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The Association of Mental Conditions with Blood Glucose Levels in Older Adults with Diabetes

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Abstract

Objectives—People with diabetes must engage in several self-care activities to manage blood glucose; cognitive function and other affective disorders may affect self-care behaviors. We examined the executive function domain of cognition, depressive symptoms, and symptoms of generalized anxiety disorder (GAD) to determine which common mental conditions that can co-occur with diabetes are associated with blood glucose levels.

Methods—We conducted a cross-sectional in-person survey of 563 rural older adults (age 60 years or older) with diabetes that included African Americans, American Indians, and Whites from eight counties in south-central North Carolina. Hemoglobin A1C (A1C) was measured from a finger-stick blood sample to assess blood glucose control. Executive function, depressive symptoms, and symptoms of GAD were assessed using established measures and scoring procedures. Separate multivariate linear regression models were used to examine the association of executive function, depressive symptoms, and symptoms of GAD with A1C.

Results—Adjusting for potential confounders including age, gender, education, ethnicity, marital status, history of stroke, heart disease, hypertension, diabetes knowledge, and duration of diabetes, executive function was significantly associated with A1C levels: every one-unit increase in executive function was associated with a 0.23 lower A1C value ($p = 0.02$). Symptoms of depression and GAD were not associated with A1C levels.

Conclusions—Low executive function is potentially a barrier to self-care, the cornerstone of managing blood glucose levels. Training aids that compensate for cognitive impairments may be essential for achieving effective glucose control.

Keywords

A1C; cognitive function; depression; anxiety; aging

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INTRODUCTION

Diabetes is a growing public health burden in the US and world-wide. In 2010, nearly 26 million Americans, or 8.3% of the population had diabetes (CDC, 2011). In many cases diabetes will result in functional decline, comorbid and cardiovascular conditions, and the extensive need for health services (CDC, 2011; Harris, 1998). Effective management of blood glucose levels is a critical element of diabetes management (Nathan et al., 2009). Large trials have demonstrated the importance of tight glycemic control for protecting against microvascular and neuropathic complications such as blindness and end-stage renal disease in individuals with diabetes (Chew et al., 2010; Ismail-Beigi et al., 2010; Patel et al., 2008; UKPDS, 1998). Effective glucose management depends largely on self-care; it requires regular self-monitoring of blood glucose and medication management that may include insulin administration. Individuals should also engage in a rigorous self-monitoring regimen including self-regulation of diet and physical activity to prevent and treat hypo- and hyperglycemia, along with regular foot, eye, and dental exams (ADA, 2010). Barriers to these self-care behaviors undermine effective blood glucose management, and likely contribute to elevated levels of poor glycemic control among older adults (Quandt et al., 2005).

Cognitive dysfunction, depression, and generalized anxiety disorder (GAD) are frequently found among individuals with diabetes: some estimates indicate that more than 90% of persons with diabetes have one or more coexisting conditions including mental disorders (Vogeli et al., 2007; Warshaw, 2006). The association of diabetes with cognitive impairment and risk of dementia is robust (Biessels, Staekenborg, Brunner, Brayne, & Scheltens, 2006; Kodl & Seaquist, 2008; Luchsinger et al., 2007; Yaffe et al., 2004); up to 80% of individuals with Alzheimer's have been reported to have either type 2 diabetes or impaired fasting glucose (Janson et al., 2004). About 11% of individuals with diabetes suffer from major depressive disorder and 31% have elevated depressive symptoms; these rates are nearly twice as many as in the general population (R. J. Anderson, Freedland, Clouse, & Lustman, 2001; Katon et al., 2004). The prevalence of GAD is substantially higher in individuals with diabetes compared to the general population (11% vs. 3%) (Grigsby, Anderson, Freedland, Clouse, & Lustman, 2002; Kessler, Chiu, Demler, Merikangas, & Walters, 2005). Elevated symptoms of GAD are present in 40% of individuals with diabetes (Grigsby et al., 2002).

Cognitive dysfunction (Munshi et al., 2006), depression (Lustman et al., 2000), and GAD (R. J. Anderson et al., 2002) have been found to be associated with poor glycemic control (R. J. Anderson et al., 2002; Lustman et al., 2000; Munshi et al., 2006), though studies have shown reciprocal relations. For example, some studies have reported that poor glycemic control leads to cognitive impairment, particularly in the executive function domain or frontal lobe function that involves abilities such as attention, working memory, organization, and persistence that are necessary for executing complex, goal-directed diabetes self-care behaviors (Brands, Biessels, de Haan, Kappelle, & Kessels, 2005; Cukierman-Yaffe et al., 2009; de Wet, Levitt, & Tipping, 2007). Conversely, it is also likely the presence of cognitive impairment affects glycemic control, largely through their relationships to behavioral mediators. That is, the presence of cognitive impairment may alter perception of disease self-management and impair patients' functioning, which may interfere good glycemic control by limiting individuals' ability to adhere to medication and other self-care behaviors (Katon et al., 2009; Schonfeld et al., 1997; Sinclair, Girling, & Bayer, 2000). Therefore mental disorders may be considered a potential barrier to self-care, the cornerstone of glucose management.

The implications of mental disorders for effective diabetes management is understudied, despite the fact that outcomes of ineffective diabetes management are known to be poor

(Bayliss, Ellis, & Steiner, 2007; Colton & Manderscheid, 2006; Gijssen et al., 2001; Iwata & Munshi, 2009). Older patients with diabetes are not often screened or evaluated for cognitive impairment and other affective disorders (Iwata & Munshi, 2009; Piette & Kerr, 2006). Screening for unrecognized barriers to successful management of diabetes may be important when complex treatment regimens are prescribed. Additionally, the research to date has largely focused on specific effects such as depression or GAD, with very few studies documenting cognitive dysfunction on glucose management in older patients with diabetes (Iwata & Munshi, 2009). Implicit in this strategy is the assumption that not all comorbidities are the same and their unique characteristics and symptoms may present different levels of disability and functioning. Different aspects of mental health may be related to blood glucose levels. The extent to which different mental conditions are associated with glycemic control is an important research topic. Older patients with diabetes often struggle with these conditions and concurrent mental distress may complicate the treatment of diabetes and diabetes care goals (Piette & Kerr, 2006; Wells, Rogers, Burnam, Greenfield, & Ware, 1991).

This study examined the extent to which cognitive function, specifically executive function, depressive symptoms, and symptoms of GAD are related to blood glucose levels in a large rural, multi-ethnic sample of older adults with diabetes. We hypothesized that certain mental health conditions may have a greater effect on glycemic control than others. Though cognitive dysfunction, depressive disorder and mood, and anxiety can co-occur (Iwata & Munshi, 2009; Potvin, Hudon, Dion, Grenier, & Preville, 2010), they are distinct conditions (DSM-IV, 2000). We therefore examined executive function, depressive symptoms, and symptoms of GAD separately to determine which conditions are associated with blood glucose levels. Research on cognitive function, depression, and GAD may contribute to a better understanding of the characteristics of mental conditions that may affect the ability of older adults with diabetes to self-manage their disease.

METHODS

Sample

Data for this study came from a larger study designed to document the beliefs and attitudes of diabetes management in rural-dwelling older adults. Data collection was conducted from June 2009 through February 2010, and consisted of an interviewer-administered, fixed response questionnaire and a finger stick blood draw to test for hemoglobin A1C. All data collection was completed by trained research personnel. This study was approved by the Institutional Review Board at the Wake Forest University Health Sciences, and all participants gave signed/written informed consent.

The research was conducted in eight south central North Carolina counties (Harnett, Hoke, Montgomery, Moore, Richmond, Robeson, Sampson and Scotland) in North Carolina. These counties were selected originally to maximize the variation in types of rural environments represented (<http://www.ers.usda.gov/Data/RuralUrbanContinuumCodes/2003>), and to contain sufficient members of ethnic minorities to constitute viable minority as well as majority communities. A total of 593 African American, American Indian, and White men and women were recruited for this study. Inclusion criteria were age 60 years or older and having had a diabetes diagnosis for at least two years. Exclusion criteria included inability to complete informed consent or end-stage renal disease. The goal of the sampling plan was to recruit 100 participants for each ethnic/gender cell, with each cell having participants spread across educational attainment categories.

Participants were recruited from various organizations and locations within each county to represent site-based sampling (Arcury & Quandt, 1999). Study staff members have

conducted research in the study counties since 1996 (Quandt, Arcury, Bell, McDonald, & Vitolins, 2001; Quandt et al., 2007). Formal and informal community leaders provided support with study recruitment by introducing the study staff to recruitment locations and by verifying the legitimacy of the research project to elder participants. The number of participants from each type of recruitment location included: 124 from community-based organizations (veteran, civic groups, senior clubs, etc.), 40 from health-related community events, 43 from churches, 13 from flyer postings and public recruitment, 81 from senior housing, and 104 from congregate meal sites. An additional 188 were recruited through social networks of participants (106), community leaders (36), interviewers (22), and lists of past participants in studies that had used site-based sampling (24). The final sample in these analyses included 563 participants who had complete data.

Personal characteristics and potential confounders

Participant personal characteristics included gender (male and female), age (continuous), education (< high school, high school graduate, and > high school), ethnicity (non-Hispanic White, American Indian, and African American), and marital status (currently married and not currently married). Self-reported medical conditions were assessed by asking participants if they had ever been told by a doctor that they had any of the following conditions: stroke, heart disease, and hypertension. The study obtained data on diabetes-related variables including duration of diabetes (measured in years) and the 16-item “Diabetes Knowledge Test” to evaluate participants’ knowledge of their diabetes in areas including nutrition, exercise, and glucose management and testing (Samuel-Hodge et al., 2009). The alpha coefficient for the Diabetes Knowledge test was .73.

Blood glucose as the main outcome

Blood glucose was assessed by measuring 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 testing (Bode, Irvin, Pierce, Allen, & Clark, 2007).

Measures of executive functioning

Three measures of executive functioning were used. The Animal Verbal Fluency test assesses language ability related to executive function (Newcombe, 1969). The Brief Attention Test is one of the most commonly used cognitive measures to assess 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 read (Schretlen, 1997). The Digit Span Backward test from the Wechsler Memory Scale-III is a well-known and validated measure of working memory (Baddeley, 1992) and executive function (Wechsler, 1981). We selected these tests because visual impairment is common in older adults with diabetes. These three widely-used, non-visual dependent executive measures 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 (Qiu et al., 2006; Stuss & Levine, 2002). The tests were administered to participants by research staff who had undergone training and supervised practice. A composite score of executive function was constructed to avoid floor and ceiling effects, and because previous factor analyses indicated all three tests loaded substantially on a single factor accounting for 33% of the variance (Nguyen, Evans, & Zonderman, 2007; Wilson et al., 2005). The composite measure was constructed by transforming the raw score of each test into z-scores, using the sample mean and standard deviation. The z-scores were averaged to produce the composite score of executive function. A higher score indicates better executive function.

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 (Bell et al., 2005; Blazer, Burchett, Service, & George, 1991). A standard cutoff score of 9 has been reported as indicative of high depressive symptoms (Blazer et al., 1991). The inventory has been extensively validated (Weissman, Sholomskas, Pottenger, Prusoff, & Locke, 1977) and is widely accepted in studies of depression in older populations (Beekman et al., 1997). A higher score indicates more depressive symptoms. The alpha for the scale was .80.

Symptoms of GAD

Symptoms of GAD were measured using the GAD subscale from the Psychiatric Diagnostic Screening Questionnaire, a self-report instrument designed to screen for the DSM-IV Axis I disorders most commonly found in medical and outpatient mental health settings (Zimmerman & Mattia, 2001). The 10-item subscale was used to assess levels of anxiety over the past six months. The instrument asks questions about levels of worrying in regards to family, daily activities, effects on sleep, concentration, and behavior. Higher scores reflect more symptoms related to GAD. The alpha for the scale was .82.

Statistical analysis

Statistical analysis was performed using SAS 9.1 (SAS Institute, Inc., Cary, NC). Descriptive statistics were used to describe the study sample. Characteristics were reported as mean $\pm$ SD unless otherwise stated. Separate linear regression models were used to examine the association of executive function, depressive symptoms, and symptoms of GAD with A1C. The base model (model 1) was adjusted for age, gender, education, ethnicity, marital status, history of stroke, heart disease, and hypertension. Model 1 also initially included interactions terms between executive function, depressive symptoms, and symptoms of GAD to determine whether the co-existence of two or more mental conditions was associated with A1C. All interaction terms were statistically non-significant and were not included in further analyses. Model 2 additionally adjusted for diabetes related variables including diabetes duration and diabetes knowledge.

RESULTS

The sample consisted of 348 women and 215 men (Table 1) and had a mean age of 70.1 years. Approximately 36% had less than a high school education, and 30% had education beyond high school. Approximately 36% were white, 30% were American Indian, and 34% were African American. About 46% of the participants were currently married. Approximately 21% had been diagnosed with a stroke, 28% with heart disease, and 60% with hypertension. The average A1C was 7.0 (SD = 1.4).

In fully adjusted models (model 2), participant personal characteristics were generally not associated with A1C values (Table 2). There were no significant differences in gender, education, ethnicity, marital status, and medical conditions. There were significant differences in age and duration of diabetes. Increased age and duration of diabetes were significantly associated with higher A1C values. Executive function was significantly associated with higher A1C values, adjusted for age, gender, education, ethnicity, marital status, stroke, heart disease, and hypertension (model 1). Specifically, a 1-unit increase in executive function was associated with a 0.25 lower A1C value ($p = 0.01$). In model 2, additional variables associated with A1C values were introduced. Adding diabetes knowledge and diabetes duration did not attenuate the association of executive function with A1C ($\beta = -0.23$, $p = 0.02$). Higher symptoms of depression were marginally associated with

elevated A1C values ($p = 0.08$), adjusting for covariates. However, the association was statistically non-significant after adjusting for diabetes knowledge and duration of diabetes. Symptoms of GAD were not associated with A1C in both reduced and fully adjusted models.

DISCUSSION

In this study, we tested the idea that mental health conditions that often coexist with diabetes may impair effective glucose management. We found a relationship between executive function and A1C, a standard metric of glucose management. This relationship is consistent with previous studies (Brands et al., 2005; Cukierman-Yaffe et al., 2009; de Wet et al., 2007; Kodl & Seaquist, 2008; Munshi et al., 2006). Adjusting for potential confounders, this study shows that a 1-unit higher executive function score was associated with a 0.23 lower A1C value. Although self-management is a cornerstone of effective blood glucose management (Glasgow, Fisher, Skaff, Mullan, & Toobert, 2007), our data suggest that low executive function may undermine self-care capacity. 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 (Stuss & Levine, 2002). This domain may be important in allowing the execution of intended behaviors aimed at managing blood glucose levels. Though we did not assess the direct causal associations between executive function and self-care capacity, previous studies have linked low executive function to self-care behaviors, including poor adherence to medication, low autonomy, and resistance to care (Qiu et al., 2006; Schillerstrom, Horton, & Royall, 2005). Other studies have found that older adults with poor cognitive function are not aware of their own limitations and less likely to have the ability to monitor and interpret symptoms, and to seek appropriate medical care or services (Murray, Burns, See, Lai, & Nazareth, 2005; Stille, Sereika, Muldoon, Ryan, & Dunbar-Jacob, 2004; Zarit & Anthony, 1986).

Our findings on symptoms of depression and GAD deserve elaboration. GAD and depression are common in medical patients, and have been reported to affect the management of several chronic conditions (DiMatteo, Lepper, & Croghan, 2000; Ziegelstein et al., 2000). In this analysis, we found that symptoms of depression and GAD were not associated with blood glucose levels. The difference between the findings of our study and previous studies may have been due to the instruments used and study samples. We examined symptoms of depression and GAD that are based on screening instruments that are sensitive to standard criteria for diagnosis of depression and GAD. In studies that determined depression, particularly major depression, and GAD from diagnostic interviews, relations to glycemic control were observed (Anderson et al., 2002; Lustman et al., 2000). Furthermore, symptoms of depression and GAD can have a waxing and waning course, especially in clinical samples; symptoms may present differently at different times. This variability may lead to conflicting results across studies. Our study included a sample of community-dwelling older adults. The means ($\pm$ SD) for depressive symptoms and symptoms of GAD were $3.9 (\pm 3.5)$ and $2.5 (\pm 3.2)$, respectively, indicating lower levels of depression and GAD in this group relative to clinical samples (Anderson et al., 2001; Grigsby et al., 2002). The low proportion of adults with higher symptoms might limit the ability to detect associations with glycemic control.

This study has several limitations. The sample was not randomly selected, so the results may not be generalizable. However, the sample was ethnically diverse and representative of rural North Carolina counties. For example, 36% of our sample did not graduate from high

school; the rate of not graduating from high school among adults > 25 years of age in these counties ranges from 37% – 47% (<http://2010.census.gov/2010census/>). We did not obtain data to differentiate between type 1 and type 2 diabetes; diabetes management issues related to the two types of diabetes may differ. We used the same strategy for determined diabetes status as is used in traditional cross-sectional surveys, such as the National Health Interview Survey (<http://www.cdc.gov/nchs/nhis.htm>) and the Behavioral Risk Factor Surveillance System (<http://www.cdc.gov/brfss/>). Further, 92% of the participants reported that they were diagnosed with diabetes after the age of 35. There is a high likelihood that our data may reflect a group of older adults with predominantly type 2 diabetes. We did not use structured diagnostic assessments to determine mental health disorders. Diagnostic assessments in community settings would be difficult. We therefore used reliable and valid screening instruments to identify unique psychosocial barriers for further study, and ones that may need to be considered by medical professionals to provide optimal care to older adults with diabetes. We did not include other potential confounders such as health behaviors and health insurance; further studies are needed to determine their potential relationship to blood glucose levels. We did not examine whether executive impairment and poor A1C values 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 (Mungas, Reed, Farias, & Decarli, 2009). However, the effects of education on A1C were not statistically significant across all models in our study. 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 blood glucose levels.

Limitations notwithstanding, this study has clinical implications. Self-care activities are a central component of effective blood glucose management (Anderson, 1995; Martin et al., 2008; Mensing et al., 2007). Our findings suggest that low executive function, whether it is exogenous or it is a complication of diabetes, may undermine patients' abilities to effectively manage blood glucose. Because deficits in executive function may affect self-care capacity, efforts to target patients for effective glycemic control should consider cognitive impairment as a risk factor. Health care providers and caregivers who care for older patients with diabetes should be alert to the possibility of low cognitive function that may interfere with their patients' ability to perform self-care. In such circumstances, changes in strategy for diabetes education and management plans may be warranted.

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Table 1

Characteristics of Participants, n =563.

Variable	N (%)	Mean (SD) [range]
Female	348 (62)	
Age		70.1 (7.1) [60 – 91]
Education		
<High school	205 (36)	
High school graduate	189 (34)	
>High school	168 (30)	
Ethnicity		
Non-Hispanic white	205 (36)	
American Indian	168 (30)	
African American	190 (34)	
Currently married	261 (46)	
Stroke	120 (21)	
Heart disease	158 (28)	
Hypertension	336 (60)	
Diabetes Knowledge Test		10.0 (2.7) [0 – 15]
Duration of diabetes, years		14.7 (12.24) [0 – 67]
Hemoglobin A1C %		7.0 (1.4) [4 – 13]
Executive function		0.05 (0.71) [–1.39 – 1.98]
Depressive symptoms		3.9 (3.5) [0 – 16]
Generalized anxiety symptoms		2.5 (3.2) [0 – 10]

Table 2

Regression coefficients describing associations of executive function, depressive symptoms, and symptoms of GAD with A1C in rural older adults with diabetes.

	Estimated coefficient (SE)			
	Model 1	P value	Model 2	P value
Executive function	−0.25 (0.10)	0.01	−0.23 (0.10)	0.02
Age	−0.02 (0.01)	0.05	−0.03 (0.01)	0.002
Female	−0.19 (0.13)	0.16	−0.18 (0.13)	0.19
> High school	0.10 (0.15)	0.48	0.17 (0.15)	0.25
American Indian	0.05 (0.16)	0.73	0.12 (0.16)	0.45
African American	−0.10 (0.15)	0.51	−0.08 (0.15)	0.57
Marital status	0.11 (0.13)	0.41	0.14 (0.13)	0.31
Stroke	−0.14 (0.15)	0.36	−0.07 (0.14)	0.58
Heart disease	−0.06 (0.14)	0.63	0.08 (0.13)	0.50
Hypertension	−0.11 (0.13)	0.39	−0.12 (0.15)	0.42
Diabetes knowledge			−0.01 (0.02)	0.52
Diabetes duration			0.02 (0.01)	0.001
Depressive symptoms	0.03 (0.02)	0.08	0.02 (0.01)	0.19
Age	−0.01 (0.01)	0.13	−0.02 (0.01)	0.01
Female	−0.18 (0.12)	0.14	−0.18 (0.12)	0.14
> High school	0.12 (0.14)	0.41	0.18 (0.14)	0.20
American Indian	0.23 (0.14)	0.10	0.27 (0.14)	0.06
African American	0.05 (0.14)	0.73	0.03 (0.14)	0.80
Marital status	0.02 (0.12)	0.84	0.04 (0.12)	0.70
Stroke	−0.09 (0.14)	0.51	−0.06 (0.13)	0.60
Heart disease	−0.06 (0.13)	0.66	0.14 (0.12)	0.23
Hypertension	0.17 (0.11)	0.14	−0.07 (0.14)	0.62
Diabetes knowledge			−0.01 (0.02)	0.63
Diabetes duration			0.02 (0.01)	0.001
Symptoms of GAD	0.03 (0.01)	0.14	0.02 (0.01)	0.19
Age	−0.01 (0.01)	0.17	−0.02 (0.01)	0.01
Female	−0.19 (0.12)	0.12	−0.19 (0.12)	0.13
> High school	0.10 (0.14)	0.50	0.17 (0.14)	0.23
American Indian	0.23 (0.14)	0.10	0.27 (0.14)	0.06
African American	0.04 (0.14)	0.74	0.03 (0.14)	0.81
Marital status	0.01 (0.12)	0.99	0.03 (0.12)	0.79
Stroke	−0.07 (0.14)	0.58	−0.07 (0.13)	0.58
Heart disease	−0.06 (0.13)	0.64	0.13 (0.12)	0.27
Hypertension	0.16 (0.12)	0.16	−0.05 (0.14)	0.70
Diabetes knowledge			−0.01 (0.02)	0.54
Diabetes duration			0.02 (0.01)	0.001

Model 1: adjusted for age, gender, education, ethnicity, marital status, stroke, heart disease, and hypertension. Model 2: Model 1 plus diabetes knowledge and diabetes duration