Diabetes, Cognitive Decline, and Mild Cognitive Impairment Among Diverse Hispanics/Latinos: Study of Latinos–Investigation of Neurocognitive Aging Results (HCHS/SOL)

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OBJECTIVE

Hispanics/Latinos are the largest ethnic/racial group in the U.S., have the highest prevalence of diabetes, and are at increased risk for neurodegenerative disorders. Currently, little is known about the relationship between diabetes and cognitive decline and disorders among diverse Hispanics/Latinos. The purpose of this study is to clarify these relationships in diverse middle-aged and older Hispanics/Latinos.

RESEARCH DESIGN AND METHODS

The Study of Latinos–Investigation of Neurocognitive Aging (SOL-INCA) is an ancillary study of the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). HCHS/SOL is a multisite (Bronx, NY; Chicago, IL; Miami, FL; and San Diego, CA), probability-sampled (i.e., representative of targeted populations), and prospective cohort study. Between 2016 and 2018, SOL-INCA enrolled diverse Hispanics/Latinos aged ≥50 years ($n = 6,377$). Global cognitive decline and mild cognitive impairment (MCI) were the primary outcomes.

RESULTS

Prevalent diabetes at visit 1, but not incident diabetes at visit 2, was associated with significantly steeper global cognitive decline ($\beta_{GC} = -0.16$ [95% CI −0.25; −0.07]; $P < 0.001$), domain-specific cognitive decline, and higher odds of MCI (odds ratio 1.74 [95% CI 1.34; 2.26]; $P < 0.001$) compared with no diabetes in age- and sex-adjusted models.

CONCLUSIONS

Diabetes was associated with cognitive decline and increased MCI prevalence among diverse Hispanics/Latinos, primarily among those with prevalent diabetes at visit 1. Our findings suggest that significant cognitive decline and MCI may be considered additional disease complications of diabetes among diverse middle-aged and older Hispanics/Latinos.

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Hispanics/Latinos (henceforth referred to here as Latinos) are the largest ethnic/racial group in the U.S. and represent nearly one-fifth of the population (1). Latinos have the highest prevalence of diabetes of any ethnic/racial group when diagnosed (13.6%) and undiagnosed (6.2%) cases are included in estimates (2,3). Additionally, Latinos have the earliest age of diabetes diagnoses of any ethnic/racial group in the country, provided they have access to health care (4,5). Similarly, age of mild cognitive impairment (MCI) and dementia onset are thought to be earlier among Latinos compared with other ethnic/racial groups (6,7). However, few studies have examined cognitive decline and disorders among middle-aged Latinos when cognitive changes are thought to begin (8). From age 40 years, diabetes prevalence rapidly increases each successive decade to nearly half (49%) of Latinos age >70 years, representing a 445% increase (9). The prevalence of MCI has an accelerating trajectory per decade similar to that of diabetes (10), which suggests that diabetes and cognitive impairment may be interrelated among Latinos.

Diabetes is associated with microvascular brain changes and stroke that manifest in cognitive decline and dementia (11). Behaviorally, diabetes is related to lower cognitive function but not generally with significant cognitive decline (12,13). In previous studies, diabetes was associated with increased MCI prevalence in older Latinos and whites, but the effects were small and explained by other cardiovascular disease (CVD) risk factors (14–16).

In general, previous studies of cognitive aging and disorders have focused on older adults (i.e., age ≥75 years) and have relied on self-reports or medical records of diabetes diagnosis. Few have used American Diabetes Association (ADA) diagnostic criteria for ascertaining diabetes. Additionally, there is a dearth of information about the length of diabetes exposure in relation to cognitive aging. Lastly, most studies have focused on whites and not examined diabetes, cognition, and MCI in other representative populations in which diabetes is highly prevalent. In this study of diverse middle-aged and older Latinos, we test the relationships between diabetes and cognitive decline and MCI and assess whether longer diabetes exposure affect relationships between cognitive decline and MCI.

RESEARCH DESIGN AND METHODS

Study Design

The Study of Latinos–Investigation of Neurocognitive Aging (SOL-INCA) is a Hispanic Community Health Study/Study of Latinos (HCHS/SOL) ancillary study. HCHS/SOL and SOL-INCA study designs and rationales are available elsewhere (17–19). HCHS/SOL is a multisite, population-based, probability-sampled, prospective cohort study of CVD and diabetes among diverse Latinos (visit 1: 2008–2011). The complex survey sampling procedures used in HCHS/SOL were designed to yield representative data for diverse Latinos in four targeted U.S. metropolitan areas: Bronx, NY; Chicago, IL; Miami, FL; and San Diego, CA. Each Field Center enrolled ~4,000 eligible self-identified Latinos (ages 18–74 years; $N = 16,415$). Biospecimens (e.g., blood) were assayed for CVD risk factors (e.g., fasting blood glucose) and stored for later studies. Detailed HCHS/SOL sampling procedures have previously been published and are available on the HCHS/SOL website: https://sites.cscc.unc.edu/hchs/ (17).

Baseline cognitive testing at HCHS/SOL visit 1 involved only middle-aged and older (ages 45–74 years) participants who were oversampled ($n = 9,714$) in the cohort. The Neurocognitive Reading Center trained and the Field Centers directly supervised bicultural/bilingual technicians who administered the brief cognitive battery, which included four tests: *1*) Six-Item Screener (SIS) (mental status) (20), *2*) Brief-Spanish English Verbal Learning Test (B-SEVLT) (verbal episodic learning and memory) (21), *3*) Word Fluency (WF) (22), and *4*) Digit Symbol Subtest (DSS) (processing speed, executive function) (23). Of all eligible participants, only 59 (<1%) did not participate due to health limitations and/or refusals. Additional information about the cognitive tests used at visit 1 and the cohort has previously been published (24).

SOL-INCA cognitive tests were administered to eligible HCHS/SOL participants who returned for visit 2, which occurred on average ~7 years after visit 1. We expanded the cognitive battery to derive an MCI research diagnosis based on National Institute on Aging–Alzheimer's Association (NIA-AA) criteria (25). In addition to visit 1 tests, we included the Trail Making Test (TMT) (parts A and B [executive function]) and NIH Toolbox Picture Vocabulary Test (PVT) (general premorbid cognitive function), self-reported cognitive decline (Everyday Cognition-12 [eCog-12]), and instrumental activities of daily living (IADL) (for functional impairment) (26,27). More detailed information about the battery of tests has previously been published (10,19). The PVT was used to assess premorbid cognitive function, since these scores remain stable with age and into later neurodegenerative stages, and to control for potential educational quality test biases (28). At HCHS/SOL visit 2, the Coordinating Center identified 7,420 potentially eligible participants for SOL-INCA. Inclusion criteria were *1*) visit 2 completion, *2*) visit 1 neurocognitive testing completion, and *3*) age ≥50 years. Of this group, 222 were determined to be ineligible (e.g., missing visit 1 data), 569 were eligible but refused, and 6,377 were eligible and agreed to participate. The overall response rate for SOL-INCA of eligible participants was 88.7%. Eligible participants returning for SOL-INCA had largely similar visit 1 characteristics compared with those in the overall pool of eligible visit 1 participants (Supplementary Table 1). Furthermore, to guard against possible biases by sample attrition, the HCHS/SOL Coordinating Center generated study-specific calibrated probability weights that adjust for nonresponse (e.g., deaths) and allow generalization of estimates to the HCHS/SOL metropolitan area target populations aged ≥50 years.

Cognitive change scores for repeated cognitive tests were calculated using regression-based methods, whereas survey linear regression models were used to predict cognitive performance at SOL-INCA as a function of visit 1 cognitive performance, with adjustment for elapsed time (in days) between cognitive assessments. Regression-based change score methods and their application to neurocognitive measures have previously been described (29). Briefly, test-specific standardized measures of change were subsequently calculated, $T2 - T2_{pred}/RMSE$, where T2 is the respondent's cognitive score at SOL-INCA, $T2_{pred}$ is their predicted score at visit 2, and RMSE is the regression-derived root mean squared error. A global cognitive change measure was subsequently generated by averaging across the change measures pertaining to each of the cognitive domains (19).

MCI diagnostic criteria were operationalized to generate four core NIA-AA criteria: *1*) any cognitive score in the mildly

impaired range, i.e., from −1 to −2 SDs compared with the SOL-INCA internal robust norms (age-, education-, sex-, and PVT-adjusted scores), *2*) significant cognitive decline (greater than or equal to −0.055 SD/year) from visit 1, *3*) self-reported cognitive decline, and *4*) no or minimum IADL impairment (25). Cognitive impairment and significant cognitive decline criteria were used to reduce false-positive bias. Individuals with severe cognitive impairment (below −2 SD relative to SOL-INCA robust norms and with significant functional impairment) were not included in these MCI prevalence estimates (10).

Diabetes assessment at HCHS/SOL visit 1 and visit 2 was based on ADA criteria: FPG ≥126 mg/dL (7 mmol/L), 2-h postload glucose level (2-h oral glucose tolerance test) ≥200 mg/dL (11.2 mmol/L), A1C level ≥6.5% (48 mmol/mol), or hypoglycemic agent use (i.e., scanned medication bottles) (9,30). We generated three groups, *1*) no diabetes, *2*) diabetes at visit 1 and visit 2 (prevalent), and *3*) new incident diabetes at visit 2 (incident), to capture associations between diabetes exposure and cognitive decline and MCI.

Covariables were included to account for confounding and other factors that could potentially explain associations of cognitive decline and MCI with diabetes, including sociocultural and CVD risk factors. All covariables, with the exception of age, were measured at visit 1.

Model covariables included Latino background (six groups), sex, age in years, education (<12 years, 12 years, >12 years), language preference (0 = English, 1 = Spanish), smoking status (0 = no, 1 = yes), a dichotomous indicator for alcohol consumption (one or more drinks per day), self-reported prevalent stroke or transient ischemic attack (TIA), myocardial infarction, and BMI based on weight measured in kilograms and height measured in centimeters. We also corrected for depressive symptoms (Center for Epidemiologic Studies Depression Scale-10 [CESD-10]) using a binary indicator to separate individual with elevated depressive symptoms (≥10) from others; the cut point for the CESD-10 was based on validation work previously conducted in HCHS/SOL (31). In addition, we tested genetic risk for cognitive decline and MCI in sensitivity analyses with apolipoprotein (apo)E genotype (34 and 44 vs. other) as a covariable in separate models (described below).

The analytic sample included 6,377 enrolled participants aged 50–86 years at HCHS/SOL visit 2. For the cognitive decline analyses, we excluded $n = 120$ participants who reported mixed Latino backgrounds and $n = 14$ participants who did not provide background information. For multivariable modeling, we also excluded $n = 150$ individuals with missing values on any of the covariates of interest. The analytic sample size was $n = 6{,}093$. For the MCI analyses, we additionally excluded $n = 91$ participants who were missing cognitive data needed to classify MCI. We also excluded $n = 80$ participants who met criteria for suspected severe cognitive impairment (<2 SD below the normative mean on any cognitive domain and functional impairment). Excluded participants had similar age, sex, and Latino background distributions relative to those included in the analytic sample.

In sensitivity analyses, we additionally adjusted (see list of included covariables above) for apoE4 genotype. These analyses focused on participants who consented for genetic data analyses. The analytic samples for these models included $n = 4{,}141$ participants. Compared with those consenting for genetic testing, nonconsenting participants were more likely to be male (40.8% vs. 47.2%; $P = 0.001$) and have <12 years of education (36.3% vs. 41.7%; $P < 0.001$). Age ($P = 0.107$) and diabetes status ($P = 0.955$) did not substantively differ between consenters and nonconsenters.

Statistical Analyses

First, we provide descriptive statistics to characterize the target population overall and by diabetes status (Table 1). Second, we describe and test the differences in means for the cognitive measures at visit 1 and at SOL-INCA for each of the cognitive domains as well as global cognition. We used survey-adjusted *t* tests to examine crude and age- and sex-adjusted mean differences between incident and prevalent diabetes, separately, versus no diabetes. For each test, we compare the crude and adjusted cognitive scores for no diabetes with those for *1*) incident diabetes and *2*) prevalent diabetes. These estimates are included in Supplementary Table 2. Third, we use survey linear regression models to test *1*) crude, *2*) age- and sex-adjusted, and *3*) covariable-adjusted associations between diabetes (reference: no diabetes) and global cognition as well as domain-specific cognitive change. The β-coefficients and SEs derived from the age- and sex-adjusted and fully adjusted estimated models are presented in Table 2. Fourth, we use survey logistic regression to model prevalent MCI as a function of diabetes status. As with the above, we fit *1*) crude, *2*) age- and sex-adjusted, and *3*) covariable-adjusted models. The estimated odds ratios (ORs) and 95% CIs from the age- and sex-adjusted and fully adjusted models are also presented in Table 2. For all the tested models, we calculated and plotted post hoc estimates of crude, age- and sex-adjusted, and full covariables–adjusted marginal means (for the continuous change measures [Fig. 1]) and probabilities (for prevalent MCI [Fig. 2]) and their 95% CIs. These plots facilitate visualization of associations between diabetes and the cognitive outcomes, in addition to showcasing the attenuations in estimated means and probabilities in each of the considered diabetes groups as a result of covariable adjustments in the models.

In sensitivity analyses, we further adjust the estimated models for apoE4. The estimates derived from the survey linear regression (for cognitive change) and survey logistic regression model (for MCI) are presented in Supplementary Figs. 1 and 2, respectively.

Ethics Committee Approval

The HCHS/SOL and the SOL-INCA studies were reviewed and approved by the institutional review boards of the University of California, San Diego, and all participating sites.

RESULTS

The target population characteristics and covariables of interest are shown in Table 1 both for the overall sample and by diabetes status. More than a quarter (28.5%) of people with diabetes were identified at visit 1 (prevalent diabetes), and 1 in 10 participants met criteria for incident diabetes (10.4%) at visit 2. For visit 2, mean ± SD age was 63.4 ± 8.2 years and 55% of subjects were females, 39.7% had <12 years' education, and 88.0% identified Spanish as their preferred language. Close to one-half met criteria for hypertension (47.0%) and 3.5% reported a prevalent stroke/TIA and 3.1% a myocardial infarction. Finally, 31.0% met CESD-10 criteria for elevated depressive symptoms.

Table 1—Descriptive statistics to characterize the population of SOL-INCA overall and by diabetes status

	No diabetes	Incident diabetes	Prevalent diabetes	Overall	*P*
Unweighted *n*	3,760	649	1,684	6,093	
Age, years, mean (SD)	62.2 (8.0)	63.2 (8.0)	66.1 (8.3)	63.4 (8.3)	<0.001
Female, %	55.1	49.2	55.3	54.5	0.169
Education, years, %					
<12	34.8	38.7	47.1	38.7	<0.001
12	21.5	24.1	21	21.6	
>12	43.7	37.2	31.9	39.7	
Spanish language preference, %	87.6	88.4	88.5	88	0.764
Latino background, %					
Dominican	9.8	9.3	10	9.8	0.051
Central American	7.8	5.4	7.8	7.5	
Cuban	27.1	29.2	25.6	26.9	
Mexican	34.4	35.3	34.1	34.4	
Puerto Rican	14.7	16.4	18.8	16	
South American	6.2	4.4	3.8	5.3	
Hypertension, %	37	53.3	66	47	<0.001
Prevalent stroke/TIA, %	2.3	2.3	6.6	3.5	<0.001
Myocardial infarction, %	2.1	3.9	5	3.1	<0.001
CESD-10 (≥10), %	28.7	33.4	35.1	31	0.002
Current smoker, %	20.4	18.6	14.1	18.4	<0.001
More than one alcoholic drink daily, %	11	11.6	7.3	10	0.007
BMI, kg/m^2, mean (SD)	28.7 (5.1)	31.3 (5.4)	31.5 (5.8)	29.7 (5.5)	<0.001
Metabolic syndrome, %	38.3	70.8	80.7	53.8	<0.001
A1C, mmol/mol, mean (SD)	37.3 (3.7)	40.4 (3.6)	57.9 (20.2)	43.5 (14.7)	<0.001

Prevalent diabetes since visit 1 and incident diabetes at visit 2. *P* values are based on survey-adjusted χ^2 tests for categorical measures and *t* tests for continuous measures. With the exception of age (in years), all other characteristics were measured at visit 1. Low mental status at visit 1 and visit 2 was measured as having a score ≤4 in the SIS.

The prevalent diabetes group was older (66.1 vs. 62.2 years old for no diabetes) and more likely to have <12 years of education (47.1% vs. 34.8% for no diabetes). The prevalent diabetes group was more likely to be hypertensive (66.0% vs. 37.0% for no diabetes), close to three times as likely to have had a stroke/TIA (6.6% vs. 2.3% for no diabetes), and 2.5 times more likely to have had a myocardial infarction (5.0% vs. 2.1% for no diabetes). With the exception of higher levels of hypertension (53.3% vs. 37.0%), the incident diabetes group had largely similar profiles for the considered characteristics compared with the no diabetes group. Finally, both prevalent (31.5 kg/m^2) and incident (31.3 kg/m^2) diabetes groups had higher average BMI relative to the no diabetes group (28.7 kg/m^2).

The prevalent diabetes group had consistently lower visit 1 and visit 2 (average 7 years later) scores on all considered cognitive tests (Supplementary Table 2). The incident diabetes group did not differ in their cognitive performance at visit 1 and visit 2 relative to the no diabetes group. In age- and sex-adjusted models for cognitive change (Table 2), the prevalent diabetes group had more pronounced levels of decline (*z* score units) compared with no diabetes for global cognition ($\beta_{GC} = -0.16$ [95% CI −0.25; −0.07]; $P < 0.001$), as well as each of the considered cognitive domains, including episodic memory ($\beta_{B\text{-}SEVLT\text{-}Sum}$ −0.10 [95% CI −0.19; −0.01]; $P < 0.05$), learning ($\beta_{B\text{-}SEVLT\text{-}Recall}$ −0.09 [95% CI −0.17; −0.01]; $P < 0.05$), verbal fluency (β_{WF} −0.16 [95% CI −0.25; −0.06]; $P < 0.01$), and processing speed (β_{DSS} −0.20 [95% CI −0.29; −0.10]; $P < 0.001$). Incident diabetes was not significantly associated with any of the cognitive measures.

The associations between prevalent diabetes and episodic learning and memory were explained by adjustments for the model covariables. The inverse associations between prevalent diabetes and global cognition (β_{GC}−0.12 [95% CI −0.20; −0.03]; $P < 0.01$), verbal fluency (β_{WF} −0.11 [95% CI −0.20; −0.02]; $P < 0.05$), and processing speed (β_{DSS} −0.14 [95% CI −0.24; −0.05]; $P < 0.01$) were attenuated but remained statistically significant after covariable adjustments (Table 2 and Fig. 1).

In age- and sex-adjusted models, prevalent diabetes increased the ORs for MCI relative to no diabetes by 74% (OR 1.74 [95% CI 1.34; 2.26]; $P < 0.001$). The higher ORs for MCI among the prevalent diabetes group were attenuated (OR 1.48 [95% CI 1.13; 1.94]; $P < 0.01$) but not explained by adjustments to the model covariables (Table 2 and Fig. 2). These results remained consistent in sensitivity analyses following adjustment to apoE4 status (Supplementary Figs. 1 and 2).

CONCLUSIONS

Diabetes was associated with significantly lower cognitive function and increased cognitive decline and MCI prevalence compared with Latinos without diabetes. Specifically, participants with diabetes at visit 1 evinced significant 7-year cognitive decline. Secondly, prevalent diabetes was associated with a marked increase in MCI prevalence. In coming decades, the Latino older adult population is projected to quadruple and have the largest increase in ADRD prevalence of any U.S. ethnic/racial group (32,33). Additionally, Latinos also have the earliest age of diabetes diagnosis and the highest rates of uncontrolled diabetes of all ethnic/racial groups in the U.S. (3,4). Therefore, preventing

Table 2—Associations of diabetes status with cognitive change and with prevalent MCI

	M1	M2
ΔGlobal cognition		
No diabetes	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)
Incident	0.06 (−0.06; 0.18)	0.07 (−0.05; 0.19)
Prevalent	−0.16 (−0.25; −0.07)***	−0.12 (−0.20; −0.03)**
ΔB-SEVLT-Sum		
No diabetes	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)
Incident	0.12 (−0.01; 0.25)	0.13 (0.00; 0.26)*
Prevalent	−0.10 (−0.19; −0.01)*	−0.05 (−0.14; 0.03)
B-SEVLT-Recall		
No diabetes	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)
Incident	0.05 (−0.06; 0.17)	0.05 (−0.07; 0.16)
Prevalent	−0.09 (−0.17; −0.01)*	−0.06 (−0.15; 0.02)
ΔWF		
No diabetes	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)
Incident	−0.01 (−0.12; 0.10)	0.01 (−0.10; 0.13)
Prevalent	−0.16 (−0.25; −0.06)**	−0.11 (−0.20; −0.02)*
ΔDSS		
No diabetes	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)
Incident	−0.02 (−0.13; 0.10)	0.01 (−0.10; 0.13)
Prevalent	−0.20 (−0.29; −0.10)***	−0.14 (−0.24; −0.04)**
Prevalent MCI at visit 2		
No diabetes	1.00 (1.00; 1.00)	1.00 (1.00; 1.00)
Incident	1.20 (0.73; 1.98)	1.10 (0.66; 1.84)
Prevalent	1.74 (1.34; 2.26)***	1.48 (1.13; 1.94)**

Data are β (95% CI) except for data for prevalent MCI at visit 2, which are OR (95% CI). Change estimates are based on survey linear regression models. MCI estimates are based on survey logistic regression models. Prevalent diabetes, since visit 1; incident diabetes, at visit 2. M1: model adjusted for age and sex. M2: model fully adjusted, including adjustment for Latino background (six groups), sex, age, education (<12 years, 12 years, >12 years), language preference (Spanish, English), whether someone is a current smoker (0 = no, 1 = yes), a dichotomous indicator for alcohol consumption (one or more drinks per day), self-reported prevalent stroke or TIA, myocardial infarction, BMI based on weight measured in kilograms and height measured in centimeters, and ≥10 on CESD-10. With the exception of age, all covariates were measured at visit 1. ***$P < 0.001$; **$P < 0.01$; *$P < 0.05$.

diabetes, early detection, and improving and increasing glycemic control for Latinos with diabetes are vital priorities for potentially mitigating diabetes complications, including reducing the risk of cognitive decline and impairment.

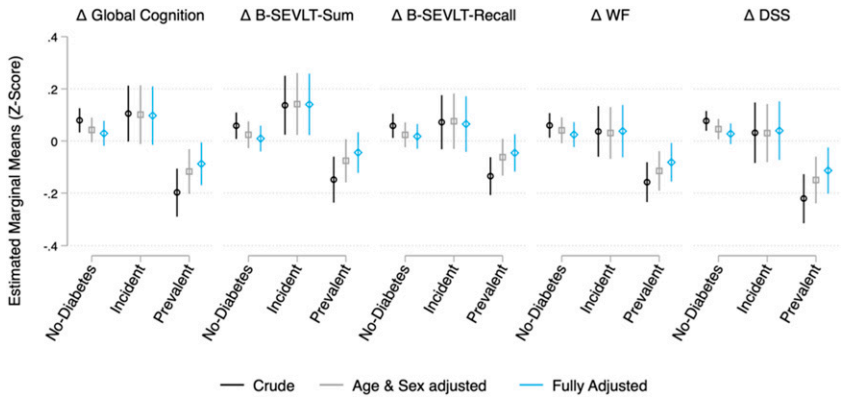

Figure 1—Estimates of crude and adjusted marginal means (and their 95% CIs) of cognitive change. Results are derived from survey linear regression estimates. Prevalent diabetes, since visit 1; incident diabetes, at visit 2. Adjusted models correct for Latino background (six groups), sex, age, education (<12 years, 12 years, >12 years), language preference (English, Spanish), whether someone is a current smoker (0 = no, 1 = yes), a dichotomous indicator for alcohol consumption (one or more drinks per day), self-reported prevalent stroke or TIA, myocardial infarction, BMI based on weight measured in kilograms and height measured in centimeters, and ≥10 on CESD-10. With the exception of age, all covariates were measured at baseline.

Previous studies of diabetes, cognitive decline, and MCI have reported mixed results. Among whites in Olmstead County, MN, diabetes was marginally associated with prevalent MCI but only when prevalent diabetes and complications were also considered (34). In the same cohort, MCI incidence was associated with longer diabetes exposures (16). Among middle-aged and older Mexican-origin Latinos and whites in a cross-sectional, mixed community-based rural and urban (i.e., dementia registry) Texas study, diabetes was not related to MCI prevalence (6). In another study of mostly older Mexican-origin Latinos, diabetes was associated with faster decline in mental status scores and higher mortality compared with no diabetes. The authors cautioned that ignoring mortality in analyses could lead to underestimates of associations between diabetes and cognitive decline (13). Among older Caribbean Latinos, diabetes was marginally associated with MCI, which was explained by competing CVD risks (14). In the same sample, diabetes was associated with lower cognitive performance but not cognitive decline (8). However, among middle-aged Caribbean Latinos, higher A1C values were associated with lower cognitive performance (35). In a study of older Germans, diabetes was not significantly related to MCI. In that study, the authors reported small (nonsignificant) associations between diabetes and psychomotor speed and cognitive flexibility (15). There are several explanations for the differences in findings between the aforementioned studies and SOL-INCA findings. Firstly, SOL-INCA is a much larger and younger cohort in which diabetes was rigorously ascertained per ADA guidelines. Secondly, we assessed both cognitive function and diabetes in midlife, whereas most previous studies retrospectively determined midlife diabetes status via self-report or medical records in relation to later-life cognitive function. Thirdly and perhaps most importantly, diabetes prevalence was higher in Latinos compared with other cohort studies of whites. Thus, our findings are consistent with previous studies that demonstrated that diabetes is associated with lower cognitive function among older Latinos. Moreover, middle age appears to be a particularly vulnerable developmental period for Latinos with diabetes for cognitive decline and MCI. Finally, our study and other studies

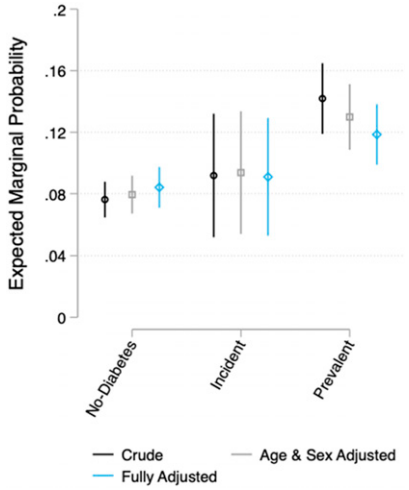

Figure 2—Estimates of crude and adjusted marginal probability (and their 95% CIs) of MCI. Results are derived from survey logistic regression models. Prevalent diabetes, since visit 1; incident diabetes, at visit 2. Adjusted models correct for Latino background (six groups), sex, age, education (<12 years, 12 years, >12 years), language preference (English, Spanish), whether someone is a current smoker (0 = no, 1 = yes), a dichotomous indicator for alcohol consumption (one or more drinks per day), self-reported prevalent stroke or TIA, myocardial infarction, BMI based on weight measured in kilograms and height measured in centimeters, and ≥10 on CESD-10. With the exception of age, all covariates were measured at baseline.

suggest that the magnitude of the problem of diabetes for Latinos regarding brain function and disease may be higher compared with other populations.

In this Latino cohort study, there were other notable correlates that explained some of the associations between diabetes, cognitive decline, and MCI. Older age, male sex, and smoking were also significantly associated with significant cognitive decline in most domains. Men with diabetes evinced more decline in verbal learning and memory, a hallmark of Alzheimer disease, than women. Higher education was generally protective of cognitive decline in all domains. For MCI, older age and hypertension were associated with increased MCI prevalence, whereas having more years of education was related to decreased MCI prevalence. Interestingly, although men showed greater cognitive decline than women, the prevalence of MCI was indistinguishable between the sexes. This finding suggests that men may report, or have, fewer subjective complaints of cognitive decline and functional impairment compared with women, which are both key components of the MCI diagnosis.

There are several strengths and weaknesses that readers may wish to consider in evaluating the results of this study. SOL-INCA is the largest study of diabetes, cognitive decline, and MCI, which improved our statistical power to detect meaningful associations. The effect sizes of statistical associations in this study were modest. However, given the representativeness of this sample, the population-level public health benefits would likely be large. Secondly, diabetes is all too common and poorly controlled in this cohort of diverse Latinos, which also amplified statistical power to detect effects (3). Thirdly, the ADA guidelines–concordant diabetes diagnostic approach used in HCHS/SOL and SOL-INCA is more rigorous than used in previous studies of cognitive function and MCI. Our study is somewhat limited by our brief cognitive assessment battery and our reliance on participant self-reported subjective cognitive decline and functional decline (e.g., handling a checkbook). Although inclusion of informant reports of cognitive and functional limitations is optional in NIA-AA criteria, SOL-INCA did not include informant reports of cognitive and functional limitations, which could have improved MCI case identifications. Secondly, we did not fully account for mortality in this study (n = 405 deaths between visit 1 and visit 2). Instead, deaths were accounted for as nonresponses in our sampling weights. This may have resulted in a small underestimation of the effect of diabetes on cognitive decline and MCI (13). Thirdly, it is possible that participants with diabetes in this study may have had poor cognitive functioning prior to developing diabetes. Given our study design, our operational definition of diabetes following ADA criteria, and the high rates of undiagnosed diabetes among Latinos (3), we were unable to accurately estimate age of diabetes onset. As such, we were unable to precisely characterize the effects of total disease duration from onset in middle age on cognitive decline and MCI. Nevertheless, our findings provide new insights into the effects of midlife diabetes on cognitive aging and impairment among diverse Latinos who are at risk for diabetes complications.

Conclusion

Diabetes was associated with marked 7-year cognitive decline and increased MCI prevalence among diverse middle-aged and older Latinos but primarily among those with diabetes at visit 1. Diabetes disease onset typically occurs in middle age, and our findings suggest that middle age is a particularly vulnerable period in life—when the effects of diabetes on cognitive function and decline begin. Our findings additionally suggest that intensive public health and clinical messaging targeting individuals with early-stage diabetes might strengthen patients' motivation for adherence to diabetes management and treatment efforts in midlife and may have important implications for controlling diabetes complications, including cognitive decline and impairment, among diverse Latinos.

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