI Change	-0.18*	0.09	-2.09
	Male	0.29	0.49	0.59
	Education	-0.21*	0.10	-2.07
Verbal Ability Change[e]	BMI Change	0.07	0.04	1.55
	Male	0.34	0.24	1.41
	Education	-0.02	0.05	-0.31
Perceptual Speed Change[f]	BMI Change	-0.09[T]	0.05	-1.84
	Male	0.30	0.28	1.07
	Education	0.01	0.06	0.13

Notes. * $p < .05$. ** $p<.01$. *** $p < .001$. T < .07
a. $R^2 = .005$. b. $R^2 = .004$
c. $R^2 = .008$. d. $R^2 = .015$
e. $R^2 = .008$. f. $R^2 = .008$

Table 5. Multivariate Regression Analysis of Change in BMI and Cognition in Older Adults

Inductive Reasoning Change[g]	BMI Change	0.13	0.09	1.55
	Male	0.19	0.41	0.48
	Education	-0.16*	0.07	-2.22
Spatial Orientation Change[h]	BMI Change	0.29**	0.11	2.68
	Male	-0.41	0.52	-0.78
	Education	0.06	0.09	0.68
Number Skills Change[i]	BMI Change	0.10	0.10	1.06
	Male	-0.24	0.47	-0.51
	Education	0.96	0.08	1.15
Verbal Memory Change[j]	BMI Change	0.42**	0.14	3.00
	Male	0.05	0.68	0.07
	Education	0.23[T]	0.12	1.87
Verbal Ability Change[k]	BMI Change	0.10	0.08	1.28
	Male	0.36	0.36	1.00
	Education	0.01	0.07	0.22
Perceptual Speed Change[l]	BMI Change	.05	0.10	0.49
	Male	-0.25	0.45	-0.56
	Education	0.07	0.08	0.86

Notes. * $p < .05$. ** $p<.01$. *** $p < .001$. T < .065
g. $R^2 = .016$. h. $R^2 = .019$
i. $R^2 = .006$. j. $R^2 = .030$
k. $R^2 = .007$. l. $R^2 = .003$

Table 6. Multinomial Regression Analysis of Change in BMI Predicting Change in Smoking Status in Midlife

Dependent Variable	Parameter	B	SE B	Wald
Previous Smoking or Current Smoking at Either Time Point	BMI Change	0.30**	0.10	8.64
	Male	-0.10	0.66	2.29
	Education	0.31*	0.14	4.67
Previous Smoking at Both Time Points	BMI Change	0.14*	0.07	4.44
	Male	-0.56	0.47	1.45
	Education	0.31**	0.10	9.17
Previous Smoking or Not Currently Smoking at Either Time Point	BMI Change	0.14	0.10	1.88
	Male	-0.75	0.62	1.43
	Education	0.30*	0.13	4.90
Not Currently Smoking at Both Time Points	BMI Change	0.15*	0.07	4.95
	Male	-1.15*	0.46	6.14
	Education	0.36***	0.10	12.12

Notes. * $p < .05$. ** $p < .01$. *** $p = .001$.

Table 7. Hierarchical Regression Analysis of Change in Smoking Status and Cognition in Midlife

Dependent Variable	Parameter	B	SE B	t
Inductive Reasoning Change[a]	Yes Both Times	-2.51*	1.13	-2.23
	Not now, but in past/yes either time	1.24	1.07	1.16
	Not now, but in the past Both Times	-0.12	0.41	-0.29
	Not now, but in the past, no either time	-0.58	1.02	-0.57
	Education	0.29	0.06	0.50
	Male	0.02	0.39	0.05
Spatial Orientation Change[b]	Yes Both Times	0.26	1.63	0.16
	Not now, but in past/yes either time	-0.64	1.54	-0.41
	Not now, but in the past Both Times	-0.38	0.60	-0.88
	Not now, but in the past, no either time	-1.30	1.47	-0.86
	Education	0.10	0.08	1.18
	Male	0.39	0.57	0.70
Number Skills Change[c]	Yes Both Times	-1.04	1.01	-1.03
	Not now, but in past/yes either time	0.50	0.95	0.52
	Not now, but in the past Both Times	-0.58	0.37	-1.57
	Not now, but in the past, no either time	1.10	0.91	1.21
	Education	0.09	0.05	1.64
	Male	0.06	0.35	0.18
Verbal Memory	Yes Both Times	-1.45	2.00	-0.72

Change[d]	Not now, but in past/yes either time	5.21**	1.89	2.77
	Not now, but in the past Both Times	-0.15	0.73	-0.21
	Not now, but in the past, no either time	2.67	1.80	1.48
	Education	-0.21*	0.10	-2.08
	Male	0.41	0.69	0.59
Verbal Ability Change[e]	Yes Both Times	-0.46	0.98	-0.47
	Not now, but in past/yes either time	-0.07	0.92	-0.08
	Not now, but in the past Both Times	0.25	0.36	0.69
	Not now, but in the past, no either time	1.04	0.88	1.18
	Education	-0.2	0.05	-0.48
	Male	0.79*	0.05	2.34
Perceptual Speed Change[f]	Yes Both Times	-0.20	1.16	-0.17
	Not now, but in past/yes either time	-1.43	1.09	-1.31
	Not now, but in the past Both Times	-0.34	0.42	-0.80
	Not now, but in the past, no either time	0.48	1.04	0.46
	Education	0.01	0.06	0.19
	Male	0.33	0.40	0.81

Notes. * $p < .05$. ** $p < .01$. *** $p = .001$.
a. $R^2 = .022$. b. $R^2 = .012$
c. $R^2 = .032$. d. $R^2 = .031$
e. $R^2 = .023$. f. $R^2 = .013$

Table 8. Hierarchical Regression Analysis of Change in BMI and Cognition with Change in Smoking Status as a Mediator in Midlife

Dependent Variable	Parameter	B	SE B	t
Inductive Reasoning Change[a]	BMI Change	-0.08	0.05	-1.54
	Smoking Both Times	-2.51*	1.13	-2.23
	Previous Smoking or Current Smoking Either Time	1.21	1.06	1.14
	Previous Smoking Both Times	-0.10	0.41	-0.25
	Previous Smoking or Never Smoked Either Time	-0.47	1.02	-0.46
	Male	0.06	0.39	0.15
	Education	0.03	0.06	0.15
Spatial Orientation Change[b]	BMI Change	0.05	0.07	0.68
	Smoking Both Times	0.26	1.64	0.16
	Previous Smoking or Current Smoking Either Time	-0.62	1.54	-0.40
	Previous Smoking Both Times	-0.39	0.60	-0.66
	Previous Smoking or Never Smoked Either Time	-1.36	1.48	-0.92
	Male	0.37	0.57	0.65
	Education	0.10	0.08	1.18
Number Skills Change[c]	BMI Change	-0.05	0.05	-1.00
	Smoking Both Times	-1.04	1.01	-1.03
	Previous	0.48	0.95	0.51

	Smoking or Current Smoking Either Time			
	Previous Smoking Both Times	-0.57	0.37	-1.54
	Previous Smoking or Never Smoked Either Time	1.16	0.91	1.27
	Male	0.08	0.35	0.24
	Education	0.09	0.05	1.64
Verbal Memory Change[d]	BMI Change	-0.17[T]	0.09	-1.90
	Smoking Both Times	-1.44	1.99	-0.72
	Previous Smoking or Current Smoking Either Time	5.15**	1.88	2.74
	Previous Smoking Both Times	-0.12	0.73	-0.16
	Previous Smoking or Never Smoked Either Time	2.91	1.80	1.61
	Male	0.49	0.69	0.72
	Education	-0.21*	0.10	-2.08
Verbal Ability Change[e]	BMI Change	0.05	0.04	1.17
	Smoking Both Times	-0.46	0.98	-0.47
	Previous Smoking or Current Smoking Either Time	-0.05	0.92	-0.06
	Previous Smoking Both Times	0.24	0.56	0.66
	Previous Smoking or Never	0.97	0.88	1.10

	Smoked Either Time			
	Male	0.76*	0.34	2.26
	Education	-0.02	0.05	-0.48
Perceptual Speed Change[f]	BMI Change	-0.14*	0.06	-2.06
	Smoking Both Times	-1.86	4.05	-0.46
	Previous Smoking or Current Smoking Either Time	1.17	3.98	0.29
	Previous Smoking Both Times	-0.06	1.62	-0.04
	Previous Smoking or Never Smoked Either Time	0.22	3.49	0.06
	Male	-0.58	1.26	-0.46
	Education	-0.04	1.20	-0.03

Notes. * $p < .05$. ** $p < .01$. *** $p < .001$. T < .06.
a. $R^2 = .026$. b. $R^2 = .012$
c. $R^2 = .034$. d. $R^2 = .037$
e. $R^2 = .025$. f. $R^2 = .020$

Youngstown
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March 23, 2015

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RE: HSRC Protocol Number: 145-2015
Title: Change in BMI and Cognition in Middle-Aged and Older Adults: The Seattle Longitudinal Study

Dear Dr. Van Dussen, et. al.:

The Institutional Review Board has reviewed the abovementioned protocol and determined that it is exempt from full committee review based on a DHHS Category 5 exemption.

Any changes in your research activity should be promptly reported to the Institutional Review Board and may not be initiated without IRB approval except where necessary to eliminate hazard to human subjects. Any unanticipated problems involving risks to subjects should also be promptly reported to the IRB.

The IRB would like to extend its best wishes to you in the conduct of this study.

Sincerely,

Dr. Scott C. Martin
Interim Associate Dean for Research
Authorized Institutional Official

SCM:cc

c: Dr. Qi Jiang, Chair
Department of Sociology, Anthropology and Gerontology