RESEARCH ARTICLE

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Vascular depression: overrepresented among African Americans?

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Objective: Our primary aim was to compare the rate of vascular depression among a clinical sample of African American and Caucasian depressed older adults. Secondary aims included characterizing the clinical and neuropsychological profile of vascular depression and comparing antidepressant response rates between patients with vascular and nonvascular depression.

Methods: This was a two-site, multi-ethnic, open 8-week trial of antidepressant medication in older adults with depression. Men and women 50 years or older meeting DSM-IV criteria for nonpsychotic unipolar depression participated in this trial. Each participant underwent a comprehensive psychiatric and neuropsychological evaluation and a brain MRI, which were performed at baseline.

Results: Forty-six patients met inclusion and exclusion criteria. Forty-two of those patients received an MRI at baseline. Sixteen patients met criteria for vascular depression. Patients with vascular depression were significantly more likely to be African American and have a higher likelihood of being female, a higher rate of hypertension and psychomotor retardation, a lower rate of family history of affective illness, and frontal systems dysfunction on neuropsychological testing. The difference in response rates between patients with vascular and nonvascular depression did not reach statistical significance.

Conclusions: This is the first study to document high rates of vascular depression in a clinical sample of African Americans and Caucasians. Our findings suggest that vascular depression may be overrepresented among African Americans, which is consistent with the high rates of cardiovascular disease, hypertension, and stroke in this population. Copyright © 2013 John Wiley & Sons, Ltd.

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Introduction

The vascular depression (VD) hypothesis proposes that cerebrovascular disease may increase risk for the development of some geriatric depressive syndromes (Alexopoulos *et al.*, 1997). Given the high rates of vascular risk factors that exist among African Americans, it is possible that they are at high risk for VD, but this association has yet to be tested. For instance, African Americans have higher rates of hypertension (60% vs. 38%) (Kramer *et al.*, 2004), diabetes (19% vs. 10%) (CDC, 2011), and obesity (45% vs. 30%) (Ogden *et al.*, 2006) than Whites. Not surprisingly, they also have higher rates of cardiovascular disease compared with Whites (37% of White men and 34% of White women versus 45% of African American men and 47% of African American women) (AHA, 2012; AHA, 2012), and cardiovascular disease is the leading cause of death in African Americans (AHA, 2005). Finally, stroke is 1.5 times more prevalent in

African Americans at every age group (Kissela *et al.*, 2004), which significantly increases risk for the development of vascular dementia. It stands to reason that the high rates of vascular risk factors also leave African Americans at higher risk for VD than Caucasians.

If we take MRI evidence of white matter hyperintensities as the definition of VD (i.e., MRI-defined VD) (Sneed *et al.*, 2008; Krishnan *et al.*, 1997), there is some indication that its clinical profile is characterized by frontal lobe symptoms, which is consistent with the VD hypothesis (Alexopoulos *et al.*, 1997; Krishnan *et al.*, 2004; Hickie *et al.*, 1995). White matter lesions among older depressed adults were associated with older age, late onset of depression (> 50 years), psychomotor retardation, and the absence of a family history of affective disorder (Hickie *et al.*, 1995). In another study, deep white or subcortical gray matter hyperintensity lesions were associated with older age (≥60 years) and later age of depression onset (> 40 years) (Krishnan *et al.*, 1997). Patients with deep white subcortical gray matter hyperintensity lesions were also found to be older, have greater levels of lassitude (as measured by the Montgomery–Asberg Depression Rating Scale), and more likely to have a self-reported history of hypertension (Krishnan *et al.*, 2004). Loss of libido and a family history of psychiatric illness have also been associated with the VD syndrome (Krishnan *et al.*, 2004).

Patients with VD may also respond poorly to antidepressant treatment (Hickie *et al.*, 1995; Simpson *et al.*, 1998; Taylor *et al.*, 2003; Navarro *et al.*, 2004; Alexopoulos *et al.*, 2002; Alexopoulos *et al.*, 2008; Gunning-Dixon *et al.*, 2010; Sneed *et al.*, 2011). For example, among depressed older adults classified as having VD on the basis of deep white matter hyperintensity (DWMH) burden, none achieved remission (Sneed *et al.*, 2011). In another recent study, depressed older adults who failed to remit following antidepressant treatment had significantly greater MRI hyperintensity burden than both patients who remitted and age-matched controls (Gunning-Dixon *et al.*, 2010).

The vulnerability of the vascular depressed patient to cognitive dysfunction has been widely discussed (Pimontel *et al.*, 2012; Culang-Reinlieb *et al.*, 2010). For instance, patients with deep white or subcortical gray matter lesion load demonstrated significantly worse performance across measures of executive functioning and nonverbal memory when compared with nonvascular depressed patients (Potter *et al.*, 2009). Although this is the only study to date that has examined this issue among patients selected for VD on the basis of MRI hyperintensities, numerous other studies have shown that depressed older adults with white matter hyperintensities demonstrate worse performance on measures of executive functioning and processing speed compared with both age-matched controls and depressed older adults without such lesions (Kramer-Ginsberg *et al.*, 1999; Lesser *et al.*, 1996; Sheline *et al.*, 2008).

Older African Americans with depression have not been studied systematically despite their high risk for adverse cardiovascular and cerebrovascular outcomes. Previous VD research has primarily been conducted in disproportionally Caucasian samples (Sneed *et al.*, 2008; Gonzalez *et al.*, 2012; Alexopoulos *et al.*, 2002; Sheline *et al.*, 2010). VD studies with ethnically diverse samples did not directly compare the rate or characteristics of VD in Caucasians with those in minority subjects (Krishnan *et al.*, 1998; Potter *et al.*, 2009). Our primary aim was to compare the rate of VD among older depressed African Americans and Caucasians presenting clinically for evaluation and treatment. Our secondary aim was to compare the demographic, clinical, and neuropsychological profiles of vascular and nonvascular depressed patients. On the basis of previous reports and the VD hypothesis, we hypothesized that patients with VD will be older with a later age of depression onset and demonstrate poorer insight, increased rates of psychomotor retardation and hypertension, and lower rates of loss of libido and family history of affective disorder than patients with non-VD. We further predicted that patients with VD would demonstrate worse performance on measures of executive functioning and psychomotor speed than those with non-VD. Although limited by a relatively small sample size, we also compared open-label antidepressant treatment response in these two groups of depressed patients, and we predicted that patients with VD would respond less well to antidepressant medication than patients with non-VD.

Methods

Study procedures

This study was a two-site (Harlem Hospital Center and New York State Psychiatric Institute), multi-ethnic, open 8-week trial of antidepressant medication in older adults with depression. At the screening visit, a comprehensive psychiatric evaluation, including a 24-item Hamilton Rating Scale for Depression (HRSD) and Mini Mental State Exam (MMSE), and a medical history were performed to assess eligibility. If the patient

was considered to have an affective disorder, a structured clinical interview for DSM-IV was completed to confirm diagnostic status.

Patients were considered eligible if they (i) were male or female 50 years or older; (ii) had a current diagnosis of major depression disorder, dysthymia, or depression not otherwise specified; (iii) had a score of ≥14 on the 24-item HRSD at initial visit; and (iv) were willing and able to give informed consent, complete neuropsychological testing, and complete the medical exam, electrocardiogram, blood tests, and urine screen. Patients were excluded from the study if they (i) had a diagnosis of bipolar disorder, obsessive compulsive disorder, psychotic disorder, or current substance abuse or dependence within the past year; (ii) had met the criteria for psychotic depression; (iii) had current suicide intent or made a suicide attempt within the past 6 months; (iv) had probable Alzheimer's disease or vascular dementia based on National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association criteria; (v) had a Folstein MMSE (range 0–30) score < 24; (vi) had started psychotherapy in the last 3 months; (vii) were currently taking triptans; (viii) had acute, severe, or unstable medical illness; and (ix) had MRI contraindications.

If a patient met inclusion and did not meet exclusion criteria, informed consent was obtained, and the patient entered the treatment protocol. The baseline assessment included a physical examination, an electrocardiogram, and routine blood work. The patient completed a Beck Depression Inventory, Second Edition, and the study physician completed the Cumulative Illness Rating Scale—Geriatrics (CIRS-G), HRSD, and the Clinical Global Impression Rating Scale. Finally, patients received baseline structural MRI and neuropsychological testing (refer to the succeeding text).

Upon completion of the baseline evaluation, patients began open treatment with either citalopram or escitalopram. If a patient failed to respond to an adequate trial of escitalopram or citalopram in the current depressive episode, he or she was alternatively treated with duloxetine or desvenlafaxine. Treatment with citalopram began at 20 mg/day for the first 4 weeks. At the end of 4 weeks, patients who did not meet remission criteria (HRSD < 8) had their citalopram dose increased to 40 mg/day for the remainder of the trial (4 weeks). If treated with escitalopram, the dosage began at 10 mg/day for 4 weeks and was increased to 20 mg/day at the end of week 4 if the patient did not meet remission criteria. Duloxetine dosing began at 30 mg/day for the first week followed by increasing doses up to a maximum of 120 mg/day, as was clinically determined by the study physician. Desvenlafaxine dosing began at 50 mg/day for 4 weeks and then was increased to 100 mg/day at the end of week 4.

At each weekly visit, depression severity was evaluated using the 24-item HRSD and Beck Depression Inventory, Second Edition. Global improvement ratings were also collected (Clinical Global Impression Rating Scale).

Neuropsychological test battery

All participants completed a comprehensive neuropsychological test battery at baseline that assessed cognitive domains likely to be affected in late-life depression (Lezak *et al.*, 2004): memory (Buschke Selective Reminding Test (Buschke and Fuld, 1974) [total learning over six trials]), language (Boston Naming Test (Goodglalss and Kaplan, 2000) [total correct]), executive functioning (Trail Making Test B (Reitan, 1958) [seconds to complete, log transformed to normalize distribution], Stroop Color/Word Test (MacLeod, 1991) [percent interference—percent change in median reaction time to color/word versus color responses, log transformed to normalize distribution], and Dementia Rating Scale-2 Initiation/Perseveration subscale (Mattis, 1989)), visuospatial functioning (Wechsler Abbreviated Scale of Intelligence Block Design), and attention/psychomotor speed (Trail Making Test A (Reitan, 1958) [seconds to complete, log transformed to normalize distribution] and complex (choice) reaction time test (Thorne *et al.*, 1998) [reaction time for correct responses, log transformed for analyses]). Two of the tests (Choice Reaction Time Test and Stroop Color/Word Test) were presented on a Macintosh laptop computer and were written in the PsyScope programming language (Cohen *et al.*, 1993), whereas all other tests were administered by hand.

MRI and VD classification

T2-weighted fluid attenuated inversion recovery images were acquired at baseline and evaluated for the presence of DWMHs. The severity of lesions was graded by a neuroradiologist using the Fazekas modified Coffey Rating Scale for signal hyperintensities (Krishnan *et al.*, 1997). DWMHs were defined as abnormalities in the frontal, parietal, temporal, or occipital lobes and scored as 0 (absent), 1 (punctate foci), 2 (beginning confluence of foci), and 3 (large confluent areas). Participants were classified as having VD if they

received a score of 2 or more on their DWMH rating (Sneed *et al.*, 2008; Krishnan *et al.*, 1997).

Data analysis

Missing data. To accommodate missing data, we used multiple imputation (Schafer and Olsen, 1998) using the multiple imputation procedure in SPSS. Multiple imputation replaces missing data with a set of plausible values on the basis of all variables in the working data set, which includes demographic, clinical outcome, and neuropsychological test variables. This report is based on 20 imputed data sets ($m=20$), which is sufficient to obtain excellent results unless rates of missing data are extremely high (Schafer, 1999). The imputed data sets were analyzed using standard statistical analyses, and the results of these analyses are combined using Rubin's rules (Schafer and Olsen, 1998; Schafer and Graham, 2002).

Statistical analyses. Descriptive statistics were calculated to characterize the total sample and the VD and non-VD subgroups. We compared baseline demographic characteristics using ordinary least squares and logistic regression analyses.

Primary aim. To compare the racial make-up of the VD and non-VD subgroups, we first conducted an omnibus chi-square test. To specifically compare the rate of VD between Caucasian and African American patients, we conducted a follow-up chi-square test on VD (non-VD = 0, VD = 1) and race (Caucasian = 0, African American = 1).

Secondary aims. To characterize the clinical profile of VD, we used logistic and ordinary least squares regression analyses to compare dichotomous and continuous variables, respectively, between the VD and non-VD subgroups. To test for differences in neuropsychological test performance at baseline between patients with and without VD, we regressed the neuropsychological test score of interest on VD status.

To test for differences in antidepressant treatment response between patients with VD and non-VD, we conducted two sets of analyses. First, we conducted logistic regression analyses on both response (50% reduction in HRSD from baseline) and remission (HRSD < 8 at week 8). Second, we conducted a regressed change analysis to test for differences in endpoint HRSD scores by VD subgroup, covarying for baseline HRSD. All statistical tests were two sided and evaluated at the $\alpha=0.05$ level for significance.

Results

Descriptive statistics

Forty-six participants met inclusion and exclusion criteria. Forty-two of these patients received an MRI at baseline. Table 1 presents unadjusted baseline demographic and clinical characteristics of the total sample as well as the VD and non-VD subgroups. Within the total sample, the average study participant was 62 years old ($SD=9.4$) and completed 3 years of college ($SD=2.9$). Fifty-two percent of the sample was women, the average depression score at baseline was 23.4 ($SD=5.5$) on the 24-item HRSD, and the average MMSE score was 28.5 ($SD=1.3$). Of the 42 patients,

Table 1 Baseline demographic and clinical characteristics for the total sample and the vascular depression subgroups

Variable	Total sample (n=42)	Vascular depression (n=16)	Nonvascular depression (n=26)
Age (years)	62.3 (9.4)	63.5 (10.8)	61.5 (8.6)
Women (%)[a]	52	75	38
Race (%)[a]			
Caucasian	48	13	69
African American	43	69	27
Hispanic	7	13	4
Education[a]	15.0 (2.9)	13.8 (3.0)	15.7 (2.7)
Age at depression onset (years)	41.0 (21.4)	35.5 (23.8)	44.3 (19.5)
FH mood disorder[a]	56	33	71
HRSD	23.4 (5.5)	23.6 (7.0)	23.3 (4.5)
CIRS-G total score	3.8 (3.2)	4.9 (2.8)	3.1 (3.3)
CIRS-G vascular score	0.6 (0.9)	0.7 (1.1)	0.5 (0.8)
Hypertension (%)[a]	41	67	25
Diabetes (%)	21	40	8

FH, family history; HRSD, 24-item Hamilton Depression Rating Scale; CIRS-G, Cumulative Illness Rating Scale– Geriatrics.
[a]Indicates statistical significance at the $p< 0.05$ level between the vascular depression and nonvascular depression groups.

30 (71%) were administered escitalopram, nine (21%) citalopram, two (5%) duloxetine, and one (2%) desvenlafaxine.

As can be seen in Table 1, 16 (38%) patients were classified as VD and 26 as non-VD (62%). Patients with VD were significantly less educated than those with non-VD ($B = -2.0$, $SE = 0.89$, 95% CI [-3.72, -0.25], $p = 0.03$). Patients with VD were also significantly more likely to be female ($B = 1.57$, $SE = 0.70$, 95% CI [1.21, 19.08], $p = 0.03$). We therefore adjusted for education and gender in all neuropsychological test analyses (Secondary Aims section). There were no statistically significant differences in age, baseline depression severity (as measured by the 24-item HRSD), medical disease burden (as measured by the CIRS-G total score), or vascular burden (as measured by the CIRS-G vascular score) between vascular and nonvascular depressed patients.

Hypothesis testing

Primary aim. We first tested the association between VD and race. The omnibus test revealed a statistically significant difference in the racial make-up of the VD and non-VD subgroups ($p = 0.001$, Fisher's exact test). Specifically, the VD subgroup ($n = 16$) was composed of two Caucasians, 11 African Americans, two Hispanics, and one biracial individual, whereas the non-VD subgroup ($n = 26$) was composed of 18 Caucasians, seven African Americans, and one Hispanic. A follow-up test (2 × 2 chi-square) revealed a significant difference in the rate of VD among African Americans and Caucasians ($\chi^2(1) = 11.0$, $p = 0.001$). Specifically, 11 of 18 or 61% of African Americans in this sample had VD, whereas two of 20 or 10% of Caucasians were classified as VD.

Secondary aims. We next characterized the clinical and neuropsychological profiles of VD. We found that patients with VD had a lower rate of family history of affective illness than patients with non-VD ($B = -1.61$, $SE = 0.73$, 95% CI [0.05, 0.84], $p = 0.03$); five of 15 (33%) patients with VD had a family history of affective illness, whereas 15 of 21 (71%) patients with non-VD had a family history of affective illness. VD was also associated with higher rates of hypertension ($B = 1.79$, $SE = 0.72$, 95% CI [1.46, 24.73], $p = 0.01$) in that a history of hypertension was reported by 10 of 15 (67%) patients with VD compared with six of 24 (25%) patients with non-VD. Finally, patients with VD demonstrated significantly more psychomotor retardation as measured by item 8 on the HRSD ($B = -0.32$, $SE = 0.16$, 95% CI [-0.64, -0.001], $p = 0.05$). There were no significant differences in level of insight (HRSD item 17) or loss of libido (HRSD item 14), or in the rate of diabetes between the two patient groups.

We further compared baseline neuropsychological test performance between the VD and non-VD subgroups. All comparisons of neuropsychological test performance were adjusted for education and gender. Table 2 presents unadjusted baseline neuropsychological test scores for the total sample and the VD and non-VD subgroups. Patients with VD demonstrated significantly worse performance on the Stroop ($B = 0.61$, $SE = 0.29$, 95% CI [0.04, 1.2], $p = 0.04$),

Table 2 Baseline neuropsychological test performance for the total sample and the vascular depression subgroups

Measure	Total sample (n = 42)	Vascular depression (n = 16)	Nonvascular depression (n = 26)
MMSE	28.5 (1.3)	28.3 (1.0)	28.5 (1.4)
Memory			
Buschke SRT	44.3 (8.9)	42.8 (8.1)	45.3 (9.5)
Language			
Boston naming test	50.6 (9.0)	48.9 (7.5)	51.6 (9.8)
Executive functioning			
Stroop[a]	0.4 (0.3)	0.5 (0.3)	0.3 (0.2)
TMT-B	123.1 (77.2)	158.4 (85.0)	102.7 (65.6)
DRS-2 I/P[a]	35.8 (2.6)	34.3 (3.5)	36.8 (0.9)
Attention/psychomotor speed			
TMT-A	41.4 (19.8)	50.5 (22.0)	36.1 (16.6)
Complex (choice) reaction time test[a]	876.4 (201.4)	963.0 (245.9)	816.2 (139.9)
Visuospatial functioning			
WASI block design	26.6 (16.5)	20.9 (12.5)	30.4 (17.9)

Table values are means and standard deviations.

MMSE, Mini mental state exam, total number correct; Buschke SRT, Buschke selective reminding test, immediate recall, total number correct; TMT, trail making test, seconds; DRS-2 I/P, Dementia Rating Scale-2 initiation/perseveration subscale, total correct; Stroop, Stroop color/word test, interference effect; WASI, Wechsler Abbreviated Scale of Intelligence.

[a]Indicates statistical significance at the $p < 0.05$ level between the vascular depression and nonvascular depression groups.

Dementia Rating Scale Initiation/Perseveration subtest ($B = -2.68$, $SE = 0.80$, 95% CI [−4.26, −1.11], $p = 0.001$), and choice reaction time test ($B = 0.15$, $SE = 0.07$, 95% CI [0.01, 0.29], $p = 0.04$) at baseline when compared with patients with non-VD. No other comparisons were statistically significant.

Finally, we compared open-label antidepressant treatment response between patients with VD and non-VD using continuous and dichotomous outcome analyses:

Continuous outcome analyses. Change in HRSD scores over time is graphically depicted in Figure 1. At endpoint, patients with VD had an HRSD score of 13.48, whereas patients with non-VD had an HRSD score of 9.16. Adjusting for baseline HRSD, this difference in endpoint HRSD scores was not statistically significant ($B = 4.31$, $SE = 2.43$, 95% CI [−0.46, 9.08], $p = 0.08$).

Responder analyses. Seven of 16 (44%) patients with VD responded to antidepressant treatment, whereas 19 of 26 (73%) patients with non-VD responded. This 29% difference in response rates, however, was not statistically significant ($B = -1.18$, $SE = 0.69$, 95% CI [0.08, 1.20], $p = 0.09$).

Remitter analyses. Five of 16 (31%) patients with VD met remission criteria at study end compared with 11 of 26 (42%) patients with non-VD. This difference of 11% in antidepressant remission rates between patients with vascular and non-VD was not statistically significant ($B = -0.54$, $SE = 0.72$, 95% CI [0.14, 2.38], $p = 0.45$).

Discussion

Our primary finding is that the rate of VD is significantly higher among African Americans than Caucasians in a clinical sample of patients seeking treatment for depression. Specifically, 61% of African Americans and 10% of Caucasians were classified as having VD. The African American community with its high rates of cardiovascular risk factors, heart disease, and stroke, therefore, appears to be at risk for a fourth vascular illness that until now has gone unrecognized. It is, therefore, more important than ever to address the observation that patients with VD respond less well to antidepressant medication than patients with non-VD (Hickie *et al.*, 1995; Simpson *et al.*, 1998; Taylor *et al.*, 2003; Navarro *et al.*, 2004; Alexopoulos *et al.*, 2002; Alexopoulos *et al.*, 2008; Gunning-Dixon *et al.*, 2010; Sneed *et al.*, 2011). Although response to antidepressant treatment did not differ significantly between VD and non-VD patients in this study, there were indications that VD patients tended to improve less over 8 weeks of treatment.

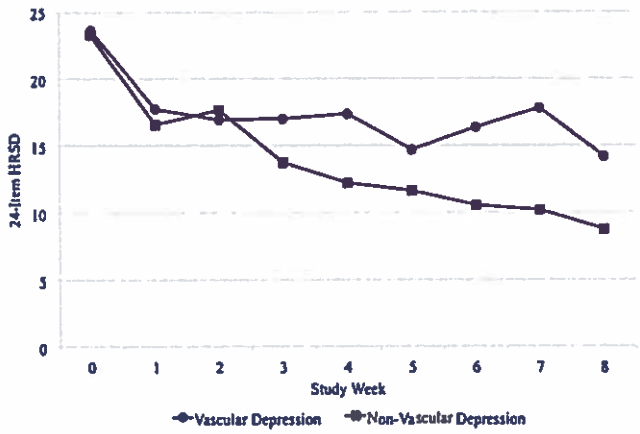

Figure 1 Change in unadjusted Hamilton Rating Scale for Depression scores over the 8-week trial for patients with vascular depression and those with nonvascular depression (complete case data).

We also found that patients with VD demonstrated a distinct clinical profile characterized by psychomotor retardation, a high rate of hypertension, and a low rate of family history of mental illness. This is generally consistent with previous studies that have examined the clinical profile of patients with MRI-defined VD (Krishnan *et al.*, 1997; Krishnan *et al.*, 2004; Hickie *et al.*, 1995). VD was also associated with a distinct neuropsychological profile that reflects frontal systems dysfunction (i.e., reduced performance in psychomotor speed and executive functioning). This finding is consistent with previous reports that document an association between white matter hyperintensities, and both psychomotor speed and executive ability among depressed older adults (Hickie *et al.*, 1995; Potter *et al.*, 2009; Lesser *et al.*, 1996). The observed neuropsychological profile of vascular depressed patients in this study also provides support for the VD hypothesis as it reflects the proposed underlying cerebrovascular pathology of the subtype (Alexopoulos *et al.*, 1997; Krishnan *et al.*, 1997).

We did not find a relationship between VD and older age or later age of depression onset. In fact, the VD group had a *younger* age of depression onset (age 36 years) than the non-VD group (age 44 years), which is the opposite of what has been reported in the literature (Krishnan *et al.*, 1997; Hickie *et al.*, 1997). One possible explanation is that a majority of the VD group in this study was African American (11 of 16 patients), a population with very high rates of vascular risk. The difference in the prevalence of hypertension between African Americans and Whites is evident as early as age 25 years, and the magnitude of that difference steadily increases with age (Geronimus *et al.*, 2007). Therefore, African Americans may be at greater risk not only for the development of VD but also

for developing it at an earlier age than Whites. This would argue against the idea that MRI-defined VD is a disorder limited to late life, especially in populations that have high rates of vascular risk factors. However, these findings should be interpreted in the context of the methodological and conceptual limitations associated with the construct of age at onset (Sneed *et al.*, 2008; Alexopoulos, 2006) and the limited sample size in our study.

Although this study documented a 29% difference in response rates to antidepressant medication between vascular and nonvascular depressed patients, this difference was not statistically significant. Seventy-three percent of the non-VD group responded, whereas 44% of the VD group responded. Although statistically nonsignificant, these findings are consistent with the idea that patients with VD respond less well to antidepressant medication than patients with non-VD. However, they also suggest that patients with VD may respond better to an initial trial of medication than is commonly reported in the literature (Gunning-Dixon *et al.*, 2010; Sneed *et al.*, 2011). It should be noted, however, that the response rate of the VD subgroup (44%) was lower than that in other open treatment trials (63%) (Karp *et al.*, 2010; Wohlreich *et al.*, 2004) in geriatric depression indicating that, although they do respond, their response may not be as robust as patients without VD.

This study should be interpreted in the context of several limitations. First, race, site, and VD were confounded in this study. It was therefore impossible to tease apart the contribution of these variables to our findings. Second, the sample size was small, and therefore, we were not able to accurately estimate the difference in response rates between VD and non-VD. Third, there was no healthy age-matched comparison group, making it difficult to determine the extent of baseline neurocognitive "impairment" among the VD subgroup. Fourth, we do not have data on history of cerebrovascular or cardiovascular disease, which could be confounding our findings given the higher rate of such illnesses in African Americans than Caucasians. Fifth, given that many patients reported having early-onset depression, it is possible that some patients had a depression with vascular disease rather than a VD; however, this was nearly impossible for us to determine given the psychometric problems of the age-of-onset construct (Sneed *et al.*, 2008; Alexopoulos, 2006; Sneed *et al.*, 2006) and the inability to determine causality in VD. Finally, past studies have reported racial differences in antidepressant use and adherence to medical treatments (Odedosu *et al.*, 2012; Bosworth *et al.*, 2008; Waldman *et al.*, 2009; González *et al.*, 2008), which may have affected our findings. However, if African Americans (predominantly classified as vascular depressed) are less likely to have received past antidepressant treatment, then they may be selective serotonin reuptake inhibitor (SSRI) naïve, making them *more* likely to respond to antidepressant medication in this study. The low rate of antidepressant treatment response in the VD group (predominantly African American) underscores the lack of response that they may actually have to SSRI treatment of depression.

The limitations of this study, however, must be assessed in the context that this is the first study of VD to include equal numbers of African Americans and Caucasians. This is critical because we documented for the first time that rates of VD are higher in African Americans than Caucasians.

Conflicts of interest

S.P.R. has received consultation fees from Pfizer and has served on the Adverse Events Board for Medtronic. D.P.D. has received research funding from Eli Lilly. For the remaining authors, none were declared.

Key points

- Vascular depression may be overrepresented among African Americans.
- Our findings are consistent with the high rates of cardiovascular disease, hypertension, and stroke in this population.

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