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RESEARCH ARTICLE

Bilingual neurocognitive resiliency, vulnerability, and Alzheimer's disease biomarker correlates in Latino older adults enrolled in the Health and Aging Brain Study - Health Disparities (HABS-HD)

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Abstract

INTRODUCTION: The effects of bilingualism on neuropsychological test performance in bilinguals with and without cognitive impairment are not well-understood and are relatively limited by small sample sizes of Latinos.

METHODS: Using analysis of covariance (ANCOVA), we explored patterns of cognitive performance and impairment across a large sample of community-dwelling bilingual and monolingual Latino older adults with ($n = 180$) and without ($n = 643$) mild cognitive impairment (MCI) enrolled in HABS-HD.

RESULTS: Bilinguals demonstrated cognitive resiliency in the form of significantly better performance on the Trail Making Test and Digit Symbol Substitution Test, observed across the cognitively unimpaired and MCI groups. In contrast, bilinguals demonstrated cognitive vulnerability in the form of significantly poorer performance and higher impairment rates on phonemic fluency in the MCI phase, only. Follow-up analyses revealed less balanced bilinguals demonstrated poorer performance and higher impairment rates on this measure, supported by lower levels of plasma Aβ 42/40.

DISCUSSION: Patterns of cognitive performance and impairment differ as a function of bilingualism. Bilingualism must be considered when evaluating cognitive and biomarker outcomes in Latino older adults.

KEYWORDS
bilingualism, cognition, cognitively unimpaired, Latino, MCI

Highlights

- Latino bilinguals perform better on measures of processing speed and coding.
- Latino bilinguals with MCI demonstrate cognitive vulnerability in verbal fluency.
- Less balanced bilinguals demonstrate greatest vulnerability anchored by Aβ 42/40.

1 | BACKGROUND

Society at large is facing a dementia epidemic, with estimates indicating that over 100 million individuals will be living with Alzheimer's disease and/or related dementias (AD/ADRDs) by 2050.[1] In the context of the United States, Hispanic/Latino/Latina (henceforth Latino) older adults are disproportionately affected by AD and demonstrate an earlier age of AD onset relative to non-Latinos whites.[2,3] This increased risk for AD has been linked to greater cardiovascular disease burden,[4,5] fewer years and lower quality of education,[6] and delays in diagnosis and access to treatment.[7–12] Although there has been a significant emphasis on understanding risk factors that influence the development of AD/ADRDs among Latinos, there is a growing appreciation for the need to examine sociocultural and linguistic factors of resiliency that may ultimately protect against cognitive decline in late life.

Bilingualism is a unique life experience that requires the constant management of two languages and has been shown to have an impact on cognitive performance across the lifespan.[13–16] Although results are somewhat mixed across samples, previous work has generally shown that bilinguals demonstrate better performance on executive function tasks,[17–20] but tend to perform more poorly on lexical retrieval tasks relative to monolinguals.[21] The pattern of poorer performance on lexical retrieval tasks may be explained by language interference, vocabulary size and depth, or language proficiency.[21–25] In neurotypical individuals and those with cognitive impairment, bilingualism has also been associated with greater gray and white matter integrity in several brain regions and fiber tracts that support language and cognitive control.[26] In the context of cognitive decline, greater gray matter volume has been observed in regions implicated in language and executive functions, sometimes in the context of poorer performance on category fluency and some executive function tasks,[27] and other times with no significant differences on such tasks[28] (although the language pairs of these studies differ in degree of typological similarity).

Bilingualism is thought to contribute to cognitive and neural reserve, leading to a later age of onset in particular dementia syndromes[29–31] (see also[32–34] reporting no association). However, the majority of work examining the effects of bilingualism has been conducted in relatively small samples of non-Latino and mixed ethnoracial groups (e.g.,[35–37]) with varying degrees of proficiency in each language.[38] As such, our understanding of the basic cognitive profiles of monolingual and bilingual Latino older adults with and without cognitive impairment is severely lacking.[7,12] Mixed findings exist with respect to potential differences in performance on cognitive screening instruments in aging bilinguals[39,40]; however, a greater degree of bilingualism has been associated with higher scores on a subset of neuropsychological measures that assess attention/processing speed and executive functions.[41] These findings indicate that further research characterizing the effects of bilingualism on neuropsychological measures is warranted.

Given that previous literature characterizing cognitive outcomes has been conducted primarily in non-Latino populations, the current study sought to address two specific aims in Latino older adults with and without mild cognitive impairment from the Health and Aging Brain: Health Disparities (HABS-HD) cohort. Our first aim was to characterize bilingual Latinos' performance on standard neuropsychological assessment relative to their monolingual Latino counterparts. We also assessed if language dominance and age of second language acquisition influenced neuropsychological test performance. We hypothesized that bilinguals would perform better than monolinguals on executive function measures, but worse on measures associated with lexical retrieval, and that bilinguals with an earlier age of second language acquisition and more balanced dominance would demonstrate the strongest effects.

Our second aim was to investigate if bilingual Latinos differ in their rates of impairment on a standard neuropsychological assessment compared to their Latino, monolingual counterparts, and again examined the association of these patterns with their language history profiles. We hypothesized that bilinguals would demonstrate greater impairment rates on measures related to lexical retrieval but lower impairment rates on measures related to executive functions.

RESEARCH IN CONTEXT

1. **Systematic review**: The authors reviewed the literature using traditional (e.g., PubMed) sources and meeting abstracts and presentations. While the neuropsychological profiles of healthy aging and mild cognitive impairment (MCI) in bilinguals has been understudied, there have been several recent relevant publications which are cited in the manuscript.
2. **Interpretation**: Our findings suggest a unique clinical phenotype of MCI in bilingual Mexican-Americans, when compared to an ethnically matched monolingual cohort of Mexican-Americans.
3. **Future directions**: Future research should consider the role of distinct bilingual factors on the longitudinal trajectories of change across diagnostic phase in bilingual speakers from historically marginalized groups, with consideration of plasma biomarkers.

2 | METHODS

2.1 | Data availability

Data from the HABS-HD Study were utilized in the current study. The HABS-HD Study is conducted at the University of North Texas Health Science Center (UNTHSC) Institute for Translational Research in Fort Worth, Texas. The HABS-HD study staff utilize community-based participatory research approaches in order to target and include traditionally underrepresented and underrecruited groups and is ded-

TABLE 1 Demographic characteristics of cohort by cognitive status and bilingualism status, means (standard deviations).

	Cognitively unimpaired ($N = 643$)			Mild cognitive impairment ($N = 180$)		
	Monolingual ($n = 267$)	Bilingual ($n = 376$)	p	Monolingual ($n = 86$)	Bilingual ($n = 94$)	p
Ethnicity (% Mexican-American)	100%	100%	1	100%	100%	1
Age (years)	62.92 (7.30)	63.61 (7.95)	0.26	63.38 (7.81)	64.77 (8.45)	0.26
Age of second language acquisition (% early)	N/A	24%	N/A	N/A	25%	N/A
Dominance (% balanced)	N/A	13%	N/A	N/A	22%	N/A
SASH Total	1.50 (1.32)	3.02 (1.51)	**<0.001**	1.19 (.85)	2.87 (1.34)	**<0.001**
Language of interview/assessment (% Spanish)	88%	44%	**<0.001**	95%	45%	
Years of U.S. residency	32.99 (16.28)	51.34 (17.45)	**<0.001**	28.17 (16.45)	52.74 (19.66)	**<0.001**
Nativity (% US Born)	13%	48%	**<0.001**	5%	47%	**<0.001**
Sex	80 M; 187 F	130 M; 246 F	0.23	31 M; 55 F	26 M; 68 F	0.26
Education (years)	7.09 (.4.08)	11.46 (3.96)	**<0.001**	7.44 (4.37)	11.50 (3.67)	**<0.001**
Income	$28,307 (48,905)	$46,710 (55,446)	**<0.001**	$20,207 (15,117)	$38,165 (31,971)	**<0.001**
MMSE (30)	25.79 (3.00)	27.84 (1.88)	**<0.001**	23.45 (3.69)	26.43 (2.40)	**<0.001**
CDR sum of boxes	0.05 (0.20)	0.04 (0.26)	0.48	0.96 (0.71)	0.71 (0.54)	**0.008**

Abbreviations: CDR, Clinical Dementia Rating; MMSE, Mini-Mental State Examination; SASH, Short Acculturation Scale for Hispanics; t-tests and chi-squared tests used where appropriate.
Bold values indicates significant differences.

icated to addressing racial/ethnic disparities in AD.[42] The Institutional Review Board at UNT approved the HABS-HD Study and written informed consent was obtained for all study participants. Exempt institutional review board (IRB) approval was obtained at the University of Texas at Austin for secondary data analysis.

HABS-HD enrollment criteria have previously been described in detail,[42] but briefly, these criteria include community-dwelling adults above the age of 50 that are fluent in English or Spanish, are willing to provide blood samples, and eligible to undergo brain magnetic resonance imaging (MRI) scans. Exclusion criteria included: type 1 diabetes, a history of severe mental illness or an active medical condition that could impact cognition (e.g., end stage renal disease, cancer), a history of a traumatic brain injury with a loss of consciousness within the past 12 months, and meeting DSM-V criteria for current alcohol or substance abuse.[43]

2.2 | Inclusion/exclusion criteria for the present study

Data for 1705 participants was available for use and downloaded on 04/18/2022. The present study consisted of 823 Latino participants that were determined to be cognitively unimpaired (CU, $n = 643$) or to have met criteria for mild cognitive impairment (MCI, $n = 180$). Each participant was required to have basic demographic information, neurocognitive testing, and language data to be included in the present study (see Table 1).

2.3 | Bilingualism status and factors

Bilingualism status was determined via a specific item administered to participants regarding their language history which is included in the Short Acculturation Scale for Hispanics.[44] More specifically, participants were categorized as bilingual if they responded "Yes" to the following question: "Do you speak a secondary language?".[45,46] A positive response to this question was taken as evidence that the participant endorsed speaking a secondary language at the time of interview. On the other hand, participants were categorized as monolingual if they responded "No" to the aforementioned question. This dichotomous grouping was used in the primary analyses outlined in the current manuscript.

In addition, two bilingual factors were examined (1) dominance and (2) age of acquisition. In the current study, bilingual individuals were categorized into one of three dominance groups: balanced, English dominant, or Spanish dominant. Individuals were categorized as balanced if they indicated that they read and speak English and Spanish to an equal extent, as English dominant if they indicated that they read and speak English better than Spanish, and Spanish dominant if they indicated that they read and speak Spanish better than English. In addition, bilingual individuals were categorized into one of two age of acquisition groups: early or late learners of a second language. Individuals were categorized as early bilinguals if they indicated that they used English and Spanish as a child, and as late bilinguals if they indicated only using Spanish or English as a child yet endorsed that they spoke a secondary language at the time of interview.

2.4 | Neuropsychological tests

Participants completed a comprehensive neuropsychological battery comprised of measures of (1) general cognitive and functional abilities as measured by the Clinical Dementia Rating Scale,[47] (2) attention/executive functioning/coding as measured by Trail Making Test Parts A and B,[48] Digit Span Test,[49] and Digit Symbol Substitution,[50] (3) verbal memory as measured by Logical Memory I and II [51] and the Spanish English Verbal Learning Test,[52] and (4) language as measured by letter and animal fluency test.[50] Individuals spoke Spanish, English, or both languages and were able to select their language of interview and testing. As such, the protocol was administered in participants' language of preference. Raw scores for each cognitive test were converted to z-scores that were based on predicted values from demographically-adjusted (age, sex, and education) regression equations from the HABS-HD Latino sample.

2.5 | CU versus MCI diagnostic status

Cognitive status was based upon z-score patterns of neuropsychological test performance. Consistent with previous work in HABS-HD,[42,53] CU status was determined by neuropsychological test scores that were broadly within normal limits (z-score > -1.5) and Clinical Dementia Rating (CDR)[47,54,55] sum of boxes score of 0, a measure that also accounts for activities of daily living. MCI diagnosis was determined by z-scores ≤ -1.5 on at least one cognitive test and CDR sum of boxes score ≥ 0.5 but < 2. Dementia diagnosis was based neuropsychological z-scores ≤ -2 on two or more cognitive tests and CDR sum of boxes score ≥ 2, which was further confirmed in a clinician consensus diagnosis meeting.

2.6 | Genetic and plasma markers

Apolipoprotein E (APOE)-ε4 positivity was determined by the possession of at least one ε4 allele. Assay preparation was completed using a custom automatic StarPlus system from Hamilton Robotics.[42] Baseline serum levels of plasma amyloid beta 40 ($A\beta_{40}$) and 42 ($A\beta_{42}$) and total tau (t-tau) were assessed using the ultra-sensitive Simoa technology platform (Quanterix.com). Lower plasma Ab42/Ab40 is indicative of greater cerebral protein accumulation and plaque formation, but higher t-tau is associated with poor clinical outcomes and increased risk for AD.[56]

Statistical analyses

All analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 26 and R version 3.5.0 (https://cran.r-project.org/). Data were checked for outliers and to ensure no basic statistical assumptions were violated. Multicollinearity statistics were performed prior to analyses and determined to be in the acceptable range for all regression models (variance inflation factor < 1.5, tolerance, < 1, all $rs < 0.4$). Analyses of covariance (ANCOVAs) controlling for age, education, and sex were used to determine whether there were significant group differences across language groups on neuropsychological test performance within each cognitive group (CU vs. MCI). Age, education and sex were included as covariates as these factors may be associated with differences in neuropsychological test performance and in biomarker levels. Tukey's Honest Significant Difference (HSD) was used to assess the significance of differences between pairs of (1) dominance or (2) age of acquisition group means. ANCOVAs controlling for age, sex, and APOE ε4 positivity were used in exploratory analyses comparing bilingual speakers with and without language impairment on plasma AD biomarkers. Effect sizes are reported as Cramer's V and phi (φ) values for the chi-square tests and as partial eta-squared (n_p^2) values for the ANCOVA.

3 | RESULTS

3.1 | Sample characteristics

In the current study, 643 individuals ($n = 267$ monolinguals) without cognitive impairment and 180 individuals ($n = 86$ monolinguals) with MCI were included from the HABS-HD cohort. Differences in sociodemographic measures and in indices of severity were examined between speaker groups and within each diagnostic phase. Across diagnostic phases, bilinguals demonstrated a greater number of years of U.S. residency, education, and higher income and Mini-Mental State Examination (MMSE) scores (all $ps < 0.001$). In the MCI cohort only, significantly lower CDR score was also observed in the bilingual group ($p = 0.008$). See Table 1.

3.2 | Group comparisons on cognitive test performance

3.2.1 | Bilingual versus monolingual by diagnostic phase

Within the CU group, results revealed that bilingual speakers performed significantly better on Trails A ($F = 10.85$, $p = 0.001$, partial $\eta^2 = 0.017$), Trails B ($F = 5.69$, $p = 0.02$, partial $\eta^2 = 0.009$), Digit Symbol Substitution ($F = 8.44$, $p = 0.004$, partial $\eta^2 = 0.013$), and Logical Memory I ($F = 4.12$, $p = 0.04$, partial $\eta^2 = 0.006$). There were no other significant differences on any other cognitive tests ($ps > 0.14$). Within the MCI group, results revealed that bilingual speakers performed significantly better on Trails A ($F = 16.72$, $p < 0.001$, partial $\eta^2 = 0.09$) and Digit Symbol Substitution ($F = 5.55$, $p < 0.02$, partial $\eta^2 = 0.03$). However, bilinguals performed significantly worse on Letter Fluency ($F = 5.22$, $p < 0.02$, partial $\eta^2 = 0.03$) and SEVLT Recall ($F = 4.48$, $p < 0.04$, partial $\eta^2 = 0.03$). No other significant between group differences were found. See Table 2.

TABLE 2 Cognitive test performance in monolingual and bilingual speakers by diagnostic status, means (standard deviations).

	Cognitively unimpaired						Mild cognitive impairment					
	Monolingual	Bilingual	F	*p*	Partial eta^2	Directionality of group comparisons	Monolingual	Bilingual	F	*p*	Partial eta^2	Directionality of group comparisons
Trails A	0.15 (0.87)	0.23 (0.70)	10.85	**0.001**	0.017	**B > M**	−1.19 (1.57)	−0.24 (0.90)	16.72	<**0.001**	0.088	**B > M**
Trails B	0.13 (0.97)	0.28 (0.77)	5.69	**0.017**	0.009	**B > M**	−0.83(1.01)	−0.75 (1.11)	0.652	0.42	0.004	
Digit substitution	0.07 (0.84)	0.28 (0.93)	8.44	**0.004**	0.013	**B > M**	−0.81 (0.90)	−0.58 (1.14)	5.55	**0.02**	0.031	**B > M**
Digit span	0.07 (0.85)	0.18 (1.03)	1.34	0.25	0.002		−0.43 (0.94)	−0.51 (1.02)	0.096	0.76	0.001	
Letter fluency	0.18 (0.92)	0.14 (0.98)	1.45	0.23	0.002		−0.34 (0.86)	−0.76 (0.97)	5.22	**0.02**	0.029	**M > B**
Animal fluency	0.18 (0.97)	0.11 (0.98)	1.73	0.19	0.003		−0.47 (0.92)	−0.53 (0.91)	0.019	0.89	0.000	
Logical memory I	0.14 (0.90)	0.26 (0.90)	4.12	**0.04**	0.006	**B > M**	−0.83 (1.02)	−0.68 (0.94)	1.20	0.28	0.007	
Logical memory II	0.16 (0.91)	0.25 (0.88)	2.16	0.14	0.003		−0.85 (0.99)	−0.69 (0.96)	1.48	0.23	0.008	
SEVLT trails 1-5	0.26 (0.88)	0.16 (0.95)	2.004	0.16	0.003		−0.68 (1.02)	−0.76 (0.85)	0.48	0.49	0.003	
SEVLT recall	0.23 (0.86)	0.24 (0.83)	0.016	0.90	0.000		−0.66 (0.95)	−1.05 (1.09)	4.48	**0.04**	0.03	**M > B**

Note. Mean z-scores and standard deviations are reported for each test.
Abbreviations: B, bilingual; M, monolingual; SEVLT, Spanish English Verbal Learning Test.
Bold values indicates significant differences.

3.2.2 | Effects of bilingualism factors by diagnostic phase

Language dominance

Within the CU group, results revealed a significant effect of language dominance on performance on Trails A (F = 6.15, p = 0.002, partial η^2 = 0.02); however, pairwise post-hoc comparisons were not significant. A significant effect of language dominance was also observed on Digit Substitution performance (F = 4.23, p = 0.02, partial η^2 = 0.01), and post-hoc analyses (Tukey's HSD) revealed that only unbalanced bilinguals performed better than monolinguals (M difference = -0.21, SE = 0. 07, p = 0.01, CI = -0.039–0.04). Within the MCI group, results revealed a significant effect of dominance on Trails A performance (F = 9.45, p < 0.001, partial η^2 = 0.10) and post-hoc analyses revealed that both balanced (M difference = −1.24, SE = 0.31, p < 0.001, CI (−1.97–0.51) and unbalanced bilinguals (M difference = -0.86, SE = 0.20, p < 0.001, CI (−1.34–0.39) performed better than monolinguals. A significant effect of dominance was also observed on Digit Substitution performance (F = 4.83, p = 0.009, partial η^2 = 0.05), and post-hoc analyses revealed that only balanced bilinguals performed better than monolinguals (M difference = -0.62, SE = 0.25, p = 0.04, CI = −1.21–0.03). See Table 3 for omnibus test results and Table S1 for pairwise post-hoc comparisons.

Age of acquisition

Within the CU group, results revealed a significant effect of age of acquisition on Trails A and B performance (F = 6.85, p = 0.001, partial η^2 = 0.02, F = 3.51, p = 0.03, partial η^2 = 0.01); however, pairwise post-hoc comparisons were not significant. A significant effect of age of acquisition was also observed on Digit Substitution (F = 6.85, p = 0.001, partial η^2 = 0.02), and post-hoc analyses revealed that only early bilinguals performed better than monolinguals (M difference = -0.35, SE = 0.11, p = 0.004, CI = -0.60–0.09). A significant effect of age of acquisition was observed on SEVLT Recall (F = 3.21, p = 0.04, partial η^2 = 0.01) and post-hoc comparisons revealed that only early bilinguals performed better than late bilinguals (M difference = -0.28, SE = 0.10, p = 0.02, CI = -0.52–0.04). Within the MCI group, results revealed a significant effect of age of acquisition on Trails A (F = 8.46, p < 0.001, partial η^2 = 0.09), with post-hoc comparisons revealing that both early (M difference = -0.95, SE = 0.29, p = 0.004, CI = −1.64 = 0.26) and late bilinguals (M difference = -0.95, SE = 0.21, p < 0.001, CI = −1.43–0.46) performed better than monolinguals. A significant effect of age of acquisition was also observed on Digit Substitution (F = 4.92, p = 0.008, partial η^2 = 0.05), with only early bilinguals performing better than monolinguals (M difference = -0.59, SE = 0.24, p = 0.03, CI = −1.15–0.04). In addition, a significant effect of age of acquisition was observed on SEVLT Recall (F = 3.08, p = 0.05, partial η^2 = 0.05) and post-hoc comparisons revealed that only early bilinguals performed better than monolinguals (M difference = 0.65, SE = 0.24, p = 0. 02, CI = 0.08–1.21). See Table 3 for omnibus test results and Table S1 for pairwise post-hoc comparisons.

3.3 | Rates of impairment on cognitive testing within MCI group

3.3.1 | Monolingual versus bilingual speakers

Results revealed that monolingual speakers had higher rates of impairment on Trails A relative to bilingual speakers (χ^2 = 16.19, p < 0.001, φ = 0.301). However, bilingual speakers had higher rates of impairment on Letter Fluency relative to monolingual speakers (χ^2 = 10.47, p = 0.001, φ = 0.241). No other significant group differences in rates of impairment were observed across any other cognitive tests (χ^2 = 0.002 to 2.03, ps = 0.11 to 0.97, φs = 0.003 to 0.194). See Table 4.

3.3.2 | Dominance

When the bilingual group was delineated by language dominance, results revealed that there were significant group differences in rates of impairment on Trails A (χ^2 = 22.19, p < 0.001, V = 0.32); pairwise comparisons revealed that monolingual speakers had higher rates of impairment on Trails A relative to unbalanced (p = 0.002, φ = 0.25) and balanced bilingual speakers (p = 0.001, φ = 0.32), but there was no significant difference in the rate of impairment between the bilingual groups (p = 0.11, φ = 0.25). Results also revealed there were significant group differences in rates of impairment on Letter Fluency (χ^2 = 13.37, p < 0.001, V = 0.28). Pairwise comparisons revealed that unbalanced bilinguals had higher rates of impairment relative to monolingual speakers (p < 0.001, φ = 0.28), but there was no significant difference in rates of impairment between balanced bilinguals and monolinguals (p = 0.41, φ = 0.08) or between the bilingual groups (p = 0.15, φ = 0.15). See Table 5.

3.3.3 | Age of acquisition

When the bilingual group was delineated by age of acquisition, results revealed that there were significant group differences in rates of impairment on Trails A (χ^2 = 16.30, p < 0.001, V = 0.30). Pairwise comparisons revealed that monolingual speakers had higher rates of impairment relative to early (p = 0.009, φ = 0.25) and late bilingual speakers (p < 0.001, φ = 0.29), but there was no significant difference in the rates of impairment between the bilingual groups (p = 0.65, φ = 0.05). Results also revealed there were significant group differences in rates of impairment on Letter Fluency (χ^2 = 12.80, p = 0.002, V = 0.27). Pairwise comparisons revealed that late bilingual speakers had higher rates relative to monolingual speakers (p < 0.001, φ = 0.28), but there no significant difference in rates of impairment between early bilinguals and monolinguals (p = 0.24, φ = 0.11) or between the bilingual groups (p = 0.20, φ = 0.13).

TABLE 3 Cognitive test performance by bilingualism factor and diagnostic status, means (standard deviations).

Language dominance												
	Cognitively unimpaired						Mild cognitive impairment					
	Monolingual ($n = 267$)	Unbalanced ($n = 325$)	Balanced ($n = 50$)	F	p	Partial eta^2	Monolingual ($n = 86$)	Unbalanced ($n = 73$)	Balanced ($n = 21$)	F	p	Partial eta^2
Trails A	**0.15 (0.87)**	**0.24 (0.71)**	**0.11 (0.59)**	**6.15**	**0.002**	**0.02**	**-1.15 (0.14)**	**-0.37 (0.15)**	**0.05 (0.28)**	**9.35**	**<0.001**	**0.10**
Trails B	0.13 (0.97)	0.27 (0.79)	0.30 (0.64)	2.85	0.06	0.009	−0.83 (1.01)	−0.74 (1.11)	−0.79 (1.12)	0.34	0.71	0.004
Digit substitution	**0.07 (0.84)**	**0.28 (0.92)**	**0.26 (0.98)**	**4.23**	**0.02**	**0.01**	**-0.81 (0.90)**	**-0.69 (1.19)**	**-0.19 (0.82)**	**4.83**	**0.009**	**0.05**
FAS	0.18 (0.92)	0.16 (0.97)	−0.007 (1.03)	1.46	0.23	0.005	−0.34 (0.86)	−0.80 (1.02)	−0.60 (0.75)	2.96	0.06	0.033
Logical memory I	0.14 (0.90)	0.27 (0.91)	0.20 (0.83)	2.21	0.11	0.007	−0.83 (1.02)	−0.67 (0.89(	−0.72 (1.10)	0.65	0.52	0.007
SEVLT recall	0.23 (0.86)	0.23 (0.82)	0.27 (0.89)	0.03	0.97	0.000	−0.66 (0.95)	−1.02 (1.05)	−1.17 (1.27)	2.37	0.10	0.03
Age of acquisition												
	Cognitively unimpaired						Mild cognitive impairment					
	Monolingual ($n = 267$)	Late ($n = 284$)	Early ($n = 91$)	F	p	Partial eta^2	Monolingual ($n = 86$)	Late ($n = 70$)	Early ($n = 24$)	F	p	Partial eta^2
Trails A	**0.15 (0.87)**	**0.20 (0.72)**	**0.30 (0.62)**	**6.85**	**0.001**	**0.02**	**-1.19 (1.57)**	**-0.24 (0.93)**	**-0.24 (0.83)**	**8.46**	**<0.001**	**0.09**
Trails B	**0.13 (0.97)**	**0.25 (0.81)**	**0.36 (0.65)**	**3.51**	**0.03**	**0.01**	−0.83 (1.01)	−0.78 (1.13)	−0.66 (1.06)	0.48	0.62	0.006
Digit substitution	**0.07 (0.84)**	**0.23 (0.94)**	**0.42 (0.88)**	**6.08**	**0.002**	**0.02**	**-0.81 (0.90)**	**-0.70 (1.06)**	**-0.21 (1.28)**	**4.92**	**0.008**	**0.05**
FAS	0.18 (0.92)	0.12 (0.98)	0.20 (0.99)	0.78	0.46	0.002	−0.34 (0.86)	−0.81 (0.97)	−0.61 (0.98)	2.95	0.06	0.03
Logical memory I	0.14 (0.90)	0.27 (0.89)	0.24 (0.91)	2.06	0.13	0.006	−0.83 (1.02)	−0.70 (0.86)	−0.60 (1.15)	0.60	0.55	0.007
SEVLT Recall	**0.23 (0.86)**	**0.17 (0.81)**	**0.45 (0.84)**	**3.31**	**0.04**	**0.01**	**-0.66 (1.05)**	**-0.96 (1.08)**	**-1.31 (1.15)**	**3.08**	**0.05**	0.04

Note. Mean z-scores and standard deviations are reported for each test.
Abbreviations: FAS, letter fluency total scores; SEVLT, Spanish English Verbal Learning Test.
Bold values indicates significant differences.

TABLE 4 Rates of impairment in monolingual and bilingual speakers with MCI, *n* (% impaired).

	Monolingual ($n = 86$)	Bilingual ($n = 94$)	χ^2	p	φ
Trails A	**31 (36%)**	**10 (11%)**	**16.19**	**<0.001**	**0.30**
Trails B	27 (34%)	26 (28%)	0.68	0.41	0.06
Digit Substitution	22 (26%)	21 (23%)	0.22	0.64	0.04
Digit Span	9 (11%)	14 (15%)	0.84	0.36	0.07
Letter Fluency	**7 (8%)**	**25 (27%)**	**10.47**	**0.001**	**0.24**
Category Fluency	9 (11%)	15 (16%)	1.17	0.28	0.08
Logical Memory I	30 (35%)	23 (25%)	2.35	0.13	0.11
Logical Memory II	25 (29%)	17 (18%)	3.03	0.08	0.13
SEVLT Trails 1-5	19 (22%)	21 (22%)	0.002	0.97	0.003
SEVLT Delayed Recall	18 (23%)	31 (34%)	2.62	0.11	0.12

Note. Data for several subjects were missing across different tests: one bilingual subject was missing data for Trails A, Digit Substitution, and Digit Span; Six monolingual and one bilingual speaker were missing data for Trails B; seven monolingual and three bilingual speakers were missing SEVLT Delayed Recall data. φ = phi effect size estimate.
Bold values indicates significant differences.

3.3.4 | Exploratory AD plasma biomarkers (Aβ 42/40 and t-tau) analyses

Exploratory ANCOVAs controlling for age, sex, and APOE ε4 positivity were conducted in an effort to better understand whether the higher rates of language impairment observed in the bilingual MCI groupings were due to genuine neurological changes associated with AD or potentially false positive diagnoses that may be due to the influence of cultural and linguistic factors on neuropsychological test performance.

3.3.5 | Bilingual speakers: Impaired versus unimpaired letter fluency comparisons

We first compared whether bilinguals with impaired scores on Letter Fluency differed from bilinguals without impairment on the same task in plasma AD biomarkers of Aβ 42/40 and t-tau. Results revealed that bilingual speakers that were impaired in Letter Fluency had significantly lower levels of plasma Aβ 42/40 relative to bilingual speakers that were not impaired in Letter Fluency (F = 5.29, $p = 0.02$, partial $\eta^2 = 0.059$). In contrast, there were no significant group differences between bilingual speakers with and without language impairment on plasma t-tau (F = 1.18, $p = 0.28$, partial $\eta^2 = 0.014$). See Figure 1.

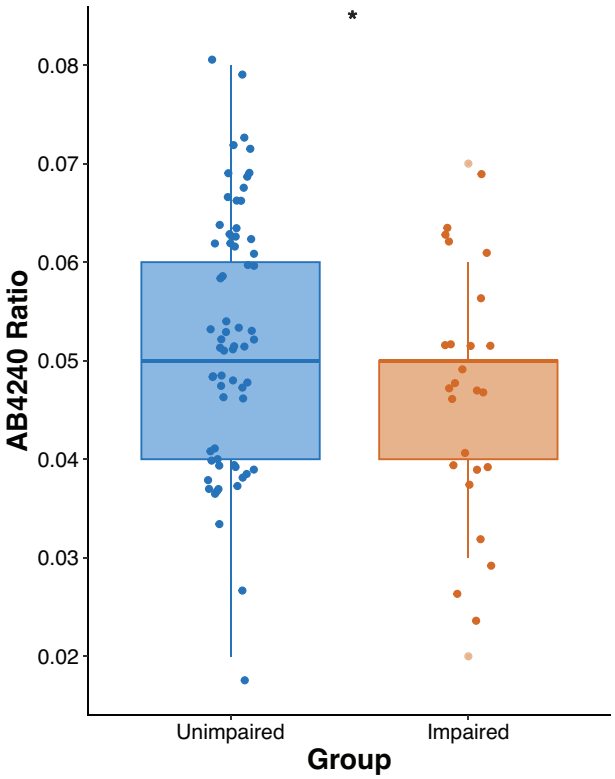

FIGURE 1 Boxplot of significant difference in plasma AB42/40 ratio for those with impaired versus unimpaired performance on letter fluency in bilinguals with MCI.

3.3.6 | Exploratory analyses of plasma levels in unbalanced bilingual speakers (dominance) and late bilingual speakers (age of acquisition) with and without impairment on letter fluency

Results revealed that unbalanced bilingual speakers that were impaired on Letter Fluency had significantly lower levels of plasma Aβ 42/40 relative to unbalanced bilingual speakers that were not impaired on Letter Fluency (F = 5.73, $p = 0.02$, partial $\eta^2 = 0.081$). There were no significant group differences between bilingual speakers with and without language impairment on plasma t-tau (F = 0.06, $p = 0.81$, partial $\eta^2 = 0.001$). Finally, there were no significant group differences between late bilingual speakers with and without language impairment on levels of plasma Aβ 42/40 (F = 2.54, $p = 0.12$, partial $\eta^2 = 0.039$) or t-tau (F = 0.23, $p = 0.63$, partial $\eta^2 = 0.004$). See Figures 2 and 3.

TABLE 5 Rates of impairment by bilingualism factors within the MCI group, *n* (% impaired).

Dominance	Monolingual (*n* = 86)	Unbalanced bilingual (*n* = 73)	Balanced bilingual(*n* = 21)	χ^2	*p*	*V*	Summary of pairwise comparisons	$\varphi_{1\text{-}2}$	$\varphi_{1\text{-}3}$	$\varphi_{2\text{-}3}$
Trails A	31 (36%)	10 (14%)	0 (0%)	22.19$^{\lambda}$	<0.001	0.32	M > U & B Bilinguals	0.25	0.32	0.19
Letter Fluency	7 (8%)	22 (30%)	3 (14%)	13.37$^{\lambda}$	0.001	0.28	U Bilinguals > Monolinguals	0.028	0.08	0.15
Age of Acquisition	**Monolingual (n = 86)**	**Early bilingual (*n* = 24)**	**Late Bilingual (*n* = 70)**	χ^2	*p*	*V*	**Summary of pairwise comparisons**	$\varphi_{1\text{-}2}$	$\varphi_{1\text{-}3}$	$\varphi_{2\text{-}3}$
Trails A	31 (36%)	2 (8%)	8 (12%)	16.30	<.001	0.30	M > E & L Bilinguals	0.25	0.28	0.05
Letter Fluency	7 (8%)	4 (17%)	21 (30%)	12.80$^{\lambda}$	0.002	0.27	L Bilinguals > M	0.11	0.28	0.13

Note. One unbalanced/late bilingual subject was missing data for Trails A. λ = likelihood ratio. Cramer's *V* or φ = phi are effect size estimates. Chi-squared statistics for omnibus test are reported within the table with effect sizes for the follow up pair-wise comparisons.
Abbreviations: B, balanced; E, early; L, late; M, monolingual; U, unbalanced.

FIGURE 2 Boxplot of significant difference in plasma AB42/40 ratio in those with impaired versus unimpaired performance on letter fluency by dominance group.

FIGURE 3 Boxplot of nonsignificant difference in plasma AB42/40 ratio in those with impaired versus unimpaired performance on letter fluency by age of acquisition group.

4 | DISCUSSION

The current study investigated bilingual relative to monolingual Latinos' performance on neuropsychological measures and their corresponding rates of impairment on these measures. These data are quite unique in that the cohort is extremely well-characterized and allows for the examination of patterns of performance *within* the Latino population, with specific languages spoken by study participants (Spanish-English). In addition to examining bilingualism as a dichotomous variable, we examined if particular bilingual factors determined which components of the bilingual experience were driving between-group differences. Exploratory analyses on plasma biomarkers were conducted in order to contextualize our findings regarding rates of impairment in the MCI sample.

4.1 | Mean levels of performance

In the CU group, our hypothesis was partially met as evidenced by bilinguals' higher performance on tasks related to executive function (i.e., Trails B), as well as on tasks related to coding and processing speed (i.e., Digit Substitution and Trails A)[57] or verbal episodic memory (i.e., Logical Memory I). Consistent with our hypothesis, bilinguals performed better on an executive function task, and none of the pairwise comparisons resulting from dominance or age of acquisition analyses survived correction. Although we did not specifically hypothesize greater performance for bilinguals on coding, processing speed, or verbal episodic memory tasks, there is emerging evidence that episodic memory may be enhanced in healthy bilinguals,[58] and may be supported by enhanced volume of hippocampal structures.[59] Our finding of higher performance in verbal episodic memory adds to the existing literature by reporting this pattern in a specific population of bilinguals, namely older Mexican-American adults. With respect to coding (i.e., Digit Substitution), differences between bilingual and monolingual speakers were driven by unbalanced or early bilinguals. Previous work found no difference between Mexican-American older adults and monolingual non-Hispanic Whites on this measure.[60] As such, our findings reflect the value of conducting analyses *within* a specific population as a means to identify how bilinguals compare to monolinguals from the same sociocultural context.

In the MCI group, our hypothesis again was partially met as evidenced by bilinguals' higher performance on a processing speed (i.e., Trails A) and coding (i.e., Digit Substitution) measure coupled with bilinguals' worse performance on letter fluency and verbal recall (i.e., SEVLT recall). Both balanced and unbalanced and early and late bilinguals performed significantly better than monolingual speakers on Trails A. This indicates a general bilingual effect on this measure of processing speed. With respect to coding, we found that differences between bilingual and monolingual speakers were driven by early or balanced bilinguals. This indicates that sustained, ongoing use of both languages is necessary to promote resilience for more general aspects of cognitive functioning in individuals with MCI.

On the other hand, the finding that bilinguals with MCI performed more poorly on letter fluency is consistent with previous reports.[61] Although analyses of dominance and age of acquisition resulted in marginal effects, pairwise analyses indicated that only late or unbalanced bilinguals performed significantly worse than monolinguals on letter fluency. With respect to verbal recall, bilinguals' worse performance was attributed to early bilingual speakers. This latter result may be driven by patterns of language decline. That is, in the context of bilingual AD, it has been documented that reversion to one's first language is common[62]; thus, our finding that bilinguals perform worse on a verbal memory task relative to monolinguals may reflect language decline as 96% of early bilinguals in this cohort selected to be tested in English (their dominant but perhaps not first language).

4.2 | Rates of impairment

With respect to rates of impairment, a similar pattern emerged such that bilinguals presented with lower rates of impairment on a measure of processing speed (Trails A) and higher rates of impairment on letter fluency. Analyses of dominance and age of acquisition again indicated a general bilingual advantage for processing speed (i.e., both unbalanced and balanced and early and late bilinguals had lower rates of impairment). On the other hand, the vulnerability of lexical access was evident only for unbalanced or late bilingual groups. Together, these findings suggest a bilingual phenotype of MCI in Mexican-Americans such that certain aspects of executive functions may be relatively spared and may be indicative of resilience, whereas performance on tasks at the intersection of executive function and language may be particularly vulnerable. Given that only late and unbalanced bilinguals performed worse than monolinguals on letter fluency, it is possible that early acquisition and more balanced dominance are prerequisites for achieving comparable performance on tasks at the intersection of executive function and language when compared to monolinguals. In addition, our ability to reveal change in performance detected between the cognitively unimpaired and MCI phases on letter fluency is likely driven by our ability to match participants in the monolingual and bilingual cohorts by ethnicity and languages spoken (i.e., Spanish-English), which is an extremely unique feature of these data. The absence of several confounding factors (e.g., collapsing across ethnicity, languages, utilizing only a non-Hispanic White monolingual cohort), greatly increases the confidence of the results reported herein. These findings have ramifications for clinical service provision as the results of neuropsychological testing in Mexican-Americans with MCI will indeed differ from their Mexican-American monolingual counterparts. Given that particular bilingual factors are associated with rates of impairment in letter fluency, it will be crucial that clinicians gather bilingualism history from patients and their families to appropriately interpret assessment results.[63,64]

4.3 | Plasma biomarkers in MCI bilingual speakers

Our exploratory analyses of plasma biomarkers documented significantly lower (worse) Aβ 42/40 levels for bilinguals impaired in verbal fluency relative to unimpaired bilinguals. With respect to bilingualism factors, this same pattern was observed only for unbalanced bilinguals. As such, dominance (taken to reflect elements of language use and proficiency) may be particularly useful when investigating the effects of bilingualism on plasma biomarkers in future studies.

The results of these exploratory analyses indicate that our observations garnered from behavioral measures do not simply reflect differences that can be explained as false positives as they are anchored by lower Aβ 42/40 levels. In other words, bilinguals with MCI had impaired scores on letter fluency coupled with worse AD pathology, which suggests that impaired language scores are not merely a consequence of bilingualism on cognitive test performance but rather that impaired language scores may be potentially caused by change in AD pathologic burden across the CU to MCI phase. The absence of such a pattern in the CU phase, together with the presence of this pattern in the MCI phase, demonstrates the need for appropriate comparison groups to avoid a premature or misdiagnosis of MCI.

This notion is supported by recent research from the Neuropsychological Norms for the U.S.-Mexico Border Region project, which has highlighted that population-specific norms are important when evaluating patterns of performance and impairment within Latinos. Researchers have shown that the utilizing norms generated from non-Hispanic White monolingual English-speakers drastically overestimate rates of impairment in the Latino, native Spanish-speaking population. However, as highlighted by a recent review, the effects of bilingualism on neuropsychological test performance in normative data for Spanish-speakers in the United States has not been thoroughly investigated.[30,33] In the current study, we utilized monolingual comparison cohorts that were recruited from the same socio-ethnic background as the bilingual cohorts. As such, our findings also provide evidence that utilizing the appropriate comparison cohorts may elucidate fundamental knowledge regarding the basic phenotypes of MCI and neurodegenerative syndromes within the context of bilingualism. Taken together, these findings indicate the significance of accounting for demographic factors, bilingualism status, and the need to develop methods that do not overestimate rates of impairment in culturally and linguistically diverse populations.

4.4 | Strengths, weaknesses, and future directions

In this study, we analyzed data from a large, well-characterized, community-based sample of Mexican-American older adults with and without cognitive impairment. Although this rich dataset allowed for examination of bilingual factors, the data utilized regarding bilingualism history still lack granularity, and future studies should include patient-friendly, detailed language history questionnaires to facilitate more fine-grained inquiries regarding bilingualism [e.g., [64]], in conjunction with objective measures [see [65–67]]. In the current study, participants could be tested in either English or Spanish based on their personal preference. Because participants are most likely to select their dominant language for testing, the results reported herein reflect differences in participants' strongest and most dominant language. Select studies of Latinos based in the United States have combined the results of English and Spanish testing as a means to represent the results of testing considered to be the most valid.[68] Although testing in a singular language of testing would provide a common ground for the stimuli utilized, testing some bilingual speakers in their nondominant language and others in their dominant language would raise many new confounds that would result serious concerns regarding interpretation of differences between speaker groups. Future research should explore different methods of testing older bilingual adults with and without cognitive impairment [e.g., [69]], as typological differences between languages could influence between-group comparisons, particularly for measures of language.

Nativity has been identified as an important demographic factor when examining cognitive impairment in Mexican-American older adults.[70–72] In the current study, most monolinguals were not born in the United States, and just over half of the bilingual cohort was born in the United States. As such, a future direction of this work is to examine the effects of bilingualism by nativity status, as a means to further characterize the effect of bilingualism in the Mexican-American population. In order to achieve this, it will be important that acculturation measures are developed and utilized which place less emphasis on language as this is only one aspect of acculturation. In addition, ongoing comparisons with bilingual cohorts that are native-born will provide information regarding the effects of bilingualism that are universal, as many bilingual effects have been replicated in bilinguals who do not have a history of immigration [see 36].

The questions we addressed in this study challenge a basic assumption with respect to established patterns of cognitive aging and impairment by considering the influence of bilingualism. By characterizing the unique experiences of historically marginalized populations, diagnosis and management will be much improved. As such, there is a need for future studies to engage individuals with these unique perspectives as a means to improve scientific discovery and clinical practice in ethnically and racially diverse populations. In addition, although the participants reported in the current study reflect individuals from a historically marginalized sub-ethnic sample (i.e., Mexican-Americans), there is much need to investigate such associations in other sub-ethnic and bilingual groups in order to establish the generalizability of the findings reported herein.

5 | CONCLUSION

The majority of research to-date that has characterized older adults with and without cognitive impairment has focused on non-Hispanic Whites. In the current study, we investigated bilingual relative to monolingual Mexican-Americans' performance on neuropsychological measures and performed exploratory analyses on plasma biomarkers to contextualize our findings regarding rates of impairment in the

MCI sample. Results suggest a bilingual phenotype of MCI in Mexican-Americans such that particular components of executive functions may be relatively spared across bilingual groups, whereas executive function tasks that interact with lexical access may be particularly vulnerable in unbalanced or late bilinguals. Clinical service providers should account for bilingual factors in the diagnostic decision-making process in order to elevate the standard of care for this historically underserved and growing segment of the population.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest. Author disclosures are available in the supporting information.

CONSENT STATEMENT

All human subjects provided informed consent for the original study and the current study performed secondary data analysis.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX

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