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Diabetes and Cognitive Systems in Older Black and White Persons

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Abstract

We examined the association of type 2 diabetes mellitus to function in different cognitive systems in older black and white persons. Participants were 1437 persons (28.1% black; 72.9% women; mean age 78.4 y, education 14.5, Mini-Mental State Examination 27.9) free of dementia, enrolled in the Minority Aging Research Study or Memory and Aging Project, 2 epidemiologic, community-based cohort studies of aging and cognition. Summary measures of 5 cognitive domains and global cognition were derived from 19 neuropsychologic tests. Diabetes, by medication inspection and history, was present in 15.3% participants, including 23.5% blacks and 12.1% whites ($P < 0.001$). In linear regression models adjusted for age, sex, education, and race, diabetes was associated with a lower level of semantic memory ($P = 0.042$), but not other cognitive domains (episodic memory, working memory, perceptual speed, and visuospatial ability) or global cognition. In separate analyses adjusted for age, sex, education, race, and diabetes, there was no interaction of diabetes with race (all P values > 0.333). In summary, diabetes was associated with semantic memory impairment in both black and white persons. We found similar effects of diabetes on cognition in both racial groups. Because diabetes is twice as common in blacks, the burden of diabetes on cognition is higher in black than white persons.

Keywords

diabetes mellitus; cognition; race

Type 2 diabetes mellitus is common and its prevalence is increasing at an alarming rate.¹ Although neurologic complications of diabetes have been recognized for long, systematic examination of the relation of diabetes to cognitive function has been mostly conducted in recent years. Many,^{2,3} but not all studies,⁴ have found that older persons with diabetes have lower levels of cognition compared with those without. Because these studies have focused predominantly on white populations, the question of whether the adverse effect of diabetes on cognition is present in diverse populations has been mostly unexplored.

There are significant and well-established racial differences in diabetes and diabetes-related health complications. In particular, black persons have a higher prevalence of diabetes and diabetes-related factors, such as hypertension, compared with whites.^{5,6} Although there is substantial data to support the associations of diabetes and related comorbidities with cognitive impairment, little is known of the association of diabetes to cognition in black persons. This

is an important question for several reasons. First, as noted, blacks have a higher prevalence of diabetes compared with whites, the disparity is still present in old age and some studies suggest that it may be growing.⁷⁻¹⁰ Second, there is growing evidence that some risk factors for cognitive impairment may operate differently in blacks and whites (eg, apolipoprotein E genotype). Finally, it is possible that the increased prevalence of other medical comorbidities in blacks could influence the association of diabetes to cognition in this population, but almost all of the studies conducted to date have been done only with white samples.

Another gap in our understanding of diabetes and cognition is whether the diabetes is associated with impairment in specific domains of cognitive function. Few studies have examined the relation of diabetes to different cognitive systems and we are not aware of any such studies conducted in a large cohort of black and white persons. We previously published a study on a subsample of participants included in this study. In that study of more than 800 older persons in the Rush Memory and Aging Project, we found that diabetes was associated with some cognitive systems, including semantic memory, but not others.¹¹ Participants in that study were predominantly white persons. This study aims to extend those findings by (1) adding a cohort of African American older adults and (2) by directly examining the potential interaction of race and diabetes on cognitive function. We combined an updated dataset from the Rush Memory and Aging Project on more than 1100 persons with more than 300 blacks participating in the Minority Aging Research Study, all living in the Chicagoland area. Thus, subjects for this study consists of more than 1000 older whites and more than 400 older blacks free of dementia, who underwent clinical evaluations including detailed neuropsychologic testing, to examine the relation of diabetes to different cognitive systems by race.

METHODS

Subjects

All subjects were enrolled in 1 of 2 epidemiologic studies of aging and cognition.

Participants in the Rush Minority Aging Research Study were older community-dwelling persons without known dementia, who signed an informed consent agreeing to annual clinical evaluations, including cognitive testing. Subjects reside in private residences or senior housing in the Chicagoland area. From August 2004 to April 2008, 346 persons enrolled in the study, of whom 10 met criteria for dementia at baseline (see Clinical Evaluation). The remaining 336 (97.1%) had a mean age of 73.1 years (SD = 5.9 y), a mean education of 14.8 years (SD = 3.6 y), and a mean Mini-Mental State Examination (MMSE) score of 27.9 (SD = 2.6); 28.9% were men and all were non-Hispanic black.

Participants in the Rush Memory and Aging Project¹² were older community-dwelling persons, from more than 40 retirement communities and senior subsidized housing facilities across the Chicagoland area. All subjects signed an informed consent agreeing to annual clinical evaluations and an Anatomical Gift act agreeing to donate their brain, spinal cord, and selected nerves and muscles at the time of death. Of the 1187 persons enrolled from January 1997 to April 2008, 70 met the criteria for dementia (see Clinical Evaluation). Of the remaining 1113 (93.8%), the mean (SD) age was 79.9 years (7.4 y), mean education was 14.3 years (3.2 y), and mean MMSE was 27.8 (2.1); 26.5% were men, 6.3% were black, 92.8% were white, and 0.9% were of other races.

Both the Minority Aging Research Study and the Memory and Aging Project were approved by the Rush Institutional Review Board of Rush University Medical Center. Both studies have essentially identical recruitment techniques, and a large overlap of identical data collection designed to facilitate analyses of racial differences through combining data from both cohorts.

Clinical Evaluations

All subjects underwent uniform, structured clinical evaluations, including a medical history, neurologic examination, and neuropsychologic testing (see below). Race was assessed by asking each participant to self-report their racial category based on questions used by the US Census Bureau (www.census.gov/population/www/socdemo/race.html). Subjects were asked to bring prescription and non-prescription medication containers, which were visually inspected. Medication names and dosages were recorded using the Medi-Span system.^{13,14} After review of all clinical data, participants were classified with respect to dementia status,¹⁴ by a physician with expertise in the evaluation of persons with dementia. Clinical data were collected on laptop computers, with forms programmed in Blaise, a Pascal-based data entry program.

Diabetes mellitus was identified at the clinical evaluation, as previously described.¹¹ Briefly, diabetes was present if the participant was taking a medication to treat diabetes (insulin or oral hypoglycemic agent) as determined by direct visual inspection of medications, or reported a history of diagnosis of diabetes.

Clinical evaluations also allowed for the identification of factors that may play a role in the relation of diabetes to cognition. The medical history and physical examination provided data on vascular factors, as previously described.¹¹ Vascular risk factors included a history of current or former smoking (“Do you smoke cigarettes now?” and if no, then “Did you ever smoke cigarettes regularly?”), and increased systolic or diastolic blood pressures as determined by direct measurement using standard procedures (average of 3 measures, 2 while sitting and 1 after standing 1 min). Vascular conditions included the presence of stroke (as determined by a clinician specialized in the evaluation of older persons), and history of myocardial infarction, congestive heart failure, and claudication. Additional data available for analyses included alcohol use (based on daily intake), depressive symptoms (based on the Center for Epidemiologic Studies—Depression Scale), and body mass index (measured as weight in kg divided by height in m²).

Neuropsychologic Testing and Summary Measures of Cognition

Subjects underwent detailed cognitive assessments, as previously reported.¹⁵ The MMSE was used for descriptive purposes only. Eighteen other neuropsychologic tests were selected to assess a broad range of cognitive abilities commonly affected in older persons. All neuropsychologic test data were reviewed by a board-certified neuropsychologist.

To minimize floor and ceiling artifacts and other sources of measurement error, composite measures of 2 or more individual tests were used in analyses. Based in part on a previous factor analysis,¹⁵ 5 cognitive domains were formed along with a measure of global cognition based on all 18 tests. Briefly, there were 2 tests of semantic memory (Verbal Fluency; Boston Naming), 7 of episodic memory (immediate and delayed recall of Story A of the Wechsler Memory Scale-Revised; immediate and delayed recall of the East Boston Story; Word List Memory; Recall; and Recognition), 3 of working memory (Digit Span forward and backward; Digit Ordering), 4 of perceptual speed (Symbol Digit Modalities Test; Number Comparison; 2 indices from a modified version of the Stroop Test), and 2 of visuospatial abilities (Line Orientation; Progressive Matrices).¹⁵ In each case, individual tests were converted to Z scores, using the mean and SD from the entire cohort, and then the Z scores were averaged to yield the composite measure. Further information about the individual tests and the derivation of these composite measures is published elsewhere.^{15,16}

Statistical Analyses

We first examined whether there were differences in demographic features and other characteristics in persons with and without diabetes, using *t* tests for continuous variables, and Pearson χ^2 tests for categorical variables. All subsequent analyses adjusted for age, sex, education, and race.

Relation of diabetes to summary measures of 5 cognitive domains and global cognition was examined using separate linear regression models controlling for demographic covariates (age, sex, education, and race).

We next tested racial differences in the association between diabetes and cognitive function by adding an interaction term for diabetes $\times$ race to the core models.

To examine for potential mechanisms linking diabetes to cognition, we next conducted analyses with vascular risk factors added to the core model.

Analyses were carried-out using SAS/STAT software version 8 on a SunUltraSparc workstation. Models were validated graphically and analytically.¹⁷

RESULTS

Subject Characteristics

Individuals were eligible for this study, if they had completed a baseline clinical evaluation, were free of dementia, and self-identified as either black or white. To test for racial differences and to increase power, all black persons enrolled in either the Minority Aging Research Study or Memory and Aging Project were grouped together in this study. Blacks in the 2 studies did not differ on key demographic features. The sample size was therefore 1437, which included 404 (28.1%) black persons (from either of the 2 studies) and 1033 (71.9%) white persons (all from the Memory and Aging Project).

For the total group of 1437 persons, the mean (SD) age was 78.4 years (7.6 y), education 14.5 years (3.3 y), and MMSE score 27.9 (2.2); and 27.1% were men. There were 220 (15.3%) persons with diabetes, of whom 134 were taking medication for diabetes (98 taking an oral hypoglycemic, 21 taking insulin, and 15 taking both), and 95 (43%) were black. Compared with those without diabetes, those with diabetes were more likely to be younger, male, black, and have a lower level of education (Table 1).

Relation of Diabetes to Cognitive Domains and Global Cognition

We first performed linear regression models, adjusted for age, sex, education, and race, to examine the association of diabetes to cognition. Compared with persons without diabetes, persons with diabetes had a 0.105 unit lower score on the measure of semantic memory, an effect that was roughly equivalent to the effect of 3 years of age (Table 2). In separate models, we did not find associations of diabetes with the other 4 cognitive domain scores (episodic memory, working memory, perceptual speed, or visuospatial ability), or global cognition (Table 2).

Relation of Diabetes to Cognition as a Function of Race

As there is a well-established difference in the prevalence of diabetes among blacks and whites, we examined the relation of diabetes to cognition as a function of race. In our study, diabetes was about twice as common in black compared with white persons (23.5% black vs. 12.1% white persons, $P < 0.001$), comparable with other large cohort studies.^{18,19} To examine whether the association between diabetes and cognition differed by race, we repeated the core models

and added a term for the interaction of diabetes $\times$ race, controlling for age, sex, and education (Table 2). There were no significant interactions of diabetes with black race for any of the cognitive domains (all P values > 0.333), suggesting that the association of diabetes to cognition was similar in black and white persons.

Given the association of diabetes with vascular factors and of vascular factors with impaired cognition,²⁰ we conducted additional analyses to examine whether vascular factors and conditions, and other factors, might account for the association of diabetes with cognition and whether the association varied by race. In the first analysis, which adjusted for vascular factors (smoking and blood pressure), as well as race, age, sex, and education, the effect of diabetes on semantic memory was similar (estimated coefficient = -0.098 , SE = 0.052 , $P = 0.060$), suggesting that these factors do not play a substantial role in the association of diabetes with cognition. Similarly, in a separate analysis controlling for vascular conditions (stroke, myocardial infarction, congestive heart failure, and claudication), results were also essentially unchanged (estimated coefficient = -0.096 , SE = 0.051 , $P = 0.061$). In separate analyses controlling for body mass index, alcohol, and depressive symptoms, the association of diabetes with cognition was no longer significant (all P values > 0.1), suggesting that these factors may play a role in the relation of diabetes with cognition. Next, we did not find evidence for a 3-way interaction of diabetes $\times$ race $\times$ vascular factors, suggesting that the influence of vascular factors on the association of diabetes with cognition was similar in blacks and whites.

DISCUSSION

In this study of more than 1400 older community-dwelling black and white persons without dementia, we found that diabetes was associated with impaired semantic memory, but not with other cognitive domains or global cognition. We did not find evidence for an interaction of diabetes with race, suggesting that the association of diabetes and cognition does not differ between older blacks and whites in these cohorts.

Results from observational community or population-based studies examining the relation of diabetes to level of cognition in older persons have been mixed. Although several studies suggest an association,^{2,3,11,21,22} others do not.⁴ For studies in which no association was found, the possibility of a small effect of diabetes on cognition cannot be excluded. For instance, in 1 study with a large cohort of older persons,⁴ only a single measure of global cognition (the MMSE) was used, raising the question of whether an association of diabetes to cognition in some, but not other cognitive domains may have been missed. Yet, few studies have examined the relation of diabetes to different cognitive functions^{11,21-23} and we are aware of only 2 that used composite measures of cognition based on 2 or more individual tests.^{11,22} One study found that diabetes was associated with lower scores of cognition based on several individual tests and on a composite measure of these, in a large cohort of older women participating in the Nurses' Health Study.²² The other study, using data from one of the cohorts in this manuscript, the Memory and Aging Project, examined the relation of diabetes to different cognitive domains, and found that persons with diabetes had lower scores in semantic memory and perceptual speed, but not other domains.¹¹ Findings from this study, which included an updated dataset with more than 200 additional persons from the Memory and Aging Project, and 300 persons from another cohort (the Minority Aging Research Study), of an association of diabetes with cognition, in particular semantic memory, are consistent with these, with one exception—we did not find an association with perceptual speed. This difference may be due to several factors. First, the under-diagnosis of diabetes (see limitations discussed below) is an issue in many large, observational cohort studies including ours, and probably even more of an issue for black compared with white persons. This likely biases results toward the null and makes it difficult to detect more modest associations of diabetes with specific cognitive domains. Second, the relation of diabetes to perceptual speed may be

weaker compared with that of semantic memory, as suggested by the substantially smaller estimate for perceptual speed compared with that of semantic memory. Indeed, diabetes was not associated with the level of perceptual speed although it was associated with other cognitive domains including semantic memory in another cohort.²⁴ Third, the relation may be weaker in cross-sectional analyses and only observed over time.²⁴ Fourth, differences in the way analyses were performed (eg, which covariates were included in the models, in particular race, the focus of this study), may have influenced the results. Further examination of the relation of diabetes to cognition in blacks and whites are needed to clarify these issues.

Given that the prevalence of diabetes is rapidly increasing in several countries including the US, and that the diabetes is more common in some minority compared with white populations, it is timely to examine the relation of diabetes to cognition as a function of race. However, to date, almost all observational studies on diabetes and cognition have been conducted in cohorts consisting exclusively of white persons or with too few nonwhite persons to examine for racial effects. In fact, few studies have examined the relation of diabetes to cognitive function in nonwhite races,²¹ and we are not aware of any that directly examined this question using data from a cohort with a large group of black persons. Indeed, although diabetes has been associated with dementia²⁵ and mild cognitive impairment¹⁸ in black persons, little is known about the relation of diabetes to cognitive function or different cognitive systems in this population. Although 2 studies have examined the relation of blood markers of diabetes to cognition in blacks, 1 study of 43 black persons could not assess for racial differences,²⁶ and the other study, with findings consistent to ours, examined relations in middle-aged adults.²⁷ We wished to directly examine the relation of diabetes to cognition as a function of race. There are significant and well-established racial differences in diabetes and diabetes-related health complications with black persons, who have a higher prevalence of diabetes and comorbidities compared with whites.^{5,6} Given that diabetes and comorbidities are associated with cognitive impairment, and the persistent disparity between blacks and whites in the prevalence of diabetes, it is surprising that little is known about the association of diabetes to cognition in black persons. We capitalized on available data from 2 existing epidemiologic studies with essentially identical assessment methods to examine the question in a large group of about 400 black and 1000 white, well-characterized, community-dwelling older persons without dementia, in whom detailed neuropsychologic data yielding 5 different cognitive domain summary scores were available. In analyses using interaction terms of diabetes by race, results suggested that the associations of diabetes to cognitive domains and global cognition were similar in black and white persons. In particular, the association of diabetes with a lower level of semantic memory did not differ for blacks compared with whites. Given that diabetes is more common in blacks, the burden of diabetes on cognition may be higher in black than white persons. This finding will need to be replicated in other cohorts with black and white persons.

The mechanism linking diabetes to impaired cognition remains unclear. One plausible explanation is that vascular factors are playing a role. Diabetes is known to be associated with vascular disease and cerebrovascular pathology is thought to increase the likelihood of the clinical expression of dementia.²⁸ We did not find strong evidence that vascular risk factors, including smoking, or vascular conditions, including stroke, affected the association of diabetes with cognition. However, the role of vascular processes needs further examination, as smoking was previously found to have an effect modification¹¹ and other factors such as BMI, seem to affect the relation of diabetes to cognition. Caution in interpretation of results is needed, as we may not have had adequate power to detect subtle vascular effects given small numbers of persons in some analyses, in particular in analyses with 3-way interactions. Another possible mechanism linking diabetes to cognition is that diabetes may be associated with another common neuropathology of aging that causes cognitive impairment, namely AD pathology. Yet, results of studies using human postmortem tissue have been mixed with some not finding a relation of diabetes with AD pathology.^{29,30} Additional factors, such as depression, also

need to be considered in the association of diabetes with cognition. Further research, using human postmortem tissue and other approaches (eg, in vivo approaches, such as neuroimaging), is needed to examine possible underlying neurobiologic mechanisms linking diabetes to impaired cognition.

Confidence in these findings is strengthened by 3 factors. First, data are derived from 2 large, well-characterized epidemiologic cohorts with essentially identical operational methods, allowing for examination of racial differences in the association between diabetes and cognition. Second, all participants underwent structured clinical evaluations allowing for identification of persons with dementia and exclusion of these from analyses. Third, detailed neuropsychologic data were available and summarized to yield previously established composite measures of 5 cognitive domains and global cognition.

This study also has several limitations. First and importantly, diabetes was identified by history and medication inspection, but without more sophisticated methods. Of specific relevance to this study, fasting blood glucose data were not available and has likely contributed to an underdiagnosis of diabetes in this cohort. Under-diagnosis is likely a bigger issue in black compared with white persons. These factors would bias results toward the null and may mask the modest associations of diabetes to specific cognitive domains. Despite this limitation, we were able to detect an association between diabetes and cognition. Second, this study had a relatively small proportion of black participants, likely limiting our power to detect a small effect of race on the association of diabetes with cognition. Yet, we are unaware of any other published studies with detailed neuropsychologic data in a large group of blacks and whites to examine the association of diabetes with function in different cognitive domains. Finally, this is a cross-sectional study, and longitudinal data from a large group of persons who are representative of the older population in race and other important demographic and clinical characteristics, would contribute to a better understanding of these associations.

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TABLE 1

Characteristics of 1437 Participants, According to the Presence or Absence of Diabetes

Characteristics	Diabetes (n = 220)	No Diabetes (n = 1217)	P
Age (y) *	75.9 (7.3)	78.8 (7.6)	< 0.001
Male sex (%)	37.7	25.1	< 0.001
Black (%)	43.2	25.4	< 0.001
Education (y) *	13.9 (3.6)	14.6 (3.2)	0.014
MMSE score/30 *	27.6 (3.0)	27.9 (2.0)	0.158

MMSE indicates Mini-Mental State Examination.

* Values are mean (SD), unless otherwise specified.

TABLE 2

Relation of Diabetes to Summary Measures of 5 Separate Cognitive Domain Scores and Global Cognition

Outcome: Cognitive Score	Model 1 [*] Estimate (SE), <i>P</i>	Model 2 [†] Estimate (SE), <i>P</i>
Semantic memory	−0.105 (0.052), 0.042	0.084 (0.104), 0.481
Episodic memory	−0.012 (0.046), 0.796	0.053 (0.093), 0.572
Working memory	0.038 (0.053), 0.475	0.011 (0.106), 0.914
Perceptual speed	−0.044 (0.054), 0.416	0.100 (0.109), 0.358
Visuospatial ability	−0.074 (0.054), 0.169	0.075 (0.108), 0.486
Global cognition	−0.025 (0.035), 0.487	0.069 (0.071), 0.334

^{*} Estimated effect of diabetes [estimated coefficient (SE), *P* value], from separate linear regression models that controlled for age, sex, education, and race.

[†] Estimated effect of diabetes × race [estimated coefficient (SE), *P* value], from separate linear regression models that controlled for age, sex, education, race, and diabetes.