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RESEARCH ARTICLE

Neurocognitive profiles are associated with subsequent brain integrity in a sample of Hispanics/Latinos: Findings from the SOL-INCA-MRI study (HCHS/SOL)

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Abstract

The Hispanic/Latino population is one of the largest and most diverse ethnoracial groups in the United States at high risk for dementia. We examined cognitive constructs and associations with subsequent hippocampal volume (HV) and white matter hyperintensity volume (WMHV). Participants were from the Hispanic Community Health Study/Study of Latinos–Magnetic Resonance Imaging Study (n = 2029). We examined confirmatory factor analysis and longitudinal invariance using neurocognitive scores at Visits 1 (2008–2011) and 2 (2014–2018) and path analyses. We obtained a longitudinally invariant two-factor episodic memory (EM) and working memory (WM) construct. Lower EM profile at both visits was associated with greater WMHV and smaller HV at Visit 2. Lower WM profile at both visits was associated with larger WMHV and smaller HV at Visit 2. Neurocognitive profiles were associated with subsequent neurodegeneration in a sample of Hispanics/Latinos. Identifying neurocognitive risk profiles may lead to early detection and intervention, and significantly impact the course of neurodegeneration.

KEYWORDS
aging, cognition, Hispanic, Latino, magnetic resonance imaging, neurodegeneration

Highlights

- Cognitive profiles predict brain integrity up to 10 years later.
- We observed two-factor latent memory constructs and longitudinal invariance.
- These findings were observed in a Hispanic/Latino cohort.

1 | BACKGROUND

Exponential growth in global dementia incidence[1] particularly among Hispanics/Latinos, coupled with inequalities in dementia diagnosis and treatment, has augmented the burden of disease for this ethnoracial group within the United States.[2] Hispanic/Latino older adults are highly diverse and are predicted to make up the largest group at elevated risk for Alzheimer's disease and related dementias (ADRD) over the next 40 years.[3] Ongoing longitudinal studies in this group describe an earlier age for mild cognitive impairment (MCI) onset and signs of neurodegeneration, but lower rates of amyloid positivity compared to non-Hispanic Whites.[3] Recent work also observed that the widely accepted biological cascade[4] composed of amyloid, tau, and neurodegeneration (AT[N]) may be differentially represented between non-Hispanic White and Mexican American groups.[5] Specifically, neurodegeneration in the Mexican American cohort was seen before deficits in other biomarkers and was uniquely associated with diabetes and sociocultural factors.[5]

Although neurocognitive decline and neurodegeneration associations have been well-described for non-Hispanic White populations,[6,7] similar research in Hispanic/Latino communities is more limited.[8] In this study, we examined whether cognitive performance at two visits (~7 years apart) is associated with structural magnetic resonance imaging (MRI) measures assessed 10 years later in a large Hispanic/Latino population cohort of middle-aged and older adults. Neurodegeneration signs and symptoms may vary significantly across and within ethnoracial groups.[9] Thus, understanding differences between cognitive trajectories and subsequent MRI measures in these groups will likely contribute to our understanding of the underlying mechanisms leading to dementia onset. Such emerging ethnoracial differences in key dementia biomarkers emphasize the need to focus on both group and person-specific heterogeneity.

Cognitive development varies significantly across the lifespan.[10] This variability is driven largely by biological factors and environmental influences,[11] particularly in minoritized ethnoracial groups.[12] Although increasing age in concert with common brain pathologies plays a fundamental role in all late-life cognitive processes,[13] cognitive trajectories are also dependent on individual-specific risk factors including those leading to Alzheimer's disease (AD).[14,15] Maximally attained ability, coupled with normative and non-normative (illness-related) factors contribute toward an individual's cognitive performance at any given time.[16] Given that "normal aging" is often accompanied by diseases that affect brain health as measured by MRI,[17] cognition across the lifespan may be a promising marker associated with differences in structural brain measures at a later date (see Figure 1). Cognitive screening may also be more cost-effective and easily accessible than structural MRI to identify individuals with high dementia risk profiles. Prior research has focused primarily on whether neurodegeneration predicts future cognitive performance and decline.[18] To our knowledge, studies that associate cognitive function with subsequent MRI measures have rarely been conducted. We examine this relationship to better understand the neurobiological underpinnings between cognitive and brain trajectories in aging.

We examine whether cognitive performance at two separate visits is associated with subsequent MRI measures. Specifically, two common age-related MRI phenotypes were examined, white matter hyperintensity volume (WMHV) and hippocampal volume (HV). Larger WMHVs have been linked to accelerated cognitive decline,[19] and this association is stronger in cognitively healthy adults and those with MCI versus those with dementia.[20] Studies also show that larger HV is positively associated with memory performance across the lifespan in cognitively normal adults.[21] Based on the availability of neuropsychological measures in our cohort, we examine seven cognitive scores representing the memory domain. Specifically, our cognitive test scores measured aspects of episodic memory (EM) and working memory (WM).

We had two sequential research aims. First, we aimed to establish a latent cognitive factor and longitudinal invariance[22] using seven manifest variables from three cognitive tests administered at both the first and second cognitive visits. We expected to observe a one- or two-factor latent memory construct at both visits and longitudinal invariance. Second, we examined the association between the derived latent cognitive scores at both visits and subsequent structural MRI measures. We hypothesized that lower memory factor scores at Visits 1 and 2 would be independently associated with subsequent larger WMHVs and smaller HVs as evidence of poorer brain health, and that this association would be strongest for the neurocognitive tests at the second visit based on its greater proximity to the MRI visit.

2 | METHODS

2.1 | Participants

We used data from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL), an ongoing prospective cohort study of Hispanic/Latino adults from four U.S. metropolitan areas (Bronx, NY; Chicago, IL; Miami, FL; and San Diego, CA).[23] General information regarding recruitment, methodological details, and participant samples are available elsewhere.[24,25] Participants for the present study are from the Study of Latino-Investigation of Neurocognitive Aging-Magnetic Resonance Imaging (SOL-INCA-MRI) study, which includes participants from the HCHS/SOL cohort and those with neurocognitive data from the SOL-INCA, an ancillary study focused on cognitive performance of adults ≈50 years and older.[8] Written informed consent was obtained for all participants. SOL-INCA-MRI and all present data procedures are in full and certified compliance with prevailing human/institutional research ethnics guidelines. SOL-INCA-MRI is an ongoing longitudinal sub-study using brain morphometry to understand how vascular risk burden influences cerebrovascular pathology and AD risk. All participants in SOL-INCA-MRI were 50 years and older, received neuropsychological testing at Visit 2 v, and were willing to undergo MRI. All subjects identified as having MCI were approached as well as a random sample of cognitively normal individuals. For

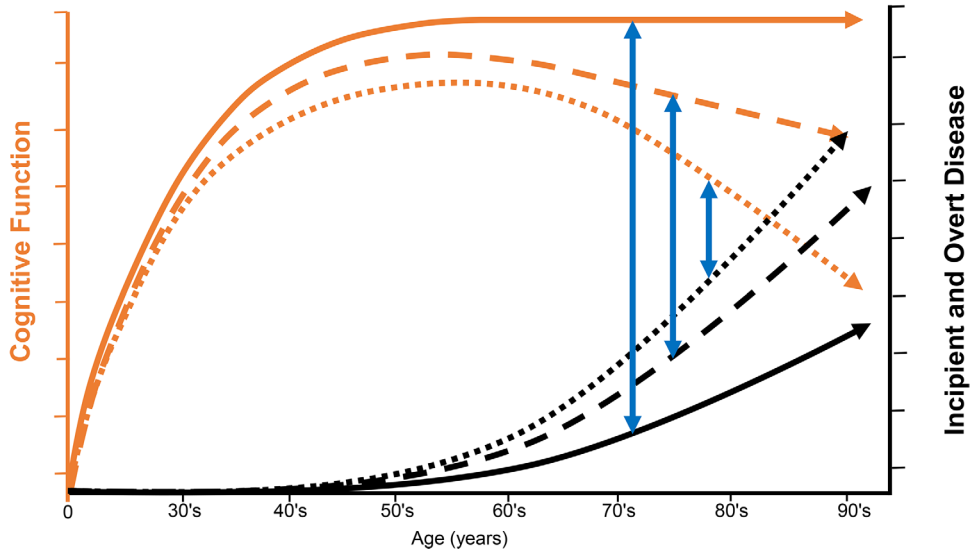

FIGURE 1 Conceptual model for cognition and incipient disease across the lifespan. As individuals age, cognitive function and incipient and overt diseases are positively correlated. Once a threshold is reached, cognitive function will show an exponential decline and incident disease will show an exponential increase. The vertical bidirectional arrows indicate the potential differences in magnetic resonance imaging (MRI) measures that could reflect this process. The dotted lines represent examples of individual trajectories of cognitive function (orange lines) and overt diseases (black lines).

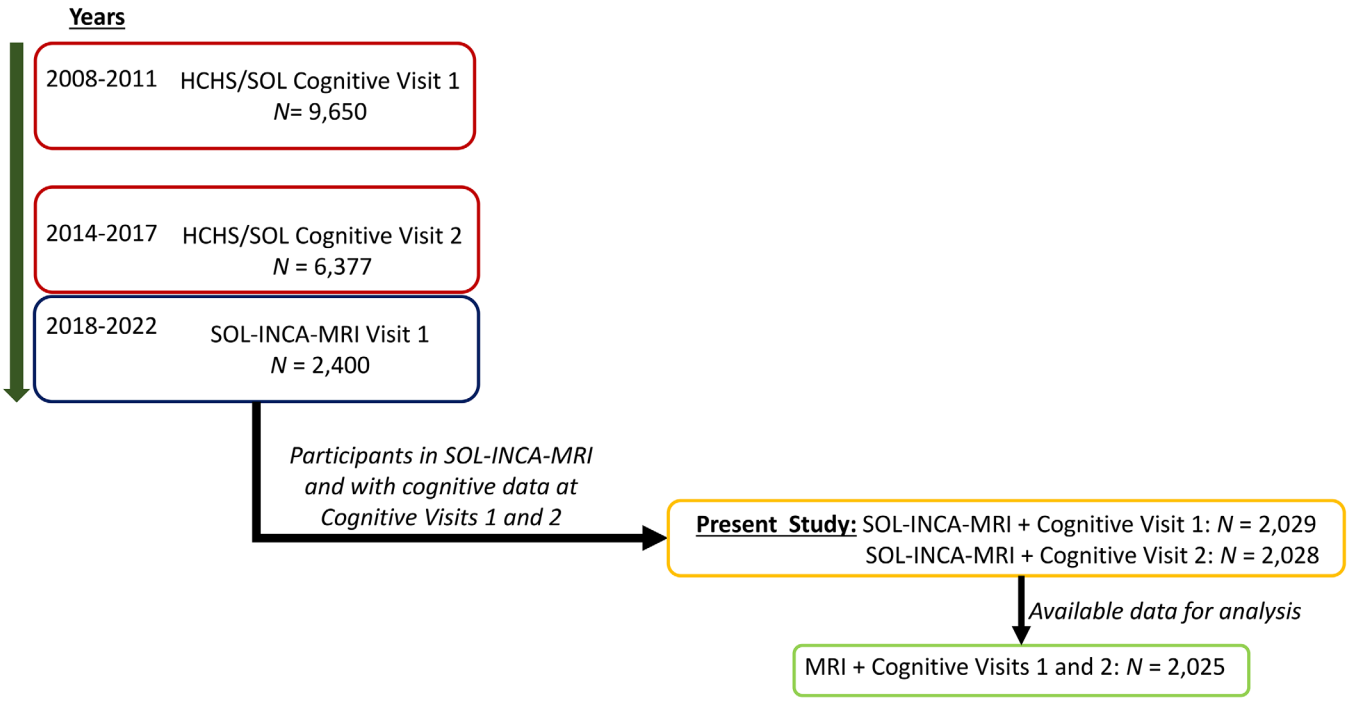

FIGURE 2 Flow chart displaying the sequence of visits leading up to present study sample based on the years that cognitive and magnetic resonance imaging (MRI) data were collected in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) and Study of Latino-Investigation of Neurocognitive Aging-Magnetic Resonance Imaging (SOL-INCA-MRI).

the present study, we included all available participants with cognitive data at Visits 1 and 2 and MRI data ≈10-years after Visit 1 as of July 1, 2023 (see Figure 2). Accordingly, we included n = 2029 older adults (mean cognitive Visit 1 age (SD) = 54.19 (6.75) years old, age range = 43- to 74-years-old, 69.5% women; see Table 1). The difference in participant numbers at Visits 1 and 2 and the MRI visit reflects only those participants with complete cognitive and MRI data.

TABLE 1 Participant demographic characteristics by neurocognitive and magnetic resonance imaging (MRI) visits.

	Neurocognitive Visit 1 (2008–2011)	Neurocognitive Visit 2 (2014–2017)	MRI visit (2018–2022)
N	2029	2028	2025
Age (years)	54.19 (6.75)	61.15 (6.85)	64.39 (6.85)
Sex (F/M)	1407/618	–	–
Education (1/2/3)	782/423/817	–	–
Background	7.8% Dominican/12.9% Central American/15.4% Cuban/36.6% Mexican/16.3% Puerto Rican/8.8% South American/1.3% More than one heritage/0.8% Other	–	–
B-SEVLT 1	5.25 (1.76)	5.31 (1.78)	–
B-SEVLT 2	8.33 (2.23)	8.33 (2.32)	–
B-SEVLT 3	9.94 (2.37)	9.97 (2.43)	–
B-SEVLT recall	8.84 (2.73)	8.62 (2.99)	–
Word Fluency (Letter A)	9.56 (3.99)	8.91 (3.92)	–
Word Fluency (Letter F)	9.44 (3.96)	9.32 (4.07)	–
Digit symbol substitution	35.56 (13.00)	33.24 (12.87)	–
Episodic memory factor score	−0.003 (0.95)	0.004 (0.99)	–
Working memory factor scores	0.007 (0.94)	−0.013 (0.96)	–
Hippocampal volume (residual cc)	–	–	0.001 (0.58)
WMHV (log residual cc)	–	–	−0.005 (1.51)

Note: F = female; M = male; education levels: 1 = less than high school, 2 = up to high school, 3 = greater than high school; MRI = magnetic resonance imaging; B-SEVLT = Brief Spanish-English Verbal Learning Test; cc = cubic centimeter; WMHV = white matter hyperintensity volume.

2.2 | MRI acquisition protocols and processing

Structural MRI scans were obtained using 3T MRI scanner (GE 3T 750, three sites; or Phillips 3T Achieva TX, one site). A combination of high-resolution T1-weighted structural (1 mm^3) and three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) images were examined in the current study. All images were processed at the Imaging of Dementia & Aging Laboratory at University of California, Davis (UC Davis). Regarding the sequence parameters, high-resolution, 3D T1 image acquisitions consisted of Inversion Recovery Spoiled Gradient Echo or Magnetization Prepared Rapid Gradient Echo at $1 \times 1 \times 1$ mm voxel size. FLAIR sequences were also acquired in 3D with $1 \times 1 \times 3$ mm voxel size. The analysis pipeline included a number of steps, including (1) removal of non-brain tissues using neural net method[26] and quality control; (2) image intensity inhomogeneity correction; (3) gray and white matter and cerebrospinal fluid measurement and segmentation, (4) WMH assessment using a modified Bayesian probability structure[27]; and (5) automatic hippocampal segmentation. Complete details on acquisition and image processing are available elsewhere.[23] In the present study, we examined measures of WMHV and HV collected between 2018 and 2022, regressed against total cranial volume (TCV). All WMHV values were natural log-transformed prior to TCV correction to account for non-normal distribution. This approach results in a nearly normal residual distribution, strengthening the statistical inference.

2.3 | Neuropsychological assessments

SOL-INCA neurocognitive data collected across two visits were used in the present study. All neurocognitive assessments were offered in both English and Spanish and administered by bilingual personnel. At SOL-INCA-MRI Visit 1 there were $n = 2029$ participants tested between 2008 and 2011 and at Visit 2, $n = 2028$ participants were tested between 2014 and 2017. In the present study, we used seven cognitive scores based on three distinct neurocognitive tests to evaluate for the best memory latent factor model. Specifically, the Brief Spanish-English Verbal Learning Test (B-SEVLT) words recalled from trials 1–3 (as three separate variables) and B-SEVLT delayed recall, as well as the digit symbol substitution, phonemic word fluency letter A, and word fluency letter F were used.[28] Additional details regarding the psychometric properties of the battery are available elsewhere.[8]

2.4 | Statistical analysis

Baseline participant characteristics by neurocognitive and MRI visits were examined. Continuous measures were summarized using means and SDs, whereas categorical measures were summarized using counts and percentages. We used structural equation modeling (SEM) for all analyses in Mplus Version 8.6.[29] All missing values were assumed to be missing at random and were estimated using maximum likelihood.

Cases with missing predictor values were removed using list-wise deletion in Mplus 8.6. The mean lag time between MRI measurements and neuropsychological assessment for cognitive Visit 1 was 10.21 (1.34) years and for cognitive Visit 2 was 3.25 (1.14) years.

2.4.1 | Confirmatory factor analysis (CFA)

We used confirmative factor analysis (CFA) to determine the best latent cognitive construct(s). Specifically, we examine loadings of all seven manifest variables (B-SEVLT trials 1–3, B-SEVLT delayed recall, digit symbol substitution, and word fluency letters A and F) on the predicted latent variable. The first model examined all cognitive scores on one latent variable. We subsequently examined solutions with two latent variables. The best-fitting model was determined with several model-fit statistics. The chi-square test of model (χ^2; $p > 0.05$) allowed for an overall indication of model fit. Additional absolute/comparative fit indices were also examined to determine model fit to the data.[30] The root-mean-square error of approximation (RMSEA ≤ 0.05), comparative fix index (CFI ≥ 0.95), and the standardized root-mean-square residual (SRMR ≤ 0.08) were used.

2.4.2 | Longitudinal measurement invariance

We tested for longitudinal invariance across the two cognitive visits for the best factor solution. Additional details are included in the supplementary materials.[30]

2.4.3 | Path analyses

Separate path analyses were performed to test the association between performance at cognitive Visits 1 and 2 and subsequent brain morphometry measures (WMHV, HV). Specifically, WMHV and HV were regressed on cognitive factor scores at Visit 1, and we repeated the same set of analyses for Visit 2. All models controlled for age at each visit, sex, education, Hispanic/Latino background, and cognitive-MRI lag time. Education was categorized into three levels (1 = no high school, 2 = up to high school, and 3 = greater than high school diploma). This path analysis was run for each cognitive construct and brain integrity measure at Visit 1 and again at Visit 2. A total of eight path analyses were examined.

We repeated path analyses using cognitive tertiles to test the association between cognitive profiles and subsequent brain morphometry. Specifically, for each cognitive latent construct, tertiles consisted of equal groupings in ascending order using the total sample. Specifically, the low-, intermediate-, and high-performing groups consisted of ≈ 676 individuals each based on their latent factor score rankings in ascending order. Cognitive tertiles were examined to identify how overall cognitive profiles in addition to specific test scores are associated with subsequent brain integrity measures. As supplementary analyses, we ran weighted analyses that account for the non-probability sampling design and survey regression methods, which include the stratification and clustering of observations. This allows for appropriate inferences to the overall HCHS/SOL target population.[23]

3 | RESULTS

Descriptive baseline characteristics of study participants by cognitive and MRI visits are displayed in Table 1.

3.1 | CFA

The one-factor parsimonious cognitive model resulted in poor model fit at both cognitive Visits 1 and 2. We then tested two factors and found that the seven indicators were best represented across two memory factors at both visits. Specifically, B-SEVLT trials 1–3 and B-SEVLT delayed recall loaded on a factor representing verbal learning and memory (henceforth EM) and word fluency letter A, word fluency letter F, and digit symbol substitution loaded on a factor representing working memory (WM) (cognitive Visit 1: $\chi^2(df) = 166.197$ (13), $p < 0.001$, RMSEA = 0.076 (0.066–0.087), CFI = 0.975, SRMR = 0.042; cognitive Visit 2: $\chi^2(df) = 245.734$ (13), $p < 0.001$, RMSEA = 0.094 (0.084–0.104), CFI = 0.965, SRMR = 0.044) (Table 2). Based on the availability of neuropsychological test scores in our cohort, we did not examine other cognitive domains such as executive function or visuospatial ability.

3.2 | Longitudinal measurement invariance

We obtained partial scalar longitudinal invariance across the two cognitive visits (see Table 2) for the two-factor memory model. Obtaining invariance at this level means there are no differences in what our latent construct represents across the two visits, and they are measuring the same factor longitudinally (see Table 2).

3.3 | Path analyses

We observed several significant associations between the two memory factor scores and two brain morphometry measures (Table 3 and Figure 3) across cognitive Visits 1 and 2. First, lower EM at Visits 1 and 2 was associated with greater WMHV burden (Figure 3A). Second, lower WM at Visits 1 and 2 was associated with greater WMHV burden (Figure 3B). Third, higher EM at Visits 1 and 2 was associated with greater HV (Figure 3C). Fourth, higher WM at Visit 2 was associated with greater HV (Figure 3D). For our tertile associations, we observed that older adults in the low, intermediate, and high groups had similar memory scores across the two visits (Figure S1). In addition, we confirmed that adjusting for language preference (Spanish vs English) does not change our significant findings. Using complex study design weights derived from the HCHS/SOL parent study and modified to best

TABLE 2 Confirmatory factor analysis and longitudinal invariance model fit statistics and chi-square difference test for episodic memory and working memory across two visits.

			Two-factor episodic and working memory				
	AIC	BIC	$X^2_M df_M$	RMSEA (90% CI)	CFI	SRMR	$X^2_D df_D$
Confirmatory factor analysis							
Visit 1	68297.967	68421.482	166.197(13); $p < 0.001$	0.076 (0.066–0.087)	0.975	0.042	–
Visit 2	68974.666	69098.191	245.734(13); $p < 0.001$	0.094 (0.084–0.104)	0.965	0.044	–
Longitudinal invariance							
Episodic memory							
	AIC	BIC	$X^2_M df_M$	RMSEA (90% CI)	CFI	SRMR	$X^2_D df_D$
Configural	63455.242	63612.471	232.108 (16); $p < 0.001$	0.082 (0.072–0.091)	0.977	0.022	–
Metric	63450.148	63590.530	233.014 (19); $p < 0.001$	0.075 (0.066–0.083)	0.977	0.022	0.906 (3)
Scalar	63460.031	63583.567	248.897 (22); $p < 0.001$	0.071 (0.063–0.079)	0.976	0.024	15.883 (3)**
Partial scalar[a+]	63448.271	63583.038	233.136 (20); $p < 0.001$	0.072 (0.064–0.081)	0.978	0.022	0.122 (1)
Working memory							
	AIC	BIC	$X^2_M df_M$	RMSEA (90% CI)	CFI	SRMR	$X^2_D df_D$
Configural	70110.539	70228.460	70.046 (6); $p < 0.001$	0.073 (0.058–0.088)	0.991	0.024	–
Metric	70110.309	70217.000	73.816 (8); $p < 0.001$	0.064 (0.051–0.077)	0.991	0.020	3.77 (2)
Scalar	70265.192	703060.652	232.699 (10); $p < 0.001$	0.105 (0.093–0.117)	0.968	0.035	158.886 (2)**
Partial scalar[b+]	70108.317	70209.393	73.824 (9); $p < 0.001$	0.060 (0.047–0.073)	0.991	0.020	0.008 (1)

Note: AIC = Akaike information criteria; BIC = Bayesian information criteria; 'X^2_M = chi-square test of model fit; df_M = degrees of freedom for model fit; RMSEA = root-mean square error of approximation; CI = confidence interval; CFI = comparative tit index; SRMR = standardized root-mean square residual; X^2_D = chi-square test of difference; df_D = degrees of freedom for difference in model fit.

*$p < 0.05$; **$p < 0.001$.

[a]Partial scalar for episodic memory, where the intercept for B-SEVLT list 1 and B-SEVLT list 2 were constrained to be equal across the two visits.

[b]Partial scalar for working memory, where the intercept for Word Fluency (Letter A) and Word Fluency (Letter F) were constrained to be equal across the two visits.

[+]Best model fit.

reflect the subset selection of the SOL-INCA-MRI study resulted in similar relationships (see Tables S1 and S2) between latent variables and subsequent MRI, although the strength of these associations was attenuated somewhat as described in the supplemental materials.

4 | DISCUSSION

The overall aims of our study were to (1) create latent cognitive constructs in a Hispanic/Latino cohort and establish longitudinal invariance across two visits, and (2) to determine whether the cognitive constructs were associated with subsequent measures of brain integrity. We established a two-factor EM and WM factor with longitudinal invariance across two visits. Following this fundamental step, we observed that the two-factor EM and WM latent scores at both visits were significantly associated with subsequent MRI measures. Specifically, lower EM scores at both visits were associated with greater WMHV and lower HV. Lower WM scores at both visits were associated with greater WMHV and lower HV only at Visit 2. Neurocognitive profiles examined as tertiles further supported that an overall higher performing neurocognitive profile was associated with larger HV and smaller WMHV measured years later. This is the first study to report cognitive risk profiles are associated with future MRI structural differences in a large Hispanic/Latino cohort. Our finding advances work on early detection and interventions for this diverse group with increased risk of dementia by identifying specific neurocognitive risk profiles that are associated with neurodegeneration ≈10 years later. Neurocognitive assessments are easier to administer and cost-effective than blood-based and neuroimaging biomarkers.[31] Thus, identifying high cognitive risk profile groups may lead to changes in clinical trials aimed at delaying dementia onset and subsequently influencing the overall burden for both caregivers and health care costs across the United States. Future work should consider testing this in other ethnoracial groups for replication.

In research aim 1, we obtained longitudinally invariant two-factor latent memory construct across two visits in our sample of Hispanic/Latino older adults. This finding establishes a latent memory model with two factors comprising seven manifest variables (B-SEVLT trials 1–3, B-SEVLT recall, digit symbol substitution, and word fluency letters A and F). A latent variable approach provides a superior and robust estimation of the memory construct where measurement errors associated with each indicator are adjusted for in the model.[22] Such latent constructs are not commonly examined or available for Hispanic/Latino populations. By accounting for more than one

TABLE 3 Path analysis results for episodic and working memory with white matter hyperintensity volume (WMHV) and hippocampal volume (HV).

	Episodic memory Visit 1 (continuous)			Episodic memory Visit 1 (tertiles)			Working memory Visit 1 (continuous)			Working memory Visit 1 (tertiles)		
	β	SE	p	β	SE	p	β	SE	p	β	SE	p
WMHV	−0.155	0.035	<0.001	−0.179	0.039	<0.001	−0.143	0.036	<0.001	−0.159	0.041	<0.001
Hippocampal volume	0.035	0.140	0.016	0.037	0.016	0.024	0.030	0.015	0.050	0.033	0.017	0.053
	Episodic memory Visit 2 (continuous)			**Episodic memory Visit 2 (tertiles)**			**Working memory Visit 2 (continuous)**			**Working memory Visit 2 (tertiles)**		
	β	SE	p	β	SE	p	β	SE	p	β	SE	p
WMHV	−0.215	0.034	<0.001	−0.224	0.040	<0.001	−0.148	0.036	<0.001	−0.146	0.041	<0.001
Hippocampal volume	0.049	0.014	0.001	0.046	0.017	0.006	0.024	0.015	0.111	0.038	0.017	0.026

Note: β = beta estimate. SE = standard error.

manifest variable, the shared common variance among multiple indicators is used to determine the underlying latent construct. Although large inter-individual differences and intra-individual variability are typically observed with age and possibly even Hispanic/Latino background, we acquired longitudinal invariance for our two-factor memory model. This fundamental step in latent construct allows us to examine the same invariant construct across two visits in our large and diverse Hispanic/Latino sample. To our knowledge, this is one of the only studies of Hispanic/Latino individuals from diverse heritage groups to establish cognitive constructs and longitudinal invariance.

In our second research aim, we observed that each factor, EM and WM, regardless of continuous or tertile measurement, was associated with differences in subsequent HV and WMHVs. Subtle changes in memory profiles across the lifespan may be a precursor to neurodegeneration[13] in late life in Hispanic/Latino adults. Validation studies should consider examining this approach as a potential screening tool for adults who are at a higher risk of brain atrophy or neurodegeneration ultimately resulting in significant ADRD-related cognitive deficits. This method may provide a relatively inexpensive and globally accessible resource for health care and early dementia diagnosis in Hispanic/Latino populations.

Memory factor scores may also indirectly represent brain reserve,[32] where the rate of subsequent neurodegeneration is composed of concurrent brain reserve and cognitive performance. Future research should consider examining longitudinal memory changes as well as their associations with brain reserve and integrity over time. As expected from prior cross-sectional and longitudinal brain-cognition findings,[33,34] the neurocognitive profile collected closest in time was more consistently associated with brain morphometry in the current study. Larger interval differences between measurements may imply greater discrepancies resulting in stronger concurrent brain-cognition associations. It is also important to note the uncertainty of risk and protective factors within this measurement interval and its impact on brain-cognition associations. Normal cognitive trajectories from early adulthood typically show a decline in memory and speed measures, whereas vocabulary and general knowledge increase up to 60 years of age.[35] Thus, identifying specific cognitive domains and their threshold or deflection points as early as possible will result in earlier detection of individuals at higher risk of accelerated cognitive decline and subsequent dementia diagnosis.

A few strengths and limitations of the present study should be noted. Regarding, limitations, first, our middle-aged and older adult sample included only a Hispanic/Latino population and may not be generalizable to other ethnoracial groups. However, our sample includes a diverse group of Hispanic/Latino adults including people of Mexican, Cuban, Dominican, Puerto Rican, and Central and South American heritages (Table 1). Second, our MRI sub-sample findings may not represent the SOL-INCA study population, as it includes only those who qualified and were generally younger and willing to have MRI. When we included weighted results as representative of the Hispanic/Latino population, the general findings remained, but were somewhat attenuated (see supplementary materials). Third, our ongoing data collection

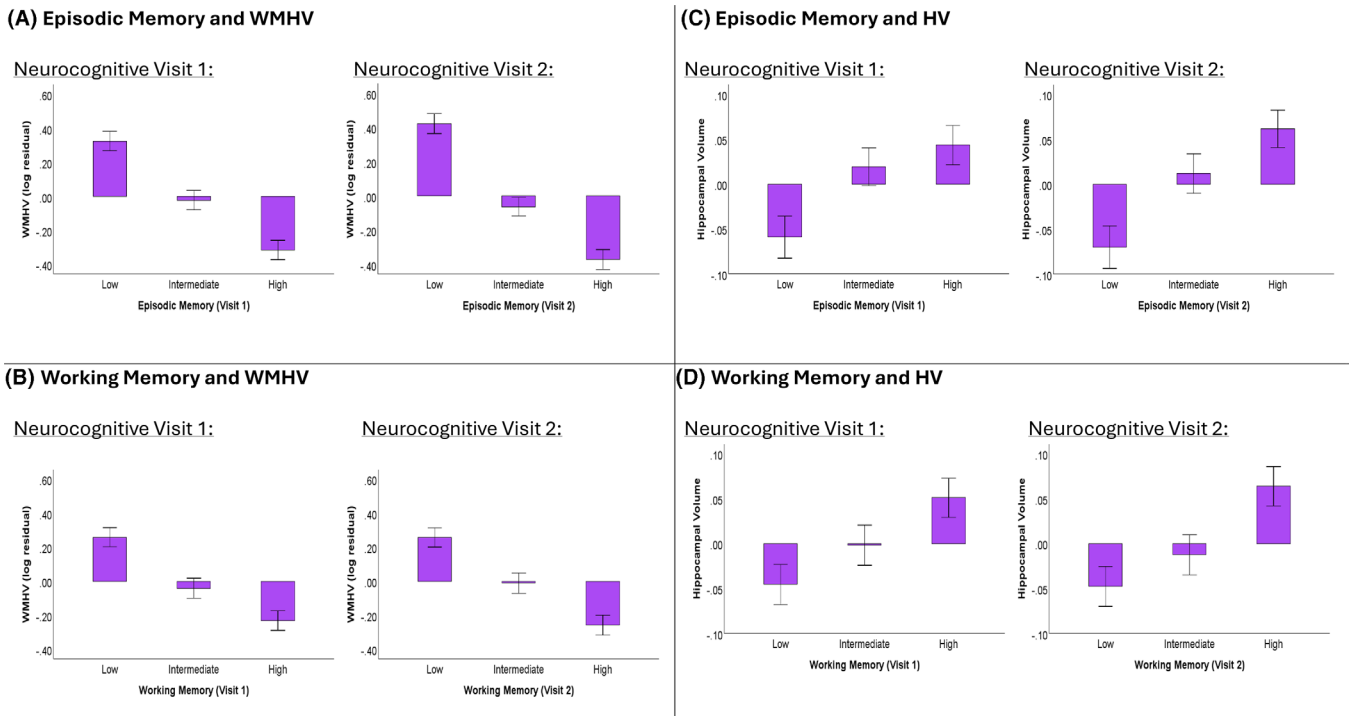

FIGURE 3 Neurocognitive profiles represented with episodic and working memory tertiles at neurocognitive Visits 1 and 2 are associated with subsequent white matter hyperintensity volume (WMHV) and hippocampal volume (HV). All tertiles were significantly different across all neurocognitive visits for brain integrity except for neurocognitive Visit 1 and HV. ± 1 standard error of the mean is shown for all figures.

and processing for longitudinal brain morphometry data limited our analysis to cross-sectional. Future work with longitudinal brain morphometry data will provide additional information to support our preliminary brain-cognition integrity results. Fourth, all cognitive tests examined were designed to study a Hispanic/Latino group typically observed in a large epidemiological study and cannot be compared with construct or loadings in a non-Hispanic White cohort as the individual tests are specific to this cohort. Fifth, although we included sex as a covariate, future work should consider examining sex differences with memory and brain integrity associations in Hispanic/Latino cohorts.[23] Sixth, structural determinants of health including economic and social policies and racism directly impact everyday living conditions in this group[36] and may not be generalizable to other ethnic groups. This includes fair access to housing, education, and health care,[37] each of which could affect cognitive performance obscuring the brain-cognition relationship while simultaneously increasing risk for late-life dementia.[38] A first strength is the large (>2000) and diverse (more than four heritage groups) sample of Hispanic/Latino adults tested longitudinally on neurocognitive performance across an ≈10-year period from an ongoing study with neuroimaging data. Second, we used seven scores from three commonly examined standard cognitive tests to represent our two-factor, longitudinally invariant, memory construct, which accounts for measurement error frequently present with single cognitive variables. Third, neurocognitive data were collected before brain morphometry measures, making our study design unique and among the first studies to examine this dynamic and complex brain-cognition relationship in a diverse Hispanic/Latino cohort.

In conclusion, we established two-factor longitudinally invariant EM and WM latent construct models of cognition in a large and diverse Hispanic/Latino cohort of middle-aged and older adults from four U.S. metropolitan areas. These neurocognitive profiles were associated with subsequent indices of WMHV and HV. This implies an accurate reflection of memory at the two visits (≈7 years apart) and suggests that neurocognitive profiles at any given time also reflect the extent of underlying brain integrity. Future studies should consider examining the impact of longitudinal memory changes to predict brain integrity as well as replication studies with other ethnoracial groups and patients with dementia. Careful monitoring of neurocognitive risk profiles in the Hispanic/Latino population may identify individuals at high risk for future neurodegeneration, and significantly lead to early detection and individualized intervention programs. Although our findings confirm an association between cognitive risk profile and future structural MRI changes, it is important to note that longitudinal studies are needed to infer a predictive relationship between neurocognitive risk and future neurodegeneration. Examining neurocognitive profiles periodically across the lifespan may detect thresholds or deflection points that accurately identify individuals at high risk of experiencing structural brain abnormalities associated with neurodegeneration. This approach can lead to early detection and opportunities for on-time and person-centered interventions that may significantly impact the course of neurodegeneration in Hispanic/Latino adult communities.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

CONSENT STATEMENT

Written informed consent was obtained from all participants.

DISCLOSURE

All authors report no disclosures relevant to the manuscript.

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SUPPORTING INFORMATION

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