Characterization of Mexican Americans with Mild Cognitive Impairment and Alzheimer's Disease

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Abstract

Objective—To provide characterization of Mexican Americans who meet criteria for Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI).

Methods—1069 participants ages 40 and above who self-identified as either non-Hispanic white (n=633) or Mexican American (n=436); were recruited using a community-based participatory research (CBPR) approach. Global cognition was assessed via the Mini Mental State Exam (MMSE), dementia severity by the Clinical Dementia Rating Scale (CDR) and depression via the Geriatric Depression Scale 30-item version. Age, gender, education, ApoEε4 allele frequency and diabetic diagnoses were also analyzed.

Results—Mexican Americans (normal controls, MCI and AD) were younger, less highly educated, performed more poorly on the MMSE, endorsed more symptoms of depression, were more likely to be diagnosed with diabetes, and possessed the ApoEε4 allele less frequently. Age was the only significant risk factor for cognitive dysfunction (AD/MCI) among Mexican Americans (OR=1.06, 95% CI = 1.03–1.09). Age (B=0.07, std=0.02, p<0.001) and ApoEε4 presence (B=0.9, std=0.4, p=0.02) were significantly related to increased disease severity.

Conclusions—Given the rapidly growing and aging Mexican American population, there is a substantial need for research into cognitive aging, MCI and AD among this ethnic group. The current findings hold important implications for both clinic and research settings and point to additional research needs.

Keywords

Mild Cognitive Impairment; Alzheimer's disease; Mexican American; Hispanic; cognition; depression; diabetes

Introduction

Alzheimer's Disease (AD) is the most common form of neurodegenerative dementia with over 5.2 million Americans suffering from the disease; every 71 seconds an American develops AD[1]. AD is the 5th leading cause of death for those over 65[1]. It is also estimated that between 10–30% of adults age 65 and above suffer from Mild Cognitive Impairment (MCI)[2], which conveys significant risk for development of AD. When combined, these estimates suggest that anywhere between 8 and 14 million Americans age 65 and above currently suffer from MCI or AD.

While volumes of literature are available on the characterization of MCI and AD among non-Hispanic whites, little research has been produced to date regarding these conditions among Mexican American elders. The population of Hispanics 65 and above will *triple* by the year 2050[3] with the rates of AD expected to grow six-fold[4]. Given that approximately 65% of the U.S. Hispanic population is Mexican American[5], this is the fastest aging segment of the population. Research from our group, and others, suggests that Mexican Americans are (1) diagnosed at more advanced stages of AD progression[6], (2) are diagnosed with AD at younger ages[6], (3) are less likely to have the ApoEε4 allele (the strongest genetic risk for AD among non-Hispanic whites)[7], and (4) suffer from a disproportionate burden of modifiable risk factors for AD (e.g. diabetes)[8]. However, whether these findings hold true among Mexican Americans diagnosed with MCI is unknown. Therefore, there is a significant need for research aimed at those diagnosed with AD and MCI among this underserved ethnic group[4, 6, 9].

The current study was undertaken to provide a characterization of Mexican Americans with MCI and AD. Based on prior work, it was hypothesized that, when compared to non-Hispanic whites, Mexican Americans with AD and MCI would (1) be younger, (2) have poorer global cognition and increased disease severity, (3) have higher rates of diabetes and depression, and (4) express a lower frequency of the ApoEε4 allele.

Materials and Methods

Participants

A total of 1069 participants age 40 and above (Mexican Americans n=436, non-Hispanic whites n=633) were recruited using a community-based participatory research (CBPR) approach. CBPR involves partnering communities with scientific groups to conduct studies of human disease. This approach is growing rapidly in terms of use and acceptance in the scientific community. CBPR is particularly useful when working with underserved communities that may not respond to classic approaches (e.g., random digit dialing, mail surveys); CBPR is supported by the National Institute of Environmental Health Sciences [10]. We partnered with the local hospitals and clinics (including multiple neurology clinics and Federally Qualified Health Centers [FQHCs]) as well as senior citizens' organizations. Our community recruiters and research personnel presented information about the study at community events, churches, food banks, as well as through door-to-door solicitation and clinic-based recruitment. Data for this study came from two independent research projects conducted by our team (Project FRONTIER [Facing Rural Obstacles to health Now Through Intervention, Education & Research] and one site of the Texas Alzheimer's

Research & Care Consortium [TARCC][*]), which have been published extensively elsewhere[11–20]. This research was conducted under an IRB approved protocol with each participant (and/or informants for cognitively impaired persons) providing written informed consent.

Methods

Each participant underwent an interview (i.e., medical history, medications, health behaviors), neuropsychological testing, blood draw, and medical examination (review of systems, Hachinski Ischemic Index scale, brief neurological screen). Global cognition was assessed via the Mini Mental State Examination (MMSE)[21] and disease severity rated according to the Clinical Dementia Rating scale[22] sum of boxes scores(CDR SB)[15, 23]. Depression was assessed with the Geriatric Depression Scale 30-item version (GDS-30)[24]. An informant interview was conducted for each research participant to obtain information regarding his/her activities of daily living (basic and instrumental). All information was presented at a weekly consensus review conference with diagnoses of Alzheimer's disease[25] and MCI[26] assigned according to published criteria by clinical experts in neurology and neuropsychology; cognitively normal control (NC) participants performed within normal limits on psychometric assessment[27]. Diabetes was diagnosed based on medication status, medical history, and when available, fasting glucose and/or HbA1c levels according to the American Diabetes Association 2011 guidelines[28]. Depression (yes/no) was codified based on GDS scores (GDS <10 = not depressed, GDS 10 = depressed). Obesity (yes/no) was categorized based on Body Mass Index Scores (BMI <30 = not obese, BMI 30 = obese). Participants were interviewed and tested in either English or Spanish, based on his/her preference. A total of 39% of the Mexican American sample was tested in Spanish. Information regarding bilingualism and acculturation was not available.

Assays

Non-fasting blood samples were collected with vacutainers tubes at the time of interview into serum-separating (tiger-top) or EDTA plasma (purple top) tubes. Buffy coats were extracted from EDTA plasma collection tubes (purple top) for DNA extraction using Puregene® isolation kits. ApoEε4 genotyped was conducted using standard PCR methods[29]

Statistical Analyses

Analyses of demographic characteristics between diagnostic and ethnic groups were conducted via t-tests (continuous) or χ^2 (categorical) analyses. The link between demographic and genetic data and clinical outcomes of global cognition (MMSE scores) and disease severity (CDR SB scores) was carried out via linear regression with age, education, and gender entered as covariates. The impact of demographic variables on disease risk (i.e., diagnosis) was carried out via logistic regression.

Results

Demographic characteristics of the sample, by diagnostic category and ethnicity, are presented in Table 1. With regards to ApoEε4 genotype, only 267 Mexican Americans (AD

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n=13, MCI n=47, NC n=207) were genotyped as compared to 548 non-Hispanic whites (AD n=121, MCI n=75, NC n=352), which precluded frequency analysis by ethnicity and diagnostic category due to cell sample sizes. Mexican Americans as a combined group, were significantly less likely to carry at least one copy of the ε4 allele (21% versus 32%, χ^2 =10.2, p=0.001). When AD and MCI groups for all participants were combined into a "cognitive impairment group," cognitively impaired Mexican Americans were less likely to carry at least one copy of the ε4 allele (28% versus 51%, χ^2 =11.3, p=0.003). As can be seen from Table 1, this pattern held across all diagnostic categories. As can be seen from Table 1, Mexican Americans were more likely to be classified as obese across diagnostic categories.

Among the NC group, the Mexican American cohort was significantly younger (t=8.5, p<0.001), achieved fewer years of formal education (t=23.4, p<0.001), performed worse on the MMSE (t=9.2, p<0.001), endorsed significantly increased symptoms of depression (t=3.8, p<0.001), were more likely to be classified as depressed (χ^2=14.4, p<0.001), and were more likely to be diagnosed with diabetes (χ^2 =26.0, p<0.001).

Among the MCI group, the Mexican American cohort was significantly younger (t=6.7, p<0.001), achieved fewer years of formal education (t=11.1, p<0.001), performed more poorly on the MMSE (t=2.5, p=0.01), endorsed significantly increased symptoms of depression (t=2.7, p=0.007), and were more likely to be diagnosed with diabetes (χ^2 =5.8, p<0.02).

Among the AD group, the Mexican American cohort was significantly younger (t=4.1, p<0.001), achieved fewer years of formal education (t=11.3, p<0.001), performed more poorly on the MMSE (t=3.5, p=0.001), endorsed significantly increased symptoms of depression (t=3.7, p<0.001), were more likely to be classified as depressed (χ^2=8.0, p=0.005), and were more likely to be diagnosed with diabetes (χ^2 =12.6, p<0.001).

Next, linear regression models were created to determine the impact of the above-outlined significant group differences on clinical outcomes of global cognition (MMSE scores) and disease severity (CDR SB scores). All diagnostic groups were collapsed in order to increase the range of scores. Among non-Hispanic whites, age (B=−0.09, std=0.28, p<0.001) and GDS total scores (B=−0.07, std = 0.03, p=0.008) were negatively related to MMSE scores while education was positively related to MMSE scores (B=0.20, std=0.01, p<0.001). Presence of the ApoEε4 allele was negatively associated with MMSE scores (B=−1.0, std=0.3, p<0.001). Gender and diabetes diagnosis were not related to MMSE scores. Among Mexican Americans, education was positively related to MMSE scores (B=0.3, std=0.1, p<0.001) whereas GDS 30 scores were negatively related to MMSE scores (B=−0.1, std=0.03, p=0.04). Women performed better on MMSE scores than did men (B=1.6, std=0.5, p=0.03). ApoEε4, age, and diabetic status were not significantly related to MMSE scores. When examining CDR SB scores, age (B=0.05, std=0.01, p<0.001) and ApoEε4 presence (B=0.9, std=0.2, p<0.001) were related to significantly increased disease severity among non-Hispanic whites. Among Mexican Americans, advanced age (B=0.07, std=0.02, p<0.001) and ApoEε4 presence (B=0.9, std=0.4, p=0.02) were associated with significantly increased disease severity.

Next, logistic regression models were created to determine the impact of ApoEε4 presence on risk of disease diagnosis. Due to the limited amount of ApoEε4 genotyping available in the Mexican American group, AD and MCI groups were collapsed into a "cognitively impaired" group. As expected, age (odds ratio [OR] =1.12, 95% CI=1.09–1.14, p<0.001), education (OR =0.83, 95% CI = 0.77–0.90, p<0.001), and ApoEε4 presence (OR =4.80, 95% CI = 3.03–7.62, p<0.001) were all significantly related to cognitively impaired status

among non-Hispanics. Among Mexican Americans, age (OR=1.06, 95% CI = 1.03–1.09), was a significant contributor to risk for a cognitive impairment diagnosis. Among Mexican Americans, ApoEε4 presence was not significantly related to increased risk for cognitive impairment (OR=1.95, 95% CI = 0.96–3.94, p=0.06).

Discussion

Our findings confirm prior work regarding AD as well as extend those findings to Mexican Americans diagnosed with MCI. Given the rapidly growing and aging Mexican American population, there is a great need for research into MCI and AD among this underserved segment of the population, which is also the fastest aging ethnic minority group. In fact, a Scopus literature search (7/31/2012) using the search terms "'Mexican American' AND 'mild cognitive impairment'" yielded a total of three articles[30–32] whereas searching for "'Mexican American' AND 'Alzheimer's disease'" yielded nine articles[7, 33–40] The Sacramento Area Latino Study on Aging (SALSA)[7], outside of the current work, is the only available study that conducted detailed neuropsychological assessments to yield careful designation of dementia, mild cognitive impairment, and normal control status. However, we are aware of no prior studies that explicitly sought to provide characterization of Mexican Americans diagnosed with MCI and AD was done here.

First, Mexican Americans diagnosed with MCI and AD were younger than their non-Hispanic counterparts. This point is important given that the average age of our Mexican American MCI cohort was 62 as compared to 74 among non-Hispanic whites. This finding has important implications for research studies examining "geriatric" cognitive aging among Mexican Americans and suggests that the standard 65 and above age of inclusion is insufficient. While the range of MCI ages for the non-Hispanic white sample was as low as 64, Mexican American MCI cases were as young as 50. Additionally, it was found that the low end of the age range for Mexican American AD cases went down to 64. Clinically, this suggests that practitioners may need to revise their notions of "cognitive aging" when working with Mexican American patients.

Educational attainment varied significantly between ethnic groups, which have important implications. Specifically, it will be important to carefully explain medication/treatment regiments to patients and family members and that opportunities for follow-up questions are offered to ensure appropriate understanding. "Non-compliance" should be addressed differently among patients who do not fully understand medication/treatment regimens. Another important finding is the increased expression of depressive symptoms among Mexican Americans both with and without cognitive impairment. In our prior work, we have shown that (1) Mexican Americans presenting to dementia specialty clinics are more likely to endorse affective complaints and (2) the link between depression and neuropsychological functioning is stronger for Mexican Americans[11]. Fitten and colleagues found levels of clinical depression to be higher than anticipated among a sample of 100 community-dwelling Hispanics in California [9]. These findings suggest the need for additional work to determine if treatment of depressive symptoms offers concomitant improvement in cognition and/or slowing of progression of cognitive decline among Mexican Americans.

The lack of a significant link between ApoEε4 and MMSE scores as well as risk of cognitive impairment (AD and MCI) among Mexican Americans was surprising. Others have documented a lower frequency of the ε4 allele among Mexican Americans and the OR of ApoEε4 for risk of cognitive impairment was similar to that found by others[7]. It is still, however, possible that this lack of a significant finding is due to sample size. This decreased ε4 frequency combined with increased diabetes diagnoses suggests the possibility of differential etiological mechanisms underlying cognitive dysfunction among Mexican

Americans. It is likely that the same mechanisms are involved across ethnicity; however, the relative weights of these mechanisms may vary. For example, the increased incidence of diabetes may suggest that inflammation is a more powerful driving factor of cognitive dysfunction among Mexican Americans. Our group is currently testing this hypothesis. In the current sample, Mexican Americans were also more likely to be classified as obese, which should also be investigated for etiological roles.

Overall, the current study highlights the significant differences in presentation and characterization between Mexican Americans and non-Hispanic whites who meet criteria for AD and MCI. Our study suffers from several limitations. First, our sample size was relatively small. Second, longitudinal analyses are necessary to determine the impact of these differences on incident and progression of MCI and AD among Mexican Americans. Our CBPR methodology also likely yielded a different cohort than would have been if patients were strictly recruited from dementia specialty clinics. This methodological difference from many other studies likely had an impact on age of participant by diagnostic group and should be confirmed across other studies. In clinic-based studies, age differences may not be present[6]. Despite these limitations, the current study offers important advancements to the extant literature on AD and MCI among Mexican Americans and highlights the need for additional work among this oft-neglected, rapidly aging, segment of the U.S. population.

Acknowledgments

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Table 1

Demographic Characteristics

	Mexican American			Non-Hispanic White		
	AD (n=35)	MCI (n=67)	NC (n=337)	AD (n=160)	MCI (n=97)	NC (n= 376)
Age (years)	73.6 (9.1)	61.9 (12.3)	58.7 (9.9)	79.4 (7.0)	74.4 (10.6)	65.6 (11.5)
Education (years)	5.9 (4.5)	6.6 (4.2)	8.1 (4.2)	13.2 (3.2)	12.4 (2.5)	14.3 (2.8)
Gender (%male)	45%	38%	29%	39%	33%	32%
MMSE	18.5 (5.0)	24.7 (3.6)	27.5 (2.8)	21.6 (4.6)	26.1 (2.7)	29.0 (1.3)
CDR SB	5.5 (3.6)	0.8 (1.0)	0.1 (0.4)	5.4 (3.3)	1.2 (1.1)	0.1 (0.4)
GDS	9.8 (5.5)	9.3 (1.5)	6.1 (5.6)	5.9 (4.4)	5.6 (0.7)	4.4 (4.7)
Depressed (%yes)	46%	44%	21%	18%	29%	10%
ApoEe4 positive	38%	26%	19%	60%	37%	23%
Diabetes	46%	51%	35%	14%	29%	16%
Obese	27%	45%	47%	13%	16%	25%