The association between cognitive decline and incident depressive symptoms in a sample of older Puerto Rican adults with diabetes

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ABSTRACT

Background: Older Puerto Rican adults have particularly high risk of diabetes compared to the general US population. Diabetes is associated with both higher depressive symptoms and cognitive decline, but less is known about the longitudinal relationship between cognitive decline and incident depressive symptoms in those with diabetes. This study investigated the association between cognitive decline and incident depressive symptoms in older Puerto Rican adults with diabetes over a four-year period.

Methods: Households across Puerto Rico were visited to identify a population-based sample of adults aged 60 years and over for the Puerto Rican Elderly: Health Conditions study (PREHCO); 680 participants with diabetes at baseline and no baseline cognitive impairment were included in analyses. Cognitive decline and depressive symptoms were measured using the Mini-Mental Cabán (MMC) and Geriatric Depression Scale (GDS), respectively. We examined predictors of incident depressive symptoms (GDS ≥ 5 at follow-up but not baseline) and cognitive decline using regression modeling.

Results: In a covariate-adjusted logistic regression model, cognitive decline, female gender, and greater diabetes-related complications were each significantly associated with increased odds of incident depressive symptoms (p < 0.05). In a multiple regression model adjusted for covariates, incident depressive symptoms and older age were associated with greater cognitive decline, and higher education was related to less cognitive decline (p < 0.05).

Conclusions: Incident depressive symptoms were more common for older Puerto Ricans with diabetes who also experienced cognitive decline. Efforts are needed to optimize diabetes management and monitor for depression and cognitive decline in this population.

Key words: diabetes, Hispanic, older adults, cognition, depressive symptoms

Introduction

Approximately 9.3% of the US population has diabetes, with older persons having higher rates than the general population (CDC, 2014). Aging with diabetes represents a major public health concern and underscores the need for better understanding of diabetes-related health outcomes in older adults. Specifically, there is evidence that people with diabetes are at higher risk for vascular problems such as myocardial infarction and stroke as well as cognitive decline due to vascular dementia and Alzheimer’s disease (Xu et al., 2010; CDC, 2014). Because older adults are already at higher risk for these conditions, an aging population with diabetes may be even more vulnerable to cardiovascular and cognitive problems. The issue of an aging population is particularly relevant in Puerto Rico, where there was a 28% increase in adults aged 65 years and over between 2000 and
2010, almost double the 15% increase seen in the USA during the same period (U.S. Census Bureau, 2011).

Furthermore, there is a recognized disparity in the prevalence of diabetes, with Hispanics at a higher risk of diabetes than non-Hispanic whites. For instance, Mexican American adults have an approximately 45% higher prevalence of diabetes compared to non-Hispanic whites (Kendzor et al., 2014). Recently, the Center for Disease Control (CDC, 2014) reported that Puerto Ricans (14.8%) and Mexican Americans (13.9%) have the highest rates of diabetes in Hispanic populations, considerably higher than the prevalence among non-Hispanic whites in the USA (7.6%). Additionally, certain minority populations including Hispanics have been found to have worse diabetes control compared to whites, not explained by differences in healthcare utilization, education or socioeconomic status (Harris et al., 1999). Worse diabetes control is related to long-term complications and makes efforts to improve treatment in this group paramount. One important factor that may contribute to poor diabetes control in this population is depression.

Studies have found that 12–20% of those with diabetes meet diagnostic criteria for major or subclinical depression, respectively (Ciechanowski, 2011), though comorbid depression may be even higher in Hispanic adults. For example, prevalence of depression was found to be 39% and 41% for Hispanic adults with diabetes in the USA and Mexico, respectively (Mier et al., 2008). It is important to note that the relationship between diabetes and depression may be bidirectional. Golden et al. (2008) found that the risk of developing diabetes increased for every point-increase in depressive symptoms longitudinally, though this association became non-significant after controlling for sociodemographic, lifestyle, metabolic, and inflammatory factors. Conversely, there was an increased risk of incident depressive symptoms in those with diabetes, which remained significant in fully adjusted models. Thus, the presence of depressive symptoms in diabetes seems to increase with progression of the disease itself, and this relationship may be more pronounced in Hispanic persons who have both higher prevalence of depression and diabetes (CDC, 2014).

Depressive symptoms may have a negative impact on health outcomes in persons with diabetes since treatment is highly reliant on self-management (Solanki et al., 2009). A person with diabetes must often make lifestyle changes that can be challenging and add to the burden of coping with the disease (Ciechanowski, 2011). Depression is a prime concern for diabetes-related health outcomes because it can negatively affect diabetes self-care (Egede and Osborn, 2010). It is recommended that individuals with diabetes adhere to a regimen that includes frequent blood glucose monitoring, medication (for some), regular physician visits, and proper dietary intake and exercise. Depression is associated with reduced self-efficacy, or perceived ability to successfully manage diabetes (Cherrington et al., 2010). In turn, lowered self-efficacy is associated with less self-care behavior, poorer blood glucose control, and poorer treatment adherence (Bernal et al., 2000; Sacco et al., 2005; Sarkar, Fisher, & Schillinger, 2006; Gao et al., 2013). Black et al. (2003) found that in an older Mexican American population, diabetes increased the risk of death, microvascular complications, and disability, but this risk of negative outcomes was even higher for those with more depressive symptoms (Black et al., 2003). Diabetes and depression together may have a synergistic effect on worsened health outcomes in older Hispanics with diabetes. Therefore, it is imperative to understand predictors of depressive symptoms within older Hispanic populations with high prevalence of diabetes.

Cognitive decline may be an important indicator of depression risk in diabetes. Studies have found greater levels of cognitive decline in older adults with diabetes (Fontbonne et al., 2001), and there is an accelerated conversion from Mild Cognitive Impairment (MCI) to dementia among those with diabetes (Xu et al., 2010). Over time, lower cognitive function may lead to worse diabetes control and increased caregiver burden (Munshi et al., 2006; Cukierman-Yaffe et al., 2009; Leroy et al., 2012). While it is often difficult to disentangle depression and cognitive impairment, depression has been linked to many of the same biological pathways as cognitive decline, including neural damage via hypothalamic pituitary adrenal dysregulation and chronic inflammation (Golden, 2007; Strachan et al., 2011). Richard et al. (2013) reported that depression was related to concurrent MCI but was not predictive of future incidence, possibly due to a shared causal manifestation.

Within a high-risk sample of Puerto Ricans (i.e. older adults with diabetes), we hypothesized that cognitive decline would be related with greater incidence of clinically significant depressive symptoms. Also, we examined whether age, education, gender, and health comorbidity had similar associations with both depressive symptoms and cognitive decline as outcomes in this sample of older Puerto Ricans with diabetes.
Methods

Participants

The Puerto Rican Elderly: Health Condition (PREHCO) study is a longitudinal population-based study of older adults in Puerto Rico. The study was conducted in two waves using a probability-based sampling technique to select homes with at least one adult over 60 years of age across the entire mainland of Puerto Rico. The first wave occurred from 2002 to 2003, with the second wave occurring from 2006 to 2007. The overall response rate was 93.9% and there were no significant differences between those who responded and those who did not respond (McEniry and Palloni, 2010). For the current study, participants were included in analyses if they reported a diagnosis of diabetes and completed cognitive testing and information on depressive symptoms at baseline and at 4-year follow-up.

Overall, 4,291 participants were recruited for PREHCO; 408 were not interviewable and 3,883 (90.5%) completed cognitive testing at baseline. Of these, 75 had incomplete data and 292 participants had cognitive impairment (7.5%). Individuals with suspected cognitive impairment, defined by scores less than 11 on the Mini-Mental Cabán (MMC), were administered informant interviewee questionnaires in lieu of self-report. An informant-report parallel measure of depressive symptoms was not included, resulting in exclusion from the current study. There was a potential sample of 3,516 participants without cognitive impairment at baseline with information on depressive symptoms. There were 456 participants who died between baseline and follow-up, and 408 who were lost to follow-up, resulting in a sample of 2,652 without baseline cognitive impairment who completed follow-up cognitive testing. A total of 2,561 had complete data on variables of interest at follow-up, with 680 (26.6%) participants who had diabetes at baseline. Our longitudinal analytic sample consisted of those with diabetes but without substantial baseline depressive symptoms (n = 480), defined as having 5 or more depressive symptoms reported on the Geriatric Depression Scale (GDS; Friedman et al., 2005).

Measures

Demographics and health problems including diabetes were self-reported. Depressive symptoms were measured using a Spanish language version of the GDS, which was developed to improve detection of depression in older adults by relying less on somatic complaints and using a yes/no response format for symptoms (Yesavage et al., 1983). The commonly used 15-item scale (GDS-15) has been shown to have acceptable reliability (Cronbach’s α = 0.77; Friedman et al., 2005) and has convergent validity with other scales of depression, including the Hamilton Self-Rating Depression Scale and the Cornell Scale of Depression in Dementia (both r’s = 0.77; Körner et al., 2006). The yes/no format of the GDS-15 was designed to decrease the cognitive demand of Likert scales. The scores range from 0 to 15, with 15 indicating the highest number of depressive symptoms. For the current study, a cut-off of 5 was used to determine substantial depressive symptoms because a recent meta-analysis showed this cut-off to have the best sensitivity and specificity to predict clinically diagnosed depression across different languages including Spanish (Pocklington et al., 2016), and there was good sensitivity (80.7%) and acceptable specificity for this cut-off among Hispanic older adults (68.7%; Aguilar-Navarro et al., 2007). Incident depressive symptoms were defined as scores surpassing the cut-off at follow-up but not at baseline.

The MMC was utilized at baseline and follow-up to assess global cognitive functioning. The MMC was designed to be more appropriate for use in Hispanic populations and those with low education levels compared to simple Spanish translation of the Mini-Mental State Examination (MMSE; Sánchez-Ayéndez et al., 2003). Scores on the MMC can range from 0 to 20 and items reflect orientation (day of week, date), verbal memory (immediate and delayed recall of three words), visual memory (immediate recall; draw complex figure after viewing for 15 sec), executive function (clock drawing, abstraction), and comprehension (follow three-step command).

The MMC was found to have superior sensitivity and specificity compared to the MMSE for detecting clinically diagnosed dementia in a clinic-based study of older adults in Puerto Rico (Sánchez-Ayéndez et al., 2003). To determine baseline cognitive impairment, MMC scores were regressed on years of age, female gender, years of education, and self-reported reading ability (yes/no). An expected score for each participant was calculated using the intercept and beta weights from the baseline regression model. Participants with MMC scores 1.5 standard deviations (SD) or more below the predicted score were classified as having cognitive impairment at baseline and not included in the longitudinal analytical sample of 480 participants. Cognitive decline was measured by subtracting follow-up MMC scores from baseline scores.

We included two health comorbidity measures in analyses: diabetes-related complications and...
vascular comorbidity. Diabetes-related complications were measured as a summed index score of self-reported history of problems with circulation, vision, foot sores, amputations, and kidney disease due to diabetes (range 0–4). Vascular comorbidity was measured as a summed index score of self-reported history of cardiovascular events including myocardial infarction, hypertension, congestive heart failure, and stroke (range 0–4).

Statistical analysis
First, we used t-tests and χ² analyses to determine differences in the sample with diabetes by presence of significant depressive symptoms at baseline. Next, to examine predictors of incident depressive symptoms, we used a logistic regression model that included age, gender, education, vascular comorbidity, diabetes complications, cognitive decline, and baseline cognitive performance. We also examined predictors of cognitive decline using multiple linear regression. Cognitive decline was regressed on incident depressive symptoms, baseline cognitive function, age, gender, education, vascular comorbidity, and diabetes complications. Last, sensitivity analyses were conducted to discern whether a higher GDS-15 cut-off would lead to different findings. Analyses were conducted using SAS Version 17 software (SAS Institute, Inc., Cary, NC, USA, 2014).

Results
Health and demographic characteristics of the sample, separated by presence of substantial depressive symptoms at baseline, are shown in Table 1. Overall, those with substantial depressive symptoms at baseline were more likely to be female and had more diabetes-related complications as well as vascular comorbidities (p < 0.05) compared to participants without depressive symptoms. Average years of education was lower for those with substantial depressive symptoms (7.4 years) compared to those with low depressive symptoms (8.5 years). In our longitudinal analytic sample of participants with no substantial depressive symptoms at baseline, average cognitive decline was 0.89 points (SD = 2.33) and 25.22% showed a decline of at least three points on the MMC between baseline and follow-up.

Results from logistic regression modeling with incident depressive symptoms as the outcome are shown in Table 2. Cognitive decline was a significant predictor of increased depressive symptoms; for every additional point of decline in cognitive score, there was a 19% increased odds of incident depressive symptoms at follow-up (95% CI: 1.07–1.33). Higher baseline cognitive performance was related to lower odds of incident depressive symptoms (OR = 0.80, 95% CI: 0.70–0.93). Women had 64% greater odds of incident depressive symptoms (95% CI: 1.01–2.66) compared to men. There were no significant associations between incident depressive symptoms and age, education, or vascular comorbidities. However, diabetes-related complications were related to greater odds of incident depressive symptoms (OR = 1.46; 95% CI: 1.14–1.86). After z-score standardization, cognitive decline had a similar size of association as diabetes complications (OR = 1.55 and 1.45, respectively) with incident depressive symptoms.

Interactions were added to the model shown in Table 2 to determine if the relationship between cognitive decline and incident depressive symptoms was moderated by any of the covariates. Results indicated that the association between cognitive decline and incident depressive symptoms did not significantly vary by gender, age, education, baseline MMC, diabetes complications or vascular complications (all p’s > 0.05).

Next, cognitive decline from baseline to follow-up was regressed on incident depressive symptoms, baseline cognitive function, age, gender, education, diabetes-related complications, and vascular comorbidities (see Table 3). Results showed

### Table 1. Characteristics of the sample with diabetes by presence of significant depressive symptoms

<table>
<thead>
<tr>
<th></th>
<th><strong>BASELINE GDS &lt; 5 (N = 480)</strong></th>
<th><strong>BASELINE GDS ≥5 (N = 200)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RANGE</strong></td>
<td><strong>M(SD)</strong></td>
<td><strong>M(SD)</strong></td>
</tr>
<tr>
<td><strong>N(%)</strong></td>
<td><strong>N(%)</strong></td>
<td><strong>N(%)</strong></td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>287 (59.8)</td>
<td>141 (70.5)</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>193 (40.2)</td>
<td>59 (29.5)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>60–89</td>
<td>60–92</td>
</tr>
<tr>
<td></td>
<td>69.12 (6.35)</td>
<td>69.98 (7.27)</td>
</tr>
<tr>
<td><strong>Education (years)</strong></td>
<td>0–16</td>
<td>0–16</td>
</tr>
<tr>
<td></td>
<td>8.46 (4.52)</td>
<td>7.39 (4.63)</td>
</tr>
<tr>
<td><strong>Vascular comorbidity</strong></td>
<td>0–4</td>
<td>0–4</td>
</tr>
<tr>
<td></td>
<td>1.05 (0.87)</td>
<td>1.41 (0.93)</td>
</tr>
<tr>
<td><strong>Diabetes complications</strong></td>
<td>0–4</td>
<td>0–4</td>
</tr>
<tr>
<td></td>
<td>0.92 (0.92)</td>
<td>1.51 (1.03)</td>
</tr>
</tbody>
</table>

*Note: t-tests and χ² analyses are used to determine p-values for difference between those with and without baseline depressive symptoms.*
significant associations between cognitive decline and incident depressive symptoms, baseline cognitive status, age, and education level. Older age was associated with greater cognitive decline ($b = 0.05$, $p < 0.01$), and more years of education was related to less cognitive decline ($b = -0.15$, $p < 0.001$). Incident depressive symptoms were associated with greater cognitive decline ($b = 0.79$, $p < 0.01$).

To address the issue of whether using a different GDS-15 cut-off would change results, we conducted sensitivity analyses using more conservative cut-offs (7, 8, and 9). In logistic regression models with incident depressive symptoms as the outcome, the relationship between cognitive decline and incident depressive symptoms remained statistically significant with a GDS-15 cut-off of 7 ($OR = 1.10$, 95% CI: 1.01–1.21) and 8 ($OR = 1.14$, 95% CI: 1.03–1.25). Using a GDS-15 cut-off of 9, the $p$-value for cognitive decline was increased to 0.06 ($OR = 1.10$, 95% CI: .99–1.23).

### Discussion

Substantial depressive symptoms were common in this sample of older Puerto Rican adults with diabetes. At baseline, approximately 30% of the sample with diabetes also had high depressive symptoms. An additional 26% of those without significant depressive symptoms at baseline reported elevated depressive symptoms (GDS $\geq 5$) 4 years later. Consistent with hypotheses, cognitive decline was significantly related to an increased risk of incident depressive symptoms after controlling for demographics and health problems, adding to research suggesting shared cognitive and mental health changes in persons aging with diabetes (Richard et al., 2013). Most of the research in this area has specifically focused on depressive symptoms as a predictor of cognitive function (e.g. Paterniti et al., 2002; Rosenberg et al., 2010). However, this study highlights the need to also consider how changes in cognition may relate to subsequent depressive symptoms in older adults with diabetes.

Baseline comparisons revealed that individuals with significant depressive symptoms reported more diabetes complications and vascular comorbidities. Depressive symptoms have been linked to increased risk of cardiovascular disease and diabetes complications in prior research (e.g. Lin...
et al., 2010). Notably, the group with high depressive symptoms at baseline had greater frequency of females and individuals with lower levels of education. This is consistent with other research in older adults, where women have been found to have a higher prevalence of depression assessed via self-reported depressive symptoms and clinical diagnoses (Steffens et al., 2000; Anderson et al., 2001). Lower education has also been associated with higher depressive symptoms in previous research (Zahodne et al., 2014). These differences may help identify older individuals with diabetes who are at greatest risk for developing depression.

This research contributes to our understanding of the interrelationship between diabetes, cognitive function, and depressive symptoms. While depressive symptoms may be a risk factor for cognitive decline, our findings showed that cognitive decline is also predictive of incident depressive symptoms in older Hispanic adults with diabetes. The pathophysiological mechanisms for these relationships are not completely understood and could not be examined in the current study; however, the role of inflammatory pathways has been proposed as central to diabetes–depression–cognition associations (e.g. Marioni et al., 2010). Diabetes-induced neural damage, potentially caused by both chronic inflammation and insulin resistance, may make older adults more vulnerable to cognitive and mental health problems (Strachan et al., 2011).

While there was an association between cognitive decline and incident depressive symptoms, there were different relationships between these outcomes and demographic and health variables. For example, female gender and diabetes-related complications were significantly associated with increased depressive symptoms but not cognitive decline. Older age and less education were associated with cognitive decline but not incident depressive symptoms. There is ample research in the general older adult population showing that individuals with higher education have lower risk of dementia (Meng and D’Arcy, 2012). One explanation for the relationship between education and cognitive decline involves the concept of cognitive reserve, which is the ability to cope with neural damage through the recruitment of compensatory neural networks or pre-existing cognitive strategies (Stern, 2013). Even in the context of aging with diabetes, people with greater education may take longer to show signs of cognitive decline.

Limitations of this study include the use of self-report measures of health and assessment at only two time points. Incident depressive symptoms were determined using a cut-off on a self-report measure of depression and not by clinical evaluation. However, the GDS is a widely used and well-validated measure of depressive symptoms in older adults (D’ath et al., 1994). The measures used in this study were designed to be quickly administered, but without compromising reliability and validity, allowing for increased feasibility of data collection in large epidemiologic samples. Because the current study included two time points, we could not examine potential non-linear trends over time or utilize more complex longitudinal modeling techniques. Also, it should be noted that associations between depressive symptoms and cognitive functioning may be underestimated due to exclusion of adults with cognitive impairment at baseline.

Current guidelines by the American Diabetes Association (ADA) recommend that physicians screen and monitor older adults with diabetes for cognitive impairment and depression (American Diabetes Association, 2016). Though not recommended for all older adults, screening is recommended for adults with diabetes who report cognitive difficulties, impairments in activities of daily living, or high depressive symptoms (Pottie et al., 2015; ADA, 2016). Screening can help clinicians detect possible cases of cognitive impairment and depression who should then be referred to specialists for further testing and possibly treatment. Screening and referral for issues such as depression and cognitive impairment presents unique challenges in Puerto Rico, where the healthcare system has been described as being on the brink of collapse (Roman, 2015). Medicare reimbursement rates in Puerto Rico are substantially less compared to states in the USA and many physicians and other healthcare professionals have left the island over the past decade. In addition, quality of care for Medicare Advantage enrollees in Puerto Rico was found to be substantially worse compared to quality for enrollees in the mainland USA (Rivera-Hernandez et al., 2016). Thus, hope for improvement in age-related health outcomes in Puerto Rico will be largely dependent on quality and availability of healthcare on the island.

Last, what can healthcare professionals do to prevent cognitive decline or reduce depressive symptoms in older adults with diabetes? Optimizing glycemic control may prevent substantial cognitive decline before the age of 70 in those with diabetes (Messier, 2005), and cardiovascular care is also thought to be important for preventing cognitive decline in this population (Takeda et al., 2010). In addition, getting older adults to engage in moderate exercise may reduce risk of cognitive decline and depressive symptoms. Several exercise...
interventions have been shown to improve cognitive function in older adults (Bherer et al., 2013) and resistance training (45 minutes, three times per week, over 16 weeks) has been shown to reduce depressive symptoms in older Puerto Rican adults specifically (Lincoln et al., 2011). Though challenging, such interventions may be especially important in older Puerto Rican adults who show the lowest rates of physical activity compared to other Hispanic subpopulations and non-Hispanic whites (Hajat et al., 2000), and exercise interventions show feasibility across different levels of cognitive dysfunction and frailty (Bherer et al., 2013). Regarding psychological interventions to reduce depressive symptoms, cognitive behavioral therapy, interpersonal psychotherapy, problem-solving therapy, and behavioral activation are effective treatments for depression in Hispanics (Cabassa and Hansen, 2007; Collado et al., 2016), especially when tailored to specific Hispanic cultures (Interian and Díaz-Martínez, 2007). For example, Rosselló et al. (2008) found that modified cognitive behavioral therapy and interpersonal psychotherapy emphasizing cultural values (e.g. *familismo*) were effective at reducing depressive symptoms in a Puerto Rican sample. Further, the ADA (2016) recommends collaborative care models, and in Puerto Rico, a collaborative model where physicians and mental health professionals worked together to coordinate antidepressant treatment and counseling provided better reduction of depressive symptoms than usual care (Vera et al., 2010). Still, any strategies for improving diabetes management and treating depression for older Puerto Ricans will only be successful to the extent that further erosion of the healthcare system on the island can be avoided.

Conflict of interest

None.

Description of authors’ roles

Tyler Bell conducted data analyses and wrote the manuscript. Ana Luisa Dávila performed data collection, helped to prepare the dataset, and revised the manuscript critically for important intellectual content. Olivio Clay, Kyriakos Markides, and Ross Andel assisted in conceptualization of the study and contributed to the manuscript by revising it critically for important intellectual content. Michael Crowe assisted in conceptualizing the study, conducting data analyses, and writing the manuscript.

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References


Cognitive decline and depressive symptoms in diabetes


