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Central obesity, cardiometabolic risk, and cognitive change in the Study of Latinos-Investigation of Neurocognitive Aging

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Abstract

Background: The relationships between obesity and cognitive decline in aging are mixed and understudied among Hispanics/Latinos.

Objective: To understand associations between central obesity, cognitive aging, and the role of concomitant cardiometabolic abnormalities among Hispanics/Latinos.

Methods: Participants included 6,377 diverse Hispanics/Latinos enrolled in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) and SOL-Investigation for Neurocognitive Aging (SOL-INCA). Participants were 45-years and older at the first cognitive testing session (Visit 1). Cognitive outcomes (z-score units) included global composite and domain specific (learning, memory, executive functioning, processing speed) measures at a second visit (SOL-INCA, on average, 7-years later), and 7-year change. We used survey linear regression to examine associations between central obesity (waist circumference ≥88 cm and ≥102 cm for women and men, respectively) and cognition. We also tested whether the relationships between obesity and cognition differed by cardiometabolic status (indication of/treatment for 2+

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CONFLICTS OF INTEREST/DISCLOSURE STATEMENT

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of the following: high triglycerides, hypertension, hyperglycemia, low high-density lipoprotein cholesterol).

Results: Central obesity was largely unassociated with cognitive outcomes, adjusting for covariates. However, among individuals with central obesity, cardiometabolic abnormality was linked to poorer cognitive function at SOL-INCA ($\Delta_{GlobalCognition} = -0.165$, $p<0.001$) and to more pronounced cognitive declines over the average 7-years ($\Delta_{GlobalCognition} = -0.109$, $p<0.05$); this was consistent across cognitive domains.

Conclusion: Central obesity alone was not associated with cognitive function. However, presence of both central obesity and cardiometabolic abnormalities was robustly predictive of cognition and 7-year cognitive declines, suggesting that in combination these factors may alter the cognitive trajectories of middle-aged and older Hispanics/Latinos.

Keywords

Obesity; Hispanics; Latinos; cognition; aging; cardiometabolic risk factors; diabetes mellitus; hyperlipidemias; hypertension

INTRODUCTION

Obesity is prevalent in 47.0% of Hispanics/Latinos in the United States, making it a one of the most common cardiovascular disease risk factors among this group [1]. Existing literature suggests that obesity increases the risk for dementia, particularly when present in middle-age [2-4]. Recently, the Million Women Study reported that obesity was more clearly linked to risk for dementia over a 15-year period than physical inactivity and low caloric intake [5]. However, a meta-analysis of 2.8 million adults reported that obesity was only associated with increased risk for vascular dementia (not other dementia-types), and this link was attenuated when cardiometabolic factors were taken into account [6].

Among individuals without dementia, evidence on the link between obesity and cognition is also mixed [7]. Some studies suggest that the relationship between obesity and cognition might be synergistic and occurs through more complex pathological mechanisms [8]. For example, in a longitudinal cohort of predominantly non-Hispanic/Latino Whites, obesity was associated with steeper cognitive decline relative to healthy weight but only among individuals with at least two cardiometabolic risk factors [9]. Otherwise, the rate of cognitive decline was similar between individuals with and without obesity. Data from a diverse group of Hispanics/Latinos enrolled in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL), over half of whom met criteria for metabolic syndrome (a cluster of cardiovascular risk factors), did not detect a link between obesity and cognition [10]. However, it is unclear whether the relationship of obesity with cognition varies by presence of cardiometabolic risk factors in diverse Hispanics/Latinos.

Alternatively, the lack of significant association between obesity and cognition in this prior study may be related to the specific measure of adiposity (i.e., body mass index rather than waist circumference) [10]. Waist circumference, a measure of central obesity, has been shown to have stronger associations with other cardiometabolic risk factors than body mass index [11], and thus might also be more closely associated with cognitive

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function. Therefore, we aimed to investigate the relationships among cognition, central obesity (based on waist circumference), and cardiometabolic risk factors similar to the approach used by Singh-Manoux and colleagues [9]. Specifically, we compared the extent to which central obesity and presence or absence of other cardiometabolic risk factors are linked to concurrent cognition, cognition 7-years later, and cognitive change over the 7-year period. We hypothesized that central obesity would be associated with poorer cognition at both time points and with greater cognitive change relative to non-obese individuals. Further, we hypothesized that these relationships would be more pronounced (i.e., worse cognition and greater cognitive change) among individuals with central obesity who also have two or more cardiometabolic risk factors (high triglycerides, hypertension, hyperglycemia, low high-density lipoprotein cholesterol). Finally, given some literature on potential sex differences in the relationships between obesity and cognition [12, 13], we also conducted an exploratory examination to test if sex modifies the associations of central obesity and cardiometabolic complications on cognition.

MATERIALS AND METHODS

Study Design

The *Hispanic Community Health Study/Study of Latinos* (HCHS/SOL) is a prospective population-based cohort study of a diverse Hispanic/Latino population ages 18-74 years. A total of 16,415 eligible diverse self-identified Hispanics/Latinos from four US metropolitan areas: Bronx, NY; Chicago, IL; Miami, FL; and San Diego, CA participated in the HCHS/SOL from 2008-2011. HCHS/SOL methods are available at the study website: https://sites.cscc.unc.edu/hchs. We used a complex survey weighted design to obtain representative data and adjust for non-response bias. Study rationales and designs are also available elsewhere [14]. Institutional review boards at each participating site approved the study protocol. Participants provided written informed consent. HCHS/SOL participants who were 45-74 years old at the first visit were invited to complete the *Study of Latinos-Investigation of Neurocognitive Aging* (SOL-INCA), a second wave of neurocognitive testing 7-years later, on average. A total of 7,420 individuals were identified by the coordinating center as eligible for participation for SOL-INCA. Furthermore, the following criteria were used to determine inclusion for SOL-INCA: (1) individuals should have participated in the Visit 1 cognitive module, (2) they were at least 50-years or older at SOL-INCA. A total of 222 individuals did not meet these criteria and were excluded. Furthermore, 569 individuals were eligible and contacted but refused participation. A total unweighted sample of 6,377 people participated in SOL-INCA (response rate = 88.7%). To avoid selection bias, the coordinating center for the study used target population characteristics to generate probability weights that adjust for non-response and allow for appropriate inferences and generalization of estimates.

Cognitive Outcomes

Visit 1 Cognitive Battery—Trained bilingual technicians administered the following cognitive tests in the participant's preferred language: (1) Brief-Spanish English Verbal Learning Test (B-SEVLT; verbal episodic learning (B-SEVLT-Sum) and memory (B-SEVLT-Recall)), (2) Word fluency (WF; verbal fluency), and (3) Digit Symbol Subtest

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(DSS; processing speed, executive function). Additional procedures and information about Visit 1 testing are available elsewhere [14]. A Global measure of cognitive performance at Visit 1 was generated by averaging the standardized scores (Z-Score) from the B-SEVLT-Sum, B-SEVLT-Recall, DSS, and WF.

SOL-INCA Cognitive Battery—SOL-INCA repeated the cognitive battery administered at Visit 1 and added the Trails Making Test parts A (TMT part A; processing speed) and B (TMT part B; executive functioning). To maintain consistency with Visit 1, a global cognitive measure for SOL-INCA was generated by averaging the standardized scores (Z-Score) from B-SEVLT-Sum, B-SEVLT-Recall, DSS, and WF.

Cognitive Change—Change scores for repeated cognitive tests were calculated using survey linear regression, regressing cognitive performance at SOL-INCA on cognitive performance at Visit 1, and adjusting for time elapsed (in days) between cognitive assessments [15]. The regression-based methods for assessing change have been previously used with cognitive data from multiple cohorts, including HCHS/SOL and SOL-INCA [16, 17]. Test specific standardized measures of change and global change were calculated using $T2 - T2_{pred}/SEE$ where $T2$ was the respondent cognitive score at SOL-INCA, $T2_{pred}$ their predicted score, using regression estimates from the model specified above, and SEE refers to the *root mean square error from the same* regression model. More detailed explanation on cognitive change can be found in Duff and colleagues [18].

Exposure

Central obesity status at HCHS/SOL (around the time of Visit 1) was our main exposure variable. Participants were coded into two groups (no central obesity, central obesity) using sex specific thresholds [19]. Women and men were classified as meeting criteria for central obesity if waist circumference (WC) was ≥88 cm and ≥102 cm, respectively. Given increased risk of cardiometabolic abnormality and mortality among individuals with morbid obesity relative to using body mass index cut-offs (35+ versus 25) [20, 21], we ran sensitivity models to test a three-category indicator of central obesity (no central obesity, moderate central obesity, high central obesity). We used previously published criteria for "very high levels of WC" to categorize high central obesity [22]. That is, women were classified with moderate central obesity if 88 ≤ WC <110 and high central obesity if WC was ≥110. Men were classified with moderate central obesity if 102 ≤ WC < 120 and high central obesity if WC was ≥120. No central obesity categories remained the same for both sexes.

Cardiometabolic Abnormality Component Factors

Blood draws and biospecimen were analyzed for cardiometabolic factors. We used the International Diabetes Federation consensus to characterize four components of cardiometabolic function at HCHS/SOL. Although there are different approaches to classifying cardiometabolic health (e.g., presence of any cardiometabolic abnormality or sum of abnormalities), we created a classification that is consistent with that of Singh-Manoux and colleagues [9]. Thus, participants meeting criteria on two or more of the following indicators were considered "metabolically abnormal": (1) High triglycerides:

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≥150mg/dL and/or reported Fibric/Nicotinic acids use; (2) High blood pressure: systolic pressure ≥130mm Hg, diastolic pressure ≥85mm Hg, and/or reported anti-hypertensive medication use; (3) Elevated fasting glucose: ≥100 mg/dL and/or reported antidiabetic medication use; and (4) low HDL Cholesterol: <40 mg/dL or <50 mg/dL for men and women, respectively and/or reported use of Fibric/Nicotinic acids.

Covariables

In adjusted models we accounted for factors that have previously been associated with cognitive functioning among Hispanics/Latinos [23]. Covariables included (1) age group (<60 years, 60-69 years, ≥70 years), sex (male, female), Hispanic/Latino background (Puerto Rican, Mexican, Central American, South American, Cuban, Dominican), educational level (<12 years, 12 years, >12), and depressive symptoms using the Center for Epidemiologic Studies Depression Scale (CES-D-10). Individuals were classified as non-depressed (CESD-10 <10) and elevated depressive symptoms (CESD ≥10) based on thresholds used previously in HCHS/SOL participants [24].

Analytic Sample

Individuals ages 50-86 years were enrolled at SOL-INCA (n = 6,377). A total of 120 individuals were excluded due to reporting mixed Hispanic/Latino backgrounds as well as 12 who did not specify their background. We excluded 215 individuals who had missing covariates, for a final analytic sample of 6,030. Individuals excluded from the analysis did not differ significantly from the analytic sample in terms of age, sex, background, education, or cardiovascular risk profile (Supplementary Table 1).

Statistical Analysis

We used the survey suite in the Stata 16 software to generate all estimates and inferential statistics. All analyses adjusted for the survey design of the SOL-INCA study including clustering, stratification, and correction for sample probability weights. First, we computed descriptive statistics to characterize individuals in the overall target population and by central obesity/metabolic status over the covariates specified above. Table 1 includes estimates of means and prevalence rates for these covariates by central obesity group stratified over metabolic abnormality status. Supplementary Table 2 includes these estimates by central obesity status and metabolic abnormality groups independently. Group differences were tested using survey adjusted chi-squared tests for categorical variables and t-tests for continuous measures. Second, we sequentially fit survey linear regressions to model the associations between the central obesity exposure and global cognition as well as global cognitive change. We included a global score because cognitive composites tend to minimize intraindividual variability [25, 26]. In each case, we fit three models to determine the 1) crude, 2) age and sex adjusted, and 3) fully adjusted coefficients and their standard errors (Table 2). To facilitate the interpretation of these associations we estimated and plotted the marginal means of cognition/cognitive change by central obesity status, derived from these models, and their 95% confidence. Third, we refit the fully adjusted models using a grouped indicator for both metabolic abnormality and central obesity (1=not obese/metabolically normal (reference), 2=obese /metabolically normal, 3=not obese/metabolically abnormal, and 4=obese/metabolically abnormal) to test whether and how complications of obesity by

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metabolic abnormality influences cognitive function and cognitive change. We used survey adjusted post-hoc Wald tests to examine the overall equality of parameter estimates across groups and ANOVA contrasts to examine and test group differences within and across the metabolic and obesity classifications (Tables 3 and 4). We calculated and plotted the estimated marginal means of (1) cognitive performance at SOL-INCA and (2) cognitive change and their 95% confidence intervals by metabolic status across central obesity groups in figure 1 and figure 2, respectively. We refit the survey linear regression models detailed in steps 2 and 3 above to each of the cognitive tests, independently. Similar post-hoc tests and plots were used to test, visualize, and report group differences. We tested for modification by sex by including an additional interaction effect in the fully adjusted models, as specified above. We conducted post-hoc tests for significance of sex interactions with central obesity within metabolic groups (Supplementary Table 3).

Sensitivity models

All analyses detailed above were repeated using a trichotomous measure of central obesity including non-obese, moderate obesity, and high obesity (see exposure section above). The results of these sensitivity analysis are provided in Tables e-4-7.

RESULTS

Descriptives

Summary statistics characterizing the target population by central obesity and metabolic status are presented in Table 1. Average age was 63-years, 55% were female, and 31% had elevated depression symptoms. About two-thirds (68.0%) of the target population met central obesity criteria and 57.3% had 2+ cardiometabolic risk factors. Individuals with presence of both central obesity and metabolic abnormality were on average older, less likely to have greater than 12-years of education, and more likely to have elevated depressive risk symptoms. As expected, individuals meeting central obesity and metabolic abnormality criteria also had the highest average BMI, lower HDL cholesterol, and higher mean glucose, systolic and diastolic blood pressure levels (Table 1). However, non-central obesity with metabolic abnormality was associated with the highest triglycerides and lowest HDL.

Central Obesity and Cognitive Performance

Adjusting for covariates, we found no statistical evidence to support a consistent association between central obesity and cognitive function. The lack of association was true for both global cognition as well as domain specific function cognitive scores (Table 2).

Cognitive Change

Central obesity was associated with more pronounced average decline in processing speed/executive functioning based on Digit Symbol Substitution ($\beta_{\Delta DSS}$=−0.11; 95%CI [−0.20;−0.02]), and this finding persisted in fully adjusted models ($\beta_{\Delta DSS}$=−0.10; 95%CI [−0.19;−0.01]; Table 2).

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Metabolic Abnormality and Central Obesity

We found consistent evidence for associations between metabolic status and cognition, particularly for individuals meeting criteria for central obesity (Table 3). Individuals meeting criteria for central obesity and metabolic abnormality had lower global cognitive function on average 7-years later, compared to those with central obesity but without metabolic abnormality (figure 1). Presence of both central obesity and metabolic abnormality was also associated with more pronounced cognitive decline (figure 2). The higher risk for cognitive deficits and cognitive decline in this group (vs. those meeting criteria for central obesity without metabolic abnormality) was consistent across cognitive domains (Table 4). We found less evidence to support differences in cognitive function or cognitive change by metabolic status among individuals not meeting criteria for central obesity. Focusing on metabolically normal participants, individuals with central obesity tended to have nominally better performance than non-obese individuals, but this was only significant for Trail A performance at SOL-INCA ($\beta_{\Delta TRAIL\ A}$= 0.14; 95%CI [0.05;0.23]).

Sex Modifications

Overall, we found no evidence to support modifications in findings by sex. Results of tests for two-way interactions are presented in Supplementary Table 3.

Sensitivity Analysis

Summary statistics characterizing the target population by severity of central obesity (3-group) and metabolic status are included in Supplementary Table 4a,b. Individuals with high central obesity and metabolic abnormality had particularly high BMI, higher average glucose, and higher prevalence of elevated depressive symptoms relative to all other considered groups. Other demographic, vascular and blood marker characteristics were similar to those with moderate central obesity.

The associations between central obesity and cognitive performance and change were consistent with the primary findings reported above (Supplementary Table 5). Overall, we found less evidence to support an association between high central obesity and cognitive performance or cognitive change.

Differentiating moderate and high central obesity did not lead to marked differences in the reported associations with metabolic status (Supplementary Table 6). As with the main results, individuals meeting criteria for moderate central obesity and metabolic abnormality had lower SOL-INCA cognitive scores, and more pronounced global and domain specific cognitive decline relative to those with moderate central obesity and without metabolic abnormality (Supplementary Table 7). The associations of metabolic abnormality among individuals with high central obesity were largely in the same direction albeit statistical significance was less consistent.

DISCUSSION

Taken together, we found evidence that central obesity negatively alters the cognitive trajectory of middle-aged and older Hispanics/Latinos only in the presence of other

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cardiometabolic risk factors. Importantly, we detected these patterns among United States Hispanics/Latinos, a group that has high rates of Alzheimer's disease and related dementias (ADRD) [27, 28] as well as high prevalence of obesity comorbid with cardiometabolic risk factors [29]. The synergistic impact of these factors on cognitive aging will likely have substantial public health consequences.

Central obesity alone was not linked to cognitive outcomes with one exception which may have been a spurious finding (i.e., greater 7-year decline in DSS among individuals with central obesity). Among groups with multiple comorbidities, separate cardiometabolic factors may have a larger impact on cognition than obesity. For example, among individuals in the Northern Manhattan Study (NOMAS), blood pressure was more closely associated with cognitive outcomes than obesity, despite obesity being most strongly linked to metabolic syndrome [30]. Obesity is a risk factor for several other cardiometabolic factors [31]. Therefore, the relationships between obesity and cognition may be attenuated by other risk factors [30]. Importantly, in the present study, central obesity alone failed to predict the majority of cognitive outcomes *prior* to adjusting for cardiometabolic factors, suggesting that the associations between central obesity and cognition were not simply overshadowed or attenuated by other cardiometabolic factors. Examining the indirect relationships of obesity and cognition, Yesavage and colleagues [32] reported a link between obesity and cardiometabolic factors related to cognitive performance. However, the relationships between cardiometabolic factors and cognition were not attributable to obesity, suggesting that obesity failed to have direct or indirect associations with cognition.

Alternatively, the relationships between obesity and cognition may be complicated by aging: obesity may have a deleterious impact on cognition and risk for ADRD when present in middle-age but not when onset in older adulthood [7]. Dubbed the "obesity paradox", obesity onset in later life may be protective against ADRD [33]. Given that we did not have detailed objective information on onset or duration of central obesity, we did not exclude older adults and instead controlled for age in all analyses. It is possible that many older adults in our sample identified as having central obesity have been so since middle-age. Future investigations are needed to examine if the relationships between obesity and cognition among Hispanics/Latinos differ in older adulthood.

Obesity played a larger role in cognitive outcomes when examined in the context of cardiometabolic status. Compared to findings from the Whitehall II Study, we detected steeper declines in cognitive performance among obese individuals with cardiometabolic abnormalities than metabolically normal obese participants whereas Singh-Manoux and colleagues [9] did not detect any such differences between obesity groups. Generally, our data more strongly support that the presence of both risk factors (obesity and cardiometabolic abnormality) has a cumulative relationship to cognition and cognitive decline. Several factors may have contributed to study differences. First, our sample was unhealthier with higher prevalence of cardiometabolic abnormalities (57% versus 31%) and obesity (68% versus 9%) compared to Whitehall II, which may have increased our sensitivity to detect associations within obesity groups. It is likely that this, in part, reflects changes in diet and physical activity over time [34]: Whitehall II and HCHS/SOL health data were collected from 1991 to 1993 and 2008 – 2011, respectively [35, 36]. Second,

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the Whitehall II cohort was younger than the HCHS/SOL cohort (49-50 years versus 63 years, on average) which may influence the extent to which obesity is linked to cognition. Third, we measured obesity using WC rather than body mass index which minimizes confounds related to muscle mass [37] but does not specify a non-obese “overweight” group. Additionally, WC is superior to body mass index in predicting mortality [22], possibly because it better captures visceral adipose tissue which is more strongly associated with cardiometabolic risk than subcutaneous adipose tissue [38].

The combination of obesity and cardiometabolic status had nuanced relations to cognition. Given our previous work linking metabolic syndrome to widespread cognitive disadvantages [10], it was unsurprising that cardiometabolic abnormality was linked to poorer cognition. The present study extends this work by demonstrating that the combination of central obesity and cardiometabolic abnormality was also associated with steeper declines in cognition over a 7-year period whereas this was not observed among participants with healthy WC. Unexpectedly, central obesity was associated with processing speed advantages among individuals without cardiometabolic abnormality. It may be that individuals with central obesity who otherwise maintain cardiometabolic health are resilient to cardiac and cognitive health problems typically associated with obesity. Another possibility is that obesity without metabolic abnormality may be tied to cognitively stimulating and higher paying but sedentary jobs. We accounted for age and education which are possible factors that may contribute to cognitive resilience in the face of risk [13, 39], suggesting that an altogether different factor (e.g., genetics) [40] may be conferring an advantage. However, our data suggest that the processing speed advantage only applies to performance, not maintenance/decline over the 7-year period.

Our results were relatively robust. We split the “central obesity” group into “moderate” and “high” central obesity and found that the “moderate” obesity group showed similar patterns with cognition as the original analysis. In contrast, high central obesity combined with cardiometabolic status was not consistently associated with cognitive outcomes. This appeared to be related to greater variability in cognitive performance, possibly due to smaller sample size, rather than floor effects. Additionally, the relationships between central obesity, cardiometabolic status, and cognition were stable across sexes unlike some previous work which examined obesity *or* cardiometabolic risk and cognition [12, 41].

There may be several mechanisms by which obesity is linked to cardiometabolic abnormality and cognition. In obesity, excess adipose cells/tissue produce pro-inflammatory cytokines some of which cross the blood brain barrier [42]. Obesity-related inflammation has been linked to both increased risk for cardiometabolic abnormalities [43] and cognitive impairment [42, 44]. At the level of the brain, obesity has been associated with blood brain barrier disruption [45, 46], decreased perfusion [47], poorer white matter integrity [48, 49], increased white matter hyperintensities [50, 51], and smaller gray matter volumes [52-54] and cortical thickness [55]. Evidence suggests that among individuals with metabolic syndrome, obesity may be connected to lower cerebral blood flow to a greater extent than other cardiometabolic abnormalities [56], reflecting the unique contributions that obesity may have to brain health. Whether obesity and other cardiometabolic abnormalities have additive versus synergistic impacts on the brain remains undetermined [49, 57].

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Limitations

Our study included some notable limitations. First, we did not examine age of onset of obesity. As noted above, obesity onset in older adulthood may be protective of cognition. Onset may be of particular importance to the Hispanic/Latino population given that Hispanics/Latinos have the highest prevalence of childhood obesity in the United States [1]. The long-term ramifications of early onset of obesity are unknown. Existing evidence points to differences in brain structure between adolescents with and without obesity [58]. Second, we only examined central obesity at one time-point, failing to account for changes in waist circumference over the 7-year period. Previous studies suggest that significant weight loss (e.g., via bariatric surgery) may be associated with sustained improvements in cognition, particularly memory [59]. However, weight loss in older adulthood has also been linked to neurodegenerative disease and increased mortality [2]. Third, we used categorical classification of exposures and covariables which may minimize variability within categories and can minimize relationships between variables. However, we did so in order to facilitate replication of Singh-Manoux and colleagues' study [9], improve clinical relevance (i.e., through use of established clinical cut-offs), and/or to account for potential non-linear relationships. Additionally, our previous work suggests that categorical use of certain covariables (e.g., age, depressive symptoms) is useful in examining cognitive aging in this population [60, 61]. Fourth, we did not examine the relationships between central obesity and cardiometabolic status on risk for cognitive impairment and dementia. Recent work from SOL-INCA has linked diabetes [62] to increased prevalence of MCI. Future studies should examine whether obesity alone or in combination with cardiometabolic factors (e.g., diabetes) increases risk for mild cognitive impairment. Fifth, we did not examine domain-specific cognitive composites, and there may be specific cognitive processes beyond the ones we considered in the present study (i.e., verbal learning and memory, phonemic verbal fluency, processing speed, task switching) that may be more sensitive to the effects of obesity. Additionally, we showed greater declines in processing speed with obesity, yet obesity was linked to advantages on processing speed performance for individuals without metabolic abnormality. Our findings warrant investigations into the mechanisms behind these nuanced relationships between obesity and processing speed. Poorer processing speed has been linked to impairments in instrumental activities of daily living among Hispanics/Latinos [60], and future studies might examine ways to compensate for cognitive slowing when managing such activities. Sixth, certain modifiable (e.g., physical activity) and non-modifiable (e.g., genetics) factors associated with increased risk for obesity [63] may have independent or interactive relations to cognition not explored in our study. Given the limited knowledge on Hispanic/Latino cognitive aging and high prevalence of obesity in this population, these are potential venues for future investigation. Finally, we did not examine factors specific to Hispanics/Latinos (e.g., acculturation) which have been associated with cardiovascular health [64] but not necessarily obesity [65].

Conclusions

Among our population-based cohort of middle-age and older diverse Hispanics/Latinos, central obesity in the presence of cardiometabolic abnormality was associated with poorer cognitive trajectories (i.e., poorer cognitive performance and steeper rate of cognitive decline) than central obesity alone. Examining the intersections of obesity and

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cardiometabolic status is critical to characterizing cognitive health and potentially risk for Alzheimer's disease and related dementias in this underserved community.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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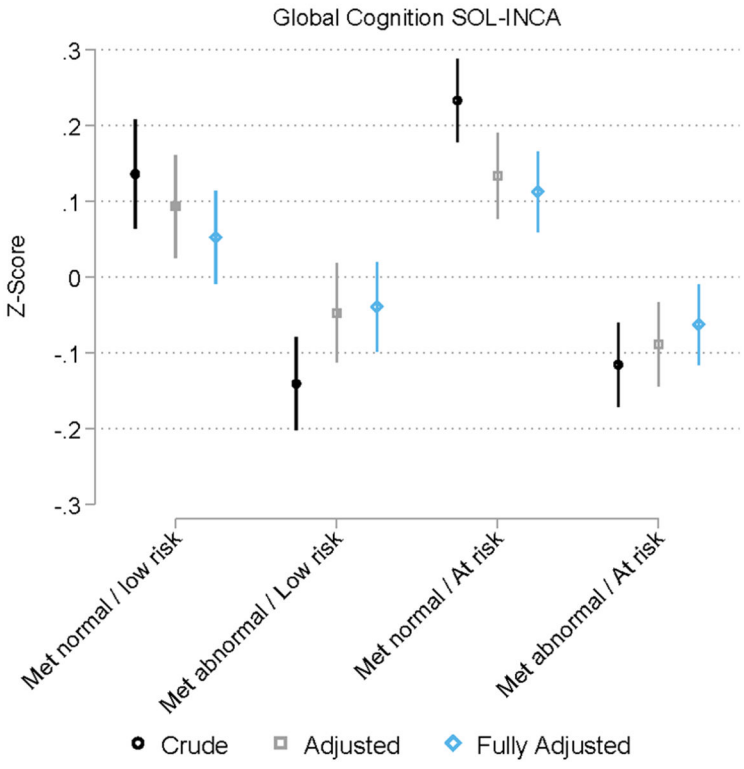
a:



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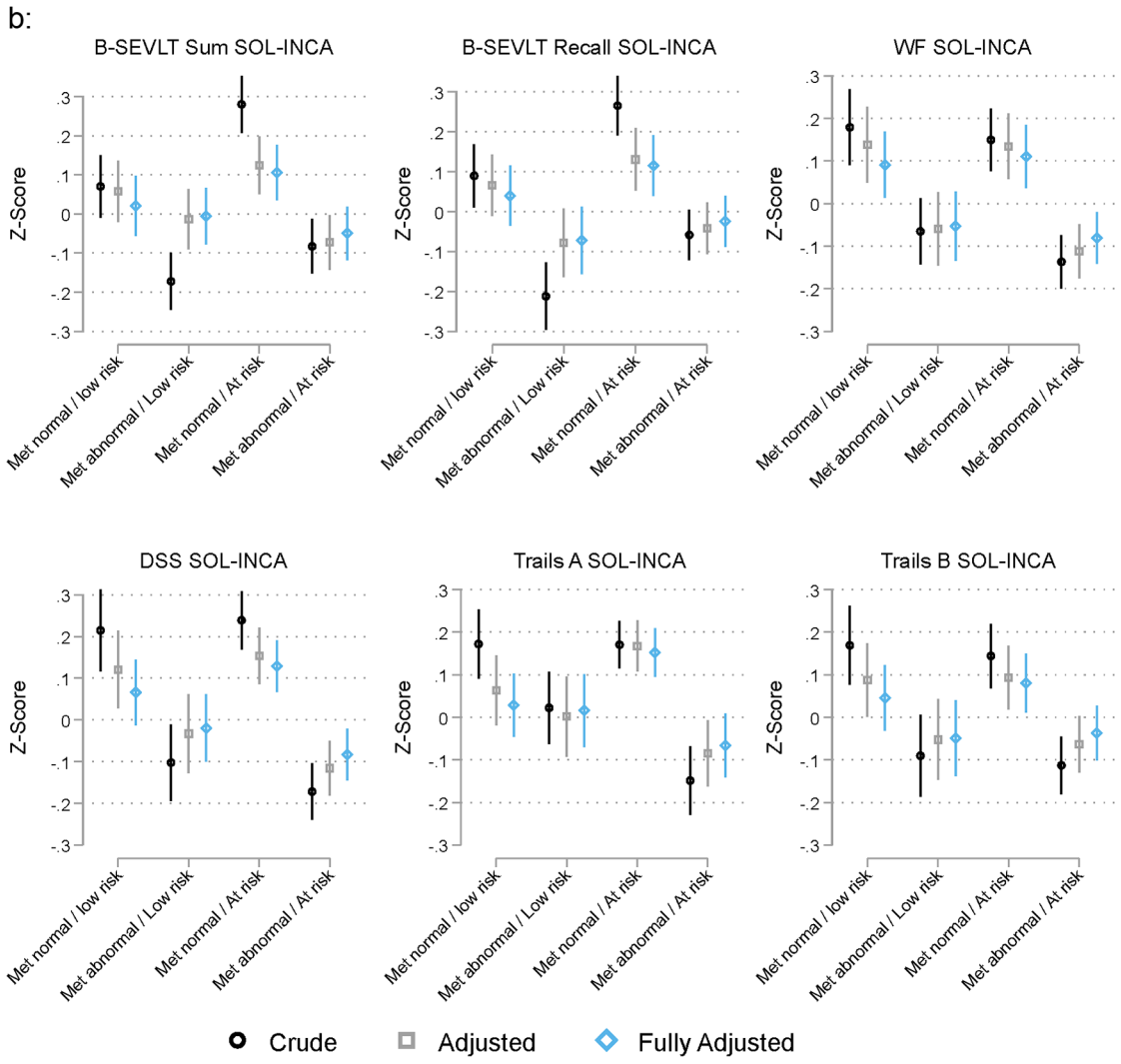

Figure 1.

Average marginal estimates (and 95% confidence intervals) of mean a) global cognitive function and b) individual test scores at SOL-INCA by central obesity[a] and metabolic abnormality.[b,c,d]

Notes:

[a] Central obesity was assessed using sex specific criteria based on individual waist circumference. For women, non-obese and obesity were measured as WC < 88 and WC ≥ 88, respectively. For men, non-obese and obesity were measured as WC < 102 and WC ≥102, respectively.

[b]Trails A and B were reverse coded so that higher values indicate better function. Under the original metric of the Trails A and B higher values (in seconds) indicate lower function.

[c]Adjusted models account for age and sex. Fully Adjusted models account for age, sex, a trichotomous indicator for education (<12, 12, 12+ years), a 6-category indicator of Hispanic/Latino background (Mexican, Puerto Rican, South American, Central American, Cuban, Dominican), and a dichotomous indicator for depression (CESD-10 <10, CESD-10 10+).

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[d]Abbreviations: B-SEVLT= Brief-Spanish English Verbal Learning Test; DSS= Digit Symbol Substitution; Met = Metabolically; SOL-INCA = Study of Latinos - Investigation of Neurocognitive Aging (i.e., second cognitive testing); WF= Word Fluency

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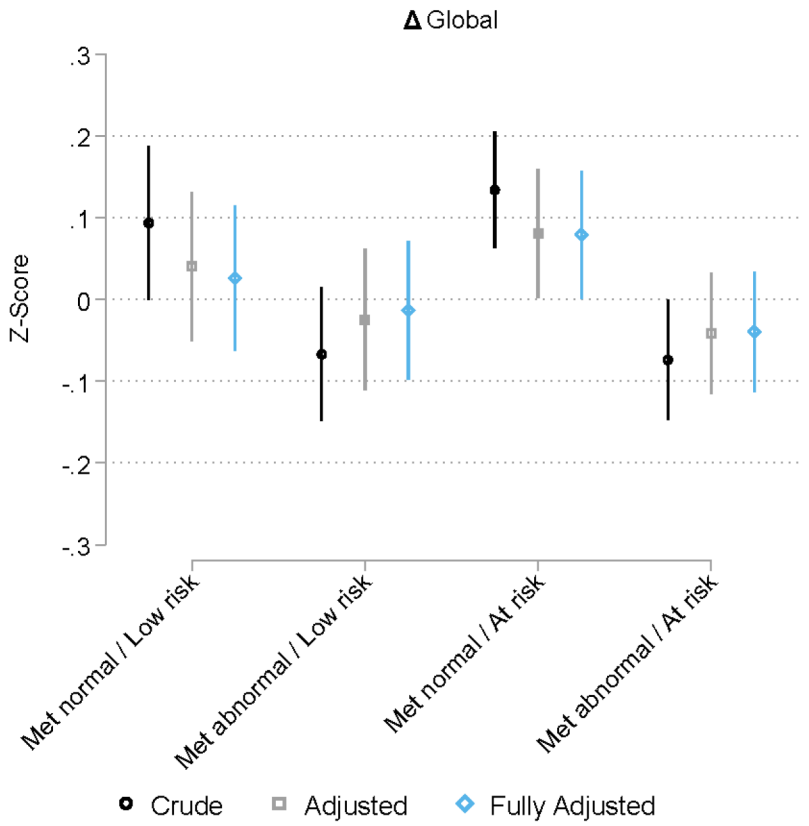
a:



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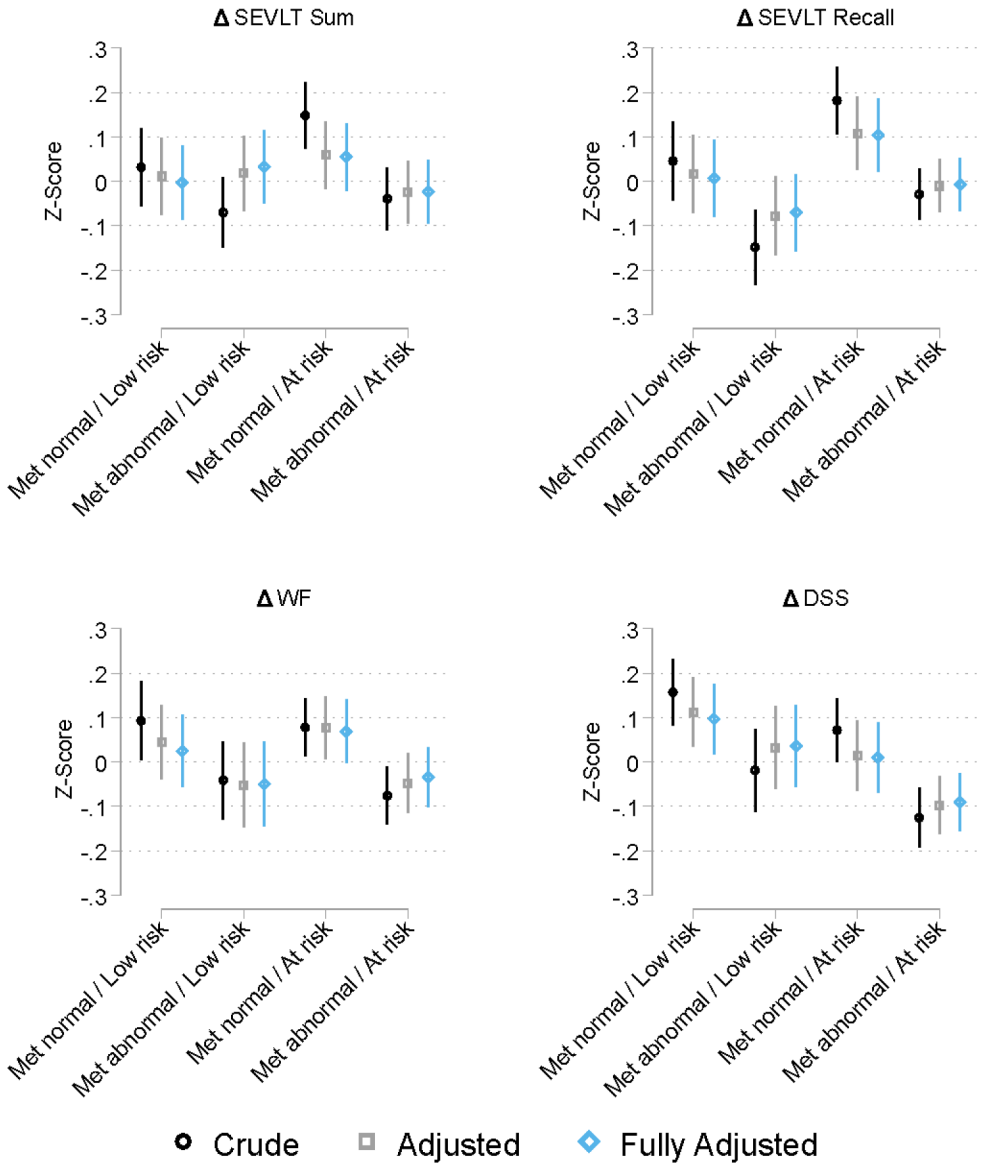

Figure 2.

Average marginal estimates (and 95% confidence intervals) of mean a) global cognitive change and b) change for individual cognitive tests by central obesity[a] and metabolic abnormality. [b,c,d,e]

notes:

[a] Central obesity was assessed using sex specific criteria based on individual waist circumference. For women, non-obese and obesity were measured as WC < 88 and WC ≥ 88, respectively. For men, non-obese and obesity were measured as WC < 102 and WC ≥102, respectively.

[b] Trails A and B were reverse coded so that higher values indicate better function. Under the original metric of the Trails A and B higher values (in seconds) indicate lower function.

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[c] Cognitive change was calculated using survey weighted linear regression, regressing cognitive performance at SOL-INCA on cognitive performance at Visit 1 and adjusting for time elapsed (in days) between cognitive assessments.

[d] Adjusted models account for age and sex. Fully Adjusted models account for age, sex, a trichotomous indicator for education (<12, 12, 12+ years), a 6-category indicator of Hispanic/Latino background (Mexican, Puerto Rican, South American, Central American, Cuban, Dominican), and a dichotomous indicator for depression (CESD-10 <10, CESD-10 10+).

[e] Abbreviations: B-SEVLT= Brief-Spanish English Verbal Learning Test; **Δ** = cognitive change (7 years since baseline); DSS= Digit Symbol Substitution; Met = Metabolically; SOL-INCA = Study of Latinos - Investigation of Neurocognitive Aging (i.e., second cognitive testing); WF= Word Fluency

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Table 1:

Descriptive characteristics for central obesity by metabolic abnormality groups.

	Metabolically Normal		Metabolically Abnormal			
Central obesity*	**Non-obese**	**Obesity**	**Non-obese**	**Obesity**	**Total**	**P-Value**
Unweighted N	1042	1530	886	2572	6030	
%	18.6	21.4	17.2	42.7	100.0	
Education						
<12 years	31.07	36.08	40.18	42.48	38.59	<0.001
12 years	22.72	21.02	20.75	21.27	21.39	
>12 years	46.21	42.90	39.07	36.25	40.02	
Sex						
Female	32.74	82.03	18.65	65.22	54.74	<0.001
Male	67.26	17.97	81.35	34.78	45.26	
Age						
<60 years	52.65	44.67	35.91	30.35	38.52	<0.001
60-69 years	30.97	35.78	35.29	37.65	35.60	
70+ years	16.38	19.55	28.80	32.00	25.88	
Hispanic/Latino Background						
Dominican	9.24	11.76	9.87	8.78	9.69	0.063
Central American	8.15	7.44	7.09	7.49	7.53	
Cuban	27.00	23.42	27.83	28.73	27.12	
Mexican	32.80	38.00	32.71	33.75	34.30	
Puerto-Rican	16.03	13.46	16.55	16.97	15.97	
South American	6.77	5.92	5.95	4.29	5.39	
Depression Score						
<10 CESD-10	75.89	68.29	74.47	64.39	69.10	<0.001
≥10 CESD-10	24.11	31.71	25.53	35.61	30.90	
Mean (SD)						
Age	60.89 (7.46)	61.94 (8.53)	63.83 (7.43)	65.12 (8.31)	63.43 (8.25)	<0.001
BMI	25.02 (2.95)	30.82 (5.28)	26.43 (2.74)	32.65 (5.27)	29.76 (5.50)	<0.001
Triglycerides mg/dL	99.33 (47.86)	105.56 (41.92)	198.1 (142.32)	179.32 (184.05)	151.87 (145.16)	<0.001
Glucose mg/dL	97.27 (27.69)	96.98 (26.78)	116.50 (42.96)	119.18 (43.45)	109.90 (39.45)	<0.001
Systolic Blood Pressure mm Hg	121.12 (13.98)	122.25 (17.28)	132.64 (15.90)	133.60 (19.01)	128.68 (18.23)	<0.001
Diastolic Blood Pressure mm Hg	70.83 (9.11)	73.34 (10.53)	76.12 (9.83)	77.41 (10.97)	75.09 (10.69)	<0.001
HDL Cholesterol mg/dL	55.31 (13.53)	57.06 (13.05)	43.85 (11.16)	45.67 (11.21)	49.59 (13.32)	<0.001

Notes:

*Central obesity was assessed using sex specific criteria based on individual waist circumference. For women, non-obese and obesity were measured as WC < 88 and WC ≥ 88, respectively. For men, non-obese and obesity were measured as WC < 102 and WC ≥102, respectively.

Abbreviations: BMI=Body Mass Index; CESD= Center for Epidemiology Studies Depression Scale; HDL= High Density Lipoprotein; SD=Standard Deviation

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Table 2:

Associations between central obesity and cognitive function at SOL-INCA and cognitive change.

	SOL-INCA		Change	
	β [95% CI]	β [95% CI]	β [95% CI]	β [95% CI]
	Adjusted	Fully Adjusted	Adjusted	Fully Adjusted
Central obesity‡	**Z-Score Global Cognition**		**Z-Score Global Cognition**	
Non-obese	ref	ref	ref	ref
Obese	−0.05 [−0.12;0.02]	−0.02 [−0.08;0.04]	−0.01 [−0.10;0.09]	−0.00 [−0.10;0.09]
	Z-Score B-SEVLT Sum		**Z-Score B-SEVLT Sum**	
Non-obese	ref	ref	ref	ref
Obese	−0.04 [−0.12;0.04]	−0.01 [−0.09;0.06]	−0.01 [−0.09;0.08]	−0.00 [−0.09;0.08]
	Z-Score B-SEVLT Recall		**Z-Score B-SEVLT Recall**	
Non-obese	ref	ref	ref	ref
Obese	0.00 [−0.08;0.09]	0.02 [−0.06;0.11]	0.05 [−0.04;0.14]	0.05 [−0.04;0.15]
	Z-Score WF		**Z-Score WF**	
Non-obese	ref	ref	ref	ref
Obese	−0.08 [−0.17;0.01]	−0.05 [−0.13;0.03]	−0.02 [−0.11;0.07]	−0.01 [−0.10;0.08]
	Z-Score DSS		**Z-Score DSS**	
Non-obese	ref	ref	ref	ref
Obese	−0.07 [−0.16;0.02]	−0.04 [−0.11;0.04]	−0.11 * [−0.20;−0.02]	−0.10 * [−0.19;−0.01]
	Z-Score Reversed Trail A		**Z-Score Reversed Trail A**	
Non-obese	ref	ref	n/a	n/a
Obese	−0.03 [−0.12;0.06]	−0.01 [−0.09;0.07]	n/a	n/a
	Z-Score Reversed Trail B		**Z-Score Reversed Trail B**	
Non-obese	ref	ref	n/a	n/a
Obese	−0.03 [−0.11;0.06]	0.00 [−0.07;0.08]	n/a	n/a

Notes:

‡ Central obesity was assessed using sex specific criteria based on individual waist circumference. For women, non-obese and obesity were measured as WC < 88 and WC ≥ 88, respectively. For men, non-obese and obesity were measured as WC < 102 and WC ≥102, respectively.

Reversed Trails A and B: The two tests were reverse coded so that higher values indicate better function. Under the original metric of the Trails A and B higher values (in seconds) indicate lower function.

Cognitive change was calculated using survey weighted linear regression, regressing cognitive performance at SOL-INCA on cognitive performance at Visit 1 and adjusting for time elapsed (in days) between cognitive assessments.

Adjusted models account for age and sex. Fully Adjusted models account for age, sex, a trichotomous indicator for education (<12, 12, 12+ years), a 6-category indicator of Hispanic/Latino background (Mexican, Puerto Rican, South American, Central American, Cuban, Dominican), and a dichotomous indicator for depression (CESD-10 <10, CESD-10 10+).

Abbreviations: β =standardized coefficient estimate; B-SEVLT= Brief-Spanish English Verbal Learning Test; CESD= Center for Epidemiology Studies Depression Scale; CI= Confidence Interval; DSS= Digit Symbol Substitution; SOL-INCA = Study of Latinos - Investigation of Neurocognitive Aging (i.e., second cognitive testing); WF= Word Fluency

*: p<0.05

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Table 3.

Estimated Fully Adjusted Average Marginal Means of cognitive function at SOL-INCA and cognitive change by central obesity and metabolic abnormality groups

	SOL-INCA			Change		
	Metabolically Normal	Metabolically Abnormal	P-Value	Metabolically Normal	Metabolically Abnormal	P-Value
	β [95% CI]	β [95% CI]		β [95% CI]	β [95% CI]	
Central obesity[‡]	**Z-Score Global Cognition**		**Overall: p<0.001**	**Z-Score Global Cognition**		**Overall: p=0.077**
Non-obese	ref	−0.10 ** [−0.17;−0.03]	0.006	ref	−0.05 [−0.17;0.06]	0.361
Obese	0.05 [−0.03;0.12]	−0.12 ** [−0.19;−0.04]	<0.001	0.05 [−0.07;0.17]	−0.06 [−0.17;0.06]	0.018
P-Value	0.203	0.700		0.393	0.959	
	Z-Score B-SEVLT Sum		**Overall: p=0.005**	**Z-Score B-SEVLT Sum**		**Overall: p=0.527**
Non-obese	ref	−0.04 [−0.14;0.06]	0.445	ref	0.02 [−0.10;0.13]	0.782
Obese	0.07 [−0.04;0.17]	−0.07 [−0.17;0.02]	<0.001	0.05 [−0.06;0.16]	−0.01 [−0.12;0.09]	0.143
P-Value	0.198	0.494		0.373	0.600	
	Z-Score B-SEVLT Recall		**Overall: p=0.001**	**Z-Score B-SEVLT Recall**		**Overall: p=0.026**
Non-obese	ref	−0.12 * [−0.23;−0.02]	0.015	ref	−0.09 [−0.21;0.02]	0.103
Obese	0.05 [−0.05;0.16]	−0.07 [−0.17;0.02]	0.002	0.08 [−0.04;0.20]	−0.02 [−0.13;0.09]	0.026
P-Value	0.327	0.355		0.204	0.178	
	Z-Score WF		**Overall: p<0.001**	**Z-Score WF**		**Overall: p=0.084**
Non-obese	ref	−0.15 ** [−0.25;−0.05]	0.004	ref	−0.06 [−0.20;0.07]	0.353
Obese	0.01 [−0.09;0.11]	−0.17 *** [−0.27;−0.08]	<0.001	0.04 [−0.07;0.14]	−0.07 [−0.17;0.04]	0.016
P-Value	0.832	0.637		0.476	0.956	
	Z-Score DSS		**Overall: p<0.001**	**Z-Score DSS**		**Overall: p=0.010**
Non-obese	ref	−0.09 * [−0.19;−0.00]	0.047	ref	−0.08 [−0.20;0.05]	0.220
Obese	0.07 [−0.02;0.16]	−0.14 ** [−0.23;−0.05]	<0.001	−0.07 [−0.18;0.05]	−0.17 ** [−0.27;−0.06]	0.030
P-Value	0.155	0.353		0.255	0.166	
	Z-Score Reversed Trail A		**Overall: p<0.001**	**Z-Score Reversed Trail A**		
Non-obese	ref	−0.01 [−0.12;0.09]	0.826	n/a	n/a	
Obese	0.14 ** [0.05;0.23]	−0.08 [−0.17;0.02]	<0.001	n/a	n/a	
P-Value	0.003	0.281		n/a	n/a	
	Z-Score Reversed Trail B		**Overall: p=0.007**	**Z-Score Reversed Trail B**		
Non-obese	ref	−0.11 * [−0.22;−0.01]	0.039	n/a	n/a	
Obese	0.03 [−0.07;0.13]	−0.08 [−0.17;0.01]	0.009	n/a	n/a	
P-Value	0.585	0.524		n/a	n/a	

Notes:

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‡Central obesity was assessed using sex specific criteria based on individual waist circumference. For women, non-obese and obesity were measured as WC < 88 and WC ≥ 88, respectively. For men, non-obese and obesity were measured as WC < 102 and WC ≥102, respectively.

Cognitive change was calculated using survey weighted linear regression, regressing cognitive performance at SOL-INCA on cognitive performance at Visit 1 and adjusting for time elapsed (in days) between cognitive assessments.

Reversed Trails A and B: The two tests were reverse coded so that higher values indicate better function. Under the original metric of the Trails A and B higher values (in seconds) indicate lower function.

All estimates are based on fully adjusted models which account for age, sex, a trichotomous indicator for education (<12, 12, 12+), a 6-category indicator of Hispanic/Latino background (Mexican, Puerto Rican, South American, Central American, Cuban, Dominican), and a dichotomous indicator for depression (CESD <10, CESD 10+).

Abbreviations: β =standardized coefficient estimate; B-SEVLT= Brief-Spanish English Verbal Learning Test; CESD= Center for Epidemiology Studies Depression Scale; CI=confidence interval; DSS= Digit Symbol Substitution; SOL-INCA = Study of Latinos - Investigation of Neurocognitive Aging (i.e., second cognitive testing); WF= Word Fluency

* = $p < 0.05$

** = $p < 0.01$

*** = $p < 0.001$. Asterisks reflect differences relative to the reference group (non-obese/metabolically normal) and are based on post-hoc ANOVA contrasts tests

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Table 4.

ANOVA contrasts (difference between metabolically abnormal and metabolically normal groups) of average marginal mean cognitive function at SOL-INCA and cognitive change among individuals with central obesity.

	SOL-INCA		Change	
	Δ	**p-value**	**Δ**	**p-value**
Global Cognition	−0.165	<0.001	−0.109	0.018
B-SEVLT Sum	−0.140	<0.001	−0.064	0.143
B-SEVLT Recall	−0.128	0.002	−0.098	0.026
WF	−0.186	<0.001	−0.105	0.016
DSS	−0.205	<0.001	−0.098	0.030
Trail A (Reverse Coded)	−0.215	<0.001	n/a	n/a
Trail B (Reverse Coded)	−0.107	0.009	n/a	n/a

Notes:

*Central obesity was assessed using sex specific criteria based on individual waist circumference. For women, non-obese and obesity were measured as WC < 88 and WC ≥ 88, respectively. For men, non-obese and obesity were measured as WC < 102 and WC ≥102, respectively.

Cognitive change was calculated using survey weighted linear regression, regressing cognitive performance at SOL-INCA on cognitive performance at Visit 1 and adjusting for time elapsed (in days) between cognitive assessments.

Reversed Trails A and B: The two tests were reverse coded so that higher values indicate better function. Under the original metric of the Trails A and B higher values (in seconds) indicate lower function.

Abbreviations: B-SEVLT= Brief-Spanish English Verbal Learning Test; **Δ** = cognitive differences between metabolically abnormal and metabolically normal; DSS= Digit Symbol Substitution; SOL-INCA = Study of Latinos - Investigation of Neurocognitive Aging (i.e., second cognitive testing); WF= Word Fluency