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Patterns of Relationships between Cardiovascular Disease Risk Factors and Neurocognitive Function in African Americans

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Abstract

Objective—The association between cardiovascular disease (CVD) risk and neurocognitive function has gathered a good deal of attention in the health and social science literature; however, the relationship among several CVD risk factors and neurocognitive function has not been fully explored in an African American sample. The purpose of this study was to examine the pattern of relationships among four CVD risk factors and five measures of higher cortical functions.

Methods—Data were collected from a sample of 106 African American community-dwelling adults in the metropolitan Washington, DC, area. A nurse collected blood pressure, waist circumference, and a blood sample (to assess triglycerides and high-density lipoprotein (HDL) cholesterol) from study participants. Participants completed the Symbol Digit Modalities Test, Trailmaking B, Stroop Colorword Task, California Verbal Learning Test-II, and Wisconsin Card Sorting Test as assessments of neurocognitive function. Canonical analysis and multiple regression analysis were the major statistical methods utilized to assess relationships between CVD risk factors and neurocognitive function.

Results—The results suggest that 1) attentional processes are associated with diastolic blood pressure levels, 2) verbal learning processes are associated with diastolic blood pressure and triglyceride levels, and 3) the ability to shift cognitive set is associated with HDL cholesterol levels.

Conclusion—As cardiovascular health worsens in our society, particularly among ethnic minorities, the neurocognitive consequences must be clearly understood. Future studies should focus on identifying and building awareness of cardiovascular and neurocognitive links through longitudinal research designs and brain imaging technology.

Keywords

Cognitive Function; African Americans; Cardiovascular Risk; Metabolic Syndrome; Cognition

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Introduction

Research suggests that neurocognitive dysfunction is associated with cardiovascular disease (CVD) risk factors such as elevated blood pressure, obesity, and dyslipidemia. In many persons these CVD risk factors form a cluster of clinical abnormalities referred to as the metabolic syndrome[1,2] that arguably place them at greater risk for neurocognitive dysfunction. The metabolic syndrome is becoming more prevalent as trends in sedentary lifestyle, obesity, diabetes, and increased longevity expand within the United States.[3] The unadjusted and age-adjusted prevalence rates of the metabolic syndrome are 21.8% and 23.7%, respectively.[4] Despite the prevalence of the metabolic syndrome, few studies have examined the relationship between CVD risk factors and neurocognitive function. To our knowledge, only one study has explored the combined effects of these CVD risk factors on neurocognitive outcomes in an African American sample. In that study investigators evaluated blood pressure, total cholesterol, and hemoglobin A1C in relation to attention, memory, and executive functions.[5] Higher diastolic blood pressure and hemoglobin A1C were positively associated with performance on Digits Forward but not associated with any of the other cognitive measures. Systolic blood pressure and total cholesterol were unrelated. The sample size used in the study was small (n=43).[5]

Because of the lack of empirical findings for African Americans, neurocognitive consequences of CVD risk factors must be examined in a larger sample. In this study, we examined four components of the metabolic syndrome: 1) systolic and diastolic blood pressure, 2) waist circumference (a measure of abdominal obesity), 3) high-density lipoprotein (HDL) cholesterol level, and 4) triglyceride level and their relation to six measures of neurocognitive function.

Methods

The participants were 106 community-dwelling African American adults (45% male). The mean age of participants was 44.3 years (standard deviation 12.4 years, range 21–73 years). Exclusion criteria included current physical, emotional, or drug abuse. Potential participants were screened by phone, and none reported a diagnosis of cognitive impairment or dementia. The number of potential participants excluded by telephone screening was not recorded. Participants received a monetary compensation of $50 at the completion of the study.

Data were collected in conjunction with the Minority Organ Tissue Transplant Education Program (MOTTEP) Stress and Psychoneuroimmunological Factors in Renal Health and Disease Study, a study aimed at identifying and reducing biological and psychosocial predictors of renal disease. The study is conducted in the metropolitan Washington, DC area, an area with a large concentration of African Americans, and employs a design consisting of physiological, neurocognitive, and psychosocial assessment.

Participants completed an assessment of several neurocognitive abilities. Scores from the following measures were employed: Symbol Digit Modalities Test (SDMT) (perceptual speed), Trailmaking B (divided attention), Stroop Colorword Task (cognitive flexibility), California Verbal Learning Test-II (CVLT-II List A Total Recall) (verbal learning), and Wisconsin Card Sorting Test 64-card computerized version (WCST) (executive function). Participants also completed the Beck Depression Inventory-II, a 21-item self-report instrument intended to assess the existence and severity of symptoms of depression.[6] This measure was included to adjust for the effect of depression on neurocognitive function. All tests were administered under testing conditions that were identical for all participants.

The study required four to six hours to complete and took place at the Howard University General Clinical Research Center. Upon arrival at the study facility, participants were given an overview of the study requirements and procedure. All participants completed an institutional review board informed consent document giving their consent to participate. Next they completed a demographic information form and a health history form.

Blood pressure was measured by using a Criticare Model 506DXNT sphygmomanometer (VitalCare DOX Model 506DXNT, Criticare Systems, Waukesha, Wisc). After sitting quietly for several minutes, one seated baseline resting measurement was obtained by the nurse on duty. Waist circumference was measured with a standard tape measure at the level of the umbilicus. Nonfasting plasma samples were obtained after the baseline resting blood pressure measurement. Four vials of blood were drawn for various laboratory assessments within the overall study. HDL cholesterol and triglyceride levels were determined by using standard enzymatic techniques. Fasting lipid samples are generally analyzed in studies of this nature; however, as part of the larger investigation, only nonfasting lipid samples were available for analysis.

Neurocognitive Assessment

Following baseline, the following neurocognitive assessments were administered: the California Verbal Learning Test (CVLT-II), Symbol Digit Modalities Test (SDMT), Stroop Color-Word Task, Trailmaking A and B (TMT), and Wisconsin Card Sorting Test (WCST). The battery was administered at the GCRC by the first author as well as other graduate students of clinical psychology and neuropsychology under identical testing conditions for all participants.

Statistical Analyses

When the goal of a research study is to analyze the overall relationships between two sets of variables, canonical analysis should be used. Canonical analysis allows common and unique pathways that may link two sets of variables to be identified. The canonical analysis conducted in the present study included the CVD risk factors as independent variables and several measures of neurocognitive function as dependent variables. Age, sex, education, and depression score were added as independent variables to adjust for their relation to neurocognitive function. Five variables were positively skewed and transformed for the analysis: triglyceride level, Trailmaking B, WCST (perseverative errors), WCST (non-perseverative errors), and Beck Depression Inventory-II. Significant canonical correlations were followed up by multiple regression analyses to clarify the differential or unique contribution of the predictors to each dependent variable.

Results

Demographic data are provided in Table 1, along with descriptive statistics for the cardiovascular risk factors and neurocognitive scores.

The omnibus test for the significance of the relationship between the set of independent variables and the set of dependent variables was significant (Wilk's lambda .23, $P<.001$). Two canonical variates were significant. Approximately 53% of the variance in the set of dependent variables was captured through variate one. An additional 9% of the variance in the set of dependent variables was captured through variate two. The first variate represented 60% of shared variance between the independent and dependent variables ($R=.74$, $P<.001$). The second variate represented 26% of shared variance between the independent and dependent variables ($R=.58$, $P<.05$). Altogether, the independent variables

helped to explain 32% of the variance in the dependent variables through the two common pathways.

Standardized canonical coefficients and correlations are found in Table 2. The latent variable represented by variate one was strongly anchored by low performance on the SDMT as well as the CVLT-II on the dependent variable side. Within the set of independent variables, age and education were most strongly related to variate one. The latent variable underlying variate two contrasted most markedly with the SDMT and perseverative errors on one hand and with CVLT-II and non-perseverative errors on the other. Within the set of independent variables, age and diastolic blood pressure were the variables that were most strongly related to the underlying construct.

After adjusting for the influence of age, sex, education, and depression score, higher systolic blood pressure was not associated with poorer performance on any of the tests of neurocognitive function. Higher diastolic blood pressure was associated with poorer recall on the CVLT-II (β=−.34, $P<.05$). Diastolic blood pressure was not related to performance on the SDMT, Trailmaking B, Stroop Colorword Task, WCST (perseverative errors), and WCST (non-perseverative errors). Greater waist circumference was not associated with poorer performance on the SDMT, Trailmaking B, Stroop Colorword Task, CVLT-II, WCST (perseverative errors), or WCST (non-perseverative errors). Higher triglyceride levels were associated with poorer performance on the CVLT-II (β=−.20, $P<.05$). Triglyceride levels were not associated with poorer performance on the SDMT, Trailmaking B, Stroop Colorword Task, or WCST (perseverative errors) or WCST (non-perseverative errors). Finally, lower HDL cholesterol levels were associated with poorer performance on the WCST (non-perseverative errors) (β=−.26, $P<.05$) but were not associated with the other neurocognitive assessments.

Age was inversely related to neurocognitive function. It was related to performance on the SDMT (β=−.50, $P<.001$), Trailmaking B (β=.42, $P<.001$), Stroop Colorword Task (β=−.36, $P<.01$), WCST (perseverative errors) (β=.21, $P<.05$), and WCST (non-perseverative errors) (β=.41, $P<.001$), but age was not related to performance on the CVLT-II. Education was related to neurocognitive function as well. Education was positively related to performance on the SDMT (β=.37, $P<.001$), Trailmaking B (β=−.28, $P<.01$), Stroop Colorword Task (β=.26, $P<.05$), CVLT-II (β=.38, $P<.001$), WCST (perseverative errors) (β=−.40, $P<.001$), and WCST (non-perseverative errors) (β=−.31, $P<.01$). Finally, sex was related to performance on the CVLT-II. Women performed significantly better on this measure than did men (β=−.25, $P<.01$). Sex was unrelated to performance on the remaining tests of neurocognitive function. All regression coefficients and significance values are found in Table 3.

Discussion

This study explored the pattern of relationships between blood pressure, waist circumference, lipids, and neurocognitive function by using a statistical procedure known as canonical analysis. Based on the links that emerged in the data, only one of the significant canonical variates suggested that a pattern of relationships exists between cardiovascular risk factors and neurocognitive function in this sample. The first latent construct was defined by performance on the SDMT and CVLT-II, as predicted from age and education, thus reflecting a biosocial influence. No cardiovascular risk factors contributed to the patterns of relationships in the first construct.

The second pattern of relationships that emerged was composed of aspects of the SDMT, CVLT-II, and WCST (both perseverative and non-perseverative errors). The interrelations among the dependent variables were such that poorer performance on the SDMT was

contrasted with better performance on the CVLT-II, while perseverative errors were contrasted to non-perseverative errors on the WCST. The latent variable is explained by the contribution of diastolic blood pressure and age, thus reflecting a more direct influence of cardiovascular risk. For older participants and participants with lower diastolic blood pressures, CVLT-II performance was better. The basic cognitive process common to all three of these tests is attention. Within this attention construct, greater age and lower diastolic blood pressure are associated with more efficient attentional processes associated with performance on the CVLT-II and less efficient attentional processes associated with performance on the WCST and SDMT.

The idea that CVD risk factors would cluster to predict neurocognitive function was not fully supported. While diastolic blood pressure and triglyceride level may work in tandem (as suggested from the canonical analysis), the relationship of HDL cholesterol level to non-perseverative cognitive errors of executive function may follow a very distinct pathway (as suggested by the multiple regression analysis). We observed no convergent and repetitive pattern that suggested that several risk factors combined are associated with broad cognitive function. Two findings clearly emerged from the present analysis: 1) beyond biosocial markers such as sex and education, some of the best known CVD risk factors may be predictive of aspects of cognitive functioning; 2) cognitive performance contrasts in terms of perseverative and non-perseverative errors may be somewhat linked to variations along some CVD risk factors. On both counts, only diastolic blood pressure was implicated in this pattern analysis.

There was a significant link between blood pressure and CVLT-II performance in the sample. Higher diastolic blood pressure was inversely related to performance. Verbal learning, as measured by the CVLT-II, is a central component of neurocognitive function, and depends on the contribution of many brain regions. Learning is the result of consolidation and implies effort and careful attention by the learner.[7] The implications of the relationship between diastolic blood pressure and verbal learning found in the current study are that 1) blood pressure, even though potentially distal, may affect the function of diverse brain regions and 2) the effect of higher blood pressure may have negative consequences for verbal abilities that are necessary for many real-world applications that require acquiring new verbal information.

Waist circumference was not related to aspects of neurocognitive function, although it has been linked to poorer neurocognitive function, independently of other CVD risk factors.[26] While waist circumference was not related to neurocognitive function in the current study, it may contribute to the CVD risk factors that are related. Thus, the relationships between blood pressure, lipids, and neurocognitive function may not exist without the presence of abdominal obesity because obesity and other CVD risk factors are generally comorbid.

Lipids were related to neurocognitive function. Higher triglyceride levels have previously been associated with a decline in verbal knowledge[8] and other psychometric measures.[9] Among participants with higher triglyceride levels, CVLT-II performance was poorer than for those with lower triglyceride levels. Lipids, in the form of cholesterol, have previously been associated with memory. Greater memory performance has been associated with a reduction in total cholesterol and low-density lipoprotein cholesterol over three years.[10] Lower HDL cholesterol levels were associated with greater errors on the WCST (non-perseverative errors), which is consistent with findings in previous studies.[11] One study suggested that increased plasma HDL cholesterol concentrations have a protective role in maintaining superior cognition into old age.[12] Based on these findings, HDL cholesterol may play a role in optimal executive functioning.

The relationship between lipids and neurocognitive function has seldom been addressed in the literature. Our findings support the notion that triglyceride levels and HDL cholesterol levels relate to neurocognitive function. In addition to the implications of the possible effect of blood pressure on verbal learning, lipid levels may also influence the acquisition of verbal information. The findings also suggest that executive function, another crucial aspect of neurocognitive function, may decrease as lipid levels increase. Executive function is used in a host of neurocognitive processes and the ability to shift cognitive set, as measured by the WCST, is typically related to damage to frontal brain regions.[7] Cognitive set shifting involves the ability to adapt and adopt a new rule or principle within an ongoing activity. This ability is necessary in novel situations and to handle distractions during an ongoing activity.

This study has a number of limitations. The availability of an African American sample to investigate our research questions was a rare and valuable opportunity; however, the cross-sectional nature of the study prevented the relationship of cardiovascular risk factors to neurocognitive function to be examined over time. Furthermore, the limited size of the sample prevented us from more comprehensively examining neurocognitive function with additional measures. While our use of nonfasting lipid measurements might be seen as a limitation, evidence suggests that the distinction between nonfasting and fasting HDL cholesterol and triglyceride levels may not be clinically significant. Concentration of HDL cholesterol and classification of patients into risk groups does not appear to be affected by the fasting/nonfasting distinction.[13,14] Furthermore, high levels of nonfasting triglycerides accurately predict myocardial infarction, ischemic heart disease, and death and, among women, are strongly associated with cardiovascular events independently of other cardiovascular risk factors.[15,16]

Conclusions

Because of the high prevalence of CVD among African Americans, identifying the effect of cardiovascular risk factors on cognition must be investigated. Longitudinal research is required to more fully validate the relationships that we found between blood pressure, lipids, learning, and executive function. The addition of imaging techniques would help to validate our findings. Adding insulin resistance as a CVD risk factor would create a fuller picture of how the metabolic syndrome may relate to neurocognitive function.

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Table 1

Demographic information, cardiovascular risk factors, and neurocognitive scores for 106 community-dwelling African American adults

	Mean	SD	Range
Age (years)	44.3	12.4	21–73
Education (years)	14.2	2.4	10–21
Systolic blood pressure (mm Hg)	131.6	17.8	90–192
Diastolic blood pressure (mm Hg)	76.9	13.3	41–113
Waist circumference (cm)	94.8	24.0	26–160
Triglycerides (mg/dL)	99.8	68.1	21–339
HDL cholesterol (mg/dL)	50.7	15.3	24–97
Symbol Digit Modalities Test (no. correct)	47.3	12.6	21–79
Trailmaking B (seconds elapsed)	92.0	55.5	28–409
Stroop Color-word Task (no. correct)	38.0	12.6	10–72
California Verbal Learning Test-II (short delay free recall, no. correct)	43.1	10.3	16–64
Wisconsin Card Sorting Test (perseverative errors)	23.1	13.2	4–80
Wisconsin Card Sorting Test (non-perseverative errors)	22.9	14.6	4–75
Beck Depression Inventory II	8.0	7.9	0–37

SD, standard deviation.

HDL, high-density lipoprotein.

Table 2

Standardized canonical coefficients and correlations between canonical variates, independent, and dependent variables

	Variate One		Variate Two	
Variables	**Correlation Coefficients**	**Standardized Canonical Coefficients**	**Correlation Coefficients**	**Standardized Canonical Coefficients**
Symbol Digit Modalities Test (written)	−.87	−.46	−.39	−.84
Trailmaking B	.74	−.002	.22	−.003
Stroop Color-word Task	−.64	−.05	−.24	−.14
California Verbal Learning Test (short delay free recall)	−.84	−.47	.44	1.00
Wisconsin Card Sorting Test (perseverative errors)	.70	.21	.003	−.44
Wisconsin Card Sorting Test (non-perseverative errors)	.55	.05	.35	.58
Systolic blood pressure	.43	−.13	−.16	.37
Diastolic blood pressure	.43	.18	−.41	−.82
Waist circumference	.33	.01	−.04	.08
Triglycerides	.37	.08	−.18	−.53
HDL	−.35	−.07	.32	−.04
Age	.62	.52	.59	.82
Education	−.83	−.62	.14	.05
Gender	.34	.26	−.45	−.31
BDI-II	.02	.05	−.24	−.09

Table 3

Cognitive test performance and corresponding parameter estimates for independent variables, controlling for age, education, sex, and BDI-II score

Independent Variables	β	t	*P*
SDMT			
Systolic blood pressure	−.11	−.82	.41
Diastolic blood pressure	.13	.995	.32
Waist circumference	−.04	−.43	.67
Triglycerides	.03	.31	.76
HDL	−.02	−.22	.83
Trailmaking B			
Systolic blood pressure	−.03	−.22	.83
Diastolic blood pressure	−.001	−.01	.996
Waist circumference	−.03	−.27	.79
Triglycerides	.02	.14	.89
HDL	−.08	−.71	.48
Stroop Color-word Task			
Systolic blood pressure	.11	.69	.49
Diastolic blood pressure	−.04	−.27	.79
Waist circumference	−.16	−1.41	.16
Triglycerides	−.04	−.35	.73
HDL	−.02	−.23	.82
CVLT-II			
Systolic blood pressure	.25	1.77	.08
Diastolic blood pressure	−.34	−2.57	.01*
Waist circumference	.06	.66	.51
Triglycerides	−.20	−2.02	.04*
HDL	.10	1.01	.32
WCST (perseverative errors)			
Systolic blood pressure	−.08	−.52	.60
Diastolic blood pressure	.15	1.02	.31
Waist circumference	.06	.56	.58
Triglycerides	−.08	−.71	.48
HDL	−.02	−.15	.88
WCST (non-perseverative errors)			
Systolic blood pressure	−.25	−1.57	.12
Diastolic blood pressure	.06	.37	.72
Waist circumference	−.08	−.72	.48
Triglycerides	−.21	−1.85	.07
HDL	−.26	−2.28	.03*

*$P<.05$