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Linking Glycemic Control and Executive Function in Rural Older Adults with Diabetes

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Abstract

OBJECTIVES—To examine the association between glycemic control and the executive functioning domain of cognition, and to identify risk factors for inadequate glycemic control that may explain this relation.

DESIGN—Cross-sectional study.

SETTING—In-person interviews conducted in participants' homes.

PARTICIPANTS—Ninety-five rural older adults with diabetes that included African Americans, American Indians, and whites from three counties in south central North Carolina.

MEASUREMENTS—Participants underwent uniform evaluations. Glycemic control was assessed using a validated method, and executive function was assessed using a previously established set of measures and scoring procedure. Information pertaining to medication for diabetes treatment, knowledge of diabetes, and diabetes self-care behaviors were obtained.

RESULTS—In linear regression models adjusting for gender, age, education, ethnicity, duration of diabetes, and depressive symptoms, executive function was significantly associated with glycemic control. A 1-point higher executive function score was associated with a 0.47 lower A1C value ($p < 0.01$). The association of glycemic control with executive function became marginally significant (p -value = 0.08) when controlling for several glycemic control risk factors, including use of diabetes medication and diabetes knowledge.

CONCLUSIONS—These results suggest that poor glycemic control is associated with impairments in performance on composite measures of executive function, and that this relation may be explained by modifiable risk factors for glycemic control such as use of diabetes medication and diabetes knowledge.

Keywords

diabetes; glycemic control; executive function

Glycemic control is an essential element of diabetes management. Glycemic control prevents microvascular complications such as blindness, end-stage renal disease, and lower limb amputations, and large trials have demonstrated the need for glycemic control among patients with diabetes ¹. Many older adults fail to achieve or maintain glycemic control ². Cognitive impairment may contribute to this. Effective glycemic control involves a series of complex goal-directed behaviors including proper nutrition, regular activity and exercise, self-monitoring of blood glucose, and medication management that may include oral medication or insulin treatment ³. A patient's cognitive ability to execute these behaviors is therefore likely to be crucial for diabetes self-management.

The association of glycemic control with cognitive function is complex. Previous studies have found that older adults with diabetes have increased risk of dementia ⁴, and that poor glycemic control leads to poorer cognitive function ⁵. Other studies suggest that cognitive capacity affects individuals' ability to achieve glycemic control, and poor glycemic control in turns impairs cognitive function in adults with diabetes ^{6, 7}. This suggests the possibility of a bidirectional association.

Executive function is a primary domain of cognition that involves a broad set of cognitive abilities such as attention, working memory, organization, and persistence that are necessary for orchestrating complex, goal-directed activities. These abilities are often referred to as frontal lobe function, because they appear to be critically dependent on the frontal cortex and its networks in other cerebral and subcortical areas ⁸. Although diabetes is related to some domains of cognition such as processing speed and memory ⁹, greater attention is now being directed to the association between diabetes and executive functioning domain of cognition. Specifically, recent data suggest that executive dysfunction is a risk factor for poor glycemic control ^{6, 7, 10}.

The executive functioning domain of cognition seems to be important in allowing the execution of intended interventions aimed at managing glycemic control. Impairments in executive function are associated with self-care capacity, including poor adherence to medication, low autonomy and inability to make decisions, low independence or instrumental activities of daily living, and resistance to care ¹¹. Patients with diabetes perform significantly worse on executive measures relative to normal comparison adults ¹². The effects of diabetes on executive function are related to underlying microvascular disease that affects frontal subcortical function ¹³.

Three issues warrant further research. First, data on cognitive function and glycemic control in rural older minorities are limited. Older adults in rural communities, particularly those of ethnic minority groups, are at increased risk for poor glycemic control ². Second, data on the impact of executive function on glycemic control is sparse, but impaired executive function has been implicated as a contributor to poor glycemic control ^{6, 7, 10}. Lastly, although the relationship between executive function and glycemic control has been found in previous studies, an investigation of recognized risk factors (e.g., self-care behaviors) for glycemic control that might explain this relation has not been undertaken.

An integrated analysis of executive function, glycemic control, and known risk factors for glycemic control among rural-dwelling older adults is needed. In this study, we examined the relation of executive function to glycemic control in a tri-ethnic sample of rural older adults that included African Americans, American Indians, and whites. We proposed a framework as a backdrop to our investigation of mechanisms in glycemic control: executive function → diabetes knowledge → self-care behaviors → glycemic control. These pathways first suggest the role that executive function plays in acquisition of diabetes knowledge, which then influences or promotes the adoption of self-care behaviors such as

taking medication for the treatment of diabetes, thereby affecting glycemic control. Although we did not seek to test these pathways explicitly, we used them to organize our investigation of how executive function influences glycemic control.

RESEARCH DESIGN AND METHODS

Participants

A total of 95 African American, American Indian, and white men and women were recruited from three counties in south central North Carolina. These counties were chosen because they contain large minority populations and because a high proportion of the population is below the federal poverty line. Inclusion criteria were age 60 years or older and having had a diabetes diagnosis for at least two years. We used three methods, including site-based sampling, word-of-mouth referral, and existing participants from previous aging studies, to provide a representative sample from the study communities¹⁴. Data collection was completed during summer of 2008 and consisted of an interviewer-administered, fixed response questionnaire and a finger stick blood draw to test for glycemic control. This study was approved by the Institutional Review Board at the Wake Forest University Health Sciences, and all participants gave informed consent.

Glycemic control as the main outcome

Glycemic control was assessed by measuring hemoglobin (A1C) from a finger stick blood sample. We used the procedures for the handheld Bayer A1cNow+ machine, which has demonstrated precision and accuracy in A1C testing¹⁵.

Measures of executive functioning

Tests of executive functioning that are not vision dependent were selected because visual impairment is common in older adults with diabetes. In addition, we chose tests that were widely used, and had good distributions in the adult population. We used three simple, well-validated and widely-used tests that draw on a variety of cognitive skills such as concentration, organization, and vigilance that are aspects of executive function and are necessary for dynamic task requirements. Some cognitive tests assess more than one domain of cognition, and were assigned to the executive function domain based on previous conventions in the literature^{8, 12}. The tests were administered to participants by research staff who had undergone training and supervised practice. We have described the tests previously¹⁶. In brief, the Animal Verbal Fluency test assesses language ability related to executive function. This test requires participants to name as many animals as they could think of in 60 seconds¹⁷. The Brief Attention Test is one of the most commonly used cognitive measures that assesses attention and executive function. It requires the examiner to read a list of letters and numbers, and the participant must keep track of how many numbers are read¹⁸. The Digit Span Backward test from the Wechsler Memory Scale-III is a well-known and validated measure of working memory and executive function¹⁹. Working memory refers to one's ability to process, maintain, and manipulate of information²⁰. Hence, language comprehension, problem solving, goal satisfaction and other high-order cognitive abilities depend on working memory.

To avoid floor and ceiling effects and because in a previous factor analysis¹⁶ all three tests loaded substantially on a single factor that accounted for 33% of the variance, we constructed a composite score of executive. As previously described^{16, 21}, the composite measure was constructed by transforming the raw score of each test into z-scores, using the sample mean and standard deviation. Then the z-scores were averaged to produce the composite score of executive function.

Recognized risk factors for glycemic control

The study obtained data on knowledge of diabetes, medication for the treatment of diabetes, and self-care behaviors. We used the Michigan's DRTC "Diabetes Knowledge Test" ²² to evaluate participants' knowledge of their diabetes in areas including nutrition, exercise, and glucose management and testing. Medication for the treatment of diabetes was based on two yes/no questions, "Are you now taking insulin?", and "Are you now taking diabetes pills?". We also included three indicators of self-care behaviors: glucose monitoring (frequency that participants checked their blood for glucose or sugar, 0 = "0 time per day", 1 = "1 per day"); diet ("how many of the last 7 days did you eat 5 or more servings of fruits and vegetables") and physical activity ("how many of the last 7 days did you participate in a specific exercise session other than what you do around the house or as part of your work").

Covariates

We adjusted the analyses for several covariates including gender, age, education, ethnicity, duration of diabetes (measured in years), and depressive symptoms. The 20-item CES-D (Center for Epidemiologic Studies-Depression) was used to assess depressive symptoms, with responses "yes" and "no" based on the validation of this modification for this population ²³

Data analysis

The relation of executive function to glycemic control was examined in a series of linear regression models. We adjusted for gender, age, education, ethnicity, depressive symptoms, and duration of diabetes in all models. In addition, any recognized risk factor (i.e., diabetes knowledge, diabetes medications, and self-care behaviors) for glycemic control, irrespective of whether it was associated with A1C in the univariate analyses, was also entered into regression models. Independent variables were entered in blocks to reflect our proposed framework: executive function was entered in block 1 (model 1); model 1 plus diabetes knowledge were entered in block 2 (model 2); model 1 plus diabetes medications were entered in model 3; and model 1 plus self-care behaviors were entered in model 4. Lastly, we tested in a separate final model (model 5) whether any recognized risk factor for glycemic control explained the association of executive function with glycemic control. Statistical analysis was performed using SAS 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

Five participants were excluded from the analyses due to missing data. Table 1 presents characteristics of the study population. Table 2 presents factors that explained the relationship between executive function and glycemic control. It also shows the results of introducing executive function into the regression model for glycemic control (model 1). As expected, executive function was significantly associated with glycemic control, adjusting for gender, age, education, ethnicity, depressive symptoms, and duration of diabetes: a 1 point higher executive function score was associated with a 0.47 lower A1C value ($p < 0.01$).

Adding diabetes knowledge to the analytic models attenuated the association of executive function with glycemic control by .10 (model 2). Further adjusting for use of diabetes pills and insulin attenuated the association between executive function and glycemic control by .08 (model 3). The addition of self-care behavior variables to the regression models increased the estimated coefficient of executive function from -0.47 to -0.52 ($p < 0.01$) (model 4). However, in the final multivariable analysis (model 5) examining all glycemic control risk factors simultaneously, the association of executive function with glycemic control was attenuated and became marginally significant ($p = 0.08$). Diabetes knowledge, use of

diabetes pills, and insulin were independently associated with glycemic control, while self-care behaviors were not associated with glycemic control.

DISCUSSION

Evidence suggests a complex association between cognitive function and glycemic control in older adults. Understanding this complex relation requires studying diverse groups and testing alternative explanations for the association. This study tested the idea that compromised executive function will impair diabetes-related knowledge and subsequent self-care behaviors, thereby interfering with glycemic control. Like previous studies^{6, 7, 10}, we observed a relationship between executive function and glycemic control, but did so in an ethnically diverse sample of rural-dwelling older adults. Adjusting for important glycemic control risk factors, this study shows that a 1 point higher executive score was associated with a 0.33 lower A1C value, but the association was marginally significant. Although self-management is a central component of achieving glycemic control³, the current data suggest that impaired executive function may interfere with older adults' ability to effectively manage their diabetes.

Although executive function may be linked to glycemic control, our understanding of the mechanisms for such an association is still limited. Pathways leading from poor executive function to poor glycemic control may involve multiple mediating mechanisms. The greatest attenuation of the executive function-glycemic control relationship resulted when controlling for diabetes medications and diabetes knowledge. The fact that executive function remained significant after adjusting for diabetes medications has clinical implications. That is, the relationship between executive function and glycemic control may not be fully explained by lower intake of medications or perhaps by poor adherence to medications. Our findings confirmed previous observations suggesting the beneficial effects of intake of medication and diabetes education on better glycemic control and other health outcomes²⁴. Whether poor executive function adversely influences glycemic control through an independent mechanism or indirectly through other determinants (e.g., medication and diabetes knowledge) has yet to be determined. Our findings further provide a rationale for future studies to determine which pathways are especially important in diabetes care and glycemic control.

This study has several strengths. First, the sample involved older adults in rural communities and those of ethnic minority groups that have not been well-represented in previous studies. These populations are particularly vulnerable to the effects of diabetes. They have significant health care barriers, including limited access to high quality specialty care and to diabetes self-management resources²⁵. Study of relatively high risk populations may provide clues to barriers that prevent effective glycemic control among all persons with diabetes. Second, the cognitive tests were chosen in accordance with other studies to detect impairments in executive function^{8, 12, 16}. We selected executive measures that do not require visual processing to minimize the confounding effect of visual impairment, one of the most common microvascular complications of diabetes²⁶. We examined composite measures of executive function instead of individual cognitive tests to minimize potential floor and ceiling effects. Lastly, our analyses suggest that modifiable health behaviors such as oral hypoglycemic agents, insulin, and diabetes knowledge explain the link between executive function and glycemic control.

This study also has several limitations. First, we did not include other measures of executive function, such as the Stroop Task²⁷ or the Wisconsin Card Sorting Test²⁸ that may be more sensitive to executive function. Unfortunately, these tests require substantial visual processing such as discriminating color. We therefore selected non-visual dependent

executive measures that draw on a variety of cognitive skills such as persistence, concentration, attention, and working memory that refers to the ability to process, maintain, and manipulate of information. These abilities are representative of the real life behavior tasks, such as taking medications and monitoring dietary consumption that are essential for achieving glycemic control. Second, we did not include other non-executive domains such processing speed and memory to determine whether they were related to glycemic control. Our selection of the executive domain was guided by previous studies ^{6, 7, 16} that support the view of executive function as a central domain that affects glycemic control. A larger scale community-based study should be conducted with a sample size adequate for exploring the impact of executive function and other cognitive domains on glycemic control. Third, we did not examine whether executive impairment and poor glycemic control were more frequent among those with low education. Previous studies have recognized the relationship between higher education attainment and higher cognitive performance, and the challenge to disentangle the effects of education from cognitive function on health outcomes ²⁹. The effects of education on glycemic control were not statistically significant across all models in our study (data not shown). However, definitive data are needed to explore the education-cognition relationship with glycemic control. Lastly, our findings are limited by the cross-sectional design and therefore cannot address causality. Longitudinal data are needed to determine whether executive function is a cause or consequence of poor glycemic control.

This study has important clinical implications. Studies have suggested that impairments in executive function are common in patients with a medical illness including diabetes. Executive function may undermine self-care capacity. Though we were not able to assess the direct causal associations between executive function and self-care capacity, we did examine the relation between executive function and diabetes knowledge, diabetes medications, and self-care behaviors. In a supplementary univariate analysis, lower executive function scores were noted among participants who took insulin ($p < .01$), and those who did not check their blood for glucose or sugar at least once per day ($p < .05$). Poorer executive function was also associated with lower diabetes knowledge ($p < .001$) and decreased self-reported days per week of exercise ($p < .05$). These results suggest associations between executive function and self-care variables. Because deficits in executive function may affect self-care capacity, efforts to target patients for effective glycemic control should consider executive function impairment as a risk factor. In addition, focusing on explicit executive measures rather than cognitive screening instruments (i.e., Mini-Mental State Examination [MMSE]) may be a better way to identify patients at risk for poor glycemic control. Studies have suggested most commonly used screening tests such as the MMSE are not sensitive to executive function ³⁰. We conclude from our findings that impaired executive function, whether it is exogenous or it is a complication of diabetes, may be key barriers to achieving treatment goals. Training aids that compensate for cognitive impairments may be essential for effective glycemic control.

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Table 1

Characteristics of Participants, n = 90.

Variable	N (%)	Mean (SD) [range]
Female	53 (53)	
Age		72.2 (7.8) [60 – 90]
Education		10 (3.8) [0 – 17]
Ethnicity		
Non-Hispanic white	31 (34)	
African American	31 (34)	
American Indian	28 (32)	
CES-D, Depressive symptoms		3.7 (4.1) [0 – 18]
Diabetes Knowledge Test		10.1 (2.1) [5 – 15]
Duration of diabetes, years		14.3 (11.6) [2 – 50]
Taking diabetes pills	63 (70)	
Taking insulin	35 (39)	
Glucose (check blood for glucose at least 1 time per day)	65 (72)	
Diet (how many of 7 days eat fruits/vegetables)		4 (2.7) [0 – 7]
Exercise (how many of 7 days exercise)		3 (3.2) [0 – 7]
Executive function, z-score		0 (0.80) [–1.77 – 1.75]
Digit span backward		4 (2.1) [0 – 9]
Verbal fluency		17 (5.9) [4 – 35]
Brief attention		4 (2.7) [0 – 10]
Hemoglobin A1C %		7.2 (1.2) [5 – 11.70]

Table 2
Changes in the Association of Executive Function with A1C After Adjusting for Diabetes-related Health Factors.

	Estimated coefficient (SE)				
	Model 1	Model 2	Model 3	Model 4	Model 5
Executive function	-0.47** (0.18)	-0.37* (0.18)	-0.39* (0.18)	-0.52** (0.19)	-0.33 [†] (0.19)
Model 1 + Diabetes Knowledge		-0.12* (0.06)			-0.15** (0.06)
Model 1 + Taking diabetes pills			-0.49 [†] (0.28)		-0.60* (0.29)
Model 1 + Taking insulin			-0.65* (0.31)		-0.85** (0.33)
Model 1 + Glucose (check blood for glucose at least 1 time per day)				0.15 (0.27)	-0.20 (0.29)
Model 1 + Diet (how many of 7 days eat fruits/vegetables)				0.05 (0.04)	0.06 (0.04)
Model 1 + Exercise (how many of 7 days exercise)				0.02 (0.04)	0.02 (0.03)

Note: Results adjusted for gender, age, education, ethnicity, depressive symptoms, and duration of diabetes.

* p < 0.05;

** p < 0.01;

[†] p = 0.08