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Diabetes and Cognitive Decline: Investigating the Potential Influence of Factors Related to Health Disparities

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Abstract

Objectives—We investigated whether factors related to health disparities – race, rural residence, education, perceived racial discrimination, vascular disease, and health care access and utilization – may moderate the association between diabetes and cognitive decline.

Methods—Participants were 624 community-dwelling older adults (49% African American, 49% rural) who completed in-home Mini-Mental State Examination at baseline and four-year follow-up.

Results—Diabetes at baseline predicted cognitive decline over four years in regression models adjusted for a number of possible confounds. Only perceived discrimination and health utilization showed significant interaction effects with diabetes. Among African Americans who reported experiencing racial discrimination, there was a stronger relationship between diabetes and cognitive decline. Among participants who reported absence of visiting a physician within the past six months, the association between diabetes and cognitive decline was substantially larger.

Discussion—Findings suggest that factors related to health disparities may influence cognitive outcomes among older adults with diabetes.

Keywords

diabetes; cognitive decline; older adults; health disparities

With aging, adults are at increased risk of developing type 2 diabetes as well as cognitive impairment, and there is mounting evidence that these conditions are strongly linked (Biessels et al., 2006; Strachan, Reynolds, Frier, Mitchell, & Price, 2008). Overall prevalence of diabetes and cognitive impairment have each been rising and are substantial contributors to reduced

quality of life in older adulthood as well as rising costs of health care. The Centers for Disease Control and Prevention (CDC) recently reported that more than 23 million Americans are thought to have diabetes, with almost half the cases occurring among individuals age 60 or older (2007). The majority of diabetes cases are due to type 2 diabetes (90–95%), which has a peak prevalence around age 70 (Biessels, Deary, & Ryan, 2008). Diabetes is a well known risk factor for cardiovascular disease and stroke, which, in turn, are associated with higher rates of cognitive impairment (Hachinski, 2008). The substantial interest in understanding the role of diabetes in cognitive decline is due to the potential for modifying risk of cognitive impairment by changing or treating factors related to diabetes.

Many existing studies of diabetes and cognitive aging have not included adequate numbers of African Americans, despite the fact that African Americans have substantially higher rates of diabetes compared to Caucasians (CDC, 2007; White, Beech, & Miller, 2009). African Americans also have higher rates of diabetes-related complications in terms of vision, nerve damage, kidney disease and amputations (Harris, 2001). In general, there has been little examination of the potential impact of race or other factors associated with health disparities on the relationship between diabetes and cognitive decline. One exception is for vascular disease, where it has been found that comorbid hypertension accelerates cognitive decline in those with diabetes (Hassing et al., 2004; Xu, Qiu, Winblad, & Fratiglioni, 2007). Also, a cross-sectional investigation found that the association between diabetes and cognitive impairment was much stronger among individuals with lower levels of education (Stewart, Richards, Brayne, & Mann, 2001).

Prior studies that focused on the influence of race on diabetes-related cognitive outcomes have yielded conflicting results. Using data from the Atherosclerosis Risk in Communities (ARIC) study, Knopman et al. (2001) reported that race did not appear to modify the association between diabetes and change in cognitive function over six years. However, the sample was limited to individuals age 70 or younger at baseline, which would exclude many older adults who are at greatest risk of cognitive decline. Highlighting the importance of advanced age in studying the interrelationship of diabetes, race, and cognitive decline, Stewart and colleagues (2003) reported no direct association between diabetes and decline but an interaction effect of diabetes and older age on three-year cognitive change in a African-Caribbean sample of adults age 55 to 75 at baseline. This particular study could not directly examine the potential influence of race since the sample was comprised solely of African-Caribbean participants. One recent study reported that race was a moderator of age-related cognitive deficits in those with diabetes (Obidi et al., 2008), but generalizability of findings is uncertain since the sample included only 25 African Americans.

To our knowledge, prior studies have not examined the effects of factors such as perceived discrimination, health care access, or health care utilization on cognitive outcomes in those with diabetes, despite reported links between these factors and various health indicators (e.g., Trivedi & Ayanian, 2006; White et al., 2009; Williams, Neighbors, & Jackson, 2003). For example, it was recently found that greater adherence to medical appointments is a strong predictor of diabetes metabolic control (Schechter, Schorling, & Voss, 2008). With regard to discrimination, pathways to negative outcomes in diabetes may include adherence to various treatment regimens as well as increased stress (Pascoe & Richman, 2009). Indicators of stress have been linked to higher levels of proinflammatory cytokines such as interleukin-6 (IL-6), which is thought to play a major role in diabetes as well as development of Alzheimer's disease (Kiecolt-Glaser, 2009).

We used data from the UAB Study of Aging (Allman, Sawyer, & Roseman, 2006) to examine the relationship between diabetes and change in cognitive function over four years. This study of community-dwelling older adults was designed to have a balanced sample size across race

(African American and Caucasian) as well as urban/rural residence. We were particularly interested in examining factors related to health disparities, such as race, rural residence, education, vascular disease, perceived racial discrimination, and health care access and utilization as potential moderators of the relationship between diabetes and cognitive decline.

METHODS

Participants

This analysis used data from the UAB Study of Aging, a longitudinal study of community-dwelling adults aged 65 and over in five counties of central Alabama (Allman et al., 2006). A random sample of older adults was initially recruited from a list of Medicare beneficiaries stratified by race (African American/Caucasian), county (rural/urban), and gender to achieve a balanced sample with respect to these factors. Letters were sent to 3,100 persons, followed by telephone calls to set an appointment for the in-home assessment. Individuals living in nursing homes or unable to schedule their own appointments were excluded. Of 2,188 persons contacted, 1,000 participants were enrolled. Data collection targeted factors related to mobility and everyday function, and was gathered during in-home interviews at baseline and four years later, with telephone follow-ups every six months. A complete description of the study design and measures has been previously published (Allman et al., 2006).

The sample for the current analysis included all participants who completed in-home assessments four years after baseline, at which time cognitive function was measured again. Of the initial 1,000 participants, 775 were alive and not living in a nursing home at four-year follow-up; 624 participants (81%) agreed to be interviewed in their homes. Non-participants did not differ from participants in terms of gender, urban/rural residence, or race ($p > .05$). However, non-participants were older and reported lower levels of education ($p < .05$).

Measures

Cognitive decline was measured using change in Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) from baseline to four years later. MMSE scores range from 0 to 30, with higher scores indicating better cognitive function. Race (African American/Caucasian), age, gender, and education were self-reported at baseline. Two of the five counties from which participants were recruited were classified as urban and three were rural (Alabama Rural Health Association, 1998). Education was collected by asking participants to report the highest grade completed, which was recorded as: sixth or less, seventh through eleventh, high school, some college, completed technical or junior college, college graduate, some graduate/professional school, or graduate/professional degree. Post-high school categories were subsequently collapsed into one level of classification.

Diabetes and vascular disease comorbidity (hypertension, peripheral arterial disease, myocardial infarction, congestive heart failure, and stroke) were ascertained by self-report with physician, hospital discharge, or medication verification at baseline. Conditions were considered verified if the participant was prescribed a medication for the condition, if the primary physician returned a questionnaire indicating the condition, or if a hospital discharge summary in the previous three years indicated the disease. An index score was created using the total number of vascular conditions listed above.

Physical activity and depressive symptoms were examined as potential confounders. Physical activity was measured using the leisure-time physical activity assessment from the Cardiovascular Health Study (Cardiovascular Health Study, 1989). Participants reported frequency and duration of participation in 15 different types of activities during the past two weeks. These activities included walking, household chores, mowing, raking, gardening,

hiking, jogging, biking, exercise cycling, dancing, aerobics, bowling, golfing, general exercise, and swimming. Physical activity was scored as kilocalories expended per week. Depressive symptoms were assessed using the 15-item Geriatric Depression Scale (GDS; Sheikh & Yesavage, 1986). This instrument involves asking participants for yes/no responses to potential depressive symptoms experienced in the past week. Higher scores reflect greater depressive symptoms.

Perceived racial discrimination, health care access, and health care utilization were considered as potential moderators in addition to race, rural residence, education, and vascular comorbidity. Perceived discrimination was measured by participant response to the question, "Over your lifetime, how often have you experienced discrimination because of your race or skin color?", and dichotomized as never versus occasionally or more often. Health care access was defined by self-report of having Medicare supplemental insurance or other private insurance in addition to Medicare. For health care utilization, participants were asked at baseline about whether a physician had been visited within the past six months.

Data Analysis

We used linear regression models to examine the association between diabetes and cognitive decline. In our basic linear model, we regressed change in MMSE score on presence of diabetes, baseline MMSE score, age, race, gender, residence (urban/rural), and level of education. In the next model, we additionally adjusted for physical activity and depressive symptoms. In the final model, we adjusted for all previous covariates as well as vascular disease comorbidity. To investigate whether the association between diabetes and cognitive decline was modified by race, rural residence, education, vascular comorbidity, health care access, or health care utilization, we refitted the basic model separately with inclusion of each potential modifier and an interaction term of the respective factor by presence of diabetes. For examination of an interaction between perceived racial discrimination and diabetes, only African Americans were included in the model given the much different meaning and relevance of discrimination to this population, as well as the very small sample of Caucasians who reported any racial discrimination ($n=29$).

In supplemental analyses, we examined whether results were affected by inclusion of individuals with baseline cognitive impairment by refitting the basic model excluding participants with initial MMSE scores <21 , a cutoff suggested for cognitive dysfunction in samples that include participants with lower levels of education (Alfaro-Acha et al., 2006; Leveille et al., 1998). We also used logistic regression to examine odds of cognitive decline as a categorical variable, with substantial cognitive decline defined using the previously reported cutoff of a change of four or more points on the MMSE within a four-year period of time indicating significant deterioration (Tangalos et al., 1996). This cutoff also corresponded to one standard deviation above mean MMSE decline in the current sample. The logistic regression analysis was performed in order to enhance interpretation of findings in terms of clinical implications. All analyses were performed using SAS Version 9 (SAS Institute, 2003).

RESULTS

Sample characteristics for the 624 participants are presented in Table 1. Average age was 74, 49% of the sample were African American, 53% were female, and 49% resided in a rural area. Approximately 44% of the sample had less than a high school level of education. Average four-year decline in MMSE score was 1.0 points ($SD=3.0$), with approximately half the sample showing some decline during this time period. A total of 138 participants (22%) had diabetes at baseline. Compared to participants without diabetes, individuals with diabetes were slightly younger and more likely to be African American. In addition, participants with diabetes showed

lower MMSE scores, less physical activity, greater depressive symptoms, and greater number of comorbid vascular conditions.

In our basic model, adjusted for baseline MMSE, age, gender, race, urban/rural residence, and level of education, there was a significant association between diabetes and change in cognitive function (Table 2). Presence of diabetes was associated with greater cognitive decline over the four-year period. In subsequent models adjusted for physical activity, depressive symptoms, and vascular comorbidity, the association between diabetes and cognitive decline was reduced by approximately 11% but remained statistically significant.

To examine potential moderation by race, rural residence, education, vascular comorbidity, perceived racial discrimination, or health care access and utilization, we refitted the basic model separately for each of these factors with inclusion of the respective interaction term. There was no evidence that the association between diabetes and cognitive decline was modified by race, rural residence, level of education, or vascular comorbidity ($p > .50$ for each interaction term). However, we found a significant interaction effect for perceived discrimination among African Americans in our sample ($p = .032$). To further explore this interaction, we performed additional analyses stratified by the discrimination variable (see Table 3). The association between diabetes and cognitive decline was larger in those reporting discrimination based on race or skin color than those who did not report discrimination.

For the health care variables, there was a significant interaction between diabetes and health care utilization (physician visit in the past six months; $p = .01$ for interaction term) but not health care access (private or supplemental insurance; $p = .39$ for interaction term) in predicting cognitive decline. Among participants who reported having seen a physician in the past six months, the parameter estimate for diabetes predicting cognitive decline was statistically significant but much smaller than the estimate for this association among those who did not report seeing a physician in the past six months (Table 3). This suggests that those with lower health care utilization experienced more cognitive decline than those with more frequent physician contact.

In the supplemental analyses, when we ran the basic model excluding participants with poor baseline cognitive function ($\text{MMSE} < 21$), diabetes remained a significant predictor of cognitive decline and the association was slightly stronger ($b = 0.84$, $p = .003$). We also examined cognitive decline as a categorical variable using logistic regression. Participants with diabetes at baseline had increased odds of substantial cognitive decline (≥ 4 points on MMSE) by about 70% compared to those without diabetes after adjustment for baseline MMSE, age, gender, race, urban/rural residence, and level of education (*odds ratio* = 1.69, 95% confidence interval 1.02–2.79).

DISCUSSION

In this sample of community-dwelling African American and Caucasian older adults, we found that diabetes at baseline predicted greater decline in cognitive function over a four-year period. This association was not explained by differences in baseline cognitive function, demographic factors, physical activity, depressive symptoms, or vascular disease comorbidity. Additionally, the relationship between diabetes and cognitive decline did not differ significantly by race, suggesting that African Americans with diabetes are not at greater risk of decline in cognitive function than Caucasians. However, perceived racial discrimination moderated the association between diabetes and cognitive decline for African Americans. The association between diabetes and decline was stronger among African Americans with a reported history of racial discrimination. Also, participants with diabetes who at baseline reported lack of physician contact within the past six months experienced greater cognitive decline than those who had

at least one physician contact in the same time period. Our findings provide further evidence that diabetes is a risk factor for cognitive decline in older adulthood and suggest that health disparities-related factors other than race itself may influence cognitive outcomes in diabetes.

Our finding of an interaction between perceived racial discrimination and diabetes in predicting cognitive decline among African Americans has several feasible explanations. Stress and negative emotions that have been linked to perceived discrimination (Pascoe & Richman, 2009; Williams et al., 2003) are associated with greater production of IL-6 and other proinflammatory cytokines (Kiecolt-Glaser et al., 2003) that are hypothesized to play an important part in the development of dementia (Peila & Launer, 2006) and type 2 diabetes (Pradhan, Manson, Rifai, Buring, & Ridker, 2001). However, there is also evidence that perceived discrimination is associated with factors such as unhealthy behaviors including smoking and alcohol abuse (Pascoe & Richman, 2009), mistrust of the medical care system (LaVeist, Nickerson, & Bowie, 2000) and lower usage of preventive health services including hemoglobin A1C testing (Trivedi & Ayanian, 2006), that may negatively influence diabetes progression. The role of perceived discrimination in diabetes outcomes is plausible and deserves further investigation regarding potential explanations.

The observed interaction between health care utilization and diabetes is consistent with the idea that greater frequency of physician contact can positively influence health outcomes in diabetes. In a prior study, Schectman et al. (2008) examined the association of diabetes metabolic control with physician appointment-keeping behavior in a rural healthcare system. Findings indicated that higher rate of missing appointments was associated with increased odds of poor diabetes control. Diabetes can be a manageable condition for many individuals, although substantial effort is required for patients with respect to monitoring the condition. Self-monitoring of blood glucose levels and adherence to treatment regimens (e.g., medications, diet, exercise, screening for complications) are recommended by the American Diabetes Association (ADA) due to associations with improved short-term health outcomes, including physiologic and microvascular outcomes (2009). Conversely, uncontrolled diabetes has been consistently found to lead to poorer health outcomes and more disease complications than controlled diabetes (Norris et al., 2002; Xu, von Strauss, Qiu, Winblad, & Fratiglioni, 2009). Although it is commonly assumed that monitoring symptoms through regular access to health care professionals is a major component of controlling diabetes, this study is the first providing evidence that health care utilization modifies the association between diabetes and cognitive decline.

Potential mechanisms to explain the increased risk of cognitive decline associated with diabetes were not examined in this study but can be found in other recent research. Studies have indicated that the presence of diabetes can induce structural changes in the brain akin to accelerated brain aging, while also modifying long-term potentiation, a synaptic process believed to underlie learning and memory (Biessels, van der Heide, Kamal, Bleys, & Gispen, 2002; Trudeau, Gagnon, & Massicote, 2004). Diabetes can also herald risk for specific types of dementias. Damage incurred to blood vessels increases the risk of vascular dementia, and links to Alzheimer's disease have also been reported (Biessels et al., 2006). Medications approved for the management of diabetes are currently being tested for their efficacy in treating Alzheimer's disease, in recognition of the potential association between insulin and blood-glucose control and cognitive function (Castillo-Quan, 2009; Zhao et al., 2004). One preliminary study found that individuals with early Alzheimer's disease who were randomized to intranasal insulin treatment showed improved performance on tests of memory and attention relative to a placebo group, as well as beneficial effects on beta-amyloid (Reger et al., 2008).

A main limitation of the current study is that data were not available regarding baseline duration, control or severity of diabetes. Longer duration of the disease, poorer blood glucose

control, and greater diabetes severity have been linked to higher risk of cognitive impairment in older adults (Munshi et al., 2006; Roberts et al., 2008). Also, because dementia diagnoses were not performed, we could not directly address this outcome. In terms of perceived discrimination, our measure was specifically focused on discrimination based on race or skin color. We acknowledge that individuals may experience discrimination based on factors other than race, such as obesity or mental illness. Thus, we did not fully capture discrimination in this study. Similarly, physician visits are just one indicator of health care utilization. For example, the ADA (2009) recommends medical care by interdisciplinary teams including dietitians, nurses, pharmacists, and mental health professionals in addition to physicians. Further data on indicators of health utilization and adherence to treatment regimens would have been informative for the present study. Another potential issue relevant to health utilization is whether baseline cognitive status may have negatively affected physician use. However, all analyses controlled for baseline cognitive function and a post hoc analysis did not show a significant association between cognitive function and health utilization controlling for comorbidity.

A general problem with studies of diabetes and age-related cognitive outcomes is that diabetes-specific measures have not been included. For example, measures designed specifically for use in populations with diabetes have been developed for areas such as diabetes-related health literacy, numeracy skills, self-efficacy, social support, and stress. One of the next steps in this line of research should be to examine diabetes-specific measures as moderators of the association between diabetes and cognitive decline in older adults. Strengths of this study include the large number of older African Americans and rural residents (both of which are understudied populations), longitudinal data on cognitive function, a high participant retention rate over the course of the study, and comprehensive determination of medical conditions at baseline.

In summary, we found that diabetes was associated with cognitive decline over a four-year period of time. We did not find evidence of greater risk of cognitive decline for African Americans compared to Caucasians with diabetes. However, given the significant interaction of diabetes and perceived racial discrimination as well as the higher prevalence of diabetes among older African Americans, our study highlights cognition as another domain of health in which older African Americans may be more vulnerable to adverse outcomes. We also found that the association between diabetes and cognitive decline was modified by contact within six months with a physician, suggesting that health care utilization may moderate the negative influence of diabetes on cognition. Patients with diabetes should be encouraged to see a health care provider relatively frequently not only to reduce the risk of physical problems but possibly also to reduce the likelihood of substantial cognitive decline. Understanding the influence of factors related to health disparities may eventually help to develop more comprehensive preventive strategies for cognitive impairment in older adults with diabetes.

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Table 1

Characteristics of Participants by Diabetes Status

Characteristic	All <i>N</i> = 624	Diabetes <i>n</i> = 138	No Diabetes <i>n</i> = 486	<i>p</i>
Age, mean (<i>SD</i>)	73.8 (5.9)	72.8 (5.0)	74.1 (6.1)	.010
African American, %	48.6	61.6	44.9	<.001
Female gender, %	53.2	55.8	52.5	.489
Rural, %	49.0	51.5	48.4	.521
Level of education				
0–6 years, %	18.6	20.3	18.1	.561
7–11 years, %	25.6	29.0	24.7	.308
12 years, %	25.5	22.5	26.3	.357
13 or more years, %	30.3	28.3	30.9	.557
Baseline MMSE (0-30), mean (<i>SD</i>)	26.1 (3.9)	25.5 (3.9)	26.3 (3.9)	.050
Follow-up MMSE (0-30), mean (<i>SD</i>)	25.2 (4.4)	24.3 (4.2)	25.4 (4.5)	.012
Physical activity (kcal/wk), mean (<i>SD</i>)	1399.9 (1989.2)	1102.5 (1756.6)	1484.4 (2044.2)	.031
Depressive symptoms (0-15), mean (<i>SD</i>)	2.0 (2.1)	2.4 (2.4)	1.9 (2.0)	.029
Vascular comorbidity index (0-5), mean (<i>SD</i>)	1.0 (0.8)	1.3 (0.8)	0.9 (0.8)	<.001

Note: *SD* = Standard deviation; *p* values obtained for comparison of those with and without diabetes using t-test or chi-square analysis.

Table 2
Parameter Estimates from Multiple Regression Models Predicting Cognitive Decline

Predictor	Model 1		Model 2		Model 3	
	Estimate	SE	Estimate	SE	Estimate	SE
Diabetes	0.695*	0.278	0.631*	0.280	0.617*	0.286
Age	0.127**	0.020	0.123**	0.020	0.123**	0.020
African American	0.059	0.269	0.068	0.270	0.066	0.271
Female	-0.677**	0.232	-0.761**	0.234	-0.759**	0.234
Rural	-0.030	0.235	-0.049	0.236	-0.050	0.236
Education (0–6 years ref.)						
6–11 years	-0.737	0.385	-0.785*	0.386	-0.785*	0.387
12 years	-1.317**	0.423	-1.267**	0.424	-1.267**	0.424
≥ 13 years	-1.770**	0.439	-1.734**	0.440	-1.731**	0.441
Baseline MMSE	0.323**	0.040	0.331**	0.040	0.331**	0.040
Physical activity			-0.00003	0.00004	-0.00003	0.00004
Depressive symptoms			0.136*	0.056	0.130*	0.057
Vascular comorbidity					0.034	0.144

Notes:

*
 $p < .05$;

**
 $p < .01$; ref. = reference group; positive estimates indicate greater decline.

Table 3

Associations Between Diabetes and Cognitive Decline Stratified by Significant Moderators

	Number	Association Between Diabetes and Cognitive Change [Estimate (SE)]	<i>p</i> -value for interaction
Perceived racial discrimination			.032
Not reported	111	−0.463 (0.654)	
Reported	192	1.167 (0.521) [*]	
Physician visit within 6 mo.			.014
No	107	3.12 (1.039) ^{**}	
Yes	517	0.616 (0.286) [*]	

Notes:

^{*} $p < .05$;^{**} $p < .01$; all models are adjusted for baseline MMSE score, age, gender, residence (urban/rural), and level of education; only African Americans were included in discrimination-stratified models and race was included as a covariate in the models stratified by health utilization.