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Vascular Risk Factors, Depression, and Cognitive Change among African American Older Adults

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Abstract

Objective—Vascular burden has been linked to future depression and cognitive change in predominately European American samples. This study investigated these relationships in older African Americans.

Methods—To examine the connection between vascular risk factors, depression, and cognitive change, this study utilized data from 435 African American elders. Specifically, the study examined the link between vascular risk at baseline with depression and cognitive functioning at a 2.5 year follow-up visit.

Results—High baseline vascular risk was associated with increased odds of future depression while controlling for age and current depression. A series of path analyses demonstrated links between baseline vascular risk, increases in depression, and decreases in processing speed.

Conclusions—These findings suggest that African Americans with greater vascular burden are at greater risk for depression and cognitive change.

Keywords

Vascular risk factors; depression; cognitive change; African Americans

Introduction

The vascular depression hypothesis asserts that vascular disease contributes to depression among older adults (Alexopoulos *et al.*, 1997a). Conditions such as stroke and heart disease often precede depression in the elderly (Alexopoulos and Kelly 2009), and vascular risk factors (VRFs) are associated with increased white matter hyperintensities (WMHs) and other cerebrovascular changes. Vascular changes visible through neuroimaging have been linked with depression as well as disorders like hypertension (Steffens *et al.*, 2002; Krishnan *et al.*, 2004; Santos *et al.*, 2009; Ikram *et al.*, 2010). The prevalence of VRFs (e.g., cardiovascular disease, angina, circulation problems, etc.) increases with age, and VRFs have been empirically linked with the onset and severity of depression in both cross-sectional and longitudinal studies (Alexopoulos *et al.*, 1997a; Alexopoulos *et al.*, 1997b; Hickie *et al.*, 2003; Kales *et al.*, 2005; Krishnan *et al.*, 1997; Lingam *et al.*, 1988; Lyness 2000; Mast *et al.*, 2005; Mast *et al.*, 2004a; Mast *et al.*, 2008; Mast *et al.*, 2004b; Nuyen *et al.*, 2007; Oldehinkel *et al.*, 2003; Steffens *et al.*, 2006; Steffens *et al.*, 2007).

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Previous literature has also shown that VRFs are related to poorer cognitive functioning in general and in patients with depression more specifically (Alexopoulos and Kelly 2009; Sheline *et al.*, 2006; Gamaldo *et al.*, 2008; Aiken Morgan *et al.*, 2010). In fact, vascular depression (i.e. the combination of depression and vascular burden) may lead to an increased risk of developing dementia (O'Brien *et al.*, 2003; Steffens *et al.*, 2007). Vascular mild cognitive impairment (MCI) may be more common than vascular dementia (O'Brien 2006), although due to the great variability within the pathology, there is no universally accepted criteria for either disorder (Jellinger 2007). Previous research also suggests that depression serves as a predictor for future cognitive impairment and dementia (Jorm 2001; Jorm 2000; Steffens *et al.*, 2006). Depression is associated with significant changes in verbal fluency, executive functioning, and perceptual speed. In addition, VRFs often serve as predictors of cognitive ability including processing speed and memory, and in terms of performance on general cognition measures such as the Mini-Mental State Examination (Freiheit *et al.*, 2012; Bielak *et al.*, 2011; Sheline *et al.*, 2006). Depression has also been linked to increased WMHs among older adults (Jorm *et al.*, 2005; Sawyer *et al.*, 2012; Alves *et al.*, 2009). In sum, individuals with greater vascular burden may be at greater risk for depression and cognitive change, and the prevalence and magnitude of these relationships requires further investigation.

Despite the attention VRFs have received as predictors of depression and cognitive change in late life (Krishnan *et al.*, 2004; Steffens *et al.*, 2002; Zimmerman *et al.*, 2009; O'Brien 2006), there has been relatively little research on older African Americans. Between-group comparisons have contributed to the understanding of multicultural aging, however, the degree to which within-group variability impacts observed differences within African Americans is not as well understood (Burton and Bengtson 1982). One longitudinal study of an 83% African American sample found that VRFs themselves did not predict decline in verbal fluency; however, depression preceded by VRFs predicted verbal fluency at three and six month follow-up. (Yochim, MacNeill, and Lichtenberg 2006). Within-group studies may help explain factors such as cohort effects and socioeconomic status (SES), each of which may be especially challenging to examine in a sample of older adults (Whitfield and Willis 1998; Whitfield *et al.*, 2008).

The impact of both depression and cognitive change are particularly concerning in light of African Americans' increased vascular risk, including high risk of stroke (Gorelick 1998), and high rates of untreated VRFs after surviving a stroke (Brenner *et al.*, 2010). African Americans are also at high risk for developing peripheral arterial disease (PAD)(Ix *et al.*, 2008; Nelson *et al.*, 2007), deep venous thrombosis (Christensen *et al.*, 2008), precursors to hypertension (Glasser *et al.*, 2011) and older African Americans also displayed high levels of WMH burden in one study (Brickman *et al.*, 2008). Overall, African American elders' many vascular vulnerabilities could substantially heighten their risk of depression and cognitive change.

The present study sought to investigate the links between VRFs, depression, and cognitive change over 2.5 years in a community dwelling sample of African American older adults. This study seeks to answer the following overarching research question: Can VRFs predict depression and cognitive change in community dwelling African American elders? This study specifically tested several hypotheses: First, a high level of vascular risk at a baseline study visit would be associated with increased depression at 2.5-year follow-up. Second, vascular risk would be associated with greater cognitive change at 2.5-year follow-up. Third, given the mixed literature concerning the interplay of depression and cognition over time, this study tested models to determine whether depression predicted subsequent change in cognition, and whether baseline cognitive functioning predicted worsening of depression over time. Memory, processing speed, and general cognition are each highly likely to be

affected by changes in depression and VRFs (Joy *et al.*, 2004; Moorhouse and Rockwood 2008; Sawyer *et al.*, 2012).

Methods

All data was collected and analyzed in accordance with the Helsinki Declaration of 1975, as revised in 1983. The procedures, data collection and ethical standards for research were approved by the Duke University Institutional review board (#1610).

Sample

The Baltimore Study of Black Aging (BSBA) is a longitudinal study of community-dwelling, African American older adults residing in the Baltimore, MD area. The analysis included 435 BSBA participants. Baseline data were collected between 2005–2007, while follow-up data was collected between 2008–2010. Each testing session lasted approximately three hours. The sample for this study had a mean age of 68.8 (SD = 9.0) and a mean of 11.7 (SD = 2.9) years of education. They had a mean of 2.1 (SD = 1.4) VRFs at the baseline visit. (A full list of sample characteristics can be found in Table 1).

Measures

Seven VRFs -- Diabetes, cardiovascular disease, high blood pressure, history of heart attack, angina, circulation problems, and history of stroke – were measured via self-report (e.g. “Has a doctor or nurse ever told you that you have ...?”) VRFs were categorized as a dichotomous variable: If a participant had multiple (i.e., two or more) conditions, they were classified as “high-risk.” Those with less than two were classified as “low-risk.” This dichotomous classification was employed based on previous findings among geriatric populations that depression rates increase significantly when two or more VRFs are present (Mast *et al.*, 2004a). Previous research has used this method to separate patients into minimal-risk and elevated-risk groups and their relative risk for depression (Zimmerman *et al.*, 2009; Azar *et al.*, 2005; Mast *et al.*, 2004b). This study used the Center for Epidemiologic Studies Depression Scale (CES-D), a well-validated self-report measure of depression among community dwelling older adults (Heller *et al.*, 2010; Lewinsohn *et al.*, 1997). CES-D was categorized as a dichotomous variable for the logistic regression model: Consistent with previous studies (Black *et al.*, 1998; Azar *et al.*, 2005; Wouts *et al.*, 2011), scores of 16 or higher were classified as evidence of clinically significant depressive symptoms. CES-D was incorporated into the path analysis models as a continuous variable.

The current analyses also included two cognitive measures. The Mini-Mental State Examination (MMSE) is a brief and repeatable measure for cognitive change among older adults in both clinical practice and research (Folstein *et al.*, 1975; Tangalos *et al.*, 1996). Among older adults, small changes in scores over time can account for reliable change at a 90% confidence level (Hensel *et al.*, 2007). The Wechsler Adult Intelligence Scale—Revised Digit Symbol task is a measure of processing speed sensitive to aging, depression, and cognitive change. It has been extensively normed across age and shown to be highly reliable (Joy *et al.*, 2004; Wechsler 1981). In this study, Digit Symbol score represents how many correct answers the participant obtained within 90 seconds, with higher scores representing better performance. MMSE and Digit Symbol scores were continuous variables within the path analysis models. An additional predictor estimating memory was also examined. The Hopkins Verbal Learning Test- Revised (HVLT-R) contains a word list which subjects attempt to learn over three consecutive trials. 20–25 minutes later, subjects attempt to recall the words without prior warning (Shapiro *et al.*, 1999).

This study also investigated impairments in activities of daily living (ADLs; Katz *et al.*, 1963) and instrumental activities of daily living (IADLs; Lawton and Brody 1969). All participants rated their facility with seventeen self-care activities. A higher total ADL score indicated greater self-reported impairment in satisfying basic needs (e.g. dressing, eating), while a higher total IADL score indicated greater self-reported impairment in satisfying complex needs of independent living (e.g. shopping, using the telephone). Physical limitations are associated with depressed mood among African American older adults (Thorpe *et al.*, 2011; Yochim, Kerkar, and Lichtenberg 2006). Controlling for ADLs and IADLs allows vascular risk factors to predict depression independent of these effects (Mast 2010).

Statistical analysis

A logistic regression analysis was conducted in which gender, age, years of education, baseline ADLs, baseline IADLs, baseline CES-D score (continuous), and vascular risk factors (dichotomous) were included as predictors of the presence or absence of 2.5-year follow-up depression. The study also employed path analysis in two additional models in order to evaluate the impact of baseline vascular risk on changes in depression and cognition over time.

Results

Baseline vascular risk and odds of depression at 2.5 year follow-up

It was hypothesized that high vascular risk at baseline would be associated with greater odds of depression at 2.5-year follow-up. Prior to estimating the logistic regression model, we examined the bivariate correlations of VRFs with the other model predictors (See Table 1). Due to the lack of significant relationships between vascular risk and HVLTL at either time-point, it was excluded from further analyses.

The logistic regression model was significantly better at predicting the presence of depression at follow-up than a constant only model, $\chi^2(7) = 96.53$, $p < 0.001$. Vascular risk was a significant independent predictor of the presence of 2.5-year follow-up depression (see Table 2). Employing the odds ratio as a measure of effect size (Field 2009), an individual classified as having a high vascular risk was 2.61 times more likely to have depression at 2.5-year follow-up than individuals with low vascular risk (OR = 2.61, 95% CI [1.28–5.33]), independent of their baseline levels of depression. Gender, age, and baseline CES-D were significant predictors, while education, ADLs, and IADLs were each not significant.

Baseline vascular risk appears to predict change in depression and cognition. The initial path analysis model contained vascular risk (dichotomous) as an exogenous variable predicting both baseline and 2.5-year follow-up versions of CES-D, MMSE, and digit symbol as endogenous variables (see Figure 1). Depression was included as a continuous variable in the path analysis model to look at changes in levels of depressive symptoms over time, as well as their relationship with cognition over time.

Baseline vascular risk was associated with higher depression scores at baseline and with lower baseline cognitive scores on the MMSE and Digit Symbol tasks (see Figure 1). Baseline vascular risk was also a significant predictor of CES-D scores at 2.5 year follow-up, suggesting that high baseline vascular risk was predictive of worsening of depression over time. Vascular risk also had a small, negative direct effect on 2.5-year follow-up Digit Symbol scores, indicating that baseline vascular risk predicted a change in processing speed over time. Vascular risk did not have a direct effect on 2.5-year follow-up MMSE score.

This first model (and the second model described below) allowed the measures of cognition to correlate (baseline and follow-up MMSE, as well as baseline and follow-up Digit Symbol). The model had overall acceptable fit ($\chi^2(10) = 47.27$, $p < 0.001$; $\chi^2/df = 4.73$; CFI = .94; RMSEA = 0.09). For the sake of simplicity, this correlation was not included in Figure 1 and Figure 2.

Relationship between depression and cognition

In addition to examining vascular risk as a predictor, this study hypothesized that baseline depression could predict 2.5 year follow-up cognitive change, and that baseline cognition could predict 2.5 year follow-up depression. A second path analysis was performed to test whether depression predicted cognition at 2.5-year follow-up (see Figure 2). In addition to each of the predictors present in the first model, this second model also examined whether either cognitive variable (MMSE or Digit Symbol) predicted 2.5-year follow-up depression. Specifically, baseline CES-D became a predictor of 2.5 year follow-up Digit Symbol and MMSE, while baseline Digit Symbol and MMSE became predictors of 2.5 year follow-up CES-D.

In this analysis, CES-D did not have a direct effect on 2.5-year follow-up MMSE or on 2.5-year follow-up digit symbol, suggesting that baseline depression was not a significant predictor of cognitive change. Baseline MMSE did not have a direct effect on changes in depression 2.5 year follow-up CES-D, but Digit Symbol had a small but unexpected positive effect, such that individuals with better Digit Symbol performance at baseline had increases in depression over time.

Discussion

The main findings show vascular burden associated with depression and cognitive change in older African Americans. These results provide support for the vascular depression hypothesis among older African Americans, such that VRFs at baseline were a useful predictor of future depression. This relationship was not accounted for by gender, age, education, ADLs, IADLs, and baseline CES-D score. These results also suggest that VRFs increase risk for mild changes in processing speed. High baseline vascular risk was associated with more depressive symptoms and slower processing speed at 2.5-year follow-up. This is consistent with previous literature, wherein baseline vascular risk was associated with greater depression and poorer cognitive function (Mast *et al.*, 2008; Sheline *et al.*, 2008). To our knowledge, this is the first study to examine this relationship in a large sample of African American elders.

Prior research has suggested that depression may be a risk factor for cognitive change, and that cognitive change may increase risk for depression. The current study did not strongly support either of these predictions. Instead, these findings suggest that although vascular burden predicts changes in both depression and cognition, they do not reliably predict one another. In this regard, the connection between better baseline Digit Symbol performance and increased depressive symptoms on the CES-D at follow-up was somewhat unexpected. Previous geriatric depression studies have shown improvements in processing speed following depression treatment (Story *et al.*, 2008). Age, depression, education, race and VRFs have each been shown to predict processing speed (Sheline *et al.*, 2006), albeit with higher vascular burden suggesting slower speed, which is consistent with our results. Recent evidence has linked improved hippocampal volume in remitted geriatric depression patients to improved performance on Digit Symbol (Hou *et al.*, 2012). Future research linking white matter imaging, processing speed, and depression treatment may help explain this finding.

Depression symptom frequency may not differ between African American and non-African American older adults (Blazer *et al.*, 1998). However, depression symptoms appear more severe among African American elders than European American elders (Spence *et al.*, 2011; Liang *et al.*, 2011). Depression may also impair work and social activities more heavily among African Americans (Williams *et al.*, 2007). Among patients with major depression, African Americans have some of the lowest use of depression psychotherapy and pharmacotherapy among commonly examined racial groups, notably lower than European Americans (González *et al.*, 2008). This may stem in part from stigma within the older African American community against the effectiveness of mental health treatment, as well as cultural reinforcement to cope alone (Conner *et al.*, 2010). Although utilization of both forms of treatment appear low, African Americans are more likely to use psychotherapy to treat major depression than pharmacotherapy (González *et al.*, 2010).

This study has helped generalize the vascular depression hypothesis and the vascular cognitive impairment concept to African American elders. These findings suggest that vascular risk factors among African Americans, like European Americans in prior studies, should be carefully monitored and could be used as an intervention target in studies aimed at preventing depression and cognitive change. These findings also suggest that providers may wish to administer depression and cognitive screens to African American patients with several VRFs, even in the absence of reported depression or cognitive change.

This study had several limitations. First, this research was conducted exclusively on African Americans from the Baltimore area, which increases the risk of cohort effects and may reduce generalizability to African Americans as a whole. Second, this study was heavily reliant on self-report data in order to gather vascular risk status: Participants who do not have regular medical care may have incomplete information and undiagnosed disorders. This study did not obtain objective measures of participant medical history, e.g. chronicity of hypertension or history of hypertension treatment. Measurements of blood pressure and other risk factors would have provided better context when classifying participants' overall vascular burden. Third, this study did not include a neuroimaging component, making it difficult to confirm the presence of cerebrovascular changes. Finally, the BSBA study did not assess all major VRFs during the baseline visits, such as participant smoking history and duration. This information could have expanded the VRF criteria and led to a more accurate portrayal of high risk vs. low risk.

Conclusion

Understanding the connections between depression and medical comorbidities could have great impact on depressed African American's care. This could include the possibility of earlier and more accurate diagnosis of depression. Depression among African Americans is also highly correlated with SES (Hudson *et al.*, 2012). Among community dwelling older adults of the 1990s, African Americans had more hospital utilization related to activities of daily living than European Americans, including mobility concerns. This suggests that merely improving economic barriers to African Americans will not equalize their standard of care to that of European Americans (Bowen and González 2008).

Future research should address the limitations outlined above in order to better understand the relationship between VRFs, depression, and cognitive change. Study data should be compared to both other racial groups and other geographic distributions of African Americans. Additionally, this study's sample was approximately 75% female. Women had greater odds of depression, although vascular risk factors predicted depression even after controlling for the effects of gender. However, future research may wish to recruit a higher percentage of depressed males to examine any gender effects on the severity of depression

(Kessler 2003). Future research should also include biomarkers such as MRI to better track vascular change. These improvements should aid in providing better diagnosis and care for older adults at risk for depression and cognitive change.

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Figure 1.
 Path Analysis Model of Depression and Cognitive Prediction. Values are standardized.
 * = $p < 0.05$, ** = $p < 0.01$

Figure 2. Path Analysis Model of Depression and Cognitive Prediction, with Depression Predicting 2.5-Year Follow-up Cognition and Cognition Predicting 2.5-Year Follow-up Depression. Values are standardized. * = $p < 0.05$, ** = $p < 0.01$

Table 1**Study Sample Characteristics and Correlations with Vascular Risk Factors**

sVariable	Mean	SD	r	p
Number of VRFs	2.1	1.4		
Age	68.8	9.0	0.19	< 0.001
Education	11.7	2.9	-0.07	0.135
ADL Total	1.8	2.3	0.25	< 0.001
IADL Total	1.0	2.0	0.24	< 0.001
CES-D	11.0	9.2	0.18	< 0.001
CES-D Follow-up	13.5	4.5	0.15	0.002
MMSE	25.8	3.0	-0.13	0.008
MMSE Follow-up	24.8	3.1	-0.09	0.062
Digit Symbol	32.8	11.9	-0.15	0.002
Digit Symbol Follow-up	31.9	13.4	-0.19	< 0.001
HVLT-R	5.3	2.9	-0.05	0.356
HVLT-R Follow-up	6.0	3.1	-0.05	0.316

n = 435 (75.6% female)

Note: VRFs = vascular risk factors

ADL = activities of daily living;

IADL = instrumental activities of daily living;

CES-D = Center for Epidemiologic Studies Depression Scale;

MMSE = Mini-Mental State Examination;

Digit Symbol = Wechsler Adult Intelligence Scale - Revised Digit Symbol;

HVLT-R = Hopkins Verbal Learning Test – Revised

Table 2**Logistic Regression Model of Depression Prediction**

Variable	Wald	p-value	95% CI for Odds Ratio		
			Lower	Odds Ratio	Upper
Constant-only model	156.633	< 0.001		0.199	
Sex	7.409	0.006	1.352	2.938	6.382
Age	11.978	0.001	0.908	0.940	0.973
Education	1.940	0.164	0.828	0.925	1.032
ADLs	0.016	0.900	0.845	0.990	1.159
IADLs	0.059	0.807	0.857	1.022	1.219
VRF Index	6.901	0.009	1.276	2.608	5.333
CES-D	36.029	< 0.001	1.074	1.111	1.151
Constant	0.120	0.729		1.666	

Note: $R^2 = .20$ (Cox and Snell); CI = confidence interval;

ADL =activities of daily living; IADL =instrumental activities of daily living;

VRF Index: 1 =two or more vascular risk factors vs. 0 =zero or one vascular risk factors;

CES-D =Center for Epidemiologic Studies Depression Scale.

All predictors were measured at the baseline visit.