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Racial Differences in Cognitive Function and Risk of Incident Stroke

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Abstract

Background and Purpose—Cognitive impairment is associated with increased risk of stroke; however, it is not known whether this association varies by race. Our objective was to examine the association of cognitive function with the risk of stroke among non-Hispanic blacks and whites with no history of stroke.

Methods—Participants were from a population-based cohort study of 7,205 older adults (61% black and 59% female) from Chicago's South Side. A standardized composite cognitive function score based on three components—global cognition (Mini-Mental State Examination), executive function (Symbol Digits Modalities test), and episodic memory (Delayed and Immediate Story Recall tests) – was used to predict risk of stroke (from Medicare hospitalization data) using a Cox model.

Results—During 72,868 person years of follow-up, 16% (N=1,185) developed stroke. After adjusting for vascular risk factors, one standard deviation lower composite cognitive function score was associated with increased risk of stroke in blacks (HR=1.76, 95% CI, 1.66 – 1.88), which was two-fold higher than whites (HR=1.38, 95% CI, 1.26 – 1.55) ($P_{\text{difference}}=0.002$). Lower global cognition and executive function were associated with a similarly increased risk of stroke in blacks and whites. Lower episodic memory (composite of recall tests) was associated with increased risk of stroke that was two-fold higher in blacks (HR=1.12, 95% CI, 1.10 – 1.14) than whites (HR=1.06, 95% CI, 1.04 – 1.09).

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Conclusions—Lower cognitive function was associated with increased risk of stroke and this association was stronger among blacks than whites. Future studies are needed to determine factors that can explain this finding.

Keywords

Cognitive Function; Stroke; Epidemiology; Minority Health

INTRODUCTION

The incidence of stroke in non-Hispanic blacks (blacks hereafter) is four times that of non-Hispanic whites (whites hereafter) with the difference declining with age.¹ Prevalence of major risk factors for incident stroke, including high blood pressure, obesity, and diabetes, is higher in blacks.² Cognitive impairment has been shown to be a potential risk factor for stroke in older adults, even after controlling for vascular risk factors, most probably due to unrecognized or silent vascular disease that is associated with cognitive impairment, such as white matter lesions, infarcts, and cerebral microbleeds.³ Blacks have lower cognitive function across several domains compared to whites,^{4–6} which may serve as a marker for future stroke and vascular dementia.^{7–10}

Several cohort studies have examined the association of cognitive impairment and incident stroke in mostly white populations. Global cognitive function was most consistently associated with increased risk of stroke.^{11–18} However, findings for memory, executive function, and language domains were generally mixed, as some prospective studies reported these domains associated with stroke risk,^{19–21} whereas others reported no significant association.^{17,22–23} Some of the differences in findings can be attributed to heterogeneous cognitive assessments, differences in stroke assessments, population variability, and thresholds for risk estimates. However, meta-analyses of several of these studies suggest that cognitive impairment across various domains is associated with risk of stroke.^{24–25} Due to the lack of heterogeneity in prospective studies from mostly white populations; it is not clear from the current literature which of the cognitive domains increases stroke risk, or whether the risks are different between blacks and whites.

To fill this gap in research, we used a prospective cohort of older adults followed over an average of 10.1 years from the Chicago Health and Aging Project (CHAP). The objectives of this investigation were to examine the association between standardized composite cognitive function scores and the risk of incident stroke in blacks and whites, and the association of global orientation and cognitive function (MMSE), executive function (Symbol Digits Modalities test), and episodic (Delayed Story Recall and Immediate Story Recall tests) raw test scores with stroke in blacks and whites, while controlling for vascular risk factors.

METHODS

Participants

Data for this investigation came from a population-based sample of older adults from the Chicago Health and Aging Project (CHAP), a biracial, longitudinal study of Alzheimer's disease and other common health conditions among adults 65 years or older performed from 1993–2012.^{26–27} The CHAP study was performed in four adjacent neighborhoods on Chicago's South Side. The interviews were conducted in the participants' homes in approximately three-year cycles during which time cognitive and self-reported stroke assessments were made. In addition to in-home interviews, electronic medical records from Medicare for all those enrolled during this period were collected.

The original sample included 10,801 participants at baseline, of whom 1,220 were excluded due to previous stroke history. Cognitive function test scores for those with previous history of stroke were significantly lower than the current study sample ($P<0.0001$). Of the remaining 9,581 participants, 115 did not provide cognitive function scores on at least one of the domains, 532 had missing vascular risk factors, and another 1,729 had no incident stroke data; these participants were thus excluded from our analysis. Participants with no incident stroke data (excluded from our study) also had lower composite cognitive function test scores compared to those included in this study ($P<0.0001$).

Cognitive Function Tests

Composite cognitive function was evaluated using a battery of four tests including two tests of episodic memory (Immediate and Delayed Story Recall) derived from the East Boston Memory Story [range: 0–12];^{28–29} a test of executive functioning and perceptual speed (Symbol Digits Modalities test [range: 0–75])³⁰ and a test of general orientation and global cognition (Mini-Mental State Examination [range: 0–30]).³¹ All four tests loaded on a single factor that accounted for about 75% of the variance. Hence, a composite standardized measure of cognitive function based on all four tests was created.³² Composite score averages the four tests together after centering and scaling to the baseline mean and standard deviation. A participant whose performance matches the average participant at baseline has a composite cognitive score of 0, and a person who performs one SD better than average on every test has a composite cognitive score of +1. Cognitive tests of executive function were based on raw symbol digits modalities test, global cognition on MMSE, and episodic memory on the average of the two recall test scores.

Demographic, Lifestyle, Cardiovascular, and Health Risk Factors

We included demographic variables, such as age (measured in years and centered at 75), sex (males or females), and education (measured in number of years of schooling completed, centered at 12). Health and lifestyle measures of body mass index (kg/m^2), heart disease, diabetes, systolic blood pressure, diastolic blood pressure, smoking status (former smoker and current smoker vs. never smoked), physical activity (total minutes of walking, jogging, yard work, dancing, calisthenics, or general exercise), and daily alcohol consumption (grams of alcohol per day) were also incorporated in the regression models. All covariates were

measured at baseline, and have been shown in previous studies to be associated with stroke risk.

Stroke Assessments

All CHAP participants were aged 65 or older, and therefore qualified for reimbursement for medical services by the Center for Medicare and Medicaid Services (CMS). We ascertained stroke from linkage to Medicare enrollment and claims data through December 31, 2009. We excluded participants from our analysis for incident stroke any time during follow up when they were actively involved in a health maintenance organization (HMO), since they would not simultaneously be enrolled in Medicare during those periods. We also excluded participants with previous history of stroke at baseline using Medicare stroke-hospitalization history, and a positive response to the self-reported question, “Have you ever been told by a doctor, nurse, or therapist that you had a stroke or brain hemorrhage?” After excluding participants for previous history of stroke and missing vascular risk factors, 90% were enrolled in Medicare and 10% in HMOs. Stroke was coded using ICD-9 codes,³³ with about 91% ischemic and the remaining 9% hemorrhagic. Our main outcome measure was hospitalization for ischemic or hemorrhagic stroke.

Statistical Analysis

Descriptive analysis was performed using means and standard deviations for continuous measures, and frequencies and proportions for categorical measures. We performed univariate comparisons for race differences using two-sample independent t-tests and a chi-squared test statistic with 1 degree of freedom. We used Cox proportional hazards regression models to estimate relative risk of time since initial assessment to time of stroke hospitalization. Our models were stratified by race. Separate regression models were performed for standardized composite cognitive function, and raw scores from each individual cognitive domain to assess the risk of stroke after adjusting for the aforementioned demographic, lifestyle, cardiovascular, and health-related risk factors. Racial differences in relative risk estimates were tested using a two-way interaction of indicator for blacks with composite and individual cognitive domains. All regression models were fitted using survival package in R software.³⁴

RESULTS

The average age of participants was 72.5 (SD=6.5) years. The sample included a higher proportion of blacks (61%) and females (59%), with an average education of 12.4 years. Descriptive cognitive, lifestyle, cardiovascular, and health characteristics stratified by race are shown in Table 1. In general, blacks were younger, had less education, and reported more adverse health conditions than whites. Blacks also showed significantly lower composite and individual cognitive function test scores than whites ($p<0.0001$).

The overall incidence of stroke was about 16% ($N=1,185$) during 72,868 person years of follow up. The average age at incident stroke was 79.7 years (95% CI, 79.5–79.9), which was about three years lower in blacks than in whites ($p<0.0001$). Participants who developed stroke were older with slightly less education and higher systolic blood pressure, and had

higher self-reports of heart disease and diabetes (Table 2). Participants who developed stroke during follow-up had significantly lower composite and individual cognitive function components at baseline than those who were free of stroke.

Composite Cognitive Function

The demographic and health-adjusted race-specific Cox models are presented in Table 3. Complete risk factor adjusted models are presented in Supplemental Table I. For every standard deviation (SD) lower the composite cognitive function, the risk of incident stroke increased by 76% among blacks (HR=1.76, 95% CI, 1.66–1.88, $p<0.0001$) and by 38% among whites (HR=1.38, 95% CI, 1.24–1.51, $p<0.0001$). The relative risk of incident stroke was about twice as high for every unit lower the composite cognitive function test score among blacks than whites ($p=0.002$).

Individual Cognitive Tests

For individual tests of cognitive function, risk-factor-adjusted relative risks are presented in Table 3. Complete risk-factor-adjusted Cox models for each cognitive test are presented in Supplemental Tables II, III, and IV. For a one-point-lower executive function, blacks and whites had similar risks of incident stroke, each with an increase in relative risk of 2% (HR=1.02, 95% CI=1.01–1.03, $p=0.0001$); therefore, a participant with a 5-point-lower executive function had an incident stroke risk about 10% higher. No racial difference in the association of executive function and stroke was observed.

We also found a significant association between MMSE and risk of incident stroke among blacks (HR=1.07, 95% CI, 1.05–1.09, $p=0.003$) and whites (HR=1.05, 95% CI, 1.03–1.07, $p=0.008$). Although the increase in relative risk was slightly elevated among blacks, it was not statistically significantly different than the risk observed among whites ($p=0.24$).

For every point lower combined raw test scores in episodic memory, the risk of incident stroke increased by 12% among blacks (HR=1.12, 95% CI, 1.10 – 1.14, $p<0.0001$), and by 6% among whites (HR=1.06, 95% CI, 1.04 – 1.09, $p=0.002$). We found significantly higher relative risk among blacks than whites for episodic memory ($p=0.004$). The risk of stroke for one-point-lower episodic memory among blacks (and 2-point-lower among whites) was similar to a 6-point-lower executive function and 2-point-lower global cognition.

DISCUSSION

The findings of this study support the hypothesis that composite cognitive function, individual domains of global cognition, executive functioning, and episodic memory are strongly associated with an elevated stroke risk among older blacks and whites. While the findings among whites confirm previous prospective studies that showed that domains of cognitive function are associated with subsequent stroke event.^{11–25} Our study identified that composite cognitive function, mostly due to episodic memory, was associated with about twice the relative risk of incident stroke among blacks compared to whites. This finding has not been previously reported in the literature, and might be of considerable interest for future research.

Increased risk of incident stroke in association with cognitive impairment in blacks compared to white may be explained by several possible mechanisms. Blacks with cognitive impairment may be more likely to have unrecognized vascular cognitive impairment or mixed dementia, reflecting a higher burden of vascular risk factors, and therefore be at higher risk of major stroke event. Indeed, risk factors, such as, systolic BP, physical activity, diet, and lifestyle measures may be related to both cognitive impairment and stroke. Alternatively, cognitive impairment may be a risk factor for lifestyle changes such as poor eating habits and lack of physical exercise, which could then be a risk factor for stroke. There are other possible reasons for the greater risk of stroke in blacks with cognitive impairment including unrecognized vascular pathways, and genetic and epigenetic processes related to vascular disease in blacks compared to whites. Further study including detailed risk factor assessment, vascular assessment, and neuroimaging for silent infarcts, white matter changes, and microbleeds in blacks compared to whites with similar episodic memory are necessary to further investigate these findings.

We are not aware of the extant literature exploring potential racial differences in cognition and stroke risk. Clinically diagnosed cognitive impairment has been associated with an increased risk of stroke in mostly white populations.⁸⁻⁹ An examination of cognitive domains from prospective studies has also found a significant association between cognitive impairment and incident stroke using global cognitive measures, such as SMPSQ¹¹ and MMSE,¹²⁻¹⁷ however the sample was drawn from predominantly white populations. Additional, one study among Hispanic whites also found a similar association between global cognition and risk of stroke.³⁵ While our previous examination found a significant association between cognitive function and incident stroke, we did not examine a race-specific association between cognitive domains and incident stroke.¹⁸

The literature is inconsistent on the role of episodic memory and risk of stroke. Batterham et al.¹⁶ found no association of stroke with episodic memory. A non-significant finding was also reported by de Moraes et al.²² using delayed word recall testing, even though their estimates showed a 19% higher risk in the lowest compared to the highest scoring groups. De Fries et al.¹⁴, using word recall testing, and Shipley et al.¹⁹, using verbal declarative memory testing, found significant associations similar to our findings between episodic memory and risk of stroke. Furthermore, memory differences were observed years before stroke, even though race-specific differences were not reported.¹⁰

Several limitations of our study must be noted. Of the original 10,801 participants, 7,205 had valid stroke assessments and risk factors, thereby giving rise to selection bias. Participants with no valid stroke assessments were mostly on HMO. We did not find any significant difference in race for those with and without stroke assessments. However, those with no stroke assessments also had lower cognitive scores and were in general less healthy than those included in this study. This might lead to underestimation of our relative risk. A large fraction of the sample was also excluded for previous history of stroke. These participants also had poor cognitive function and worse health measures.

Our stroke assessments were based on participants enrolled in Medicare plans, and no medical record validation of stroke and mostly importantly silent stroke is possible.

Participants hospitalized for stroke are much more likely to be larger and more significant, and unrecognized or silent strokes may have been completely missed. About 80% of blacks and 75% of whites were enrolled in Medicare and provided all relevant data. A higher percentage of blacks than whites were on Medicare therefore, it is unlikely that our estimates were biased differentially for blacks than for whites. However, our findings among whites were consistent with previous research. Our sample also had 90% ischemic stroke, which is somewhat larger than 80% population average. In a sensitivity analysis, we removed hemorrhagic stroke cases, and found our relative risk estimates to be similar to that full sample. We used cognitive function tests from our baseline assessment to examine the risk of stroke, but cognitive function is dynamic, and change in cognitive function might also increase the risk of incident stroke. Future analysis should examine the racial differences in the association of change in cognitive function with the risk of stroke.

In conclusion, we found that composite cognitive function and episodic memory were more strongly associated with risk of stroke among blacks than among whites. Individual cognitive tests for global cognition and episodic function were associated with similar strengths among blacks and whites. The intriguing findings from this study may have clinical relevance, particularly among blacks. The immediate implication would be that stroke and the related further cognitive decline could be delayed or prevented if treating physicians focus on vascular health, especially in their black patients with cognitive impairment. Further studies are needed to determine if blacks have more severe white matter changes, microbleeds, and vascular disease that may account for both the episodic memory loss and future risk of stroke.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Baseline Characteristics of 7,205 Participants from a Biracial Sample of Blacks (N=4,401) and Whites (N=2,804) with No History of Stroke

	Overall Mean (SD)	Blacks Mean (SD)	Whites Mean (SD)
Age (years)	72.5 (6.5)	71.2 (5.5)	74.5 (7.2)
Education (years)	12.4 (3.5)	11.4 (3.3)	13.9 (3.2)
Composite cognitive function	0.27 (.71)	0.12 (0.71)	0.51 (.64)
Global cognition	26.8 (3.8)	26.1 (4.0)	27.8 (3.1)
Executive function	30.7 (13.7)	26.6 (12.8)	37.3 (12.3)
Episodic memory	8.4 (2.6)	8.1 (2.7)	9.0 (2.4)
Systolic BP (mm Hg)	138.2 (19.3)	138.8 (19.2)	137.3 (19.4)
Diastolic BP (mm Hg)	77.8 (11.3)	79.2 (11.5)	75.6 (10.6)
Body mass index, kg/m ²	27.8 (6.0)	28.6 (6.3)	26.6 (5.2)
Alcohol consumption (gm/day)	0.5 (1.2)	0.4 (1.2)	0.7 (1.2)
Females, %	4246, 59%	2583, 59%	1663, 59%
Former smokers, %	2852, 40%	1706, 39%	1146, 41%
Current smokers, %	1052, 15%	746, 17%	306, 11%
Heart disease, %	921, 13%	551, 13%	370, 13%
Diabetes, %	490, 7%	402, 9%	88, 3%

Table 2

Baseline Characteristics of 7,205 Participants from a Biracial Sample of Those Free of Stroke (N=6,020) and Those Who Developed Stroke (N=1,185)

	Free of Stroke Mean (SD)	Developed Stroke Mean (SD)
Age (years)	72.3 (6.4)	73.7 (6.3)
Education (years)	12.4 (3.5)	12.0 (3.4)
Composite cognitive function	0.30 (.70)	0.14 (.72)
Global cognition	26.9 (3.7)	26.3 (4.2)
Executive function	31.2 (13.6)	28.4 (13.7)
Episodic memory	8.5 (2.6)	7.9 (2.7)
Systolic BP (mm Hg)	137.5 (19.1)	141.7 (19.4)
Diastolic BP (mm Hg)	77.8 (11.3)	77.6 (11.2)
Body mass index, kg/m ²	27.9 (6.0)	27.6 (5.9)
Alcohol consumption (gm/day)	0.5 (1.2)	0.5 (1.3)
Females, %	3552, 59%	694, 59%
Blacks, %	3697, 61%	704, 59%
Former smokers, %	2383, 40%	469, 40%
Current smokers, %	865, 14%	187, 16%
Heart disease, %	712, 12%	209, 18%
Diabetes, %	369, 6%	121, 10%

Table 3

Relative Risk of Composite and Cognitive Domains on Risk of Incident Stroke in a Biracial Sample of 7,205 Older Adults[/]

Cognitive Tests	Blacks HR (95% CI)	Whites HR (95% CI)
Composite cognitive function	1.76 (1.66 – 1.88)	1.38 (1.27 – 1.51)
Global cognition	1.07 (1.05 – 1.09)	1.05 (1.03 – 1.07)
Executive function	1.02 (1.01 – 1.03)	1.02 (1.01 – 1.03)
Episodic memory	1.12 (1.10 – 1.14)	1.06 (1.04 – 1.09)

[/] Relative risk estimates were summarized from separate Cox models after adjusting for demographic, lifestyle, cardiovascular, and health-related risk factors. Complete risk-factor-adjusted models are presented in Supplemental Tables I – IV.