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Authors

O'Bryant, Sid E
Petersen, Melissa
Hall, James
et al.

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Characterization of Mild Cognitive Impairment and Dementia among Community-Dwelling Mexican Americans and Non-Hispanic Whites

Sid E. O'Bryant, PhD[a,+], **Melissa Petersen, PhD**[a,b], **James Hall, PhD**[a], **Leigh A Johnson, PhD**[a,c], **Robert Barber, PhD**[c], **Nicole Phillips, PhD**[c], **Meredith N. Braskie, PhD**[d], **Kristine Yaffe, PhD**[e,f], **Robert Rissman, PhD**[g,h], **Arthur Toga, PhD**[i],

HABS-HD Study Team

[a]Institute for Translational Research, University of North Texas Health Science Center, Fort Worth, Texas, USA

[b]Department of Family Medicine, University of North Texas Health Science Center, Fort Worth, Texas, USA

[c]Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, USA

[d]Imaging Genetics Center, USC Stevens Neuroimaging and Informatics Institute, Keck School of Medicine of USC, University of Southern California, Los Angeles, CA, USA

[e]Department of Psychiatry, Neurology, and Epidemiology and Biostatistics, University of California, San Francisco, CA, USA

[f]San Francisco VA Medical Center, San Francisco, CA, USA

[g]Department of Neurosciences, University of California, San Diego, La Jolla, CA

[h]Veterans Affairs San Diego Healthcare System, San Diego, CA, USA

[i]Laboratory of Neuro Imaging, USC Stevens Neuroimaging and Informatics Institute, Keck School of Medicine of USC, University of Southern California, Los Angeles, CA, USA

Abstract

Background: Despite tremendous advancements in the field, our understanding of mild cognitive impairment (MCI) and Alzheimer's disease (AD) among Mexican Americans remains limited.

Objective: The aim of this study was to characterize MCI and dementia among Mexican Americans and non-Hispanic whites.

[+]**Address correspondence** to: Sid O'Bryant, PhD, University of North Texas Health Science Center, 3500 Camp Bowie Blvd, Fort Worth, Texas, 76107 USA; sid.obryant@unthsc.edu; 1+817-735-2962.

Conflict of Interest Statement: SEO has multiple patents on precision medicine for neurodegenerative diseases and is the founding scientist of Cx Precision Medicine. No other authors reported any potential conflicts of interest.

Methods: Baseline data were analyzed from n=1705 (n=890 Mexican American; n=815 non-Hispanic white) participants enrolled in the Health and Aging Brain Study- Health Disparities (HABS-HD).

RESULTS: Among Mexican Americans, age (OR=1.07), depression (OR=1.09) and MRI-based neurodegeneration (OR=0.01) were associated with dementia, but none of these factors were associated with MCI. Among non-Hispanic whites, male gender (OR=0.33), neighborhood deprivation (OR=1.34), depression (OR=1.09) and MRI-based neurodegeneration (OR=0.03) were associated with MCI while depression (OR=1.09) and *APOE*ε4 genotype (OR=4.38) were associated with dementia.

CONCLUSIONS: Findings from this study revealed that the demographic, clinical, sociocultural and biomarker characteristics of MCI and dementia are different among Mexican Americans as compared to non-Hispanic whites.

Keywords

Alzheimer's disease; mild cognitive impairment; health disparities; Hispanic

INTRODUCTION

Despite the rapid growth in research on Alzheimer's disease (AD) over the last decade, diverse communities remain largely unrepresented in AD clinical research[1]. For example, approximately 90% of participants in the Alzheimer's Disease Neuroimaging Initiative (ADNI)[2] and over 80% of the participants in the NIA-funded Alzheimer's Disease Centers[3] are non-Hispanic white. African Americans currently suffer the highest burden of AD and AD-related disorders (ADRDs), and Hispanics in the U.S. (65% of which are Mexican American) will experience the largest increase in AD and ADRDs by 2060[4]. Therefore, there is an urgent need to understand AD among diverse communities, which will facilitate a greater understanding of the disease. The Health & Aging Brain – Health Disparities (HABS-HD) study is an ongoing, community-based, multi-ethnic study of health disparities in AD among the largest racial/ethnic groups in the U.S. including Mexican Americans and non-Hispanic whites.

Recent work suggests that factors associated with AD are different among Mexican Americans as compared to non-Hispanic whites. For example, prior work has demonstrated that (1) Mexican Americans have a lower prevalence of the *APOE*ε4 genotype[5–7], the single greatest genetic risk factor for late-onset AD, (2) blood-based proteomic profiles of MCI and AD are different among Mexican Americans as compared to non-Hispanic whites[8–10], and (3) Mexican Americans experience cognitive loss[11] and MRI-based neurodegeneration[12] at significantly younger ages as compared to non-Hispanic whites. More recent data suggests that amyloid (A), tau (T), and neurodegeneration (N) of the (AT[N])-based AD biomarkers are differentially expressed and less strongly associated with MCI and AD diagnosis among Mexican Americans as compared to non-Hispanic whites[11,13]. Here we sought to characterize mild cognitive impairment (MCI) and dementia among Mexican Americans and non-Hispanic whites of the HABS-HD study.

MATERIALS and METHODS

Participants & Assessment

The Health & Aging Brain Study – Health Disparities (HABS-HD; formally the Health & Aging Brain study among Latino Elders, HABLE study) study is an ongoing, longitudinal, community-based project examining health disparities in MCI and AD among Mexican Americans as compared to non-Hispanic whites [9,11–13]. The HABS-HD methods have been published elsewhere[11] and are briefly outlined below. The data included in this study encompasses baseline data from Mexican American and non-Hispanic white participants. Inclusion criteria for the study includes 1) self-reported ethnicity of Mexican American or non-Hispanic white, 2) willingness to provide blood samples, 3) capable of undergoing neuroimaging studies, 4) age 50 and above, and 5) fluent in English or Spanish. Exclusion criteria includes 1) Type 1 diabetes, 2) presence of active infection, 3) current/recent (12 month) cancer (other than skin cancer), 4) current severe mental illness that could impact cognition (other than depression), 5) recent (12 months) traumatic brain injury with loss of consciousness, 6) current/recent alcohol/substance abuse and 7) active severe medical condition that could impact cognition (e.g., end stage renal failure, chronic heart failure, chronic obstructive pulmonary disease).

Participant recruitment for HABS-HD includes a community-based participatory research (CBPR) approach [14]. The CBPR approach has been used successfully as a recruitment modality for reaching underserved and minority populations. It involves collaborating with local communities through outreach (holding community events, seminars), word of mouth, marketing modalities (newspaper, television, radio), and providing information (clinical lab work, MRI clinical reads, neuropsychological test results) back to the participants and their health care providers. The HABS-HD protocol includes an interview, functional exam, blood draw for clinical labs and biobanking, neuropsychological testing and 3T MRI of the brain. All aspects of the study protocol can be conducted in Spanish or English. The HABS-HD study is conducted under IRB approved protocols and each participant (or his/her legal representative) signs written informed consent. All HABS-HD data is available to the scientific community through the UNTHSC Institute for Translational Research (ITR) website[15].

Clinical and Sociocultural

An interview is conducted as part of the HABS-HD protocol, which includes an interview and neuropsychological testing with the following battery: Mini Mental Status Exam (MMSE)[16], Wechsler Memory Scale- Third Edition (WMS-III) Digit Span and Logical Memory[16], Digit Symbol Substitution, Trail Making Test Parts A and B[16], Spanish-English Verbal Learning Test (SEVLT)[17], Animal Naming (semantic fluency) [16], FAS (phonemic fluency)[16] as well as the American National Adult Reading Test (English-speakers)[16], and Word Accentuation Test (Spanish-speakers)[18]. Z-scores were calculated based on normative references generated from the HABS-HD cohort stratified by education (i.e., 0–7 years, 8–12 years and 13+ years), primary language (English or Spanish) and age (median split <=65 and >=66)[11]. An informant interview was also conducted for completion of the Clinical Dementia Rating (CDR) Scale[19] by clinicians with expertise in

dementia to evaluate for functional declines. For the current study, the sociocultural factor included in analyses focused on neighborhood disadvantage using the Area Deprivation Index (ADI). The ADI is a validated measure of U.S. socioeconomic disadvantage[20,21]. The ADI uses 17 U.S. Census and American Community Survey poverty, education, housing and employment indicators to characterize these social determinants within neighborhoods (i.e., block-groups) using methods described previously[20,21]. The ADI has been linked with cognitive[22], imaging[23] and neuropathological[24] AD outcomes. The functional exam includes the Timed Up and Go test (TUG)[25] and Short Physical Performance Battery[26].

Blood Biomarkers

Blood samples were collected, processed and stored per previously published international guidelines[27]. Assay preparation was completed using custom automated StarPlus system from Hamilton Robotics. Plasma markers of amyloid ($A\beta_{42}$, $A\beta_{40}$), tau (total-tau) and neurodegeneration (neurofilament light chain [NfL]) were assayed using the ultra-sensitive SIMOA (single molecule array) technology platform on the HD-X (Quanterix.com)[10,11]. *APOE*ε4 genotyping was performed using commercially available TaqMan assays.

Neuroimaging

MRI Data.—The HABS-HD MRI protocol[11] is based on that of ADNI3 using a 3T Siemens Magnetom SKYRA whole-body scanner. We acquired the following scan sequences: T1-weighted whole brain volumetric spoiled Magnetization-Prepared Rapid Gradient (MPRAGE), whole brain volumetric fluid attenuated inversion recovery (FLAIR), susceptibility-weighted imaging (SWI), diffusion tensor MRI (dMRI), 3D arterial spin labeling (3DPASL), resting-state functional (rsfMRI), and high resolution (0.4 × 0.4 mm × 2 mm) T2-weighted hippocampal high resolution (HHR) scans. For this study, the neurodegeneration (i.e. N) component of the AT(N) framework[28] was derived as outlined by Jack et al[28] as the "meta-ROI", which comprises the surface-area weighted average of the mean cortical thickness in individual ROIs of the entorhinal cortex, fusiform, inferior temporal gyri, and middle temporal gyri. N+ was determined based on a cut-off of 2.68 mm for cortical thickness[28]. Participants who failed quality checks (quality assurance [QA]) for the FreeSurfer software version 5.3.0 segmentation for at least one of the individual ROI sections (referenced above) were excluded when calculating meta-ROI. Meta-ROI was calculated based on the sum of each region in each hemisphere * the surface area for that region divided by the sum of surface areas for all regions included.

Diagnostic Classification

The classification of the cognitive continuum was based on cognitive testing and functional ratings (self and informant), independent of any biomarker profiles, in alignment with the 2018 AT(N) research framework[29]. Cognitive diagnoses[11] were assigned algorithmically (decision tree) and verified at consensus review as follows: Cognitively Unimpaired (CU) = no cognitive complaints, CDR sum of boxes score of 0[30,31] and cognitive tests scores broadly within normal limits (i.e. performance greater than that defined as meeting diagnostic criteria for MCI [i.e. ≤ 1.5 standard deviations below the

normative range]). Of note, participants with an isolated cognitive test score ≤ 1.5 SD below adjusted z-scores, who had no cognitive or functional complaints were assigned as CU; Mild Cognitive Impairment (MCI): cognitive complaint (self or other), CDR sum of boxes score between 0.5– 2.0[30,31] and at least one cognitive test score falling ≤ 1.5 standard deviation below normative ranges; Dementia: CDR sum of boxes score ≥ 2.5[30,31] and at least two cognitive test scores 2 standard deviation below normative ranges. Note that biomarker assignment of amyloid and tau were not available in the current database and, therefore, biomarker assignment of AD or non-AD dementia (or MCI) was not assigned. Medical diagnoses were assigned by licensed clinicians for hypertension, dyslipidemia, and diabetes based on current medications, fasting clinical labs and blood pressure readings.

Statistical Analyses

Statistical Analyses were conducted in SPSS 25 (IBM). Chi-square, ANOVA and ANCOVAs were utilized to compare groups on demographic, sociocultural, clinical and biomarker variables. Logistic regression models were run to determine the impact of each of these variables on cognitive impairment (MCI and dementia). Logistic regression models were run separately for Clinical, Sociocultural, and Biomarker variables with all predictors entered into multi-variate models. Age, gender and education were entered as covariates across models. Analyses were conducted split by ethnicity and diagnostic status. Due to the number of statistical tests conducted, statistical significance was set at $p<0.01$; however, p-values of $p<0.05$ and $p<0.001$ are provided.

RESULTS

Demographic Factors

Table 1 summarizes the demographic characteristics of the cohort by ethnicity and cognitive categorization. Regarding demographic characteristics, Mexican American participants classified as CU ($F=166.95$, $p<0.001$) and MCI ($F=33.01$, $p<0.001$) were younger than non-Hispanic whites in these categories. Therefore, as we demonstrated previously, Mexican Americans appear to develop MCI at significantly younger ages as compared to non-Hispanic whites. There was no significant age difference in the dementia groups. Rates are as follows for Mexican Americans, 74% were diagnosed as CU, 18% as MCI and 7% as Dementia and for Non-Hispanic whites, 82% were diagnosed as CU, 12% as MCI, and 6% as Dementia. Mexican Americans across all cognitive groups had significantly lower levels of formal education completed. There were significantly fewer males in the Mexican American CU ($\chi^2=18.52$, $p<0.001$) and MCI ($\chi^2=18.84$, $p<0.001$) groups. Hypertension was significantly more prevalent in the Mexican American CU group ($\chi^2=7.10$, $p=0.008$) and dyslipidemia was more frequent in the Mexican American dementia group ($\chi^2=5.16$, $p=0.03$) as compared to the non-Hispanic white CU and dementia groups, respectively. Diabetes was significantly more prevalent among the Mexican American CU ($\chi^2=100.24$, $p<0.001$), MCI ($\chi^2=8.89$, $p=0.003$) and dementia ($\chi^2=13.43$, $p<0.001$) groups compared to the same cognitive groups for non-Hispanic whites. Cardiovascular disease was more prevalent in the non-Hispanic white CU ($\chi^2=9.26$, $p=0.002$) group compared to Mexican American CU group. There was no difference found between groups and diagnostic category in history of stroke.

Table 2 and 3 presents the odds ratios of MCI and dementia by ethnicity. MCI Factors: In linear regression models, male gender approached significance with lower prevalence of MCI among Mexican Americans (OR=0.66, 95% CI 0.47–0.95, p=0.02) whereas male gender (OR=0.33, 95% CI 0.21–0.53, p<0.001) was significantly associated with MCI among non-Hispanic whites while age (OR=1.03, 95% CI 1.001 – 1.05, p=0.04) and education (OR=0.91, 95% CI 0.84–0.98, p=0.02) approached significance. None of the medical diagnoses were related to MCI once age, gender and education were entered into the models. Dementia Factors: Among Mexican Americans, age (OR=1.07, 95% CI 1.04–1.11, p<0.001) was associated with dementia while male gender (OR=0.57, 95% CI 0.31–0.89, p=0.02) and education (OR=0.93, 95% CI 0.88–0.98, p=0.01) approached significance. Among non-Hispanic whites, male gender (OR=0.52, 95% CI 0.29–0.96, p=0.04), education (OR=0.88, 95% CI 0.79–0.98, p=0.03) and diagnosis of dyslipidemia (OR=0.51, 95% CI 0.28–0.94, p=0.03) all approached significance for dementia.

Sociocultural Factors

Table 1 summarizes the ADI frequencies by quintile of the cohort by ethnicity and cognitive categorization. ADI quintiles varied among the CU (χ^2=373.49, p<0.001), MCI (χ^2=59.64, p<0.001) and dementia (χ^2=46.15, p<0.001) groups. Overall, Mexican Americans were more likely to reside in areas of greatest neighborhood disadvantage across all cognitive categories. Table 2 and 3 present the odds ratios of MCI and dementia by ethnicity. MCI Factors: Among Mexican Americans, ADI quintiles approached significance for MCI (OR=1.14, 95% CI 0.98–1.34, p=0.09). ADI was significantly associated with MCI among non-Hispanic whites (OR=1.34, 95% CI 1.10–1.63, p=0.004). Dementia Factors: ADI quintiles were not associated with dementia.

Clinical Measures

Table 1 summarizes the clinical characteristics of the cohort by ethnicity and cognitive categorization. Regarding clinical factors, Mexican Americans across all cognitive groups had lower MMSE scores; however, CDR sum of boxes (CDR SB) scores were not different between any groups. Given that MMSE and CDR scores are used in the diagnostic process, these were not included in the logistic regression models. Mexican Americans in the CU (F=32.87, p<0.001) and dementia (F=5.17, p=0.03) groups had higher GDS scores. Table 2 and 3 present the odds ratios of MCI and dementia by ethnicity. Among Mexican Americans, GDS scores were associated with MCI (OR=1.05 95% CI 1.02–1.08, p<0.001) and dementia (OR=1.09, 95% CI 1.05–1.13, p<0.001). Among non-Hispanic whites, GDS scores were also associated with MCI (OR=1.09, 95% CI 1.05–1.14, p<0.001) and dementia (OR=1.09, 95% CI 1.04–1.15, p<0.001).

Biomarkers

Table 1 summarizes the biomarker characteristics of the cohort by ethnicity and cognitive categorization. *APOE*ε4 prevalence was lower among Mexican Americans diagnosed as CU (χ^2=19.52, p<0.001), MCI (χ^2=10.57, p=0.002) and dementia (χ^2=6.69, p=0.012) compared with non-Hispanic whites. Mexican Americans had significantly less neurodegeneration compared to non-Hispanic whites in the MCI grouping based on the MetaROI values (F=13.44, p<0.001) and neurodegeneration (N) positivity rates (χ^2=8.71,

p=0.005). Consistent with the MRI markers of neurodegeneration, Mexican Americans had significantly lower plasma NfL values in the CU (F=29.23, p<0.001) and MCI (F=11.91, p=0.001) groups though there was no significant difference in the dementia group. Plasma Aβ40 levels were significantly lower among the Mexican American CU (F=62.63, p<0.001) and MCI (F=15.90, p<0.001) groups when compared to non-Hispanic whites without any differences in the dementia group. Plasma Aβ42 levels were lower among the Mexican American CU group (F=6.03, p=0.014) compared with the non-Hispanic white CU group. The ratio of Aβ42/Aβ40 was higher among the Mexican American CU (F=24.16, p<0.001) and MCI (F=11.12, p=0.001) groups compared to the non-Hispanic white groups. Plasma total tau levels were significantly higher among the Mexican American CU group (F=17.86, p<0.001) compared with the non-Hispanic white CU group.

Table 2 and 3 present the odds ratios for MCI and dementia by ethnicity with CU as the comparison group. Of note, 217 participants meet exclusion criteria based on failed quality checks for Freesurfer and were excluded from MetaROI analyses. MCI Factors: In a combined model of all biomarker factors (with age, gender and education included as covariates), none of the biomarkers were associated significantly with MCI among Mexican Americans. Among non-Hispanic whites, the MetaROI (OR=0.03 95% CI 0.004–0.33, p=0.003) was significantly associated with MCI. Dementia Factors: Among Mexican Americans, *APOE*ε4 genotype (OR=2.34, 95% CI 1.11–4.95, p=0.03) and MetaROI (OR=0.01, 95% CI 0.00–0.07, p<0.001) were significantly associated with dementia. Among non-Hispanic whites, *APOE*ε4 genotype (OR=4.38, 95% CI 1.62–11.88, p<0.004) was significantly associated with dementia as well as MetaROI (0.00, 95% CI 0.00 – 0.001, p<0.001) although given the OR, the MetaROI does not appear to serve as a sensitive predictor for this group.

DISCUSSION

The current study adds significantly to the extant literature. First, we demonstrate that the demographic, clinical, sociocultural and biomarker characteristics of MCI and dementia are different among Mexican Americans as compared to non-Hispanic whites. We also demonstrate that many of the links between these factors and cognitive diagnostic group vary by ethnicity. These findings are of significance as there are many ongoing, or previously completed, interventions targeting many of these factors. If the prevalence and clinical impact of established "risk factors" varies by racial/ethnic group, then the associated prevention and intervention strategies need to be appropriately tailored to the community of interest. This study also presents the prevalence rates of MCI and dementia in a community-based sample of Mexican Americans and non-Hispanic whites. Although the rates are comparable to other epidemiological studies, they remain lower than that observed among clinic-based cohorts. Discrepancy in disease rates is important to examine as efforts seek to understand AD among minority groups including Hispanics, which are traditionally underrepresented in research and clinical trials.

In our prior examination of 463 Mexican Americans and 633 non-Hispanic whites from the Texas Alzheimer's Research and Care Consortium and Project FRONTIER, we found that Mexican Americans developed cognitive impairment (MCI) at significantly younger ages

and had lower rates of *APOE*ε4 positivity when compared to non-Hispanic whites[7]. In that work, we also found that the prevalence rates of medical comorbidities were different between ethnic groups[7]. Here we replicate those findings in an independent, larger cohort. In the current work, we also expand upon prior findings demonstrating that the prevalence and expression of sociocultural and biomarker factors vary between groups. For example, neurodegeneration as measured by both MRI and plasma measures, were lower among Mexican Americans classified as CU and MCI as compared to non-Hispanic whites. We also found that plasma amyloid and tau markers varied by both diagnostic and ethnic group.

The current findings, in combination with our prior work, further suggests that the MCI stage is different among Mexican Americans as compared to non-Hispanic whites. Specifically, Mexican Americans develop both MCI and neurodegeneration[13] at significantly younger ages; however, overall neurodegeneration is less when compared to non-Hispanic white MCI groups. This may be due to the age discrepancy. However, the prevalence of medical comorbidities also varied, with diabetes being more common among Mexican Americans in the MCI group as compared to non-Hispanic whites. This is in alignment with our recent work where we found that blood-based markers related to metabolic function were of primary importance in the MCI stage among Mexican Americans[9]. Recent work among cognitively unimpaired Mexican Americans also revealed higher levels of medical variables such as triglycerides, glucose, HbA1c, and systolic blood pressure (p-values<0.001) suggesting that Mexican Americans experience changes in medical factors (including metabolic variables) prior to cognitive decline [32]. In line with this, models that considered demographic and medical measurements (e.g., triglycerides, glucose, HbA1c, blood pressure, HDL, eGFR), found that Mexican Americans had lower levels of Aβ40 as well as higher levels of total tau and Aβ42/Aβ40 ratio when compared to non-Hispanic whites[32]. Although the findings from our current study did not reveal a significant link between medical factors and cognitive diagnosis once demographic factors were included in the model, it will be important for future work to examine and better explore the potential mechanisms underlying the conditions that are likely impacted by demographic characteristics particularly among this ethnic group and how this in turn impacts cognitive change and AD biomarkers. Additional work is ongoing within our own group to determine exactly which individuals have a metabolically driven MCI and how factors such as age might impact the course and relationship between metabolic factors and AD biomarkers. This development would inform a novel, precision medicine approach for targeted metabolic-related interventions. In fact, in our recent work, we demonstrated that there is a subgroup of AD patients who specifically benefit from rosiglitazone therapy[33] and, therefore, it is possible that such approaches may be applicable to a sizable portion of Mexican Americans in the MCI stage.

The current work, in combination with prior work, also suggests that heterogeneity of pathology may be greater among Mexican Americans at the MCI and dementia stages. For example, neighborhood disadvantage and depression were both significantly related to risk for cognitive impairment; however, the prevalence of these factors is greater among Mexican Americans. The same is true regarding diabetes. By contrast, pathological factors commonly studied in primarily non-Hispanic white cohorts such as *APOE*ε4 genotype, cerebral amyloid and neurodegeneration appear to be less frequent among Mexican Americans and

the strength of the association of these pathological markers and AD outcomes also seems to vary. These factors combined suggest that the generalizability of the traditional AT(N) framework may need to be adjusted for evaluating AD risk in different ethnic and racial groups as the underlying etiology for Mexican Americans may be more likely related to non-AD etiology as currently defined by available biomarkers in the proposed framework. While the framework itself likely is relevant to diverse communities, the sequence, trajectories and clinical impact of these markers is not established with the current data, suggesting they are different. Therefore, additional work is needed to understand these factors longitudinally, which is ongoing in the HABS-HD study.

There are weaknesses to the current study. First and foremost, the current data is cross-sectional in nature. However, longitudinal examinations are ongoing within the HABS-HD cohort and future studies will examine these factors over time. A second weakness is the exclusion criteria of the study. While the HABS-HD study is far less restrictive than most dementia studies, some conditions such as Type 1 Diabetes, COPD and chronic heart failure were excluded. Therefore, the current results may not necessarily be generalizable to individuals with those diagnoses. A third weakness to the study is the lack of representation of African Americans in the analyses. African Americans, Mexican Americans and non-Hispanic whites represent the three largest racial/ethnic groups in the U.S. HABS-HD is currently enrolling 1,000 African American participants and, therefore, future studies will examine all of these factors across all three racial/ethnic groups. An additional limitation was the sample size of the cohort, which might have impacted the models as a number of analyses revealed significant group differences despite similar odds across groups (reflected in odds ratios close to 1). A final limitation is the lack of known amyloid and tau pathology per the AT(N) framework; however, HABS-HD is currently collecting both amyloid and tau PET scans with future studies to examine these factors. Therefore, pathological markers will soon be available to fully characterize all cognitive diagnostic groups. Therefore, at this time, the contributions to the current results that can be attributed to AD-specific pathology is unknown. Overall, the current study adds substantially to the extant literature demonstrating that the prevalence and clinical impact of many "traditional" factors associated with AD are different among Mexican Americans as compared to non-Hispanic whites.

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Table 1:

Descriptive Characteristics of the Cohort

	Mexican American			Non-Hispanic White					
	CU N=659 Mean (SD)	**MCI N=164 Mean (SD)**	**Dementia N=67 Mean (SD)**	**CU N=669 Mean (SD)**	**MCI N=97 Mean (SD)**	**Dementia N=49 Mean (SD)**	**CU F-value Chi Square (χ^2) p-value**	**MCI F-value Chi Square (χ^2) p-value**	**Dementia F-value Chi Square (χ^2) p-value**
Demographics									
Age, years	63.23 (7.70)	64.55 (8.08)	68.54 (8.73)	68.93 (8.34)	70.97 (9.72)	71.10 (10.54)	F=166.96 p<0.001	F=33.02 p<0.001	F=2.04 p=0.155
Education, years	9.72 (4.52)	9.25 (4.57)	7.48 (4.78)	15.59 (2.58)	15.07 (2.65)	14.92 (2.13)	F=847.59 p<0.001	F=131.17 p<0.001	F=103.47 p<0.001
Gender, % Male	31%	40%	46%	42%	68%	55%	χ^2=18.52 p<0.001	χ^2=18.84 p<0.001	χ^2=0.883 p=0.452
Hypertension, % yes	65%	67%	73%	58%	68%	61%	χ^2=7.10 p=0.008	χ^2=0.02 p=0.892	χ^2=1.84 p=0.227
Diabetes, % yes	35%	36%	49%	11%	19%	16%	χ^2=100.24 p<0.001	χ^2=8.89 p=0.003	χ^2=13.43 p<0.001
Dyslipidemia, % yes	66%	67%	72%	63%	71%	51%	χ^2=1.37 p=0.251	χ^2=0.61 p=0.492	χ^2=5.16 p=0.032
Cardiovascular Disease, % yes	6%	5%	5%	10%	10%	12%	χ^2=9.26 p=0.002	χ^2=2.80 p=0.128	χ^2=2.38 p=0.165
History of Stroke, % yes	1%	5%	6%	2%	2%	2%	χ^2=0.97 p=0.452	χ^2=1.31 p=0.331	χ^2=1.09 p=0.392
Sociocultural									
ADI Quintiles							χ^2=373.49 p<0.001	χ^2=59.63 p<0.001	χ^2=46.15 p<0.001
ADI 1 %	9%	6%	7%	41%	28%	35%			
ADI 2 %	14%	9%	8%	31%	28%	35%			
ADI 3 %	16%	16%	8%	15%	22%	17%			
ADI 4%	30%	34%	33%	10%	17%	13%			
ADI 5%	31%	35%	44%	3%	5%	0%			
Clinical									
CDR SB	0.00 (0.00)	1.08 (0.58)	4.48 (3.23)	0.00 (0.2)	0.99 (0.53)	3.94 (1.87)	F=0.98 p=0.321	F=1.49 p=0.223	F=1.096 p=0.297
MMSE	26.94 (2.66)	25.01 (3.38)	19.85 (6.52)	29.19 (1.02)	28.09 (1.51)	24.04 (4.47)	F=419.06 p<0.001	F=72.40 p<0.001	F=15.02 p<0.001
GDS	5.90 (5.97)	7.82 (6.43)	10.27 (7.66)	4.22 (4.69)	6.77 (6.18)	7.04 (7.36)	F=32.87 p<0.001	F=1.66 p=0.198	F=5.17 p=0.025
Biomarker									
*APOE*ε4 positive	17%	15%	36%	28%	33%	61%	χ^2=19.52 p<0.001	χ^2=10.57 p=0.002	χ^2=6.69 p=0.012
MetaROI thickness (mm)	2.75 (0.13)	2.73 (0.13)	2.58 (0.22)	2.74 (0.13)	2.65 (0.16)	2.48 (0.27)	F=1.07 p=0.299	F=13.44 p<0.001	F=2.82 p=0.097
N Positive	29%	34%	66%	30%	56%	68%	χ^2=0.24 p=0.635	χ^2=8.71 p=0.005	χ^2=0.02 p=1.00

	Mexican American			Non-Hispanic White					
	CU N=659 Mean (SD)	**MCI N=164 Mean (SD)**	**Dementia N=67 Mean (SD)**	**CU N=669 Mean (SD)**	**MCI N=97 Mean (SD)**	**Dementia N=49 Mean (SD)**	**CU F-value Chi Square (χ^2) p-value**	**MCI F-value Chi Square (χ^2) p-value**	**Dementia F-value Chi Square (χ^2) p-value**
Plasma NfL	16.46 (11.48)	18.38 (13.69)	28.49 (25.63)	19.87 (11.01)	26.57 (23.63)	28.03 (16.42)	F=29.23 p<0.001	F=11.91 p=0.001	F=0.011 p=0.916
Plasma Aβ40	236.42 (64.42)	245.21 (71.89)	255.81 (92.88)	264.98 (64.37)	282.56 (69.73)	267.57 (67.52)	F=62.63 p<0.001	F=15.90 p<0.001	F=0.533 p=0.467
Plasma Aβ42	11.77 (3.36)	12.29 (3.65)	11.90 (4.17)	12.22 (3.12)	12.75 (3.44)	12.09 (3.80)	F=6.03 p=0.014	F=0.98 p=0.323	F=0.062 p=0.803
Plasma total tau	2.55 (0.92)	2.64 (1.57)	2.82 (1.31)	2.33 (0.93)	2.47 (1.78)	2.58 (1.14)	F=17.86 p<0.001	F=0.634 p=0.427	F=0.980 p=0.324
Aβ42/ Aβ40 Ratio, Mean (SD)	0.051 (0.015)	0.051 (0.013)	0.049 (0.013)	0.047 (0.013)	0.046 (0.011)	0.046 (0.012)	F=24.16 p<0.001	F=11.12 p=0.001	F=1.76 p=0.186

MCI = Mild Cognitive Impairment, CU = Cognitively Unimpaired, ADI = area deprivation index, Meta ROI = Jack et al meta ROI of neurodegeneration, N positive = neurodegeneration positive based on Meta ROI, CDR SB = clinical dementia rating scale sum of boxes score, MMSE = Mini Mental State Exam, GDS = geriatric depression scale (30-item)

Table 2:

Odds Ratios (95% CI for Odds Ratio) for Mild Cognitive Impairment

	Mexican American N=164	Non-Hispanic White N=97
Demographics		
Age	1.02 (0.99–1.04)	1.03* (1.00–1.05)
Education	0.98 (0.95–1.02)	0.91* (0.84–0.99)
Gender	0.66* (0.47–0.95)	0.33*** (0.21–0.53)
Hypertension	0.97 (0.66–1.43)	1.12 (0.69–1.81)
Diabetes	0.99 (0.68–1.43)	1.36 (0.75–2.46)
Dyslipidemia	0.98 (0.67–1.42)	1.18 (0.72–1.91)
Sociocultural		
ADI Quintiles	1.14 (0.98–1.34)	1.34** (1.10–1.63)
Clinical		
GDS	1.05*** (1.02–1.08)	1.09*** (1.05–1.14)
Biomarker		
APOEε4 positive	0.73 (0.41–1.31)	1.26 (0.69–2.29)
MetaROI	0.47 (0.08–2.76)	0.03** (0.00–0.33)
Plasma NfL	0.99 (0.98–1.02)	1.26 (0.69–2.29)
Plasma Aβ40	1.00 (0.99–1.00)	1.00 (1.00–1.01)
Plasma Aβ42	1.04 (0.85–1.26)	0.96 (0.86–1.07)
Plasma total tau	1.03* (0.85–1.26)	1.14 (0.93–1.41)

NOTE:

*** p<0.001,

** p<0.01,

* p<0.05,

MCI = Mild Cognitive Impairment, ADI = area deprivation index, Meta ROI = Jack et al meta ROI of neurodegeneration, N positive = neurodegeneration positive based on Meta ROI, GDS = geriatric depression scale (30-item), OR= odds ratio. CU group is referent group for comparison purposes.

Table 3.

Odds Ratios (95% CI for Odds Ratio) for Dementia

	Mexican American N= 67	Non-Hispanic White N=49
Demographics		
Age	1.07*** (1.04–1.11)	1.03 (0.99–1.07)
Education	0.93** (0.88–0.98)	0.88* (0.79–0.99)
Gender	0.53* (0.31–0.89)	0.52* (0.29–0.96)
Hypertension	0.95 (0.52–1.74)	0.96 (0.51–1.80)
Diabetes	1.49 (0.87–2.54)	1.38 (0.61–3.15)
Dyslipidemia	1.18 (0.66–2.13)	0.51* (0.28–0.94)
Sociocultural		
ADI Quintiles	1.20 (0.94–1.54)	0.98 (0.74–1.30)
Clinical		
GDS	1.09*** (1.05–1.13)	1.09*** (1.04–1.15)
Biomarker		
APOEε4 positive	2.34* (1.11–4.95)	4.38** (1.62–11.88)
MetaROI	0.01*** (0.00–0.07)	0.00*** (0.00–0.001)
Plasma NfL	1.03 (0.99–1.05)	1.04* (1.01–1.07)
Plasma Aβ40	1.00 (0.99–1.01)	0.99 (0.98–1.0)
Plasma Aβ42	0.96 (0.86–1.08)	1.13 (0.92–1.38)
Plasma total tau	0.86 (0.58–1.28)	1.35 (0.81–2.23)

NOTE:

*** p<0.001,

** p<0.01,

* p<0.05,

ADI = area deprivation index, Meta ROI = Jack et al meta ROI of neurodegeneration, N positive = neurodegeneration positive based on Meta ROI, GDS = geriatric depression scale (30-item), OR= odds ratio. CU group is referent group for comparison purposes.