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

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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 relationship.

DESIGN: Cross-sectional study.

SETTING: In-person interviews conducted in participants’ homes.

PARTICIPANTS: Ninety-five rural older African Americans, American Indians, and whites with diabetes mellitus (DM) from three counties in south-central North Carolina.

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

RESULTS: In linear regression models adjusting for sex, age, education, ethnicity, duration of DM, 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 glycosylated hemoglobin value (P = .01). The association between glycemic control and executive function became nonsignificant (P = .08) when controlling for several glycemic control risk factors, including use of DM medication and DM knowledge.

CONCLUSION: These results suggest that poor glycemic control is associated with impairments in performance on composite measures of executive function and that modifiable risk factors for glycemic control such as use of DM medication and DM knowledge may explain this relationship. J Am Geriatr Soc 58:1123–1127, 2010.

Key words: diabetes mellitus; glycemic control; executive function

Glycemic control is an essential element of diabetes mellitus (DM) 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 in patients with DM.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 DM self-management.

The association between glycemic control and cognitive function is complex. Previous studies have found that older adults with DM have a greater risk of dementia4 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 that poor glycemic control in turn impairs cognitive function in adults with DM.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 DM is related to some

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domains of cognition such as processing speed and memory, \textsuperscript{9} greater attention is now being directed to the association between DM and the executive functioning domain of cognition. Specifically, recent data suggest that executive dysfunction is a risk factor for poor glycemic control. \textsuperscript{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 ability to perform instrumental activities of daily living, and resistance to care. \textsuperscript{11} Patients with DM perform significantly worse on executive measures than adults without DM. \textsuperscript{12} The effects of DM on executive function are related to underlying microvascular disease that affects frontal subcortical function. \textsuperscript{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 greater risk for poor glycemic control. \textsuperscript{2} Second, data on the effect of executive function on glycemic control is sparse, but impaired executive function has been implicated as a contributor to poor glycemic control. \textsuperscript{6,7,10} Last, 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 in rural-dwelling older adults is needed. The current study examined the relationship between executive function and glycemic control in a tri-ethnic sample of rural older adults that included African Americans, Native Americans, and whites. A framework to the investigation of mechanisms in glycemic control (executive function $\rightarrow$ DM knowledge $\rightarrow$ self-care behaviors $\rightarrow$ glycemic control) was proposed as a backdrop. These pathways first suggest the role that executive function plays in acquisition of DM knowledge, which then influences or promotes the adoption of self-care behaviors such as taking medication for the treatment of DM, thereby affecting glycemic control. Although the goal was not to test these pathways explicitly, they were used to organize the investigation of how executive function influences glycemic control.

**RESEARCH DESIGN AND METHODS**

**Participants**

Ninety-five African-American, Native-American, 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 aged 60 and older and having had a DM diagnosis for at least 2 years. Three methods (site-based sampling, word-of-mouth referral, and existing participants from previous aging studies) were used to provide a representative sample from the study communities. Data collection was completed during the summer of 2008 and consisted of an interviewer-administered fixed-response questionnaire and a finger-stick blood draw to test for glycemic control. The institutional review board at the Wake Forest University Health Sciences approved the study, and all participants gave informed consent.

**Glycemic Control as the Main Outcome**

Glycemic control was assessed by measuring glycosylated hemoglobin (HbA1c) from a finger-stick blood sample. The procedures for the handheld Bayer A1cNow+ Headquarters (Sunnyvale, CA), which has demonstrated precision and accuracy in HbA1c testing, was used. \textsuperscript{14}

**Measures of Executive Functioning**

Tests of executive functioning that are not vision dependent were selected because visual impairment is common in older adults with DM. In addition, tests that were widely used and had good distributions in the adult population were chosen. Three simple, well-validated and widely used tests were used 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. \textsuperscript{8,12} Research staff who had undergone training and supervised practice administered the tests to participants. The tests have been described previously. \textsuperscript{13} In brief, the Animal Verbal Fluency test assesses language ability related to executive function. It requires participants to name as many animals as they can think of in 60 seconds. \textsuperscript{16} The Brief Attention Test is one of the most commonly used cognitive measures that assesses attention and executive function. The examiner reads a list of letters and numbers, and the participant must keep track of how many numbers are read. \textsuperscript{17} The Digit Span Backward test from the Wechsler Memory Scale-III is a well-known and validated measure of working memory and executive function. \textsuperscript{18} Working memory refers to the ability to process, maintain, and manipulate information. \textsuperscript{19} 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 analysis \textsuperscript{15} all three tests loaded substantially on a single factor that accounted for 33% of the variance, a composite score was constructed of executive function. As previously described, \textsuperscript{15,20} 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 DM, medication for the treatment of DM, and self-care behaviors. The Michigan Diabetes Research and Training Center "Diabetes Knowledge Test" \textsuperscript{21} was used to evaluate participants' knowledge of their DM in areas including nutrition, exercise, and glucose management and testing. Medication for the treatment of DM was based on two yes/no questions, "Are you now taking insulin?" and "Are you now taking
diabetes pills?" Three indicators of self-care behaviors were also assessed. This included one question from the DM module of the Behavioral Risk Factor Surveillance System to obtain the frequency that participants checked their blood for glucose or sugar (0 = 0 time per day, 1 = \geq 1 times per day). Two questions from the Summary of Diabetes Self-Care Activities\textsuperscript{22} were used to assess diet (How many of the last 7 days did you eat five 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
The analyses were adjusted for several covariates: sex, age, education, ethnicity, duration of DM (measured in years), and depressive symptoms. The 20-item Center for Epidemiologic Studies Depression Scale was used to assess depressive symptoms, with responses of yes and no, based on the validation of this modification for this population.\textsuperscript{23}

Data Analysis
The relationship between executive function and glycemic control was examined in a series of linear regression models. Sex, age, education, ethnicity, depressive symptoms, and duration of DM were adjusted for in all models. In addition, any recognized risk factor (DM knowledge, DM medications, and self-care behaviors) for glycemic control, regardless of whether it was associated with HbA1c in the univariate analyses, was also entered into regression models. Independent variables were entered in blocks to reflect the proposed framework; executive function was entered in block 1 (Model 1), Model 1 plus DM knowledge were entered in block 2 (Model 2), Model 1 plus DM medications were entered in Model 3, Model 1 plus self-care behaviors were entered in Model 4, and whether any recognized risk factor for glycemic control explained the association between executive function and glycemic control was tested in a separate final model (Model 5). Statistical analysis was performed using SAS 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS
Five participants were excluded from the analyses because of missing data. Table 1 presents characteristics of the study population. Table 2 presents factors that explained the relationship between executive function and glycemic control and shows the results of introducing executive function into the regression model for glycemic control (Model 1). Executive function was significantly associated with glycemic control, adjusting for sex, age, education, ethnicity, depressive symptoms, and duration of DM; a 1-point-higher executive function score was associated with a 0.47-lower HbA1c value (\(P = .01\)).

Adding DM knowledge to the analytical models attenuated the association between executive function and glycemic control by 0.10 HbA1c value (Model 2). Further adjusting for use of DM pills and insulin attenuated the association between executive function and glycemic control by 0.08 HbA1c value (Model 3). The addition of self-care behavior variables to the regression models increased the estimated coefficient of executive function from \(-0.47\) to \(-0.52 (P = .007)\) (Model 4), although in the final multivariable analysis (Model 5) examining all glycemic control risk factors simultaneously, the association between executive function and glycemic control was attenuated and became nonsignificant (\(P = .08\)). DM knowledge and use of DM pills and insulin were independently associated with glycemic control, whereas self-care behaviors were not.

DISCUSSION
Evidence suggests a complex association between cognitive function and glycemic control in older adults. Understanding this complex relationship requires studying diverse groups and testing alternative explanations for the association. The current study tested the idea that compromised executive function will impair DM-related knowledge and subsequent self-care behaviors, thereby interfering with glycemic control. Like previous studies\textsuperscript{6,7,10}, a relationship was found between executive function and glycemic control in an ethnically diverse sample of rural-dwelling older adults. Adjusting for important glycemic control risk factors simultaneously, the association between executive function and glycemic control was attenuated and became nonsignificant (\(P = .08\)). DM knowledge and use of DM pills and insulin were independently associated with glycemic control, whereas self-care behaviors were not.

Table 1. Characteristics of Participants (\(N = 90\))

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Female, n (%)</td>
<td>53 (53)</td>
</tr>
<tr>
<td>Age, mean ± SD (range)</td>
<td>72.2 ± 7.8 (60–90)</td>
</tr>
<tr>
<td>Education, mean ± SD (range)</td>
<td>10 ± 3.8 (0–17)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>31 (34)</td>
</tr>
<tr>
<td>African American</td>
<td>31 (34)</td>
</tr>
<tr>
<td>Native American</td>
<td>28 (32)</td>
</tr>
<tr>
<td>Center for Epidemiologic Studies Depression Scale score, mean ± SD (range)</td>
<td>3.7 ± 4.1 (0–18)</td>
</tr>
<tr>
<td>Diabetes Knowledge Test, mean ± SD (range)</td>
<td>10.1 ± 2.1 (5–15)</td>
</tr>
<tr>
<td>Duration of diabetes mellitus, years, mean ± SD (range)</td>
<td>14.3 ± 11.6 (2–50)</td>
</tr>
<tr>
<td>Taking diabetes pills, n (%)</td>
<td>63 (70)</td>
</tr>
<tr>
<td>Taking insulin, n (%)</td>
<td>35 (39)</td>
</tr>
<tr>
<td>Check blood for glucose at least 1 time per day, n (%)</td>
<td>65 (72)</td>
</tr>
<tr>
<td>How many of 7 days eat fruits and vegetables, mean ± SD (range)</td>
<td>4 ± 2.7 (0–7)</td>
</tr>
<tr>
<td>How many of 7 days exercise, mean ± SD (range)</td>
<td>3 ± 3.2 (0–7)</td>
</tr>
<tr>
<td>Executive function, z-score, mean ± SD (range)</td>
<td>0 ± 0.80 (–1.77–1.75)</td>
</tr>
<tr>
<td>Digit span backward</td>
<td>4 ± 2.1 (0–9)</td>
</tr>
<tr>
<td>Verbal fluency</td>
<td>17 ± 5.9 (4–35)</td>
</tr>
<tr>
<td>Brief attention</td>
<td>4 ± 2.7 (0–10)</td>
</tr>
<tr>
<td>Glycosylated hemoglobin, %, mean ± SD (range)</td>
<td>7.2 ± 1.2 (5–11.70)</td>
</tr>
</tbody>
</table>

SD = standard deviation.
Although executive function may be linked to glycemic control, understanding of the mechanisms for such an association is limited. Pathways leading from poor executive function to poor glycemic control may involve multiple mediating mechanisms. The greatest attenuation of the relationship between executive function and glycemic control resulted when controlling for DM medications and DM knowledge. The fact that executive function remained significant after adjusting for DM medications has clinical implications. That is, lower intake of medications or perhaps poor adherence to medications may not fully explain the relationship between executive function and glycemic control. These findings confirm previous observations suggesting the beneficial effects of intake of medication and DM education on glycemic control and other health outcomes.\(^\text{24}\) Whether poor executive function adversely influences glycemic control through an independent mechanism or indirectly through other determinants (e.g., medication and DM knowledge) has yet to be determined. The findings of the current study provide further rationale for future studies to determine which pathways are especially important in DM 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 DM. They have significant healthcare barriers, including limited access to high-quality specialty care and to DM self-management resources.\(^\text{25}\) Study of relatively high-risk populations may provide clues to barriers that prevent effective glycemic control in all persons with DM. Second, the cognitive tests were chosen in accordance with other studies to detect impairments in executive function.\(^\text{8,12,15}\) Executive measures that do not require visual processing were selected to minimize the confounding effect of visual impairment, one of the most common microvascular complications of DM.\(^\text{26}\) Composite measures of executive function were examined instead of individual cognitive tests to minimize potential floor and ceiling effects. The analyses suggest that modifiable health behaviors such as oral hypoglycemic agents, insulin, and DM knowledge explain the link between executive function and glycemic control.

This study also has several limitations. First, other measures of executive function, such as the Stroop Task\(^\text{27}\) or the Wisconsin Card Sorting Test\(^\text{28}\) that may be more sensitive to executive function were not included. Unfortunately, these tests require substantial visual processing such as discriminating color. Non-visual dependent executive measures that draw on a variety of cognitive skills such as persistence, concentration, attention, and working memory that examine the ability to process, maintain, and manipulate information were therefore selected. 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, whether other nonexecutive domains such processing speed and memory were related to glycemic control was not examined. Previous studies\(^\text{6,7,15}\) that support the view of executive function as a central domain that affects glycemic control guided selection of the executive domain. A larger-scale community-based study should be conducted with a sample size adequate for exploring the influence of executive function and other cognitive domains on glycemic control. Third, whether executive impairment and poor glycemic control were more frequent in those with low education was not examined. Previous studies have recognized the relationship between higher education attainment and higher cognitive performance; the challenge is to disentangle the effects of education from cognitive function on health outcomes.\(^\text{29}\) The effects of education on glycemic control were not statistically significant across all models in the current study (data not shown), but definitive data are needed to explore the relationship between glycemic control, education, and cognition. Last, the cross-sectional design limited the findings, and therefore causality cannot be addressed. 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 medical illness, including DM.\(^\text{12,13}\) Executive function may undermine self-care capacity. Although it was not possible to assess the direct causal associations between executive function and self-care capacity, the relationship between executive function

### Table 2. Changes in the Association Between Executive Function and Glycosylated Hemoglobin After Adjusting for Diabetes Mellitus–Related Health Factors

<table>
<thead>
<tr>
<th>Estimated Coefficient (Standard Error)</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive function</td>
<td>–0.47 (0.18)**</td>
<td>–0.37 (0.18)*</td>
<td>–0.39 (0.18)*</td>
<td>–0.52 (0.19)**</td>
<td>–0.33 (0.19)**</td>
</tr>
<tr>
<td>Model 1 + diabetes knowledge</td>
<td>–0.12 (0.06)*</td>
<td>–0.15 (0.06)**</td>
<td>–0.49 (0.28)*</td>
<td>–0.60 (0.29)*</td>
<td>–0.85 (0.33)**</td>
</tr>
<tr>
<td>Model 1 + taking diabetes pills</td>
<td>–0.65 (0.31)*</td>
<td>–0.85 (0.33)**</td>
<td>–0.49 (0.28)*</td>
<td>–0.60 (0.29)*</td>
<td>–0.85 (0.33)**</td>
</tr>
<tr>
<td>Model 1 + check blood for glucose at least 1 time per day</td>
<td>0.15 (0.27)</td>
<td>–0.20 (0.29)</td>
<td>0.05 (0.04)</td>
<td>0.06 (0.04)</td>
<td>0.02 (0.03)</td>
</tr>
<tr>
<td>Model 1 + how many of 7 days eat fruits and vegetables</td>
<td>0.02 (0.04)</td>
<td>0.02 (0.03)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Results adjusted for sex, age, education, ethnicity, depressive symptoms, and duration of diabetes mellitus. \(P < *.05, **.01, ^{*} P = .08.\)
and DM knowledge, DM medications, and self-care behaviors was examined. In a supplementary univariate analysis, lower executive function scores were noted in participants who took insulin ($P = .01$) and those who did not check their blood for glucose or sugar at least once per day ($P = .045$). Poorer executive function was also associated with lower DM knowledge ($P < .001$) and fewer self-reported days per week of exercise ($P = .045$). 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 (Mini-Mental State Examination (MMSE)) may be a better way to identify patients at risk for poor glyemic control. Studies have suggested that most commonly used screening tests such as the MMSE are not sensitive to executive function. It can be concluded from the findings of the current study that impaired executive function, whether exogenous or a complication of DM, may be an important barrier to achieving treatment goals. Training aids that compensate for cognitive impairments may be essential for effective glycemic control.

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Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

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Author Contributions: H.T. Nguyen: study concept and design, analysis and interpretation of data, and preparation of manuscript. J.G. Grzywacz, T.A. Arcury, J.K. Kirk, and R.A. Bell: study concept and design, interpretation of data, and preparation of manuscript. C. Chapman: acquisition of subjects and data and preparation of manuscript. E.H. Ip: analysis and interpretation of data and preparation of manuscript. S.A. Quandt: study concept and design, acquisition of subjects and data, analysis and interpretation of data, and preparation of manuscript.

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