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Chronic Health Illnesses as Predictors of Mild Cognitive Impairment Among African American Older Adults

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Abstract

Approximately 5.5 million individuals are diagnosed with Alzheimer's disease (AD) dementia, a number which includes those with mild cognitive impairment and asymptomatic individuals with biomarkers of AD. There is a higher incidence of mild cognitive impairment (MCI) in African American populations as compared to White populations, even when controlling for sociodemographic factors. The existing body of ethnically/racially targeted research on MCI has been limited by few studies with the ability to generalize to African Americans communities. This study sought to examine whether medical conditions which occur at a higher rate in African American individuals increase the hazard of subsequent MCI development.

A secondary data analysis of the National Alzheimer's Coordinating Center Uniform Data Set was employed to examine the associations between health conditions (congestive heart failure, traumatic brain injury, diabetes, hypertension, hypercholesterolemia, B12 deficiency, thyroid disease) and their relationship to MCI. The analytic sample included 2847 participants with 9872 observations. Binary logistic generalized estimating equation modeling was used to examine repeated measures over the course of 1–11 observations. Education was associated with MCI development, specifically those with some college or college graduates ($p < 0.001$) and more than college ($p = 0.002$). Female sex was associated with development of MCI ($p < 0.001$). African Americans with traumatic brain injury (TBI) were more likely to develop MCI ($p < 0.001$) compared to those with no reports of a TBI. Inactive thyroid conditions decreased the risk of MCI development ($p = 0.005$) compared to those without thyroid disease.

Though vascular factors are often attributed to higher mortality and neurodegeneration in African Americans, congestive heart failure, diabetes, high cholesterol, hypertension, diabetes, nor

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seizures were associated with an increased risk of MCI development. Findings from this study provide formative data to develop targeted interventions for subsets of the African American community, including those with higher educational levels, those with TBI, and those with a history of thyroid disease. While it may not be possible to prevent MCI development, it is possible to modify lifestyle behaviors contributing to these health conditions, such as falls that are often experienced by older adults. Practitioners can increase awareness, knowledge, and resources relevant to clients.

Approximately 5.5 million individuals are diagnosed with Alzheimer's disease (AD) dementia, a number which includes those with mild cognitive impairment and asymptomatic individuals with biomarkers of AD.¹ It is well-established in the literature that ethnic minority populations have higher incidence rates of cognitive impairment, dementia, and AD compared to White populations.^{2–10} Manly and Mayeux⁵ reported a 4.2% per person-year standardized AD incidence rate for older non-Hispanic Blacks and 3.8% per person-year for Caribbean Hispanics, which was significantly higher than that of non-Hispanic White individuals, while controlling for educational disparities that may exist among these populations. An increase in education is linked to cognitive reserve, in which the brain of more highly educated individuals is hypothesized to be able to withstand more pathology than those with more limited education.^{11–13}

According to the World Health Organization International Classification of Diseases (ICD) 10 criteria,¹⁴ AD is identified by either the onset or rapid progression of reading and writing difficulty, aphasia, apraxia, as well as difficulty with comprehending, learning, and recalling new information. A condition commonly identified as a risk of AD is mild cognitive impairment (MCI). MCI is characterized by mild, noticeable, and measurable changes in the individual's thinking capabilities in performing daily activities.¹⁵ Tabert et al.¹⁶ concluded that MCI related decline in verbal memory, psychomotor speed, and executive function may predict AD development. Therefore, it remains critical to continue to investigate possible relationships to better understand how to potentially slow the pathophysiological AD progression. However, the existing body of ethnically/racially targeted research on MCI has been limited by few studies with the ability to generalize to African American communities. The prevalence of MCI is lower among non-Hispanic White individuals as compared to African Americans,¹⁷ with some studies reporting rates at 19.1% vs. 27.3%, respectively.¹⁸ In fact, with controls for mediating variables such as level of education and literacy, the higher incidence of MCI remains statistically significant in African American populations as compared to White populations.¹⁹

The differences in risks between racial groups may be attributed to disparities in lifestyle, health, and socioeconomic status.^{19–21} The impact of these differences might also be explained by health conditions that are more prevalent among African Americans, which increase the risk of MCI development. These health conditions include: seizures, traumatic brain injury, thyroid disease, diabetes, hypertension, hypercholesterolemia, B12 deficiency, and congestive heart failure.²⁰

African Americans are more likely to experience seizures than White individuals (Bautista & Jain, 2011). Seizures are often associated with epilepsy.^{22,23} In addition, among U.S.

Medicare beneficiaries, older than 65 years of age, the average incidence rates of seizures were highest in the African American population (4.1 per 1000) compared to the White population (2.3 per 1000).^{24,25} compared the neuropsychological test results of seniors with epilepsy, seniors with MCI, and normal seniors and found that seniors undergoing antiepileptic polytherapy (AEDp) demonstrated the most severe cognitive impairments, which suggests that African Americans may be at risk for significant cognitive impairments. Seizures are a potential consequence of TBI.²⁶ More than two-thirds of TBIs in adults over the age of 65 years are caused by falls²⁷ and African Americans have the highest rates of TBI compared to any other population.²⁸ In fact, African American men are 1.5 times more likely to experience a TBI than African American women.²⁹ Evidence indicates that TBI has also been linked to an increased risk of MCI.^{30,31} Survivors of TBI may suffer neurological deficits, short and long term brain damage, cognitive, and behavioral and emotional impairments. Neurological deficits in cognition are due to atrophy of hippocampus and damage of white matter tract.³² There is also evidence to indicate that β -amyloid peptide ($A\beta$) may be deposited in the brain at higher or faster rates in reaction to brain injury,³³ though the role of $A\beta$ in the development and progression of MCI remains under debate.

Two other conditions associated with TBI are thyroid disease and diabetes.^{34–38} TBI may cause hormone problems at any point after the injury and can injure the pituitary gland and the hypothalamus, components of the endocrine system. This possibly results in hypothyroidism subsequently occurring whereas diabetes is a problem that can occur immediately after the TBI.

The prevalence of mild thyroid disorder is higher in White non-Hispanic individuals (5.8% as compared to African Americans (1.2%).³⁹ Literature indicating the rate of thyroid disease by race and ethnicity is largely unavailable, though many reports indicate that while thyroid cancer occurs at a lower rate in African Americans, their five-year survival rate is lower than that of White non-Hispanic individuals. In addition, a higher rate of anaplastic thyroid cancer, follicular cancer and an increased size of tumors associated with these cancer subtypes.⁴⁰ Existing research on the association between thyroid disease and MCI is divided. Kalmijn et al.⁴¹ reported an association between subclinical hyperthyroidism among the elderly and increased risk of AD dementia after controlling for differences in age, sex, atrial fibrillation, or potential other confounders, while Park et al.⁴² observed no association between thyroid disease and decreased scores on neuropsychological tests.

Diabetes is a well-recognized condition among African Americans, as African Americans are 1.7 times more likely to develop diabetes than non-Hispanic White individuals. Though Type 1 diabetes is more common in White individuals, Type II diabetes is 1.4–2.3 times more likely to occur in African Americans.⁴³ Diabetes increases the risk of many serious health conditions, and is linked to cognitive decline.⁴⁴ Roberts et al.⁴⁵ reported an association between type 2 diabetes and an increased risk of MCI. In addition to an association between diabetes, resulting vascular changes, and cognitive dysfunction, Sims et al.⁴⁶ noted an association between poor cardiovascular health and decreased cognitive function. In light of mounting evidence of the aforementioned associations, Sims et al.⁴⁶ specified that, “blood pressure is a significant predictor of performance on measures of executive function, working memory, attention, verbal learning, mental status, visual

tracking, speed of information processing, and reasoning:" a finding consistent with Saxby et al.⁴⁷ and Waldstein et al.⁴⁸ Hypertension is the most important risk factor for cardiovascular diseases, which include congestive heart failure, hypocholesterolemia, and dementia.^{49,50}

Hypertension disproportionately affects African Americans, in all age groups, including elderly adults.^{51,52} Forty-one percent of African American men and 45% of African American women over the age of 20 are diagnosed with hypertension.⁵³ and hypertension is associated with MCI.⁵⁴ Sierra et al.⁵⁴ report that the pathways to explain hypertension-related cognitive changes are not yet fully understood although high blood pressure, particularly among older adults, is linked to cognitive decline and dementia. Reitz et al.⁵⁵ indicate that a history of hypertension is associated with a higher risk of MCI and in fact, the relationship is stronger with non-amnesic MCI compared to amnesic MCI. Recently,⁵⁶ found that rennin-angiotensin system anti-hypertensives, which cross the blood-brain-barrier, led to a delayed progression from MCI to AD among African Americans. This effect was noted in the same study population as utilized for the current investigation.

African American individuals have the highest risk of congestive heart failure (CHF) in the United States.⁵⁷ Even among younger cohorts (18–30 years of age), the prevalence of CHF among African Americans is 20 times that of non-Hispanic White individuals. This increase in risk is largely due to other prevalent factors discussed herein, such as hypertension.⁵⁸ MCI is one of the most common conditions among older adults with CHF with incidence rates varying from 25% to 70–80% depending on demographics and the severity of the disease and measures utilized to assess cognition.^{59,60} Other evidence^{61,62} suggests that MCI is prevalent among African Americans with CHF.

Hypercholesterolemia, or elevated serum cholesterol, is not only associated with thyroid conditions, but also cardiovascular conditions.⁶³ African Americans have the highest levels of hypercholesterolemia compared to White individuals.⁶⁴ Hypercholesterolemia in midlife reportedly contributes to an increased risk of MCI later in life.⁶⁵

Elevated levels of homocysteine are a risk factor for heart disease and empirical evidence suggests that adequate amounts of B12 may help keep homocysteine levels low.⁶⁶ Evidence indicates that African Americans have a better B12 health status than White individuals, although the reasons for this are not clear.⁶⁷ However, due to the high rates of heart disease among African Americans and the possible association to elevated levels of homocysteine, research warrants examining the role of B12 in this investigation. Further, research indicates that low folate and B12 levels combined with high levels of homocystein significantly increase the risk of MCI and AD.^{68,69} In addition, preliminary studies have demonstrated the potential efficacy of homocystein-lowering B12 treatment in slowing the onset of cognitive impairment, a relationship that supports the need for further research.⁷⁰

Other studies suggest that under-diagnosis of MCI, as well as other diseases that may contribute to MCI diagnoses, may be more prevalent among African American individuals. Additionally, African Americans are less likely to seek medical attention for MCI symptoms, which can be attributed to feelings of mistrust and fear of discrimination in

healthcare treatment.⁷¹ Furthermore, African Americans are less likely to seek medical attention for illnesses that have been linked to the possible development of MCI.⁷² Whether it is an illness that has been linked to MCI, or symptoms of MCI specifically, under-diagnosis continues to be an issue for African Americans. Thus, the purpose of this study is to examine common chronic health conditions that have been associated with MCI for African Americans, and their relationship to MCI.

METHODS

A secondary data analysis of the National Alzheimer's Coordinating Center (NACC), Uniform Data Set (UDS) was employed to examine the associations between health conditions (congestive heart failure, traumatic brain injury, diabetes, hypertension, hypercholesterolemia, B12 deficiency, thyroid disease) and their relationship to MCI. The NACC UDS is a NIA-funded repository for the data collected at each of the ADCs.⁷³ Observations from yearly visits by participants to one of 34 Alzheimer's Disease Centers (ADCs) between September 2005 to December 2015 were examined. The data file was split and only African American participants were included in the current analysis. Mild cognitive impairment (MCI) was the dependent variable in all analyses. MCI included amnesic and non-amnesic types, and was a categorical variable indicating the presence or absence of the condition. MCI was diagnosed following a complete physical and neuropsychological exam by a physician or a consensus from the respective team working with the participant. Additional information about the NACC UDS is well-reported by Beekly et al.⁷⁴ and described in detail on the NACC website.⁷³

Health conditions were examined in relation to MCI development, and were independent variables. Information on health conditions are self-reported by participants and/or informants, who are required to accompany participants to yearly visits. The conditions included in the analysis were: seizures, traumatic brain injury (TBI), thyroid disease, diabetes, hypertension, high cholesterol, B12 deficiency, and congestive heart failure. TBI required a response of yes or no, indicating the presence of an existing TBI. Participants were required to state whether the following health conditions were absent, remote or inactive, or recent and active: Seizures, thyroid disease, diabetes, hypertension, high cholesterol, B12 deficiency, and congestive heart failure. Age, sex, and education were also entered into the models as main effects (Table 1), and as covariates (Table 2, Model 2 and all three models in Table 3). Age was recoded to the following ranges: 38-64, 65-75, 76-84, and 85-101 years. Education was recoded as less than high school, high school, some college/college, more than college. Biological sex included men and women.

A chi-square analysis was performed to examine the distribution of cases with respect to the absence and presence of MCI. The sample size corresponding to each level of each independent variable, and for the absence and presence of MCI was calculated. Further, using an alpha of 0.05, the statistical relationship of health condition or demographic variable was calculated.

Binary logistic generalized estimating equation modeling was used to examine repeated measures in an analytic sample of 2847 African American men and women. After main

effects were determined, all subsequent analyses were adjusted for age, sex, and education. These first two models are displayed in Table 2. Table 3 displays the results for the statistically significant health conditions from Table 2, as they are entered into their own models as independent factors, and when held constant. All analyses in Table 3 are adjusted by age, sex, and education. All independent variables were tested for multicollinearity using both the Variance Inflation Factor (VIF) and Tolerance statistic. None of the tolerance values were below .2, and in fact, all ranged from .904 to .984. The VIF ranged from 1.008 to 1.106; far below the generally used cut-off of 10,⁷⁵ or even a more conservative cut-off of 4.⁷⁶

RESULTS

There were 2847 participants with 9872 observations. The range of visits was between 1 and 11, with a mean of 3.11 visits (SD: 2.120). The minimum observed time to MCI diagnosis was 224 days, and the maximum was just over 10 years.

The initial chi-square analysis examined the level of independence of each independent variable across the two levels of the dependent variable: MCI present or MCI absent. A statistically significant relationship was found between sex and MCI, $X^2(1, N=9872) = 51.743, p = .000$, age and MCI $X^2(3, N=9872) = 11.578, p = .009$, as well as education and MCI $X^2(3, N=9872) = 82.219, p = .000$. Among the biological conditions predictors, there was a statistically significant relationship between seizures and MCI $X^2(2, N=9391) = 14.024, p = .001$, TBI and MCI $X^2(2, N=9362) = 59.506, p = .000$, diabetes and MCI $X^2(2, N=9368) = 11.513, p = .003$, and as thyroid disease and MCI $X^2(2, N=9374) = 23.969, p = .000$. Hypertension, high cholesterol, B12 deficiency, and congestive heart failure were not statistically related to MCI absence nor presence.

Binary logistic generalized estimating equation modeling was used to examine repeated measures over the course of 1–11 observations. All health conditions and covariates were added into the first model. In Table 2, the results of the full main effects and adjusted models are displayed. Education was associated with decreased MCI development, specifically those with some college or college graduates ($p < .001$; 95% CI $-.861$ to $-.302$) and more than college ($p = .002$; 95% CI $-.637$ to $-.139$). Female sex was associated with development of MCI ($p < .001$; 95% CI $-.483$ to $-.117$), though age was not. African Americans with TBI were more likely to develop MCI ($p < .001$; 95% CI $.328$ to $-.840$) compared to those with no reports of a TBI. Inactive thyroid conditions decreased the risk of MCI development ($p = .005$; 95% CI -1.05 to $-.190$) compared to those without thyroid disease. Though vascular factors are often attributed to higher mortality and neurodegeneration in African Americans, congestive heart failure, diabetes, high cholesterol, hypertension, diabetes, nor seizures were associated with an increased risk of MCI development.

DISCUSSION

This study sought to examine the associations between health conditions common among African Americans and MCI development. Through an analysis of observations obtained from African American participants presenting to ADCs throughout the United States,

findings indicated that TBI and inactive thyroid conditions along with education and sex are factors that can contribute to MCI development partially supporting our hypotheses that all chronic health conditions would be associated with MCI.

Not surprising was the evidence supporting the relationship between TBI and MCI development. African Americans have the highest rate of death from traumatic brain injury. These findings support that for those reporting a TBI, the risk of MCI development was elevated. As discussed earlier, evidence indicates that African Americans are more likely than White individuals to suffer multiple TBIs in their lifetime, to suffer TBI due to violence, and to have worse functional outcomes after TBI due to underdiagnoses, lack of appropriate care, not seeking care.^{77–79} TBI has functional effects that impact cognitive domains that are known to be linked to dementia, including thinking, language, and emotion.⁸⁰ Barnes et al.⁸¹ reported an additive association between TBI and other conditions and the risk of dementia. “TBI in older veterans was associated with a 60% increase in the risk of developing dementia over 9 years after accounting for competing risks and potential confounders.”⁸¹ LoBue et al.³¹ highlighted an increasingly prevalent hypothesis “that TBI activates a neurodegenerative process which may interact with age and other factors over time.” Furthermore, TBI causes short-term disorientation, loss of memory, loss of learning ability, and comprehension difficulty, all of which are symptoms of chronic traumatic encephalopathy (CTE), mild cognitive impairment, and other forms of dementia.⁸² Incidence of TBI has been linked to dementia, but more research is needed to fully explain the strength of the relationship and its dependence on other variables such as genetics, number of TBIs, and severity of TBIs. Furthermore, as discussed earlier, falls are a risk factor for TBI. Falls are common among older adults. In this age cohort, falls are the top cause of fatal injury, and are the most common factor in non-fatal trauma hospitalizations among older adults.⁸³

Given this relationship in this investigation, it is increasingly critical to not only identify TBI early and often particularly for African American populations most at risk, but to consider environmental changes that contribute to the prevalence of TBI. For example, practitioners should work together (physicians, social workers, gerontologists) to prevent falls in older adults by ensuring that the necessary modifications in their homes are in place.

Findings from this investigation contribute to the mixed evidence on the relationship between thyroid disease and MCI development. Extant literature indicates that hypothyroidism is associated with an increased risk of death in African Americans but not in White older adults.⁸⁴ Therefore, we expected that there would be a relationship. Findings from the study reported here suggest that hypothyroidism does not increase risk for MCI. In fact, a history of thyroid disease may be associated with a protective advantage with respect to MCI as an endpoint. Kalmijn et al.⁴¹ demonstrated that reduced thyroid-stimulating hormone (TSH) levels at baseline produced a more than threefold increased risk of dementia (RR 3.5, 95% CI: 1.2 ± 10.0) and Alzheimer’s disease (RR 3.5, 95% CI: 1.1 ± 11.5), after controlling for age and sex. Furthermore, statistically significant, but clinically irrelevant associations were found between TSH levels and anxiety and cognition.⁸⁵ Osterweil et al.⁸⁶ reported an association between hypothyroidism in non-demented older adults and impairments in certain cognitive categories such as “learning, word fluency, visual-spatial

abilities, and some aspect of attention, visual scanning, and motor speed” (p. 325). The statistical significance of the aforementioned association(s) depends on the severity of T4 hypothyroidism.⁸⁶ Further research exploring the potential protective effect of a history of thyroid disease, including the possible role of anti-thyroid medication,⁸⁷ should be explored to understand the mechanism driving this association with MCI.

The finding that African Americans with more education have a higher risk of MCI development compared to those with lower educational levels, is inconsistent with the literature,^{88,89} which suggests that the cognitive and neurological reserves have a protective effect on MCI development. A possible reason for this finding may have to do with cumulative disadvantage theory that suggests that compounding effects of early disadvantages in resources produce trajectories of health that over time differ with age. Specifically, the number of possible risk factors (e.g., health behaviors, socioeconomic status) for declining health problems and possible risk factors for MCI development – although not significant in this investigation (e.g. hypertension, diabetes) – outweigh the high educational status. There is some evidence⁹⁰ that for every year past the average level of education (approximately 13 years), African Americans experienced a health deficit that increased with age. While there is no evidence to support this with MCI, it is a possible hypothesis worth further research. The other possibility is to consider the role of health literacy. It is critical to be able to accurately assess populations with lower education levels for cognitive decline. In fact, there is an association between low educational levels and low health literacy.⁹¹ Recent evidence suggests that cognitive tests should be adapted to accurately measure cognitive levels among lower educated populations.⁹² Furthermore, poor cognitive function may affect health literacy and poor cognitive function is established as a risk factor for individuals with diabetes. While not significant in this investigation, cognitive function is associated with health literacy in older adults with diabetes.⁹³ Thus, efforts to accurately assess cognitive decline among all literacy levels remains crucial to truly understand the role of education in the development of MCI. Finally, consistent with empirical evidence,^{94,95} females were more likely than males to experience an increased risk of MCI development. Some reasons for the gender differences include longer life expectancy of women, socio-cultural factors⁹⁵ and a neurobiological vulnerability.⁹⁶ Men may die earlier due to causes of complications of MCI and eventually AD.⁹⁷ This persistent finding among this investigation and others increases the need for sex-specific research and interventions to better understand how to slow the process of MCI and AD progression among women.

Limitations to this study exist. This secondary data analysis utilized a data set of more than 34,000 individuals from 34 ADCs across the United States. Even still, this is not a nationally representative sample and is best characterized as a clinical case series of voluntary participants from each ADC. Association studies of this nature rely on survey data, which increases the power and sample size for analysis, but does not allow for an independent look at laboratory results. Recruitment methods, requirements for participation, and data collection protocols vary by ADC, which may affect consistency and generalizability. While this study focused on MCI among African American participants, the results cannot be generalized beyond the scope of these participants due to the aforementioned limitations. Further studies are needed to determine whether these results occur in a nationally

representative sample. The current study can serve as a strong justification for such studies given the robust measures and sizeable sample size.

Despite the limitations, the strengths of this investigation are the ability to look at intra-racial differences. There is increasing recognition about the intra-group differences that exist among ethnic and minority populations.^{98,99} Targeted interventions should not be universal to one population, but specific to the needs of groups of individuals within a population. Given the dearth of evidence to understand MCI development and potentially AD in African Americans, findings from this study provide formative data to develop targeted interventions for subsets of the African American community, including those with higher educational levels, those who are (male/female), those with TBI or the potential for TBI, and those with a history of thyroid disease. While it may not be possible to prevent MCI development, it is possible to modify lifestyle behaviors that contribute to these health conditions, such as falls that are often experienced by older adults. Practitioners can increase awareness, knowledge, and resources relevant to clients. Assistive mobility devices as well as healthcare options for mobility and vision related care are particularly important to the elderly. Basic home maintenance and recreational safety education can also help to decrease the incidence of falls which may lead to TBI and thus dementia.⁸² In addition, improving healthcare utilization among African Americans is crucial given the substantial literature suggesting that African Americans have decreased healthcare service utilization for medical conditions,¹⁰⁰ and a decrease in quality of healthcare can contribute to quicker cognitive declines. Practitioners can continue to work diligently to identify and treat TBI early and increase awareness about the role of thyroid disease in MCI development.

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Table 1

Chi-square analysis of predictors and covariates.

Parameters	MCI Present		MCI Absent		Chi-Square	df	P
	N	%	N	%			
Sex					51.743	1	.000
Female	5789	22.1	5789	77.9			
Male	714	29.3	1726	70.7			
Education					82.219	3	.000
More than college	406	19.1	1716	80.9			
Some college	929	22.1	3272	77.9			
High School	667	28.3	1700	71.8			
Less than high school	355	30	827	70			
Age					11.578	3	.009
38–64 years	305	24.6	934	75.4			
65–75 years	924	22.6	3168	77.4			
76–84 years	846	25.7	2443	74.3			
85–101 years	282	22.5	970	77.5			
Congestive Heart Failure					3.912	2	.141
Absent	2189	24.5	6740	75.5			
Remote/Inactive	27	17.9	124	82.1			
Recent/Active	67	22.9	226	77.1			
Seizures					14.024	2	.001
Absent	2220	24.1	6974	75.9			
Remote/Inactive	43	30.3	99	69.7			
Recent/Active	24	43.6	31	56.4			
Traumatic Brain Injury					59.506	1	.000
No	2003	23.3	6581	76.7			
Yes	278	35.7	500	64.3			
Diabetes					11.513	2	.003
Absent	1550	23.6	5020	76.4			

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Parameters	MCI Present		MCI Absent		Chi-Square	df	P
	N	%	N	%			
Remote/Inactive	49	33.3	98	66.7			
Recent/Active	684	25.8	1967	74.2			
Hypertension					1.674	2	.433
Absent	440	23.3	1451	76.7			
Remote/Inactive	76	23.9	242	76.1			
Recent/Active	1773	24.7	5409	75.3			
Hypercholesterolemia					2.514	2	.285
Absent	869	23.6	2814	76.4			
Remote/Inactive	118	23.5	384	76.5			
Recent/Active	1288	25	3864	75			
B12 deficiency					4.769	2	.092
Absent	2130	24.6	6534	75.4			
Remote/Inactive	48	18.7	209	81.3			
Recent/Active	82	23.9	261	76.1			
Thyroid disease					23.969	2	.000***
Absent	1969	25	5918	75			
Remote/Inactive	48	13.8	300	86.2			
Recent/Active	261	22.9	878	77.1			

Row percents are Displayed, df = degrees of freedom.

* p < .05,
** p < .01,
*** p < .001.

Table 2

Main and Adjusted Effects for All Possible Biological Factors Related to MCI Development using Generalized Estimating Equations.

Parameter	Model 1 (Main effects for Predictors) n = 2847				Model 2 (Main effects, Adjusted) n = 2847			
	B	SE	p	95% CI	B	SE	p	95% CI
Intercept	-.680	.1734	.000	-1.02 – -.340	-.121	.2432	.620	-.597 – -.356
Sex	-.300	.0934	.001	-.483 – -.117	-.297	.0933	.001	-.479 – -.114
Education ^a					-.220	.0432	.000	-.305 – -.136
More than college	-.582	.1426	.000	-.861 – -.302				
Some college	-.388	.1272	.002	-.637 – -.139				
High School	-.066	.1328	.621	-.326 – .195				
Age ^b					.001	.0447	.976	-.086 – .089
65–75 years	.077	.1093	.482	-.291 – .137				
76–84 years	.062	.1190	.602	-.171 – .295				
85–101 years	-.129	.1474	.382	-.418 – .160				
Congestive Heart Failure								
Remote/Inactive	-.377	.3202	.239	-1.01 – .250	-.402	.3237	.214	-1.04 – .233
Recent/Active	-.156	.2239	.485	-.595 – .283	.187	.2252	.406	-.629 – .254
Seizures								
Remote/Inactive	.316	.2784	.256	-.229 – .862	.331	.2753	.230	-.209 – .870
Recent/Active	-.754	.4336	.082	-.095 – 1.60	-.721	.4296	.093	-.121 – 1.56
Traumatic Brain Injury	.584	.1305	.000	.328 – .840	.590	.1308	.000	.333 – .846
Diabetes								
Remote/Inactive	.495	.2925	.091	-.079 – 1.07	.503	.2921	.085	-.069 – 1.08
Recent/Active	.056	.0932	.546	-.126 – .239	.056	.0931	.551	-.127 – .238
Hypertension								
Remote/Inactive	-.021	.1866	.909	-.387 – .344	-.037	.1874	.845	-.404 – .331
Recent/Active	.012	.1004	.908	-.185 – .208	.014	.1005	.893	-.183 – .211
Hypercholesterolemia								
Remote/Inactive	.036	.1605	.823	-.279 – .350	.039	.1606	.810	-.276 – .353

Parameter	Model 1 (Main effects for Predictors) n = 2847				Model 2 (Main effects, Adjusted) n = 2847			
	B	SE	p	95% CI	B	SE	p	95% CI
Recent/Active	-.057	.0871	.515	-.114 – .228	.059	.0871	.501	-.112 – .229
B12 deficiency								
Remote/Inactive	-.300	.2617	.252	-.813 – .213	-.324	.2612	.215	-.836 – .188
Recent/Active	-.100	.1713	.558	-.436 – .235	-.105	.1707	.540	-.439 – .230
Thyroid disease								
Remote/Inactive	-.631	.2181	.004	-1.06 to -.203	.620	.2196	.005	-1.05 to -.190
Recent/Active	-.040	.1202	.738	-.276 – .195	.025	.1208	.839	-.261 – .212

DV: MCI.

^aCompared to less than high school.

^bCompared to 38–64 year olds.

Table 3

Generalized estimating equations for statistically significant parameters in full model.

Parameter	Model 1 – TBI only, adjusted Total sample: n = 2908 TBI present: n = 778 (8.3%)				Model 2 – thyroid only, adjusted Total sample: n = 2912 Remote/Inactive: n = 348 Recent/Active: n = 1139				Model 3 – Both TBI and Thyroid n = 2898			
	B	SE	p	95% CI	B	SE	p	95% CI	B	SE	p	95% CI
Intercept	.011	.2295	.963	-.439 – .460	.140	.2262	.536	-.303 – .583	.002	.2304	.992	-.449 – .454
Sex	-.331	.0913	.000	-.510 to -.152	-.355	.0914	.000	-.534 to -.176	-.314	.0924	.001	-.495 to -.132
Education	-.230	.0423	.000	-.313 to -.148	-.228	.0424	.000	-.311 to -.145	-.231	.0425	.000	-.315 to -.148
Age	-.001	.0434	.974	-.086 – .084	-.011	.0436	.807	-.096 – .075	-.001	.0435	.975	-.087 – .084
Traumatic Brain Injury	-.558	.1284	.000	.306 – .810	–	–	–	–	.556	.1291	.000	.303 – .809
Thyroid disease												
Remote/Inactive	–	–	–	–	.663	.2261	.003	–	-.665	.2230	.003	–1.10 to -.228
Recent/Active	–	–	–	–	.035	.1191	.772	–	-.028	.1191	.812	-.262 – .205

DV: MCI.