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Mild Cognitive Dysfunction Does Not Affect Diabetes Mellitus Control in Minority Elderly Adults

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Abstract

OBJECTIVES—To determine whether older adults with type 2 diabetes mellitus and cognitive dysfunction have poorer metabolic control of glycosylated hemoglobin, systolic blood pressure, and low-density lipoprotein cholesterol than those without cognitive dysfunction.

DESIGN—Prospective cohort study.

SETTING—A minority cohort in New York City previously recruited for a trial of telemedicine.

PARTICIPANTS—Persons aged 73.0 ± 3.0 (N = 613; 69.5% female; 82.5% Hispanic, 15.5% non-Hispanic black).

MEASUREMENTS—Participants were classified with executive or memory dysfunction based on standardized score cutoffs (<16th percentile) for the Color Trails Test and Selective Reminding Test. Linear mixed models were used to compare repeated measures of the metabolic measures and evaluate the rates of change in individuals with and without dysfunction.

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RESULTS—Of the 613 participants, 331 (54%) had executive dysfunction, 202 (33%) had memory dysfunction, and 96 (16%) had both. Over a median of 2 years, participants with executive or memory dysfunction did not exhibit significantly poorer metabolic control than those without executive function or memory type cognitive dysfunction.

CONCLUSION—Cognitive dysfunction in the mild range did not seem to affect diabetes mellitus control parameters in this multiethnic cohort of older adults with diabetes mellitus, although it cannot be excluded that cognitive impairment was overcome through assistance from formal or informal caregivers. It is possible that more-severe cognitive dysfunction could affect control.

Keywords

cognition; diabetes mellitus; control; elderly

Appropriate self-management of diabetes mellitus is important for the prevention of diabetes mellitus– related complications and other adverse outcomes.[1] Poor self-management can lead to a greater incidence of diabetic complications, such as micro- and macrovascular disease, and death.[2] Individuals with diabetes mellitus have been shown to have a risk of cognitive decline that is 1.2–1.5 times as great as that of individuals without diabetes mellitus.[3] Executive function and memory declines are the most frequently reported cognitive deficits in the setting of diabetes mellitus.[4] Executive or memory dysfunctions may cause inappropriate self-management behaviors, including mishandling of or poor adherence to medication regimens, incorrect administration of insulin, and nutritional imbalance in daily meals, which can result in poor metabolic and physical outcomes. There is a dearth of studies addressing diabetes mellitus in older adults.[5] The long-term effect of diabetes mellitus–related cognitive decline on disease self-management in older adults, specifically the effect on measures of metabolic control, is understudied. This question is particularly important in Hispanics and non-Hispanic blacks, who have a higher prevalence of concomitant diabetes mellitus and cognitive impairment.[6]

Few studies have quantified the association between cognitive dysfunction and poor self-management in individuals with diabetes mellitus.[7–15] Findings relating cognitive dysfunction to metabolic control are conflicting. One study found greater executive dysfunction to have no effect on glycemic control,[8] whereas two others found global cognitive dysfunction[10] and executive dysfunction[15] to be associated with higher glycosylated hemoglobin (HbA1c) levels. Methodological concerns, including, small sample sizes, limited clinical measures of diabetes mellitus control, and the cross-sectional nature of these studies limit their interpretation.

The risk of cognitive dysfunction in the setting of diabetes mellitus is high.[6] Thus, it was hypothesized that cognitive dysfunction would affect diabetes mellitus control in elderly persons with diabetes mellitus. This hypothesis was tested by studying the longitudinal relationship between cognitive dysfunction and changes in parameters of diabetes mellitus control, HbA1c, systolic blood pressure (SBP), and low-density lipoprotein cholesterol (LDL-C) in a sample of predominantly minority elderly adults with diabetes mellitus residing in northern Manhattan.

METHODS

Study Population and Design

Participants in these analyses were a subsample recruited for a cognition ancillary study from the New York City sample of the Informatics for Diabetes Education and Telemedicine (IDEATel) Project.[16] IDEATel was designed to assess the feasibility and effectiveness of telemedicine for disease management in a sample of minority older adults with type 2 diabetes mellitus living in New York State.[16] Their primary care providers recruited participants from New York City (Columbia University) and upstate New York (State University of New York Upstate Medical University at Syracuse). They were randomized between 2000 and 2002 to the intervention (a home-based interactive telemedicine unit used for televisits with a nurse educator, transmission of self-measured glucose and blood pressure data electronically, and web access in addition to usual care) or usual care alone. The primary endpoints were changes in HbA1c, blood pressure, and LDL-C. Participants (N = 1,665) were individuals aged 55 and older with a physician or medication-defined diagnosis of diabetes mellitus who were Medicare beneficiaries and resided in a federally designated medically underserved area. Participants were excluded if they were moderately to severely cognitively impaired; had a severe visual, mobility, or motor impairment; had a severe comorbid condition, a communication impairment, or no electrical outlet for the telemedicine unit; or planned to reside in another location for longer than 3 months. Details regarding inclusion and exclusion, the randomization scheme, the intervention, and evaluation of primary endpoints are described elsewhere.[16,17]

An ancillary cognition study was initiated in the second phase (2004–08) of IDEATel at the Columbia University site. Five hundred participants who completed the first phase at this site (n = 775) continued on to the second phase. An additional 150 subjects were recruited to participate in the second phase. The only exclusion criteria for this ancillary study were unwillingness or inability to begin or complete the cognitive assessments. In addition to the global cognition measures administered in the first phase, an extended neuropsychological assessment with measures of memory, executive function, language, attention, and construction were administered in this ancillary study at 1-year intervals. Six hundred thirteen participants were included in this 5-year prospective analysis of the ancillary study data, 538 (87.7%) of whom had one follow-up visit, 437 (71.2%) two follow-up visits, 350 (57.1%) three follow-up visits, 231 (37.7%) four follow-up visits, and 90 (14.7%) five follow-up visits. Written informed consent was obtained from participants. The Columbia University institutional review board approved all protocols for this study.

Assessment of Cognitive Dysfunction

Cognitive dysfunction was classified as executive and memory dysfunction because these types seem to be most relevant to the management of diabetes mellitus. Executive dysfunction is broadly defined as the ability to plan, initiate, and execute complex tasks[18] (e.g., planning and completing diabetes mellitus treatment), whereas memory is defined as the ability to recall (e.g., remembering to take diabetes mellitus medications).[19] Executive dysfunction was assessed based on the participant's performance on the Color Trails Test Part 2, a test of executive functioning and mental flexibility.[20] The Color Trails Test is

similar in form to the Trail-Making Test Part B,[21] but it removes the cultural bias associated with unfamiliarity with the English alphabet.[22] The majority of the cohort was Hispanic, and this test is well suited to individuals whose first language is not English. Instead of connecting numbers to Arabic letters, the Color Trails Test requires participants to connect numbers and colors. Each number is overlaid on a colored circle, pink or yellow.[22] Participants are asked to connect the numbers 1–25 in ascending order but to alternate between colors (pink-1, yellow-2, pink-3, yellow-4, etc.).[22] A cutoff for an abnormal score was defined as performance in less than the 16th percentile (roughly 1 standard deviation (SD) below the standardized test score mean).[23,24] This cutoff was used because test performance 1 SD below the mean is typically used in clinical settings to categorize individuals as having abnormal cognitive functioning.[23,24] Studies of cognition, in general, are increasingly studying this range of cognitive dysfunction[25] as compared to the more frequently used classification of mild cognitive impairment (MCI), which uses 1.5 SDs as a cutoff for normal cognitive performance.

Memory dysfunction was assessed based on the participant's performance on the total immediate memory task of the Selective Reminding Test (SRT), a 12-item list-learning verbal memory test.[26] SRT total score was converted to a T-score based on the participant's age, sex, education, and race and ethnicity. An abnormal T-score was defined as performance in under the 16th percentile (1 SD below the standardized test score mean) of SRT immediate recall T-scores in the sample.[23,24] Based on this criterion, a participant with a T-score <28 on the SRT immediate recall task was classified with memory dysfunction.

Cognitive dysfunction was examined in terms of executive function and memory as an exposure in two ways: relating cognitive dysfunction at baseline to the outcomes and using all available follow-up data on cognitive dysfunction and classifying participants as ever or never having cognitive dysfunction. There was little difference in results between using the baseline cognitive dysfunction status definition and using the ever–never definition.

Outcomes

Changes in measures of metabolic control (HbA1c, SBP, LDL-C) were evaluated. Twelve-hour fasting blood samples were collected to assess HbA1c and lipid levels. HbA1c was analyzed using boronate affinity chromatography using high-performance liquid chromatography (Primus CLC 385; Primus, Kansas City, MO). Lipid levels were analyzed using enzymatic colorimetric methods (Vitros; Johnson & Johnson, New Brunswick, NJ). LDL-C was calculated using the Friedwald equation.[27] SBP was determined as the average of the last two of three readings taken 1 minute apart (Dinamap PRO 100; Critikon, Tampa, FL).[28]

Statistical Analysis

Descriptive analyses were conducted using chi-square tests for categorical variables and the Kruskal–Wallis test for continuous variables to test for significant differences in participant characteristics between individuals with and without cognitive dysfunction, executive and memory type separately.

Linear mixed models[29] were used to examine the longitudinal relationship between ever versus never presence of executive or memory dysfunction and changes in parameters of metabolic control (HbA1c, SBP, LDL-C). Models included random effects for intercepts (individuals) and clustering within primary care provider, which was the unit of recruitment in IDEATel.[19] To estimate the association between executive or memory dysfunction and changes in measures of metabolic control, an interaction term between cognitive dysfunction status (executive or memory type) and time was included. Nonlinearity was assessed and goodness-of-fit statistics were used (Akaike Information Criterion and Schwarz's Bayesian Information Criterion) to assess model fit. Model fit was not improved with inclusion of a quadratic (group by time^2) or exponential term (group by e^{-time}) for time. Demographic characteristics that are known to be associated with cognitive dysfunction and the metabolic measures (age, sex, years of education, race and ethnicity) were adjusted for. To account for residual effects of the IDEATel treatment, the randomization group assignment was included in the final model. Symptomatology of depression and cognitive dysfunction are similar and often mistaken for one another, so the presence or absence of depressive symptoms, as measured using the SHORT Comprehensive Assessment and Referral Evaluation Depression questionnaire,[30] was included in the final model. Insulin, metformin, sulfonylurea, or thiazolidinedione medication use was further adjusted for in models of HbA1c to account for possible confounding by indication. Analyses were performed using Stata 13.0 (Stata Corp, College Station, TX).

RESULTS

Six hundred thirteen participants were included in this analysis (Table 1). The mean age was 73, and 70% were women. Participants had an average of 7.5 years of education. Most participants were Hispanic (82.5%) or non- Hispanic black (15.5%), with fewer than 1.0% reporting non-Hispanic white race.

In terms of executive dysfunction, 331 of 613 participants (54%) performed in the lowest 16th percentile of test scores for the Color Trails Test Part 2 at a minimum of one visit throughout follow-up (Table 1). Age, sex, education, and race and ethnicity were not statistically different between participants classified with and without executive dysfunction. There was no difference in adjusted baseline measurements or rates of change in metabolic measures between participants with and without executive dysfunction (Table 2).

Thirty-three percent of participants (n = 202) were classified with memory dysfunction (Table 1). Women were more likely to have memory dysfunction than men, and participants with memory dysfunction had attained, on average, one less grade of education. No significant adjusted baseline differences were observed between participants with diabetes mellitus with and without memory dysfunction (Table 3). Significant longitudinal differences were observed in SBP. Participants with memory dysfunction had more declines, as opposed to increases, in SBP across follow-up than those without (Table 3).

Whether ever having executive or memory dysfunction was related to diabetes mellitus control was explored; 437 (71.2%) participants demonstrated ever having any type of dysfunction, but this exposure was not longitudinally related to HbA1c, SBP, or LDL-C.

Sixteen percent (n = 96) of participants had executive and memory dysfunction throughout follow-up. No significant baseline or longitudinal differences were observed between participants with comorbid executive and memory dysfunction and those without executive and memory dysfunction (n = 176).

DISCUSSION

Neither executive dysfunction nor memory dysfunction in the mild range were independently associated with diabetes mellitus control in longitudinal analyses in this sample of older adults with diabetes mellitus.

These results both conflict and agree with the results of prior research. A cross-sectional study of older African Americans with diabetes mellitus found that HbA1c values were 0.23 units lower for each unit increase in higher executive function score.[15] Another cross-sectional study of older adults reported that global cognitive dysfunction was inversely correlated with HbA1c.[10] In comparison, a small study of older adult men found no correlation between executive dysfunction and HbA1c, lipid levels, or blood pressure.[8] Differences in findings may be due to heterogeneity in study populations but may also be due to the cognitive measures selected. The findings with the Color Trails Test, an executive functioning task, and SRT, a verbal test of memory, were similar. Most prior studies of cognitive dysfunction and metabolic control have examined only executive dysfunction as it relates to metabolic control. Diabetes mellitus self-management requires complex thought processing with mental flexibility, which is an attribute of executive functioning. Memory may also be important for diabetes mellitus self-management, specifically for tasks related to meal preparation, medication adherence, and administration of diabetes mellitus medications, and should be examined. Appropriate self-management of diabetes mellitus is important for the prevention of diabetes mellitus–related complications and adverse outcomes, such as micro- and macrovascular disease and death.[1] Mild dysfunction in executive functioning and memory did not seem to affect self-management of diabetes mellitus in this sample of older adults.

Several limitations should be considered. First, the examination of cognition relied on a discrete number of tests, particularly for executive dysfunction, which is complex and difficult to measure.[18] It is possible that a more-comprehensive battery would have found that cognition affects diabetes mellitus control, but the current authors found that ever having cognitive dysfunction was not associated with diabetes mellitus control. Second, the sampling frame for this study was participants in a randomized controlled trial (RCT), and the potential for selection bias in RCTs is high, with the healthiest and most educated individuals likely to enroll. It is possible that the results are not generalizable to clinic-based samples. It is also possible that the minority sample with a relatively low educational achievement was somewhat homogeneous from diabetes mellitus control and cognitive performance standpoints, explaining the null findings. Third, data were not available to estimate change in diabetes mellitus medication use to account for the possible confounding by indication, with individuals who control their diabetes mellitus with insulin being observed to have greater baseline executive dysfunction. Last, it is possible that the Medicare recipients with diabetes mellitus in the sample received assistance from formal

(e.g., nurses) or informal (e.g., relatives) caregivers, but related data were not collected, so this could not be taken into account. Participants with cognitive impairment could have overcome its effects on diabetes mellitus control through the assistance of formal or informal caregivers. Collection of these data was not part of the original design of the study, although mild cognitive dysfunction of any type was not associated with diabetes mellitus self-care activities or self-efficacy. If third-party assistance explained the null findings, one would expect to find a relationship between cognitive dysfunction and these self-care variables but not between cognitive dysfunction and direct measures of diabetes mellitus control. Nonetheless, it would be useful to collect data on third-party assistance in relation to cognitive dysfunction in diabetes mellitus. Significant strengths of the study include the large sample size and detailed longitudinal data on cognition and diabetes mellitus control parameters. More-severe cognitive dysfunction (e.g., dementia) could affect diabetes mellitus control, but this study addressed mild dysfunction, which is the most common in clinical practice.

Diabetes mellitus is a complex disease that requires a substantial amount of self-management. Identifying what factors may inhibit ideal self-management is important so that it may be addressed in the clinical setting, where the provider can provided targeted education. Mild cognitive dysfunction was not related to diabetes mellitus control in this sample of elderly diabetics. Future studies need to explore whether assistance prompted by cognitive dysfunction, which could not be addressed, could explain these null findings.

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Table 1

Characteristics of Study Population (n = 613) According to Executive and Memory Dysfunction Status, Informatics for Diabetes Mellitus Education and Telemedicine (IDEATel) Project, 2004–2008

Characteristic	Total Sample, N = 613	Never Executive Dysfunction ≥16th percentile, n = 282	Ever Executive Dysfunction <16th percentile, n = 331	Never Memory Dysfunction ≥16th percentile, n = 411	Ever Memory Dysfunction <16th percentile, n = 202
Age, mean ± SD	73.0 ± 6.5	73.6 ± 6.6	72.5 ± 6.4	73.1 ± 6.3	72.8 ± 7.0
Female, n (%)	426 (69.5)	191 (67.7)	235 (71.0)	273 (66.4)	153 (75.7)a
Education, years, mean ± SD	7.5 ± 4.1	7.3 ± 4.2	7.6 ± 4.1	7.7 ± 4.2	6.9 ± 4.1a
Race and ethnicity, n (%)					
Hispanic	506 (82.5)	234 (83.0)	272 (82.2)	333 (81.0)	173 (85.6)
Non-Hispanic black	95 (15.5)	42 (14.9)	53 (16.0)	70 (17.0)	25 (12.4)
Insulin, n (%)	164 (26.8)	74 (26.2)	90 (27.2)	108 (26.3)	56 (27.7)
Metformin, n (%)	291 (47.5)	124 (44.0)	167 (50.5)	188 (45.7)	103 (51.0)
Sulfonylurea, n (%)	228 (37.2)	102 (36.2)	126 (38.1)	150 (36.5)	78 (38.6)
Thiazolidinedione, n (%)	153 (25.0)	70 (24.8)	83 (25.1)	105 (25.5)	48 (23.8)
Depressive symptoms, n (%)	218 (35.6)	100 (35.5)	118 (35.6)	136 (33.1)	82 (40.6)
IDEATel intervention group	309 (50.4)	143 (50.7)	166 (50.2)	209 (50.9)	100 (49.5)
Glycosylated hemoglobin, %, mean ± SD	7.4 ± 1.4	7.4 ± 1.5	7.5 ± 1.4	7.4 ± 1.3	7.6 ± 1.6
Systolic blood pressure, mmHg, mean ± SD	140.2 ± 21.1	139.2 ± 22.2	141.1 ± 20.1	139.2 ± 20.9	142.2 ± 21.3
Diastolic blood pressure, mmHg, mean ± SD	69.6 ± 10.9	69.0 ± 11.0	70.1 ± 10.7	69.2 ± 10.7	70.6 ± 11.2
Total cholesterol, mg/dL, mean ± SD	169.6 ± 41.2	169.4 ± 42.1	169.8 ± 40.5	168.6 ± 39.7	171.7 ± 44.1
High-density lipoprotein cholesterol, mg/dL, mean ± SD	48.6 ± 15.7	48.8 ± 15.4	48.5 ± 16.0	48.7 ± 16.2	48.5 ± 14.7
Low-density lipoprotein cholesterol, mg/dL, mean ± SD	96.5 ± 38.0	96.6 ± 39.5	96.5 ± 36.8	95.4 ± 36.8	98.8 ± 40.2

SD = standard deviation.

[a] $P < .05$.

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Table 2

Random Effects Models for the Associations Between Executive Dysfunction Status and Differences in Baseline Measures and Rates of Change in Metabolic Measures, Informatics for Diabetes Mellitus Education and Telemedicine (IDEATel) Project, 2004–08

	Adjusted Baseline Values of Metabolic Measures				Annual Rate of Change (Slopes) in Metabolic Measures over 5-Year Follow-Up			
	Never Executive Dysfunction, n = 282	Ever Executive Dysfunction, n = 331	Difference[a]	*P*-Value	Never Executive Dysfunction, n = 282	Ever Executive Dysfunction, n = 331	Difference[b]	*P*-Value
Metabolic Measure	**Estimate (95% CI)**				**Estimate (95% CI)**			
Glycosylated hemoglobin, %[c]	8.2 (6.2 – 10.1)	8.2 (6.3 – 10.2)	0.05 (−0.2 – 0.3)	.67	0.09 (0.04 – 0.1)	0.07 (0.03 – 0.1)	−0.02 (−0.08 – 0.04)	.51
Systolic blood pressure, mmHg[d]	131.1 (103.6 – 158.6)	132.5 (105.2 – 160.0)	1.4 (−1.7 – 4.5)	.37	–0.2 (−1.0 – 0.5)	−0.04 (−0.6 – 0.6)	0.2 (−0.7 – 1.1)	.70
Low-density lipoprotein cholesterol, mg/dL[d]	167.8 (118.9 – 216.8)	166.5 (117.9 – 215.2)	−1.3 (−6.7 – 4.1)	.63	−1.8 (−3.3 to −0.4)	−1.7 (−2.8 to −0.6)	0.2 (−1.5 – 1.9)	.84

CI = confidence interval.

Models include random intercepts and clustering within primary care provider.

[a] Executive dysfunction group variable in model.

[b] Interaction term of executive dysfunction group by time.

[c] Models adjusted for age; race; sex; education; insulin, metformin, sulfonylurea, and thiazolidinedione use; depressive symptoms; and IDEATel treatment group.

[d] Models adjusted for age, race, sex, education, depressive symptoms, and IDEATel treatment group.

Table 3

Random-Effects Models for the Associations Between Memory Dysfunction Status and Differences in Baseline Measures and Rates of Change in Metabolic Measures, Informatics for Diabetes Mellitus Education and Telemedicine (IDEATel) Project, 2004–08

	Adjusted Baseline Values of Metabolic Measures				Annual Rate of Change (Slopes) in Metabolic Measures over 5-Year Follow-Up			
	Never Executive Dysfunction, n = 411	Ever Executive Dysfunction, n = 202	Difference[a]	*P*-Value	Never Executive Dysfunction, n = 411	Ever Executive Dysfunction, n = 202	Difference[b]	*P*-Value
Metabolic Measure	**Estimate (95% CI)**				**Estimate (95% CI)**			
Glycosylated hemoglobin, %[c]	8.2 (6.2–10.1)	8.3 (6.4–10.3)	0.2 (−0.03 –0.4)	.09	0.09 (0.05–0.1)	0.06 (0.003–0.1)	−0.03 (−0.1 –0.03)	.28
Systolic blood pressure, mmHg[d]	131.8 (104.4–159.2)	134.5 (107.0–162.0)	2.7 (−0.5–6.0)	.10	0.3 (−0.3–0.9)	−0.8 (−1.6–0.007)	−1.1 (−2.0 to −0.1)	.03
Low-density lipoprotein cholesterol, mg/dL[d]	166.3 (117.6–215.0)	168.2 (119.3–217.1)	1.9 (−3.8–7.6)	.51	−1.7 (−2.7 to −0.6)	−1.9 (−3.4 to −0.3)	−0.2 (−2.0–1.6)	.86

CI = confidence interval.

Models include random intercepts and clustering within primary care provider.

[a] Memory dysfunction group variable in model.

[b] Interaction term of memory dysfunction group by time.

[c] Models adjusted for age; race; sex; education; insulin, metformin, sulfonylurea, and thiazolidinedione use; depressive symptoms; and IDEATel treatment group.

[d] Models adjusted for age, race, sex, education, depressive symptoms, and IDEATel treatment group.