Preservation of Cognitive Function With Antihypertensive Medications

A Longitudinal Analysis of a Community-Based Sample of African Americans

Michael D. Murray, PharmD, MPH; Kathleen A. Lane, MS; Sujuan Gao, PhD; Rebecca M. Evans, MD; Frederick W. Unverzagt, MD; Kathleen S. Hall, PhD; Hugh Hendrie, MB, ChB

Background: Results of previous studies of white older adults suggest that antihypertensive medications preserve cognition. We assessed the long-term effect of antihypertensive medications on cognitive function in a community sample of African American older adults.

Methods: We conducted longitudinal surveys and clinical assessment of cognitive function in a random sample of 2212 community-dwelling African Americans 65 years and older. We identified 1900 participants without evidence of cognitive impairment at baseline, 1617 of whom had subsequent follow-up information, and 946 of whom had blood pressure measurements. Cognitive function was measured at baseline and at 2 and 5 years by means of scores on the Community Screening Instrument for Dementia and neuropsychological and clinical assessment for dementia and cognitive impairment. Prescription and nonprescription medication use was derived from in-home inspection of medications and participant and informant reports.

Results: Of 1900 participants, 288 (15.2%) developed incident cognitive impairment. Using logistic regression to control for the effects of age, sex, education, baseline cognitive scores, and hypertension and angina or myocardial infarction, we found that antihypertensive medications reduced the odds of incident cognitive impairment by 38% (odds ratio, 0.62; 95% confidence interval, 0.45-0.84). Corresponding analysis using blood pressure measurements on the subset of participants was inconclusive.

Conclusion: Antihypertensive medication use is associated with preservation of cognitive function in older African American adults.

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lar protective medications were associated with a reduced risk of cognitive impairment and dementia primarily owing to the effect of antihypertensive medications. However, such a cross-sectional study is more likely to reveal associations wherein the timing between cognitive assessment and drug use is near (ie, acute effects), whereas a longitudinal design would be better suited to ascertain the temporal relationship of long-term drug effects. Because we now have 5 years of longitudinal data with assessments at baseline, 2 years, and 5 years, we conducted a longitudinal analysis to ascertain the long-term effects of antihypertensive medications used by members of the same cohort of older adult African American participants as in our previous cross-sectional analysis. The purpose of this study is to report the long-term effects of antihypertensive medications on cognitive performance in older adult African Americans by means of a longitudinal study design.

### SUBJECTS AND METHODS

#### PARTICIPANTS

The target geographic sampling frame for the study was 29 contiguous census tracts within Indianapolis. According to the 1990 US Census, 80% of the population within these census tracts was African American, representing two thirds of all elderly African Americans living within the city. Using data provided by the Indianapolis Water Company, we drew a simple random sample of 60% of the residents. The sample was representative of elderly African Americans throughout Indianapolis and Indiana in its age, sex, and socioeconomic composition. Interviewers who were members of the targeted community canvassed the neighborhoods and, with randomized address lists, identified homes to interview African American participants 65 years and older. When possible, a close relative within the subject's household participated in the interview as an informant to provide, verify, or supplement data.

Of the 7590 residential addresses provided by the public utility, 4915 households were ineligible because none of the members of the household were 65 years or older and 383 households had no African American family members (282 households had 2 interviews and 4 households had 3 interviews). Of the 2582 eligible participants, 249 refused participation and 121 were too ill to participate. A total of 2212 participants completed the baseline in-home interviews, and 1495 of these participants had accompanying informants during their interviews.

#### RESEARCH DESIGN

The Indiana University–Purdue University at Indianapolis Institutional Review Board approved the study, and all participants provided their written informed consent. The research design has been comprehensively described previously.20 For the purposes of this article, an overview of relevant methods is provided. The Figure shows the study design. All study waves (baseline, wave 1, and wave 2) were conducted in a 2-stage design involving an initial screen for cognitive impairment (stage 1) followed by clinical assessment (stage 2). To determine the prevalence of dementia, baseline interviews were conducted from 1992 to 1993 in participants’ homes by trained interviewers to screen for cognitive and functional impairment, ascertain medical and medication histories, and determine activities of daily living. Within a year of the stage 1 baseline screening interview, stage 2 in-home clinical assessments were conducted by means of a sampling scheme that oversampled persons with a high likelihood of dementia (Figure). The rationale for oversampling was to assess participants with the greatest propensity for dementia given limits on resources to conduct comprehensive assessments. These clinical assessments included a neuropsychological evaluation, a physical examination, and a structured interview with the informant.

To determine incident cases of dementia after the baseline interview and clinical assessments, 2 waves of follow-up interviews were conducted between 1994 and 1995 (wave 1) and again between 1997 and 1998 (wave 2). As with the baseline prevalence study, these incidence studies were performed in 2 stages: in-home screening followed by a full diagnostic evaluation primarily of those with a high probability of dementia.

On the basis of cognitive and clinical assessments as described below, we excluded 65 participants who were diagnosed as having dementia, 106 as having cognitive impairment, and 141 participants who were poor performers at baseline as defined below. As shown in the Figure, of the 1900 participants in the inception cohort, 323 participants were unavailable for wave 1 cognitive or clinical assessments because of death (n=133), refusal of assessment (n=58), or our inability to locate them or other reasons (n=132). Of these 323 participants, 129 who were unavailable at wave 1 were reascertained for wave 2. At wave 2, 447 participants were unavailable for cognitive and clinical assessments.

#### COGNITIVE AND CLINICAL ASSESSMENT

The screening instrument used at stage 1 of each wave was the Community Screening Instrument for Dementia, developed by Hall and colleagues21 while studying the Cree in Manitoba and subsequently harmonized for African Americans in Indianapo-
lis. The instrument was developed to measure 2 primary dimensions, cognition and function. The cognitive scale excluded literacy-dependent items to assess language, memory, recall, orientation, judgment, comprehension, and construction. A separate section completed by the informant assessed the subject’s activities of daily living and social function. The scores from the cognitive scale and activities of daily living were combined into a single screening outcome measurement (the cognitive score). A discriminant function score was derived from the combined cognitive and informant scores, which in one study demonstrated 100% sensitivity and 79% specificity in distinguishing demented and nondemented persons. For this study, we used the same methods for distinguishing performance groups as we have for previous studies. When informants were available, we used discriminant scores to distinguish 3 performance groups at baseline and at each wave (poor, intermediate, and good). When informants were unavailable, we used cognitive scores only to distinguish performance groups. The performance groups for follow-up also take into account participants’ decline from previous waves.

Clinical assessment of the participant at stage 2 of each wave was conducted with the informant present and had 4 components: history of the subject’s cognitive function, performance of activities of daily living, a review of the medical and noncardiovascular disorders, such as the use of antihypertensive medications. However, we previously reported on the effects of a broad category of vascular risk–mediating medications that included antihypertensive, antiabetic, antihyperlipidemic, and antiplatelet medications. Therefore, we provide information on these latter medications as well. (A document giving the classification of these medications is available on request from the authors.)

**BLOOD PRESSURE MEASUREMENT AND HYPERTENSION**

Blood pressure was measured during all clinical assessments and during the screening interview at wave 2. However, only the blood pressure measurement taken during the wave in which the end point was reached was used in the analysis. At each assessment, blood pressure was measured twice and the average of the measurements was recorded. Of the 1617 participants, 471 (29.1%) reached their end point at wave 1 and 1146 (70.9%) reached it at wave 2. Of the 471 participants from wave 1, 96 had a clinical assessment, of whom 86 had their blood pressure measured at that point. Of the 1146 from wave 2, 891 had their blood pressure measured at their end point. When the variable describing medication use on all participating visits was added, 86 participants from wave 1 and 860 participants from wave 2 had complete medication information. Thus, 946 participants were available for the analysis involving blood pressure.

The present of hypertension was determined on the basis of results from the screening interview at baseline. We asked both the subject and the informant whether a physician had ever told the subject that he or she had either hypertension or high blood pressure. If either answered yes, then the subject was considered to have hypertension.

**ANALYSIS**

We compared demographic characteristics and vascular risk factors for participants with or without incident cognitive impairment by means of t tests for continuous variables and χ² tests for categorical variables. Age was the participant’s age at end point. Using logistic regression, we ascertained the effect of baseline and follow-up medication use on the risk of incident cognitive impairment. Odds ratios, 95% confidence intervals, and P values were calculated from models controlling for participant age, total years of education, sex, baseline cognitive scores from the Community Screening Instrument for Dementia, history of angina or myocardial infarction, and hypertension. Many medications used to control hypertension may also be used for other cardiovascular disorders, such as coronary artery disease, or even noncardiovascular disorders, such as the use of β-adrenergic antagonists for migraine headache. Because hypertension is a risk factor for dementia as well as a confounding bias in the way drugs are prescribed, we controlled for hypertension and angina or myocardial infarction. Since these analyses were exploratory, not confirmatory, we did not adjust the significance levels used for each test to control for the overall type 1 error.

A separate analysis was also performed on participants who had blood pressure measurements taken at their end point. An
Antihypertensive medication usage was categorized into 6 levels by a combination of the blood pressure measurements at the end point and the subject’s antihypertensive medication usage throughout the study. If either the average systolic level was greater than or equal to 140 mm Hg or the average diastolic level was greater than or equal to 90 mm Hg, then the subject was considered to have uncontrolled blood pressure at that time. Participants who used antihypertensive medication during all waves were classified into 2 levels: continuous usage with controlled blood pressure and continuous usage with uncontrolled blood pressure. Similarly, intermittent usage was also broken into 2 levels: intermittent usage with controlled blood pressure and intermittent usage with uncontrolled blood pressure. The last 2 levels included participants who did not use antihypertensive medications with controlled blood pressure, and those who did not use antihypertensive medications but had uncontrolled blood pressure.

We used χ² tests for categorical variables and t tests for continuous variables to compare participants with blood pressure measurements and participants without this information. Logistic regression was then used to identify differences in incident cognitive impairment among the 6 antihypertensive medication usage groups described in the preceding paragraph. The reference group was the group of participants with uncontrolled blood pressure who reported no use of antihypertensive medication. The model controlled for participants’ age, total years of education, sex, baseline cognitive scores from the Community Screening Instrument for Dementia, history of angina or myocardial infarction, and hypertension.

Incident cognitive impairment occurred in 288 (15.2%) of the 1900 participants in wave 1 (n = 108) and wave 2 (n = 180). Of 1577 participants available for cognitive screening and clinical assessment at wave 1, 18 (1.1%) met our criteria for dementia, 22 (1.4%) were cognitively impaired, and 68 (4.3%) were poor performers. At wave 2, of 1151 participants available for cognitive screening and clinical assessment, 50 (4.3%) met our criteria for dementia, 51 (4.4%) were cognitively impaired, and 79 (6.9%) were poor performers. Table 1 compares demographic and vascular factors for participants with and without incident impaired cognition. Participants with incident cognitive impairment were older, had fewer years of formal education, and had lower baseline cognitive scores from the Community Screening Instrument for Dementia. Although not statistically significant, participants with incident cognitive impairment were less likely at baseline to have diabetes or use alcohol.

**RESULTS**

Table 1 shows the long-term effect of medications on incident cognitive impairment. Antihypertensive medi-
cations reduced the odds of cognitive impairment by 38% compared with persons not using these drugs (odds ratio, 0.62; 95% confidence interval, 0.45-0.84). Effects of the individual antihypertensive medication subclasses were not statistically significant, but each odds ratio for subgroups was less than 1, suggesting a trend of protective effect on cognition among subclasses. The exception was β-adrenergic antagonists, which was slightly but not significantly higher than 1.

In our previous analysis of cross-sectional data from this same cohort, we observed a reduced odds of cognitive impairment among participants prescribed vascular risk factor–mediating medications (antidiabetic, antihypertensive, antihyperlipidemic, and antiplatelet medications). In the current study of longitudinal data, this broad group of medications reduced the odds of incident dementia by 40% compared with those not using these drugs (odds ratio, 0.60; 95% confidence interval, 0.45-0.81). As in our earlier study, this protective effect on cognition largely derived from the medications used for the treatment of hypertension.

Because some participants had changes to their baseline prescription regimens, we conducted separate analyses to compare the risk of cognitive impairment from drugs administered either continuously or intermittently to the risk in participants who had reported never receiving these medications. Of these participants, 46 were not used in the analysis because they were missing medication data at wave 1 but had data at wave 2. As shown in Table 3, the effects of continuous administration of antihypertensive drugs were consistent with the favorable effects observed in Table 2.

**EFFECTS ON BLOOD PRESSURE CONTROL**

Table 4 contains the results of the analysis of reported antihypertensive medication use and blood pressure control. Of the 946 participants with blood pressure measurements, 116 (12.3%) were considered to have continuous usage with controlled hypertension, 274 (29.0%) had continuous usage but uncontrolled hypertension, 100 (10.6%) were intermittent users with controlled hypertension, 214 (22.6%) were intermittent users with uncontrolled hypertension, 91 (9.6%) did not take antihypertensive medications and had controlled blood pressure, and 151 (16.0%) did not take antihypertensive medications but had uncontrolled blood pressure. Incident cognitive impairment was 0.1% greater among participants who did not receive antihypertensive medications and whose blood pressure was uncontrolled than among those with continuous use and controlled blood pressure, but this odds ratio was not statistically significant (odds ratio, 0.63; 95% confidence interval, 0.31-1.25).

As shown in Table 5, differences in demographic and vascular risk factors between participants with and without blood pressure data were not statistically significant. Baseline cognitive scores were greater in participants in the blood pressure assessment study than in par-

### Table 3. Risk of Incident Cognitive Impairment by Continuous or Intermittent Antihypertensive Medication Usage Patterns in 1571 African Americans

<table>
<thead>
<tr>
<th>Medication Drug Use*</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any antihypertensive</td>
<td>Continuous 0.69 (0.46-1.02)</td>
<td>.06</td>
</tr>
<tr>
<td></td>
<td>Intermittent 1.13 (0.78-1.62)</td>
<td>.53</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor</td>
<td>Continuous 0.75 (0.39-1.44)</td>
<td>.39</td>
</tr>
<tr>
<td></td>
<td>Intermittent 0.99 (0.67-1.46)</td>
<td>.95</td>
</tr>
<tr>
<td>Antiadrenergic</td>
<td>Continuous 0.25 (0.03-1.91)</td>
<td>.18</td>
</tr>
<tr>
<td></td>
<td>Intermittent 1.24 (0.70-2.20)</td>
<td>.47</td>
</tr>
<tr>
<td>β-Adrenergic antagonist</td>
<td>Continuous 0.76 (0.29-2.00)</td>
<td>.57</td>
</tr>
<tr>
<td></td>
<td>Intermittent 1.30 (0.80-2.09)</td>
<td>.29</td>
</tr>
<tr>
<td>Calcium channel</td>
<td>Continuous 0.88 (0.56-1.39)</td>
<td>.59</td>
</tr>
<tr>
<td>antagonist†</td>
<td>Intermittent 0.97 (0.68-1.37)</td>
<td>.85</td>
</tr>
<tr>
<td>Central</td>
<td>Continuous 0.74 (0.25-2.19)</td>
<td>.59</td>
</tr>
<tr>
<td></td>
<td>Intermittent 0.80 (0.37-1.75)</td>
<td>.58</td>
</tr>
<tr>
<td>Sympathomimetic</td>
<td>Continuous 0.92 (0.62-1.35)</td>
<td>.66</td>
</tr>
<tr>
<td></td>
<td>Intermittent 1.15 (0.82-1.60)</td>
<td>.42</td>
</tr>
<tr>
<td>Reserpine</td>
<td>Continuous 3.10 (0.27-35.84)</td>
<td>.37</td>
</tr>
<tr>
<td></td>
<td>Intermittent 1.28 (0.38-4.33)</td>
<td>.69</td>
</tr>
</tbody>
</table>

*Odds of incident cognitive impairment by logistic regression for continuous or intermittent drug use compared with no reported use of a drug from each category. Continuous use refers to participants who reported use of a particular drug category at all participating waves. Intermittent use refers to use of drugs at least during 1 wave but not at all participating waves. Models controlled for age, sex, years of formal education, baseline cognitive score from the Community Screening Instrument for Dementia, and history of hypertension and angina or myocardial infarction. There were 46 people for whom medication usage information was missing at wave 1 but who had information at wave 2.

†CI indicates confidence interval.

‡See last footnote to Table 2 for calcium channel antagonist subclassification. The effects of calcium channel antagonist subclasses were not statistically significant.

### Table 4. Risk of Incident Cognitive Impairment by Reported Antihypertensive Medication Use and Blood Pressure (BP) in 946 Participants

<table>
<thead>
<tr>
<th>Medication Usage</th>
<th>No. of Subjects</th>
<th>Incident Cognitive Impairment, %</th>
<th>Odds Ratio* (95% CI)†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous usage with BP control</td>
<td>116</td>
<td>13.79</td>
<td>0.63 (0.31-1.25)</td>
<td>.19</td>
</tr>
<tr>
<td>Continuous usage with uncontrolled BP</td>
<td>274</td>
<td>17.52</td>
<td>0.95 (0.56-1.61)</td>
<td>.85</td>
</tr>
<tr>
<td>Intermittent usage with BP control</td>
<td>100</td>
<td>21.00</td>
<td>0.99 (0.52-1.90)</td>
<td>.97</td>
</tr>
<tr>
<td>Intermittent usage with uncontrolled BP</td>
<td>214</td>
<td>19.16</td>
<td>1.13 (0.58-2.20)</td>
<td>.99</td>
</tr>
<tr>
<td>No usage with BP control</td>
<td>91</td>
<td>21.98</td>
<td>1.13 (0.58-2.20)</td>
<td>.72</td>
</tr>
<tr>
<td>No usage with uncontrolled BP</td>
<td>151</td>
<td>19.87</td>
<td>1.00 (Referent)</td>
<td>. . .</td>
</tr>
</tbody>
</table>

*Odds of cognitive impairment for medication use over time and status of blood pressure control at the subject's end point by logistic regression controlling for age, sex, years of formal education, baseline cognitive score from the Community Screening Instrument for Dementia, and history of hypertension and angina or myocardial infarction. Blood pressure was considered controlled when both means of the 2 systolic and diastolic measurements taken at the subject’s end point were less than 140 mm Hg and less than 90 mm Hg, respectively.

†CI indicates confidence interval.
participants not in the blood pressure study. However, these scores were controlled in the analysis of data in Table 4.

COMMENT

A cornerstone of geriatric medicine is the preservation of cognitive function. The most common and devastating threats to cognition in elderly people are vascular dementias and Alzheimer disease. Even though the many recent advances in medicine prolong life, their impact is dampened by a lack of progress in preventing cognitive decline. Thus, it is especially relevant to search for strategies to preserve cognition in older adults.

The results of this longitudinal analysis of long-term drug effects indicate that antihypertensive medications reduce the risk of cognitive impairment in older African Americans. Previous longitudinal analyses of older adult cohorts indicate that the beneficial effects of antihypertensive medications on preservation of cognitive function are due to their effects in controlling blood pressure in midlife. We attempted to replicate these previous findings by using blood pressure measurements taken at the last screening or clinical contact with the participants. Unfortunately, our results were inconclusive. These discrepant findings may be explained by the shorter duration of blood pressure monitoring in our study. To demonstrate that the effect of antihypertensive medications is mediated through blood pressure control, it is probable that blood pressure monitoring would need to be conducted over a longer period than occurred in our study.

Most longitudinal studies of cognitive function in older adults have been conducted in populations predominated by whites. This study is, to our knowledge, the largest longitudinal study of the cognitive effects of drugs in older adult African Americans. It is widely known that African Americans have a greater prevalence of hypertension, which is more severe, results in poorer outcomes, and responds differently to pharmacotherapy. It is also well-known that effective treatment of hypertension protects African Americans from adverse vascular outcomes associated with prolonged exposure to high blood pressure such as stroke, myocardial infarction, and end-stage renal disease. The results of our study indicate that antihypertensive therapy may also preserve cognitive function.

Recently, Knopman and colleagues published their findings from the Atherosclerosis Risk in Communities Study involving 8729 white and 2234 African American participants primarily from Jackson, Miss. Their 6-year multiracial longitudinal study showed that hypertension and diabetes are risk factors for cognitive impairment even among younger persons. However, this study was limited by a lack of cognitive follow-up on 40% of their African American cohort. Furthermore, the effects of antihypertensive medications were not specifically addressed. Finally, ascertainment of medication use in the study was conducted by asking participants to bring their medications to the clinic, which has recently been shown to be inaccurate.

Our findings are consistent with our previous cross-sectional analysis. In the earlier study, we found a protective effect of the broad category of vascular risk factor–mediating medications. However, this effect was predominantly due to antihypertensive medications. In this more rigorous longitudinal analysis of incident cognitive impairment in a cohort of cognitively intact individuals, the protective effect of antihypertensive medications was confirmed.

The one exception between our earlier cross-sectional study and the current longitudinal analysis was that, in the current study, centrally acting sympathomimetic drugs such as clonidine and methyldopa were not risk factors for cognitive impairment or dementia. There are 2 primary reasons for this finding. First, the longitudinal analysis is more appropriate for ascertainment of long-term drug effects, whereas cross-sectional analysis is more appropriate for associations between the acute effects of drugs and cognitive effects. Centrally acting sympathomimetic drugs are not necessarily known to have a greater propensity to produce hypotension compared with other antihypertensive medications. However, withdrawal of clonidine can produce rebound hypertension, which could produce unfavorable effects on cognition. Yet, patients tolerating these drugs may have the same long-term preservation of cognitive function as occurs with other antihypertensive medications.

Limitations of this study must be noted. First, medication data were limited to the names of drugs reportedly being used by participants at the time of their interview. We do not have data on indication, precise duration of use, frequency of administration, dosage, and adherence of the participant to prescribed regimens. Although ascertainment of medication use by participant report is limited by participant recall, our interviews were conducted in participant homes where interviewers recorded most medication names directly from the container labels of prescription and nonprescription drugs currently being used by participants.

Second, blood pressure measurements were available primarily at wave 2, thereby limiting our inferences pertaining to blood pressure. Although we lack longitudinal blood pressure measurements, data from longitudinal studies already exist that demonstrate the complex relationship between blood pressure and cognitive function and reinforce the critical impact of blood pressure control with medications in preserving cognitive function.

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Table 5. Demographics and Vascular Risk Factors Between Participants Included in the Analysis of Blood Pressure (BP) Measurements

<table>
<thead>
<tr>
<th></th>
<th>In BP Study (n = 946)</th>
<th>Not in BP Study (n = 671)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>77.7 ± 6.3</td>
<td>77.7 ± 7.0</td>
<td>.91</td>
</tr>
<tr>
<td>Women, %</td>
<td>67.0</td>
<td>66.0</td>
<td>.68</td>
</tr>
<tr>
<td>Education, mean ± SD, y</td>
<td>10.1 ± 2.9</td>
<td>9.8 ± 3.1</td>
<td>.06</td>
</tr>
<tr>
<td>Baseline cognitive score, mean ± SD</td>
<td>31.3 ± 1.6</td>
<td>30.9 ± 1.7</td>
<td>.01</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>66.8</td>
<td>63.5</td>
<td>.17</td>
</tr>
<tr>
<td>Stroke, %</td>
<td>10.4</td>
<td>11.2</td>
<td>.59</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>25.8</td>
<td>25.9</td>
<td>.80</td>
</tr>
<tr>
<td>Heart disease, %</td>
<td>26.2</td>
<td>28.9</td>
<td>.23</td>
</tr>
<tr>
<td>Regular alcohol use, %</td>
<td>40.2</td>
<td>39.3</td>
<td>.72</td>
</tr>
</tbody>
</table>

*From the Community Screening Instrument for Dementia.
†Defined as report of angina or myocardial infarction or heart attack.
Despite these limitations to our data, we conclude that use of antihypertensive medications is associated with the preservation of cognition in older adult African Americans. Although we cannot state with certainty from our study that this effect is mediated by blood pressure control, the results provide additional rationale and impetus for guidelines indicating the need for heightened efforts to detect hypertension, adequately treat it, and carefully monitor patients with the disease. In doing so, not only would known adverse outcomes from poorly controlled vascular disorders such as stroke, myocardial infarction, and end-stage renal disease be prevented, but it is also likely that cognitive function would be preserved in persons who are at greatest risk of suffering vascular insult, namely, older African Americans.

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Corresponding author and reprints. Hugh Hendrie, MB, ChB, Regenstrief Institute for Health Care, Regenstrief Health Center, Sixth Floor, 1050 Wishard Blvd, Indianapolis, IN 46202-2872 (e-mail: hhendri@iupui.edu).

REFERENCES