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Association of Vascular Risk Factors With Cognition in a Multiethnic Sample

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Objectives. To examine the relationship between cardiovascular risk factors (CVRFs) and cognitive performance in a multiethnic sample of older adults.

Method. We used longitudinal data from the Washington Heights-Inwood Columbia Aging Project. A composite score including smoking, stroke, heart disease, diabetes, hypertension, and central obesity represented CVRFs. Multiple group parallel process multivariate random effects regression models were used to model cognitive functioning and examine the contribution of CVRFs to baseline performance and change in general cognitive processing, memory, and executive functioning.

Results. Presence of each CVRF was associated with a 0.1 *SD* lower score in general cognitive processing, memory, and executive functioning in black and Hispanic participants relative to whites. Baseline CVRFs were associated with poorer baseline cognitive performances among black women and Hispanic men. CVRF increase was related to baseline cognitive performance only among Hispanics. CVRFs were not related to cognitive decline. After adjustment for medications, CVRFs were not associated with cognition in Hispanic participants.

Discussion. CVRFs are associated with poorer cognitive functioning, but not cognitive decline, among minority older adults. These relationships vary by gender and medication use. Consideration of unique racial, ethnic, and cultural factors is needed when examining relationships between CVRFs and cognition.

Key Words: Cardiovascular disease—Cognitive decline—Ethnic differences—Racial differences.

CARDIOVASCULAR risk factors (CVRFs) and diseases are prevalent among older adults such that by age 60, approximately 70% of Americans have at least one cardiovascular disease (Go et al., 2013). Rates of many CVRFs and diseases are higher among Hispanic and non-Hispanic black (black) adults compared with non-Hispanic white (white) adults (Go et al., 2013). Minority older adults also have an elevated risk for cognitive impairment and dementia (Manly et al., 2008). CVRFs such as diabetes (Bangen et al., 2013; Cahana-Amitay et al., 2013; Köhler et al., 2012), and vascular diseases such as hypertension (Sims, Madhere, Callender, & Campbell, 2008; Waldstein, Brown, Maier, & Katzel, 2006), and stroke (Köhler et al., 2012; Rafnsson, Deary, Smith, Whiteman, & Fowkes, 2007) are associated with poorer cognition and may also be implicated in the progression of mild cognitive impairment (Luchsinger et al., 2009; Manly et al., 2008) and Alzheimer's disease (Manly et al., 2008). In the present study, we investigated the relationship between CVRFs and cognition.

Cognitive Functioning and CVRFs

Asymptomatic vascular changes likely begin prior to the fourth decade of life and disruption of the frontostriatal pathway results from these cerebrovascular changes in

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both subcortical structures and the white matter pathways that connect these structures to the frontal lobes (Craft, 2007). Cognitive changes related to CVRFs typically include executive dysfunction (Brickman et al., 2011; Elias et al., 2004), slowed information processing speed (Laughlin et al., 2011), impaired attention (Elias et al., 2004), and worsening general cognitive performance (Van den Berg, Kloppenborg, Kessels, Kappelle, & Bissels, 2008). However, CVRFs have also been associated with declines in verbal and nonverbal learning and memory (Elias et al., 2004; Laughlin et al., 2011; Luchsinger et al., 2005; Sims et al., 2008), visuospatial abilities (Elias et al., 2004), and language (Cahana-Amitay et al., 2013). It is possible that CVRFs such as diabetes have a direct effect on increasing Alzheimer's pathology (Craft, 2007), which would manifest as deficits in learning and memory.

Longitudinal Effects of CVRFs

The long-term effects of CVRFs on changes in cognitive functioning remain unclear. Studies measuring midlife CVRFs have reported significant associations between CVRFs and cognitive decline (Bangen et al., 2013; Laughlin et al., 2011); however, the amount of follow-up time needed to sufficiently capture cognitive changes due to vascular factors varies between studies (Duron & Hanon, 2008). A restricted follow-up time period (e.g., less than 3 years) may account, in part, for null findings given the progressive onset of many vascular conditions (Bowler & Gorelick, 2009; Spiro & Brady, 2011).

Findings regarding the effect of CVRFs on cognition differ for specific vascular diseases and vascular risk factors, as well as whether participants have received treatment for a vascular condition (Spiro & Brady, 2011; Starr et al., 2004) and by demographic factors such as race/ethnicity and gender (Insel, Merkle, Hsiao, Vidrine, & Montgomery, 2012; Waldstein & Katzel, 2004). Consideration of overall CVRF burden is also important as a greater number of CVRFs may increase risk for cognitive decline beyond the presence of a single vascular risk factor alone (O'Brien et al., 2003). Single risk factors, namely stroke (Rafnsson et al., 2007), diabetes (Laughlin et al., 2011; Stanek et al., 2009), and hypertension (Sims et al., 2008; Waldstein et al., 2006), account for significant proportions of variance in the difference in cognitive scores between those with and without several CVRFs (Van den Berg et al., 2008). However, multiple CVRFs may contribute to greater cognitive decline in an additive manner (Unverzagt et al., 2011).

Disparities in Vascular Risk Factors and Cognitive Impairment Among Minority Populations

Due to a greater prevalence of vascular conditions in minority older adults (Noble, Manly, Schupf, Tang, & Luchsinger, 2012), it is of particular interest to examine how CVRFs are associated with cognitive functioning in this population. Disparities in cognitive impairment have been partly explained by the higher prevalence of specific diseases, such as diabetes, in minorities (Noble et al., 2012); however, racial/ethnic factors contribute to these discrepancies at multiple levels (Sisco et al., forthcoming; Whitfield, Edwards, & Nelson, 2010). Factors such as perceived discrimination (Pascoe & Richman, 2009), immigration patterns (Turra & Goldman, 2007), health behaviors (Morrissey et al., 2007), genetic differences (Kalinowski, Dobrucki, & Malinski, 2004), self-perceptions regarding aging (Williams & Mohammed, 2009), and socioeconomic status (SES; Sims et al., 2011) determine access to and quality of health care, as well as diagnosis and treatment of health conditions. Education, particularly quality of early life education, is also a contributor to racial/ethnic differences in the relationship between CVRFs and cognition functioning (Barnes et al., 2011; Brickman et al., 2011).

In this study, we examined the association of CVRFs with level and longitudinal change in general cognitive processing, memory, and executive functioning in a large population-based sample of ethnically, linguistically, and educationally diverse older adults. We contrasted the effect of CVRFs on cognitive functioning in white, black, and Hispanic older adults. We hypothesized that black and Hispanic older adults would demonstrate lower baseline cognitive functioning and would experience steeper rates of cognitive decline over time, and further that vascular burden would be associated with both baseline level of cognitive functioning and accelerated decline in these groups.

Method

Participants

Longitudinal data collected as part of the Washington Heights-Inwood Columbia Aging Project (WHICAP) were used for this study. WHICAP is an ongoing study of Medicare recipients aged 65 or older residing in three contiguous census tracts in Northern Manhattan, NY, and in the neighborhoods of Washington/Hamilton Heights and Inwood. The population from which participants were drawn was comprised of English- or Spanish-speaking individuals from several countries of origin representing Caribbean Hispanic (Hispanic), black, and white older adults. Participants were invited to participate in a study of aging, cognitive function, and dementia during two recruitment efforts in 1992 and 1999 and were contacted for follow-up approximately every 18–30 months. In each interview, participants completed an extensive set of questions about their health, cognitive function, and early life experiences. Details of the sampling strategies, recruitment outcomes, and study design and procedures have been published previously (Tang et al., 2001). Institutional review boards at Columbia Presbyterian Medical Center,

Columbia University Health Sciences, and the New York State Psychiatric Institute approved this project. All individuals discussed the study with a trained research assistant and provided written informed consent before their baseline visit and at each follow-up visit.

There were data from 4,108 Hispanic, black, and white participants for use in the present study. We excluded observations in which a neuropsychological battery was not performed (n = 31). This resulted in a sample size of 4,077 participants.

Assessment Procedures

Racial/ethnic group.—Race and ethnic group were determined by self-report using the format of the 2000 U.S. Census (United States Office of Management and Budget, 2007). Participants were first asked whether they were Hispanic. In a second question, participants were asked to report their race (i.e., American Indian/Alaska Native, Asian, Native Hawaiian or other Pacific Islander, black or African American, or white). We excluded the small number of participants who were not white, black, or Hispanic (n = 51).

CVRFs and medications.—At the initial visit and each follow-up, a physician recorded medical history and medications in a semistructured formal interview. Neurological and physical examinations were performed. Diabetes mellitus and hypertension were defined by self-report at baseline and at each follow-up interval or by self-reported use of disease-specific medications. Hypertension was also defined by systolic blood pressure equal to or greater than 140 mmHg or diastolic blood pressure equal to or greater than 90 mmHg (Chobanian et al., 2003). Heart disease was defined by a history of atrial fibrillation or other arrhythmias, myocardial infarction, congestive heart failure, or angina pectoris. Smoking was classified by self-reported current smoking. Hip and waist measurements were taken at baseline and follow-up. Central obesity was defined as a waist–hip ratio of 1.0 and 0.9 for men and women, respectively (World Health Organization, 2008). Stroke was defined by World Health Organization criteria (Hatano, 1976). We had self-reported information on medications without doses, which were classified as follows for the purpose of characterizing the treatment of the vascular risk factors: for diabetes, oral hypoglycemic medications and insulin; for hypertension, angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, calcium channel blockers, or diuretics; for heart disease, aspirin and other antiplatelet medications. These classes were assigned a value of 1 if taken, and 0 if not taken. For those CVRFs for which multiple indicators of disease were considered (e.g., diabetes, hypertension, heart disease), participants were coded as having that CVRF if any one of those indicators was present (i.e., self-report, physiological measurements, medication).

Neuropsychological battery.—The evaluation included measures of learning and memory, orientation, abstract reasoning, language, and visuospatial ability. The neuropsychological battery was specifically designed for administration to both Spanish and English speakers. Specific ability areas and tests administered include verbal list learning and memory (Selective Reminding Test; Buschke & Fuld, 1974), nonverbal memory (multiple-choice version of the Benton Visual Retention Test; Benton, 1955), orientation (items from the Mini-Mental State Examination; Folstein, Folstein, & McHugh, 1975), verbal reasoning (Similarities subtest of the Wechsler Adult Intelligence Scale-Revised [WAIS-R]; Wechsler, 1981), nonverbal reasoning (Identifies and Oddities subtest of the Mattis Dementia Rating Scale [I/O MDRS]; Mattis, 1976), mental flexibility (Color Trail Making Test, Part A and B; D'Elia, Satz, Uchiyama, & White 1994), naming (15-item version of the Boston Naming Test; Kaplan, Goodglass, & Weintraub, 1983), attention (two cancellation tasks involving the detection of a shape form and a consonant trigram from an array of shape and phonemic distractions, respectively; Ben-Yishay, Diller, Mandleberg, Gordon, & Gerstman, 1974). letter fluency Benton, Hamsher, & Sivan (1976), category fluency for animals, repetition (high-frequency phrases of the Boston Diagnostic Aphasia Examination [BDAE]; Goodglass & Kaplan, 1983), auditory comprehension (first six items of the Complex Ideational Material subset of the BDAE; Goodglass & Kaplan, 1983), visuoconstruction (Rosen Drawing Test; Rosen, 1981), and visuoperceptual skills (multiple-choice matching of figures from the Benton Visual Retention Test; Benton, 1955).

Analysis Plan

The analysis plan followed five steps. First, demographic, clinical characteristics, and mean cognitive scores were compared across racial/ethnic groups. Continuous variables were compared by analysis of variance, and categorical variables were compared by chi-square tests. Second, we derived composites using factor analysis for general cognitive performance, memory, and executive functioning. Third, we created a sum score for CVRFs and diseases (Luchsinger et al., 2005). Fourth, we modeled cognitive functioning over time, including data from all available follow-up evaluations, and examined associations with CVRFs. Fifth, sensitivity analyses were performed in which subgroups (male/female participants; CVRF changers/nonchangers) were examined using the same model. Finally, medication classes were entered into the model to ascertain the contributions of vascular risk factor treatment to the association between cognition and CVRFs.

Neuropsychological tests were assigned to domains based on their content, expert opinions from teams of clinical neuropsychologists (see Gross, Jones, Fong, Tommet, & Inouye, 2014), and empirical examination of dimensionality. Composite scores were constructed for general cognitive

performance (GCP), memory (MEM), and executive function (EF) from factor analyses of the neuropsychological battery consisting of 11 tests. Each composite was scaled to have a mean of 50 and a standard deviation (*SD*) of 10. The composites were scaled to national norms using measures that were administered in both the WHICAP study and the Aging, Demographics, and Memory Study, part of the Health and Retirement Survey. The MEM composite was created using total recall, delayed free recall, and delayed recognition from the Selective Reminding Test. The EF composite was created using the Color Trail Making Test (Parts A and B), WAIS-R Similarities, I/O MDRS, cancellation tests (shape and trigram), and category fluency. All of the above variables, as well as letter fluency, Boston Naming Test, repetition, and comprehension contributed to the composite for GCP. GCP was significantly associated with both MEM (Pearson's $r = .92$; $p < .05$) and EF (Pearson's $r = .84$; $p < .05$). EF and MEM composite scores were also significantly correlated (Pearson's $r = .65$; $p < .05$). These correlations likely reflect the shared variance among neuropsychological tests attributable to global cognitive processes. We decided to consider all domains, as a goal of this study was to examine whether CVRFs were associated with both general and specific cognitive processes and because the domains were defined a priori based on clinical input.

Vascular risk factors and diseases were assigned a value of 1 if present and 0 if absent. Each risk factor was treated as a time-dependent covariate specified by the follow-up date when the diagnosis was made. Because waist measurements were not taken until 1999, data were missing for the central obesity variable in the 1992 cohort. Values for the first available waist measurements for participants from the 1992 cohort replaced these missing values. We summed the time-varying vascular risk factors (diabetes, hypertension, smoking, central obesity, heart disease, and stroke) into a composite score, which has been used in previous WHICAP studies (Luchsinger et al., 2005). For Model 2, each medication group was entered separately into the model as a time-invariant variable and those medications that significantly contributed to the model were retained.

Levels and changes in GCP, MEM, and EF were modeled together using parallel process multivariate random effects regression (Johnson et al., 2012) utilizing data from all follow-up evaluations. Participants contributed time between their first and final study visit in which a neuropsychological test battery was administered. Age was used as the timescale of interest instead of time in study to enhance interpretability of the model results. Age was centered at 75 years to make the model intercept interpretable. We adjusted for retest effects by including an indicator coded as 0 at each participant's first study visit and the difference in time between a participant's second and first visits for subsequent visits (Gross et al., forthcoming). In addition to CVRFs, all models were adjusted for age, sex, race (white, black, Hispanic), education (continuous), recruitment cohort (1992 or 1999), and apolipoprotein E (APOE) ε4 status (ε4 carrier or noncarrier). All covariates were centered at their means. Model 2 was additionally adjusted for medications as time-invariant variables. Models were adjusted for selective attrition due to death using logistic regression to predict death based on age, sex, general cognitive status, APOE ε4 status, years of education, recruitment cohort, and time-varying vascular risk factors. Attrition weights were the inverse of the predicted probability from this regression.

Analyses were conducted with Mplus version 7.0 (Muthén & Muthén, 1998–2012) using a robust maximum likelihood estimation procedure that assumed outcome observations are missing at random, conditional on covariates in the model (Little & Rubin, 1987). Fit of modeled trajectories to the data was assessed with an empirical R^2 statistic for each outcome, which represents the proportion of variability in the observed data explained by the model (Singer & Willet, 2003). The empirical R^2 is calculated by squaring the correlation between observed and model-estimated outcome scores. A p value cutoff of less than .01 was employed to determine significance of our findings.

Results

Sample Characteristics

Sample characteristics are provided in Table 1. Median years of follow-up was 5.41 years. Participants who were excluded for having no neuropsychological testing data tended to be older ($p < .001$), were recruited in 1992 ($p < .001$), had fewer years of education ($p = .01$), were less likely to have hypertension ($p = .001$), and thus fewer CVRFs ($p = .03$). Counts of CVRFs by race/ethnicity and study visit indicated that most participants of each racial/ethnic group had one or two CVRFs (see Supplementary Table 1). The number of CVRFs remained constant in 52.5% of the participants across time (see Supplementary Graphic 1).

Racial and Ethnic Differences in Cognition

Findings of the parallel process multivariate random effects analysis adjusted for sex, race, years of education, recruitment cohort, practice effects, APOE ε4 status, and attrition are summarized in Table 2. Pseudo-R^2 statistics reported in Table 2 indicated excellent fit of the model to observed data (GCP pseudo-$R^2 = .88$; MEM pseudo-$R^2 = .81$; EF pseudo-$R^2 = .82$). On average, white participants aged 75 in WHICAP performed at levels comparable with or slightly above the U.S. population of older adults (mean $T = 50$). Each point difference seen in Table 2 signifies a 0.1 *SD* difference in each cognitive score. GCP among black and Hispanic participants aged 75 was approximately 0.4–0.5 *SD* below that of white participants. A similar pattern was observed for EF and MEM performances though the difference in performances of white participants with

Table 1. Baseline Demographic, Vascular, and Cognitive Characteristics of the Sample: Results From WHICAP (n = 4,077)

Variable	White	Black	Hispanic	p Value for group differences[a]
Sample size	1,014	1,375	1,688	
Age at baseline, mean (*SD*)	78.0 (7.4)	77.8 (7.1)	76.6 (6.7)	<.001[b,c]
Male, *n* (%)	370 (36.5)	393 (28.6)	520 (30.8)	<.001[d]; .002[b]
Years of education, *n* (%)				<.001[b,c,d]
7 years or less	144 (14.3)	438 (32.0)	1301 (77.1)	
8 or more years	864 (85.7)	932 (68.0)	386 (22.9)	
Recruitment cohort, *n* (%)				<.001[b,d]; .01[c]
1992 cohort	370 (36.5)	669 (48.7)	897 (53.1)	
1999 cohort	644 (63.5)	706 (51.3)	791 (46.9)	
Apolipoprotein ε4 carrier, *n* (%)	185 (18.2)	365 (26.5)	369 (21.9)	<.001[c,d]
Vascular risk factors				
Sum of vascular risk factors, *n* (%)				.01[d]; .03[b]
None	263 (25.9)	269 (19.6)	354 (21.0)	
One	342 (33.7)	481 (35.0)	588 (34.8)	
Two	278 (27.4)	404 (29.4)	489 (29.0)	
Three or more	131 (12.9)	231 (16.1)	257 (15.2)	
Heart disease, *n* (%)	264 (26.0)	307 (22.3)	342 (20.3)	.04[d]; <.001[b]
Self-reported hypertension or elevated blood pressure, *n* (%)	641 (63.2)	972 (70.7)	1141 (67.6)	<.001[d]; .02[b]
Current smoker, *n* (%)	94 (9.3)	203 (16.1)	175 (11.4)	<.001[c,d]
Diabetes, *n* (%)	100 (9.9)	245 (17.8)	357 (21.1)	<.001[b,d]; .02[c]
Stroke, *n* (%)	66 (6.5)	80 (5.8)	79 (4.7)	.04[b]
Central obesity, *n* (%)	145 (18.8)	201 (21.8)	291 (25.1)	.001[b]
CVRF increase, *n* (%)	459 (45.2)	643 (46.7)	835 (49.5)	.03[b]
Cognitive composite scores, mean (*SD*)				
General cognitive performance	52.8 (12.0)	45.9 (12.0)	42.7 (10.2)	<.001[b,c,d]
Memory	54.3 (10.3)	49.2 (10.3)	48.1 (8.8)	<.001[b,d]; .002[c]
Executive functioning	51.7 (11.2)	44.4 (10.7)	41.1 (9.0)	<.001[b,c,d]
Medications, *n* (%)				
Diuretics	206 (20.3)	374 (27.2)	354 (21.0)	<.001[c,d]
Insulin/oral hypoglycemics	94 (9.3)	207 (15.1)	304 (18.0)	<.001[b,d]; .03[c]
Calcium channel blockers	261 (25.7)	448 (32.6)	501 (29.7)	<.0001[d], .03[b]
Antiplatelet medications	353 (34.8)	377 (27.4)	517 (30.6)	< .001[d]; .02[b]; .05[c]
ACE inhibitors	5 (0.5)	17 (1.2)	18 (1.1)	
Beta-blockers	172 (17.0)	154 (11.2)	165 (9.9)	<.001[b,d]

Notes. CVRFs = cardiovascular risk factors; *SD* = standard deviation. Sum vascular risk factors: summation of diabetes, hypertension, smoking, central obesity, heart disease, and stroke; CVRF increase indicates that the participant's overall number of CVRFs increased by at least one during the study period.

[a]Based on analysis of variance for continuous data and chi-square test for categorical data.

[b]Significant difference between white and Hispanic groups.

[c]Significant difference between black and Hispanic groups.

[d]Significant difference between white and black groups.

black and Hispanic participants was slightly less (approximately 0.3–0.4 *SD*).

With regard to change in cognitive functioning over the follow-up period, compared with black and Hispanic participants, white participants exhibited the steepest rates of cognitive decline in GCP (−0.07 *SD* per year), MEM (−0.07 *SD*), and EF (−0.06 *SD*). Black participants and Hispanic participants also demonstrated cognitive decline, although the annual change was attenuated by approximately 0.01–0.02 *SD* compared with that of white participants.

Vascular Burden as a Predictor of Cognitive Function

Each additional CVRF was associated with a 0.14 *SD* and 0.10 *SD* lower score in GCP among black and Hispanic participants, respectively, at age 75 (see Figure 1). The association was in the same direction but not statistically significant among white participants. For MEM, each additional CVRF was associated with a 0.12 *SD* and 0.09 *SD* lower memory score for black and Hispanic groups, respectively. CVRFs were not associated with MEM among white participants at age 75. For EF, each additional CVRF was significantly associated with a 0.11 *SD* and 0.10 *SD* lower executive functioning score among black and Hispanic participants, respectively. A trend for an association between EF and CVRFs (p = .5) was found among white participants. There were no significant differences in the effect of CVRFs on cognitive performance between racial/ethnic groups.

Vascular Burden as a Predictor of Cognitive Change

CVRFs were associated with a small though significant attenuated decline in MEM (0.01 *SD*) in black participants, but not among white or Hispanic participants for any

Table 2. Parallel Process Latent Growth Model of Changes in General Cognitive Processing, Memory, and Executive Functioning (N = 4,077)

Parameter	General cognitive performance Estimate (95% CI)	Memory Estimate (95% CI)	Executive functioning Estimate (95% CI)
White (n = 1,014)			
Mean level at age 75	51.90* (47.78, 56.02)	53.79* (50.71, 56.87)	49.60* (45.76, 53.44)
Mean annual change	−0.74* (−0.86, −0.62)	−0.66* (−0.78, −0.54)	−0.59* (−0.71, −0.47)
Level on CVRFs	−0.68 (−1.72, 0.36)	−0.33 (−1.31, 0.65)	−1.20 (−2.26, −0.14)
Annual change on CVRFs	−0.03 (−0.13, 0.07)	0.00 (−0.10, 0.10)	−0.03 (−0.13, 0.07)
Black (n = 1,375)			
Mean level at age 75	46.85* (43.17, 50.53)	50.12* (47.49, 52.75)	44.82* (41.39, 48.25)
Mean annual change	−0.60* (−0.68, −0.52)	−0.58* (−0.66, −0.50)	−0.42* (−0.50, −0.34)
Level on CVRFs	−1.39* (−2.29, −0.49)	−1.20* (−2.04, −0.36)	−1.14* (−1.90, −0.38)
Annual change on CVRFs	0.10 (0.02, 0.18)	0.11* (0.05, 0.17)	0.02 (−0.06, 0.10)
Hispanic (n = 1,688)			
Mean at Age 75	47.76* (45.31, 50.21)	51.01* (49.09, 52.93)	46.06* (44.06, 48.06)
Mean annual change	−0.57* (−0.65, −0.49)	−0.53* (−0.59, −0.47)	−0.48* (−0.56, −0.40)
Level on CVRFs	−0.95* (−1.54, −0.36)	−0.87* (−1.40, −0.34)	−1.02* (−1.57, −0.47)
Annual change on CVRFs	0.06 (−0.02, 0.14)	0.06 (0.00, 0.12)	0.02 (−0.06, 0.10)
Group differences in the association with CVRFs			
Mean level at age 75			
White–black	0.72 (−0.65, 2.09)	0.87 (−0.42, 2.16)	−0.06 (−1.37, 1.25)
White–Hispanic	0.27 (−0.93, 1.47)	0.54 (−0.58, 1.66)	−0.17 (−1.37, 1.03)
Black–Hispanic	−0.45 (−1.53, 0.63)	−0.33 (−1.33, 0.67)	−0.11 (−1.05, 0.83)
Annual change			
White–black	−0.12 (−0.26, 0.02)	−0.11 (−0.23, 0.01)	−0.05 (−0.17, 0.07)
White–Hispanic	−0.09 (−0.23, 0.05)	−0.06 (−0.18, 0.06)	−0.04 (−0.16, 0.08)
Black–Hispanic	0.04 (−0.06, 0.14)	0.05 (−0.05, 0.15)	0.01 (−0.09, 0.11)
Pseudo-R^2	.88	.81	.82

Notes. APOE = apolipoprotein E; CI = confidence interval; CVRFs = cardiovascular risk factors. Results from multiple group parallel process multivariate random effects regression models of general and domain-specific cognitive functioning over age. Models are adjusted for sex, years of education, recruitment cohort, and APOE ε4 status.

*$p < .01$.

cognitive domain (see Figure 2). There were no significant differences in the associations of CVRFs and cognitive decline among groups.

Sensitivity Analyses for Specific CVRFs, Gender, and Change in CVRFs

No major conclusions were changed when components of the CVRF composite replaced the overall composite score. The presence of diabetes was significantly associated with a 0.3–0.4 *SD* lower EF score at age 75 among all participants, as well as with approximately 0.3 *SD* lower score at age 75 in both MEM and GCP among black and Hispanic participants. In black participants, heart disease was associated with a 0.3 *SD* lower score in GCP and MEM at age 75 as well as a small though significant attenuation in MEM decline (0.03 *SD*). Black participants with a history of stroke exhibited lower performance at age 75 in all three cognitive domains, which were on average 0.4–0.5 *SD* lower than those without stroke. White participants with a history of stroke demonstrated an approximately 0.05 *SD* decline in GCP and EF. Current smoking was associated with a 0.1–0.2 *SD* decline in GCP and MEM among white participants. No significant associations were found for hypertension or central obesity with cognitive performance at age 75 or cognitive decline.

Sensitivity analyses for gender revealed that among black women, CVRFs were associated with poorer performances in GCP (−0.15 *SD*) and MEM (−0.14 *SD*) at age 75, as well as with attenuated decline in these domains (0.01 *SD*). No significant associations were found for CVRFs with baseline cognition or cognitive change for black men. Among Hispanics, each additional CVRF was associated with a 0.09 *SD* lower score in EF for women as well as a 0.14–0.18 *SD* lower score in all three cognitive domains for men. As before, there were no significant associations between CVRFs and cognitive performance at age 75 among white older adults or with cognitive change for Hispanic or white older adults.

Sensitivity analyses for participants whose CVRFs increased compared with those whose CVRFs remained constant over the study period were consistent with findings from the main analysis with the exception of Hispanics. Among those Hispanic participants whose CVRFs increased over the study period (i.e., changers), each additional CVRF at age 75 was associated with an approximately 0.1 *SD* lower cognitive performance. Number of CVRFs in neither changers nor nonchangers was related to cognitive change. The lack of findings for black participants may reflect loss of power due to a reduced sample size combined with use of a stringent p value for determining significance ($p < .01$).

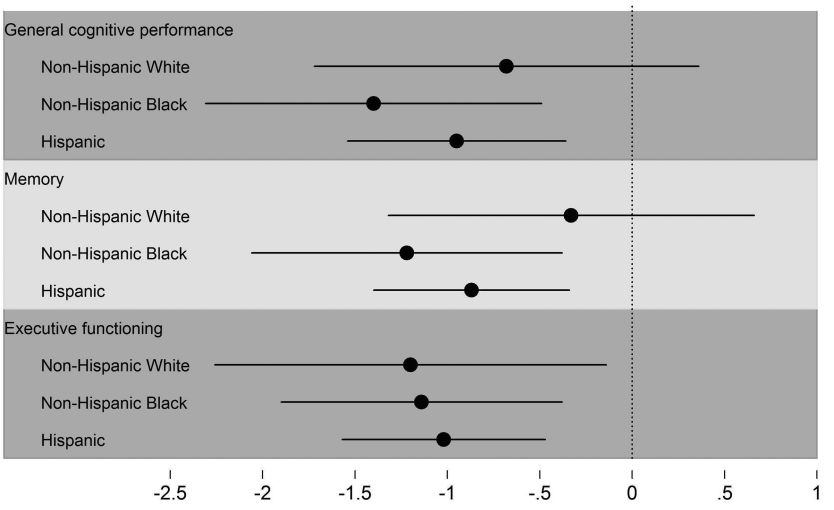

Figure 1. Regressions of age 75 performance in general cognitive performance, memory, and executive functioning on vascular risk factors among white, black, and Hispanic participants (N = 4,077). Horizontal bars indicate 95% confidence intervals. The vertical dotted line at 0 indicates a null association between model-estimated cognitive function at age 75 and the composite of vascular risk factors.

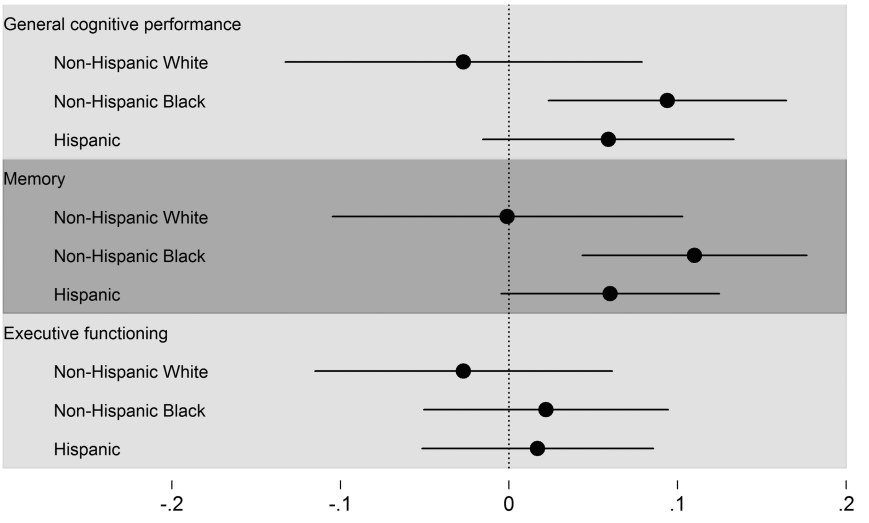

Figure 2. Regressions of annual change in general cognitive performance, memory, and executive functioning on vascular risk factors among white, black, and Hispanic participants (N = 4,077). Horizontal bars indicate 95% confidence intervals. The vertical dotted line at 0 indicates a null association between model-estimated change in cognitive functioning and the composite of vascular risk factors.

Effect of Medication on the Association Between Vascular Risk Factors, Cognition, and Cognitive Change

To examine the impact of medications on the association between CVRFs and cognition, we entered disease-specific medications into the model. Diuretics, insulin/oral hypoglycemics, calcium channel blockers, and antiplatelet medications were significant predictors of GCP and were retained; ACE inhibitors and beta-blockers were not statistically significant and were excluded from the model. Differing from the first model, relationships between CVRFs, cognitive functioning at age 75, and cognitive change were significant upon entry of medications only for black participants. Each additional CVRF was associated with a 0.15 *SD* lower score in GCP, a 0.15 *SD* lower score in MEM, and a 0.13 *SD* lower score in EF among black participants at age 75. CVRFs were associated with a small though significant attenuated decline in GCP and MEM (0.01 *SD*) after adjustment for medication. CVRFs were not significantly associated with change in EF over time among black older adults. There were no significant relationships between CVRFs and cognitive functioning at age 75 or cognitive decline among white and Hispanic participants and no significant group differences were found.

Discussion

This study explored the association of vascular burden and cognitive functioning in a sample of participants with diverse ethnic, linguistic, and educational backgrounds. Among black and Hispanic participants, a greater number of CVRFs, as measured by the presence of heart disease, diabetes, hypertension, stroke, smoking, and central obesity, was associated with lower scores on measures of GCP, MEM, and EF at age 75. A trend was found between CVRFs and EF at age 75 for white participants. In clinical terms, these findings suggest that for each CVRF, black and Hispanic participants perform approximately one T-score point worse in these cognitive domains at age 75 compared with their peers without any CVRFs. We found that approximately half of participants experienced an increase in CVRFs. Persistence of these CVRFs over time was not significantly associated with cognitive change with the exception of an attenuated memory decline in black participants, which remained after consideration of medication use. No significant between-group differences were found for the effect of CVRFs on cognitive function at age 75 or over the follow-up period.

The cognitive performance of black and Hispanics was below that of white participants at age 75 and black and Hispanic participants demonstrated declines in cognition over the follow-up period that were slightly less than their white peers. This is in line with recent work using the WHICAP data (Sisco et al., forthcoming), and other studies demonstrating relatively larger race/ethnicity differences in cross-sectional cognitive functioning versus cognitive change (Castora-Binkley, Peronto, Edwards, & Small, forthcoming). Given that our analyses were adjusted for attrition of participants due to death, our findings likely cannot be attributed to selective loss of minority participants due to illness, death, or dementia, but rather to the tendency for individuals with higher education to experience steeper cognitive decline (Scarmeas, Albert, Manly, & Stern, 2006). White participants in our study had significantly more years of education, a contributor to cognitive reserve. The cognitive reserve hypothesis suggests that individuals with high cognitive reserve may be able to tolerate more brain pathology before demonstrating cognitive changes at a relatively rapid rate of decline, whereas those with lower cognitive reserve may demonstrate cognitive declines earlier and at a gradual rate (Stern, 2012).

These findings do not support the notion that the association of CVRFs with cognition in minority older adults is significantly greater than in white older adults but is in line with literature indicating that vascular burden may be associated with functioning in a broader range of cognitive domains among minority older adults (Köhler et al., 2012; Luchsinger et al., 2005; Unverzagt et al., 2011). Though a relationship of greater magnitude between CVRFs and executive impairment among minority older adults compared with whites has been demonstrated by others (Robbins, Elias, Elias, & Budge, 2005), our findings suggest that minority older adults may not be at a greater risk for executive impairment due to vascular factors. Work on the association of domains of cognition other than executive functioning and vascular disease has not demonstrated a consistent pattern among black (Robbins et al., 2005; Sims et al., 2008; Unverzagt et al., 2011) or Hispanic older adults (Yaffe et al., 2007), as well as white older adults (Elias et al., 2004; Laughlin et al., 2011; Waldstein & Katzel, 2004).

Sensitivity analyses revealed that having a greater number of CVRFs was significantly associated with poorer performances in two cognitive domains among black women, but none among black men, as well as all with poorer performances across three cognitive domains among Hispanic men, but only with poorer executive functioning among Hispanic women. These findings suggest that black women and Hispanic men may be at a greater risk for cognitive impairment due to vascular factors. Previous work has reported differing associations between CVRFs and cognition by gender (Insel et al., 2012; Waldstein & Katzel, 2004), and our findings suggest that these gender-specific relationships may also vary within racial/ethnic groups.

Upon consideration of medications, the associations between vascular risk and cognition were no longer significant for Hispanic older adults. These results should be interpreted with caution as medication use was based solely on self-report and we were unable to ascertain whether medications led to control of conditions such as diabetes. We can only speculate that the use of medications could be a proxy for better control of vascular risk factors. Increase of CVRFs over time may be an indicator of poorer control and may explain our finding of the poorer cognitive functioning observed in Hispanic participants whose CVRFs increased over the study period. It is reported that conditions such as hypertension and congestive heart failure do not have the same response across ethnic groups (Taylor & Wright, 2005; Taylor et al., 2004) and treatment regimens tailored to blacks have been proposed. This might explain the residual association of CVRFs with lower cognitive performance in blacks after controlling for medications. Our findings are also supported by studies demonstrating diminished health disparities between Hispanic and white adults after controlling for SES (Crimmins, Kim, Alley, Karlamangla, & Seeman, 2007). As such, medication use may also serve as an indicator of SES, but further work is needed to examine social correlates of medication use in our study. Additionally, complex race/ethnicity-specific relationships have been reported regarding disparities in the use of medical services and adherence to medical interventions (Kim, Ford, Chiriboga, & Sorkin, 2012). Cardiovascular medication use and adherence is lower among subgroups of minority older adults (Qato, Lindau, Conti, Schumm, & Alexander, 2010; Traylor, Schmittdiel, Uratsu, Mangione, & Subramanian, 2010). Minority older adults are also more likely to have delayed medical treatment (Kim et al., 2012). These factors may

limit the ability of medications to hinder the effects of vascular disease processes on cognitive functioning and account for within-group differences in cognitive functioning.

Hispanic participants whose CVRFs increased over the study period had poorer baseline cognitive functioning, which is in line with previous work demonstrating that poorer baseline cognition is associated with increased risk of CVRF onset (Skoog et al., 2005). With the exceptions of a small though significant attenuated memory decline among black older adults with heart disease, as well as in general cognitive processing among black women, our analyses did not find an effect of CVRFs on cognition over time. CVRF increase was not associated with cognitive change, suggesting that gaining additional CVRFs does not contribute to cognitive decline, at least over an approximately 5-year period after age 75. Interpretation of these results is complicated by the fact that many of our participants were taking medications. The relationships between CVRFs and cognition may have therefore been partially masked, especially in cases in which diseases were well managed. Our findings indicating that CVRFs were no longer related to cognitive functioning in Hispanic older adults after entry of medications provide support for this, yet evidence of whether medications may lower risk for cognitive impairment remains unclear and findings vary by medication class (Starr et al., 2004) and whether diseases are adequately managed by medications (Cahana-Amitay et al., 2013). Careful consideration of adjustment variables is therefore needed when examining relationships between CVRFs and cognition. Further work utilizing methods closely monitoring disease control would improve understanding of how medications and preventative interventions may affect the relationship of vascular factors with cognition. Future analyses should consider whether differences between CVRF changers and nonchangers among Hispanics may be due to factors such as overall poorer health among changers, inadequate medication, or disease control, as well as SES (e.g., access to care).

Our hypothesis that a steeper rate of cognitive decline would be associated with greater vascular burden was not supported. It may be that the association between vascular diseases and cognition is less profound with increased age (Verhaegen, Borchelt, & Smith, 2003). By age 75, the neurological consequences of long-term vascular risk factors may have already occurred resulting in less significant cognitive changes due to continued vascular burden after this age. Secondly, though significant associations between CVRFs and cognitive change have been reported over similar time periods (Duron & Hanon, 2008), our follow-up period of an average of 5 years may have been insufficient. Due to the slow, progressive nature of vascular disease, shorter follow-up times (i.e., 3 years or less) may be insufficient to capture long-term changes due to vascular disease (Bowler & Gorelick, 2009) and some authors argue that 10–20 years of follow-up may be necessary (Spiro & Brady, 2011). Studies examining midlife vascular risk factors and cognitive decline have found significant relationships (Bangen et al., 2013) and such longitudinal studies could extend upon our work to determine if there are critical treatment periods for the prevention of vascular-related cognitive declines. For example, by examining the earliest cognitive changes attributable to vascular burden or whether ongoing treatment from time of diagnosis is sufficient to prevent or delay cognitive declines (Spiro & Brady, 2011).

Although we found no between-group differences in the association of CVRFs with cognition, it is notable that the relationship between CVRFs and cognition was significant only among minority older adults. Reasons that are apparent in our data are that the sample size and the prevalence of CVRFs for whites were smaller than for blacks and Hispanics, resulting in less power to find an association between CVRFs and cognition. Biobehavioral models suggest that health disparities may be understood through the examination of the complex interactions between early life, midlife, and late-life risk factors as well as consideration of sources of within-group heterogeneity (e.g., SES; Whitfield et al., 2010). Cognitive reserve (Brickman et al., 2011), which may be lower in minorities in Northern Manhattan with lower educational attainment, could account for the lack of an association in whites. Although years of education are often used as an indicator of cognitive reserve (Barnes et al., 2011), educational quality, reading ability, and engagement in lifelong cognitively stimulating events also contribute to cognitive reserve (Manly, Schupf, Tang, & Stern, 2005) and disparities in late-life cognition (Sisco et al., forthcoming) but were not considered in our study.

Consistent with previous work, among CVRFs, diabetes and stroke had the greatest effects on cognition (Köhler et al., 2012; Luchsinger et al., 2005; Van den Berg et al., 2008) and diabetes was more prevalent among minority older adults, specifically black participants. The impact of stroke on cognitive functioning generally depends on infarct location and size (O'Brien et al., 2003); however, the association of diabetes with cognition is less well understood and is likely related to factors such as glycemic control, effectiveness of treatment, and presence of microvascular complications (Sullivan et al., 2013; Van den Berg et al., 2008). Significantly higher prevalence rates of diabetes found in minority older adults may contribute to diabetes having a greater effect on cognitive functioning within minority elders (Gregg et al., 2000; Luchsinger, Tang, Stern, Shea, & Mayeux, 2001; Noble et al., 2012). However, prevalence rates alone likely do not fully explain differences in cognitive functioning as previous WHICAP studies have demonstrated that consideration of vascular burden, and specifically disparities in Type 2 diabetes, only partially reduces disparities in cognitive functioning between white and minority older adults (Noble et al., 2012; Sisco et al., forthcoming). Consideration of unique modifiers by ethnic/racial group including SES, access to health care, cultural attitudes regarding health care and aging,

perceived discrimination, and migration history (Williams, Mohammed, Leavell, & Collins, 2010) is needed to better understand group differences that contribute to greater risk.

A strength of this study is the inclusion of a large sample of older adults not only representing major ethnic and racial groups in the United States but also with diverse socioeconomic, health, and educational backgrounds. Administration of neuropsychological measures and interviews in Spanish likely allowed for more accurate measurement of cognitive functioning and data collection from Spanish-speaking older adults. The neuropsychological battery was comprised of a wide range of well-validated measures, normative data used were based on a nationally representative cross-sectional sample of older adults. Importantly, this study included time-varying CVRFs and adjusted for potential confounders and practice effects, which potentially reduces bias and allows for a more accurate examination of the relationship between CVRFs and cognition over time.

Despite these strengths, there are also limitations to our study. Data for all medications and CVRFs, except central obesity and hypertension, were obtained through self-report and we were unable to ascertain factors such as medication adherence. Self-reported rates of health conditions may not be accurate and rates are generally higher than diagnosed, particularly in minority populations. Though participants were asked in several different ways about their health conditions and medications, and self-report is commonly used in research, it may be a weakness when gathering health-related information (Spiro & Brady, 2011). Our method of coding CVRFs when multiple indices were available (e.g., for diabetes, hypertension, and heart disease) represents a conservative approach to disease identification but may be a strength of our study as this method has the advantage of not relying solely on self-report. Finally, we did not exclude individuals based on current cognitive functioning or dementia; however, we did use APOE ε4 status as a covariate in our analyses as it has been shown to affect the relationship between vascular risk factors and cognitive decline (Bangen et al., 2013), and the presence of vascular disease may contribute to the progression and onset of disorders such as Alzheimer's disease and vascular dementia. As our goal was to study cognitive aging among a wide range of older adults, exclusion of participants based on memory impairment would have limited the generalizability of our findings.

In conclusion, this study showed that in a large multiethnic sample, vascular risk factors were associated with cognitive functioning within minority older adults at age 75; however, they were not associated with cognitive decline over time. Vascular risk factors were significantly associated with poorer cognitive performances primarily in black women and Hispanic men. An increase in CVRFs over the study period was associated with baseline cognitive performance only among Hispanics. Among risk factors, diabetes and stroke had the largest associations with cognitive functioning. Consideration of unique ethnic and cultural influences on the relationship between vascular burden and cognition in minority older adults is needed to improve understanding of the factors contributing to cognitive impairment among this group of older adults.

Supplementary Material

Supplementary material can be found at: http://psychsocgerontology.oxfordjournals.org/

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