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RESEARCH ARTICLE

Impact of neighborhood disadvantage on cardiometabolic health and cognition in a community-dwelling cohort

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Abstract

INTRODUCTION: Neighborhood disadvantage may be an important determinant of cardiometabolic health and cognitive aging. However, less is known about relationships among individuals with mild cognitive impairment (MCI).

METHODS: The objective of this study is to investigate the relationship between neighborhood disadvantage measured by national Area Deprivation Index (ADI) rank with measures of cardiometabolic health and cognition among Wake Forest (WF) Alzheimer's Disease Research Center (ADRC) participants, with and without MCI.

RESULTS: ADI was positively associated with blood pressure and cardiometabolic index (CMI), and negatively associated with global and Preclinical Alzheimer's Cognitive Composite (PACC5) scores, in cognitively unimpaired (CU) individuals. ADI was only positively associated with hemoglobin A1c (HbA1c) in MCI.

DISCUSSION: Neighborhood disadvantage is associated more strongly with measures of cardiometabolic health and cognition among CU individuals rather than MCI. These findings demonstrate a need for structural solutions to address social determinants of health in an attempt to reduce cardiometabolic and cognitive risks.

KEYWORDS
Alzheimer's disease and related dementias, health equity, neighborhood disadvantage, place-based determinants of health, social determinants of health

1 | INTRODUCTION

Stark disparities exist in the prevalence of Alzheimer's disease (AD) based on socioeconomic status and poverty,[1] with numerous studies demonstrating that inequitable access to socioeconomic assets such as education, employment, income, and housing is associated with an increased risk for AD and AD-related dementias (ADRD).[2] Additionally, significant disparities in the incidence of dementia exist based on race and ethnicity, with consistently higher incidence rates among Black and Hispanic individuals compared with White individuals.[3] Despite these identified inequities, the social determinants of health (SDoH) in AD/ADRD remain relatively understudied. SDoH are defined as the conditions in the environment where people live, work, learn, and play,[4] and are known to significantly impact the distribution of health disparities. Neighborhood disadvantage is one novel SDoH measure that incorporates indicators of other existing SDoH at a neighborhood level, such as area-based education, employment, housing quality, and poverty, and can be measured using the Area Deprivation Index (ADI).[5]

In a study of community-dwelling older adults, individuals from neighborhoods with higher ADI scores had poorer performance on tests of executive function, verbal learning, and memory,[6] and had an increased risk for progression to dementia when compared to participants residing in the least deprived neighborhoods.[7] Among older Veterans, a linear association was seen between residence in areas with higher ADI and the risk of developing dementia, and these relationships persisted when adjusting for other risk factors such as traumatic brain injury and other medical and psychiatric comorbidities.[8] In another middle-to-older aged adult study sample in Wisconsin, living in the 20% of most disadvantaged neighborhoods was associated with a yearly loss of 0.02 mm cortical thickness in brain regions prone to ADRD, and lower scores on cognitive testing, such as a revised version of the Preclinical Alzheimer's Cognitive Composite (PACC5).[9,10]

Cardiometabolic risk factors including diabetes, hyperlipidemia, and hypertension are linked with the development of ADRD, especially when present at midlife.[11] Diabetes and AD are known to increase in prevalence with aging, and on a fundamental level, insulin resistance and metabolic dysfunction are known to accompany both disease processes.[12] Additionally, higher levels of low-density lipoprotein (LDL) cholesterol in midlife are associated with increased risk for dementia,[13] while higher levels of high-density lipoprotein (HDL) cholesterol in late life are associated with reduced risk of incident AD.[14] Elevated blood pressure as well as impaired glucose tolerance is associated with lower cognitive function,[15] and lower overall cardiometabolic health at older age is associated with an increased risk of cognitive decline and dementia.[16] Importantly, higher ADI scores have been associated with a higher incidence of cardiometabolic disease,[17,18] along with poorer management of chronic diseases among cognitively unimpaired (CU) individuals.[19] A higher ADI score has been shown to be a predictor of worse control of blood pressure, diabetes, and cholesterol,[19] and is associated with increased mortality.[20]

Although neighborhood disadvantage has been previously studied in association with measures of cardiometabolic health and cognition among CU individuals,[9,18] little is known regarding the impact of neighborhood disadvantage on cardiometabolic health and cognitive function at the MCI stage. It is critical to understand how neighborhood characteristics might impact those who have already progressed to cognitive impairment, and whether neighborhood disadvantage would exacerbate or alleviate ADRD risk associated with cardiometabolic health and cognitive decline since prior studies demonstrated a positive relationship between neighborhood disadvantage and dementia risk.[7] With studies suggesting higher proportions of cardiometabolic disease among individuals with prevalent MCI rather than CU individuals,[21] it is important to consider how neighborhood disadvantage might account for the prevalence of cardiometabolic risk factors among individuals with MCI. Additionally, neighborhood disadvantage is associated with reduced cognitive reserve,[22] higher odds of MCI, progression to dementia, and slightly faster cognitive decline[7]; hence, it is possible that the relationships of neighborhood disadvantage with higher cardiometabolic risk and reduced cognitive function are stronger among individuals with MCI. In this study of community-dwelling older adults, we investigated the associations of neighborhood disadvantage with numerous measures of cardiometabolic health and cognition, stratified by cognitive status (CU or MCI), and in a combined sample of older adults without dementia. We hypothesized that higher neighborhood disadvantage would be associated with poorer outcomes in measures of cardiometabolic health and cognition and that these relationships would be stronger among those with MCI, a population where this has not been studied previously.

2 | METHODS

2.1 | Participants

Adults above the age of 55 were recruited into the Wake Forest (WF) Alzheimer's Disease Research Center (ADRC) Healthy Brain Study (HBS) from the surrounding communities in North Carolina between 2016 and 2021 and underwent standard evaluation at their initial visit, including the National Alzheimer's Coordinating Center (NACC) protocol for clinical data collection, clinical exams, neurocognitive testing, neuroimaging, and genotyping for apolipoprotein E (*APOE*) ε4, as described previously.[23] The current study, as it focused on early stages of cognitive decline, excluded patients diagnosed with dementia and only included participants with a clinically adjudicated cognitive diagnosis of CU or MCI that did not incorporate biomarkers. Race was self-reported. We use it as a sociopolitical construct, conceptualized and operationalized as a proxy for exposure to systemic racism.[24] Exclusion criteria for the HBS included: large vessel stroke (participants with lacunae or small vessel ischemic disease were eligible); other significant neurologic diseases that might affect cognition other than AD; evidence of organ failure, active cancer treatment, uncontrolled clinical depression, or psychiatric illness; current use of insulin; and history of substance abuse or heavy alcohol consumption within previous 10 years. All activities described were approved by the WF Institutional Review Board. Written informed consent was obtained from all participants and/or their legally authorized representatives.

2.2 | Neighborhood disadvantage

Neighborhood disadvantage, the primary independent variable in the study, was measured using the ADI, which uses 17 census indicators of poverty, education, housing, and employment to generate a composite score corresponding to census block groups to which individuals belong.[20,25] Home addresses from initial visits for ADRC HBS participants were used to generate Federal Information Processing Systems (FIPS) codes. Census block group-level ADI national scores were accessed using the Neighborhood Atlas,[5] and linked to FIPS codes. While ADI scores are available at both the state and national level, some participants live outside the state of North Carolina; thus, only national scores were feasible to use in this study.

2.3 | Cardiometabolic measures

Cardiometabolic measures used in the study include measures of cardiovascular and metabolic health available through the WF ADRC, that are relevant to ADRD risk, including but not limited to diabetes, hyperlipidemia, and hypertension.[11–14] Systolic and diastolic blood pressure measurements were determined, as described previously,[15] using brachial blood pressure readings measured using a DINAMAP automated blood pressure device (GE Healthcare) in a seated position after 5 min of rest. If the initial blood pressure reading was greater than 160 mm Hg systolic or 90 mm Hg diastolic, a second blood pressure was measured after another 5-min rest. HDL and LDL cholesterol, triglycerides, and hemoglobin A1c (HbA1c) were assessed using blood draws from initial visits which were processed by LabCorp (Winston-Salem, NC). Cardiometabolic measures used as dependent and continuous variables in the analyses include systolic blood pressure, HDL and LDL cholesterol, HbA1c, and cardiometabolic index (CMI).

2.4 | CMI

CMI was calculated within the WF ADRC HBS cohort, using a similar formula to that used in the Multi-Ethnic Study of Atherosclerosis,[26] with a few additional measures. CMI was calculated using the following variables: systolic blood pressure, pulse pressure, average heart rate, HbA1c, waist-to-hip circumference, oral glucose tolerance testing (OGTT) at 0 (fasting) and 120 min, HDL and LDL cholesterol, and triglycerides. HbA1c and blood pressure were measured as stated above; triglycerides, HDL, and LDL cholesterol were assessed using blood draws from initial visits which were processed domestically. Pulse pressures were recorded by calculating the difference between the systolic and diastolic blood pressures. OGTT was measured as described previously,[15] where at study entry, fasting participants without diabetes completed serial blood draws. Initially, glucose measurement was drawn before glucose ingestion this was recorded as the fasting OGTT. Participants then ingested a glucose challenge—75 g of glucose in solution. Blood was then sampled at 120 min post-ingestion; this was recorded as OGTT at 120 min. Blood glucose was determined using the Hemocue whole blood glucose analyzer. Participants with a diagnosis of diabetes, severe cognitive impairment, and those who refused OGTT did not complete OGTT. Each of the 10 CMI components was standardized using common clinical cutpoints and standard deviations of the cohort. These *z*-scores were then averaged to create the CMI. If more than five of the components were missing, CMI was not calculated. CMI was utilized as a dependent and continuous variable in the analysis.

2.5 | Cognitive testing

As described previously,[15] participants underwent cognitive testing with the Uniform Data Set Version 3 (UDSv3)[27] test battery, including Montreal Cognitive Assessment (MoCA), Craft Story, Benson Figure, Number Span, Verbal Fluency (letters CFL), Category Fluency, Trail Making Test, and the Multilingual Naming Test. Additionally, supplemental tests commonly used to estimate the participant's current and past cognitive status were also administered, as described previously[23]: Mini-Mental State Examination (MMSE), American National Adult Reading Test, Digit Symbol Substitution Test (DSST), Free and Cued Selective Reminding Test (FCSRT), and the Rey Auditory Verbal Learning Test (AVLT). A PACC5 score[28] was created from five cognitive tests: the MMSE, AVLT, verbatim recall of the Craft Story, DSST, and category fluency. MoCA, MMSE, and PACC5 scores were utilized as dependent and continuous variables in the analyses. MoCA and MMSE are global cognitive measures that we used to assess the overall degree of cognitive function, with MMSE helpful in the early detection of dementia in those with MCI.[29] PACC5, which is also a global cognitive composite, has been shown to be more sensitive to cognitive differences at the CU stage.

2.6 | Adjudication

An expert panel conducted adjudication of cognitive diagnosis by consensus following the review of all available clinical and cognitive data in accordance with current National Institute of Aging-Alzheimer's Association guidelines for the diagnosis of MCI.[30] The panel consisted of investigators and clinicians with extensive experience assessing cognitive status and identifying cognitive impairment in older adults.

2.7 | Statistical analysis

The analysis included 537 CU and MCI participants enrolled in the WF ADRC HBS for whom ADI scores had been linked and consensus diagnosis had been adjudicated. Participant demographics were compared between cognitive groups of CU and MCI using chi-squared tests for categorical variables and *t*-tests for continuous variables. All measures of cardiometabolic health and cognition used in the analysis were from initial visits of participants in the ADRC, and were not available on all 537 participants, with analyses constrained to smaller samples of

participants based on availability. Sample sizes for all measures are indicated in Table 1. Unadjusted analyses used simple linear regression models between ADI and cardiometabolic and cognitive measures, stratified by cognitive status of MCI, CU, and a combined sample. Adjusted analyses used sequential multivariable linear regression models between ADI and cardiometabolic and cognitive measures, similarly stratified by MCI, CU, and a combined sample when applicable: Model 1a adjusted for the demographic variables, age, sex, and education, while Model 2a additionally adjusted for diagnosis. Models 1b and 2b additionally adjusted for participants' self-reported race along with other demographic covariates included in Models 1a and 2a. Race was added sequentially in the second model to assess for any effect modification as a result of race, as it is conceptualized and operationalized as mentioned above.[31] Probability of interactions of ADI with sex and diagnosis were identified. For all analyses, *p*-values less than 0.05 were considered statistically significant.

3 | RESULTS

3.1 | Sample characteristics

The study sample comprised 537 CU and MCI participants enrolled in the WF ADRC HBS cohort (Table 1). Participants had a mean age of 69.9 (standard deviation [SD]: 8.0), mean years of education of 15.7 (SD: 2.5), were 19.4% Black or African American individuals, 67.8% women, and 39.3% were adjudicated to have MCI. Individuals with MCI were significantly older, had lower levels of education, and had higher ADI scores on average. Among cardiometabolic and cognitive measures, significant differences were observed between those with MCI and CU in systolic blood pressure, LDL cholesterol, MoCA, and PACC5. Individuals with MCI were more likely to have higher systolic blood pressures, lower LDL cholesterol levels, and lower MoCA and PACC5 scores.

3.2 | Unadjusted analyses

Figure 1 shows unadjusted analyses of ADI scores with cardiometabolic measures. Higher ADI scores were associated with higher systolic blood pressure and HbA1c measurements in our combined (CU+MCI) sample, but not in either cognitive group alone (Figure 1A,D). ADI scores were not associated with measures of HDL or LDL cholesterol in individuals with CU, MCI, or the combined sample (Figure 1B,C). However, higher ADI scores were significantly associated with higher composite CMI scores in participants with CU and the combined sample, but not the MCI group alone (Figure 1E).

In Figure 2, higher ADI scores were significantly associated with lower scores on the MMSE (Figure 2A), MoCA (Figure 2B), and PACC5 (Figure 2C) in the combined sample. Among CU participants, higher ADI scores were associated with lower scores on MoCA (Figure 2B) and PACC5 (Figure 2C). ADI was not associated with cognitive performance in the MCI group.

3.3 | Adjusted analyses

Table 2 and 3 display adjusted multivariable linear regression analyses examining the relationships between ADI and measures of cardiometabolic health and cognition. In Model 1a, in the combined sample of participants, ADI scores were associated with higher systolic blood pressure, HbA1c, and CMI scores, and lower HDL cholesterol, MoCA, and PACC5 scores. Among participants with MCI, a positive relationship was observed between ADI scores and HbA1c, and no relationships with other cardiometabolic or cognitive measures. The relationships observed were driven by the CU participants, where a significant positive relationship of ADI scores was seen with systolic blood pressure, and negative relationships were seen with scores on MoCA and PACC5. In Model 2a, additionally adjusting for diagnosis, a positive relationship was seen with HbA1c, while negative relationships were preserved with MoCA and PACC5. No significant relationships of ADI were observed with LDL cholesterol and MMSE in Models 1a or 2a.

In Model 1b, along with demographic variables adjusted for in Model 1a, race was added as a covariate and showed preserved negative relationships of ADI with MoCA and PACC5 among those who were CU, and negative relationships of ADI with HDL cholesterol, MoCA, and PACC5 were preserved among the combined sample. In Model 2b, none of the relationships seen in Model 2a were observed.

4 | DISCUSSION

In this study, we investigated the associations of neighborhood disadvantage with numerous measures of cardiometabolic health and cognition among community-dwelling older adults adjudicated to be CU or have MCI. First, we observed that individuals with MCI had higher levels of neighborhood disadvantage in our cohort. We observed numerous associations between neighborhood disadvantage and several individual and composite measures of cardiometabolic health and cognition in unadjusted and adjusted analyses. Specifically, we saw positive relationships between neighborhood disadvantage and several cardiometabolic health measures in unadjusted models among our combined sample. In analyses adjusted for age, sex, and education, neighborhood disadvantage was only associated with higher HbA1c among individuals with MCI, and with higher systolic blood pressure among CU individuals. With regard to cognitive measures, negative relationships of neighborhood disadvantage were seen with MoCA and PACC5 in CU individuals in unadjusted analyses. Adjusted models showed preserved negative relationships of MoCA and PACC5 among CU individuals and the combined sample. These results indicate the presence of numerous cross-sectional relationships between neighborhood disadvantage and measures of cardiometabolic health and cognition, that persist when controlling for demographic variables and cognitive diagnostic status. When additionally adjusting for race, the relationships of neighborhood disadvantage with various measures of cardiometabolic health were no longer seen, while the relationships

TABLE 1 Characteristics of the WF ADRC HBS cohort with mean values of cardiometabolic and cognitive measures within the cohort.

Characteristics	MCI[a]	CU[a]	Total	*p*-value
Age				
Mean (SD)	71.8 (7.7)	68.6 (8.0)	69.9 (8.0)	**<0.0001**[g]
N	211	326	537	
Race				
White	157 (74.4%)	270 (82.8%)	427 (79.5%)	**0.0499**[h]
Black/African American	52 (24.6%)	52 (16.0%)	104 (19.4%)	
AI/AN	1 (0.5%)	0 (0%)	1 (0.2%)	
Asian	1 (0.5%)	4 (1.2%)	5 (0.9%)	
Years of education				
Mean (SD)	15.2 (2.6)	16.0 (2.3)	15.7 (2.5)	**0.0011**[i]
N	211	326	537	
Sex				
Male	83.0 (39.3%)	90.0 (27.6%)	173.0 (32.2%)	**0.0011**[j]
Female	128.0 (60.7%)	236.0 (72.4%)	364.0 (67.8%)	
ADI national rank[b]				
Mean (SD)	53.5 (19.9)	47.3 (22.0)	49.7 (21.4)	**0.001**[g]
N	211	326	537	
Systolic blood pressure[c]				
Mean (SD)—mmHg	134.3 (16.9)	130.5 (18.3)	132.0 (17.8)	**0.0155**[g]
N	210	322	532	
HDL cholesterol[d]				
Mean (SD)—mg/dL	60.4 (20.0)	63.6 (19.7)	62.3 (19.9)	0.0512[g]
N	152	218	370	
LDL cholesterol[d]				
Mean (SD)—mg/dL	98.9 (34.8)	107.0 (34.8)	103.7 (35.0)	**0.0433**[g]
N	139	202	341	
HbA1c[d]				
Mean (SD)	5.8 (0.5)	5.7 (0.5)	5.8 (0.5)	0.5617[g]
N	148	218	366	
CMI[e]				
Mean (SD)	−0.7 (0.4)	−0.8 (0.4)	−0.7 (0.4)	0.0610[g]
N	193	305	498	
MMSE				
Mean (SD)	27.3 (2.0)	29.0 (1.2)	28.3 (1.7)	**<0.0001**[i]
N	209	323	532	
MoCA				
Mean (SD)	21.8 (3.2)	26.3 (2.4)	24.5 (3.5)	**<0.0001**[i]
N	210	326	536	

(Continues)

TABLE 1 (Continued)

Characteristics	MCI[a]	CU[a]	Total	*p*-value
PACC5[f]				
Mean (SD)	−1.2 (0.7)	0.01 (0.6)	−0.5 (0.9)	**<0.0001**[i]
N	207	320	527	

Abbreviations: ADI, Area Deprivation Index; ADRC, Alzheimer's Disease Research Center; CMI, cardiometabolic index; CU, cognitively unimpaired; HbA1c, hemoglobin A1c; HBS, Healthy Brain Study; HDL cholesterol, high-density lipoprotein cholesterol, LDL cholesterol, low-density lipoprotein cholesterol; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; PACC5, Preclinical Alzheimer's Cognitive Composite; WF, Wake Forest. Bolded values indicate statistically significant *p*-values.

[a]Cognitive diagnosis of MCI and CU was adjudicated by an expert panel by consensus following a review of all available clinical, brain imaging, and cognitive data by current National Institute on Aging-Alzheimer's Association guidelines for the diagnosis of MCI.

[b]ADI national rank was calculated for participants at initial visits to the WF ADRC.

[c]Systolic Blood Pressure was measured using brachial blood pressure readings using a DINAMAP automated blood pressure device in a seated position after 5 min of rest, with values represented in mm of Hg.

[d]HDL and LDL cholesterol along with HbA1c was assessed using blood draws from initial visits, processed by LabCorp.

[e]CMI was calculated within the WF ADRC HBS cohort similar to the formula used in the Multi-Ethnic Study of Atherosclerosis[1], using systolic and diastolic blood pressures, pulse pressure, average heart rate, HbA1c, waist-to-hip circumference, oral glucose tolerance testing (OGTT) at 0 and 120 min, HDL and LDL cholesterol, and triglycerides. Higher CMI scores indicate poorer cardiometabolic health.

[f]Preclinical Alzheimer's Cognitive Composite scores were generated from five cognitive tests (PACC5): Mini-Mental State Examination, Rey Auditory Verbal Learning Test (AVLT), verbatim recall of the Craft Story, Digit Symbol Substitution Test, and category fluency.

[g]Equal variance two-sample *t*-test.

[h]Chi-squared test.

[i]Unequal variance two-sample *t*-test.

[j]Fisher's exact test.

with cognitive measures were preserved. However, when both race and diagnosis were included in the models, no significant relationships were observed. This suggests that neighborhood-level socioeconomic disadvantage is closely linked with cognitive function related to ADRD, regardless of one's age, sex, education, and race, among CU individuals but may not apply to MCI. Additionally, neighborhood disadvantage is linked with measures of cardiometabolic health, regardless of age, sex, and education status, but one's racialized experience may account for this relationship.

While this is not the first study to demonstrate a relationship between neighborhood disadvantage and various cardiometabolic and cognitive factors associated with ADRD, to our knowledge, it is the first study to examine these relationships of ADI with cardiometabolic health and cognitive function among individuals with MCI. Additionally, while other studies have investigated the relationships of neighborhood disadvantage with risk factors associated with ADRD in other geographic regions, to our knowledge this is the first study to explore these relationships among individuals with MCI in the US South. Prior studies have demonstrated that, among CU individuals, living in the most disadvantaged neighborhoods is associated with lower cerebral and hippocampal volumes,[32] accelerated neurodegeneration in regions prone to ADRD, and cognitive decline.[9] In another study examining cognitive outcomes among older Mexican American adults, aging in disadvantaged neighborhoods was associated with worse cognitive functioning.[33] Among Veterans, residence in more disadvantaged neighborhoods was found to be associated with a higher incidence of dementia.[8] Finally, in neuropathological studies, neighborhood disadvantage has also been found to be associated with greater AD pathology, in the form of neurofibrillary tangles[34] and amyloid plaques.[35]

In the WF ADRC HBS sample, neighborhood disadvantage correlated more strongly with measures of cardiometabolic health and cognition among CU individuals, rather than those who live with MCI. This is similar to previous studies discussed above that examine the relationship of neighborhood disadvantage with measures of cardiometabolic health and cognition among CU individuals.[9,18] While it is possible that neighborhood disadvantage does not have an impact on those with MCI, it is more likely that MCI is attributable to various risk factors for ADRD, including biomarkers that are more proximate to cognitive impairment than CMI. In other words, it is possible that CMI and ADI may play a small role in the progression to MCI but are likely more upstream factors in this pathway. Future studies investigating the relationships of ADRD biomarkers with ADI among individuals with MCI are needed.

ADI itself correlates with historical redlining policy[36] and the resulting residential segregation that occurred on the basis of race, and represents a form of structural racism-mediated disadvantage conferred upon a neighborhood. Relationships between neighborhood disadvantage and measures of cardiometabolic health were not preserved when race was added as a covariate to the model, indicating that racialized experiences may account for the impact of ADI on the measures of cardiometabolic health. Since ADI is correlated with the impacts of structural racism,[37] it is possible that structural racism in the form of neighborhood disadvantage may serve as one potential determinant of cardiometabolic health and, thus, attenuated the observed relationships. However, multidimensional models that directly capture the components of structural racism are needed to more accurately measure the impact of structural racism on measures associated with ADRD,[38] and must be a topic of future study. Additionally, interpersonal racism in the form of individual experiences of

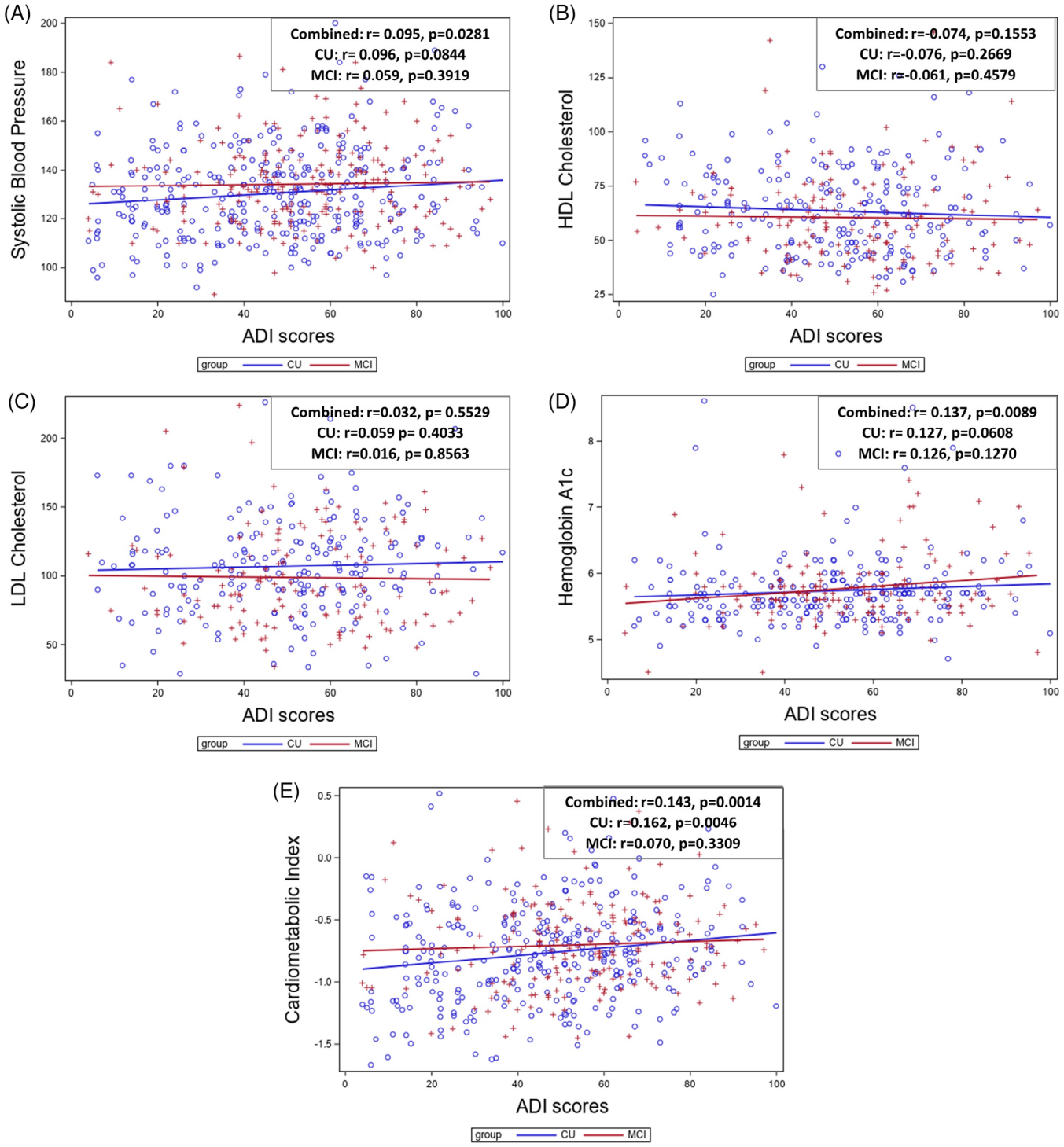

FIGURE 1 Unadjusted regression analyses between ADI scores and measures of cardiometabolic health. Unadjusted analyses used simple linear regression models between ADI and cardiometabolic measures, stratified by the cognitive status of MCI and CU. Cardiometabolic measures used include (A) systolic blood pressure, (B) HDL cholesterol, and (C) LDL cholesterol, (D) HbA1c, and (E) CMI. Cardiometabolic measures were collected as described in the footnotes of Table 1 and in the Methods section. ADI, Area Deprivation Index; CMI, cardiometabolic index; CU, cognitively unimpaired; HbA1c, hemoglobin A1c; HDL cholesterol, high-density lipoprotein cholesterol; LDL cholesterol, low-density lipoprotein cholesterol; MCI, mild cognitive impairment.

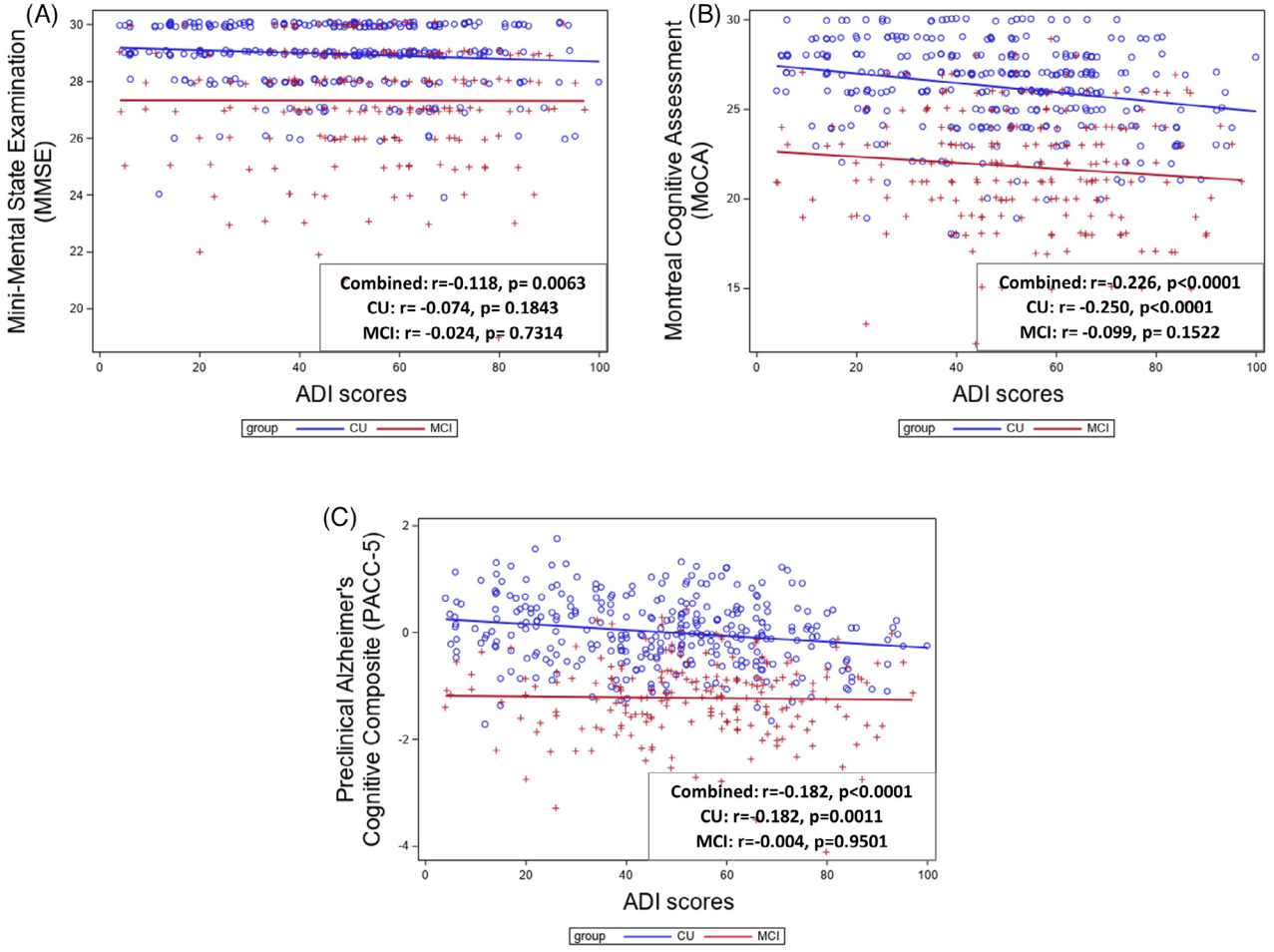

FIGURE 2 Unadjusted regression analyses between ADI scores and variables related to measures of cognition. Unadjusted analyses used simple linear regression models between ADI and cognitive measures, stratified by the cognitive status of MCI and CU. Cognitive measures used include (A) MMSE, (B) MoCA, and (C) PACC5. Cognitive measures were collected as described in the footnotes of Table 1 and in the Methods section. ADI, Area Deprivation Index; CU, cognitively unimpaired; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; PACC5, Preclinical Alzheimer's Cognitive Composite.

racial discrimination may compound the effects of structural racism,[39] in agreement with studies suggesting associations between allostatic load and dementia risk.[40] On the other hand, relationships between neighborhood disadvantage and cognitive measures were preserved among CU individuals even when race was added as a covariate, implying that one's residence may impact cognitive functioning irrespective of their racial identity.

This study has several limitations. First, the study sample lacks further racial and ethnic diversity. Among the combined sample, 79.5% of participants self-identified as White and 19.4% as Black. Further outreach to other communities in the region that are underrepresented in AD/ADRD research, including Hispanic/Latino, American Indian/Native American, and Asian American communities, is necessary to accurately represent the US South. Second, this study was conducted in a single center in the US South. While these findings offer a unique perspective on a population with specific health needs and challenges as a result of historical policy, these findings may not be generalizable outside of this geographic region and also cannot be unreservedly extrapolated to the rest of the South, due to the widespread heterogeneity of this region. Third, this sample included all ADRC participants with MCI without accounting for the various subdomains (e.g., amnestic vs. non-amnestic MCI), due to small sample sizes within each subgroup. This may have resulted in any significant differences between MCI subgroups being obscured. Last, all of the data presented here were cross-sectional. We utilized participants' addresses from initial visits to calculate their neighborhood disadvantage and did not account for the life course of participants in examining their risk for dementia. The cardiometabolic and cognitive measures used were also cross-sectional and collected from participants' initial visits and were not assessed over time, limiting the ability to highlight cardiometabolic and cognitive risk among participants. Further research is needed to longitudinally assess one's risk based on their different areas of residence through the course of their life, the complex pathways through which structural racism operates, and to study how AD relates to biomarkers of brain health.[38]

TABLE 2 Adjusted analyses examining associations of ADI with cardiometabolic factors and cognitive measures, with demographic covariates including age, sex, education (Model 1a), and cognitive status through consensus diagnosis (Model 2a).

Adjusted regression analyses of ADI scores with cardiometabolic factors and cognitive measures								
	Model 1a: Adjusted for age, sex, and education						Model 2a: Adjusted for age, sex, education, and diagnosis	
	MCI		CU		Combined		Combined	
Cardiometabolic factors and cognitive measures	Estimate (S.E.)	*p*-value	Estimate (S.E.)	*p*-value	Estimate (S.E.)	*p*-value	Estimate (S.E.)	*p*-value
Systolic blood pressure	0.0001 (0.0587)	0.998	0.100 (0.0457)	**0.029**	0.071 (0.0357)	**0.046**	0.068 (0.0361)	0.061
HDL cholesterol	−0.077 (0.0820)	0.348	−0.093 (0.0613)	0.131	−0.097 (0.0485)	**0.046**	−0.092 (0.0488)	0.059
LDL cholesterol	−0.075 (0.1539)	0.627	−0.012 (0.1198)	0.922	−0.045 (0.0932)	0.633	−0.028 (0.0936)	0.769
HbA1c	0.005 (0.0022)	**0.022**	0.002 (0.0018)	0.378	0.003 (0.0014)	**0.033**	0.003 (0.0014)	**0.037**
CMI	0.0004 (0.0013)	0.714	0.002 (0.0010)	0.076	0.002 (0.0008)	**0.043**	0.002 (0.0008)	0.059
MMSE	−0.002 (0.0068)	0.737	−0.002 (0.0029)	0.399	−0.006 (0.0034)	0.060	−0.002 (0.0031)	0.478
MoCA	−0.012 (0.0109)	0.288	−0.021 (0.0057)	**0.0002**	−0.029 (0.0065)	**<.0001**	−0.018 (0.0054)	**0.001**
PACC5	−0.001 (0.0030)	0.691	−0.003 (0.0013)	**0.009**	−0.007 (0.0016)	**<.0001**	−0.003 (0.0014)	**0.039**

Note: Results with statistical significance ($p < 0.05$) are highlighted. Cardiometabolic and Cognitive measures were collected as described in the footnotes of Table 1 and in the Methods section. Bolded values indicate statistically significant *p*-values.

Abbreviations: ADI, Area Deprivation Index; CMI, cardiometabolic index; CU, cognitively unimpaired; HbA1c, hemoglobin A1c; HDL cholesterol, high-density lipoprotein cholesterol; LDL cholesterol, low-density lipoprotein cholesterol; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; PACC5, Preclinical Alzheimer's Cognitive Composite.

TABLE 3 Adjusted analyses examining associations of ADI with cardiometabolic factors and cognitive measures with demographic covariates including age, sex, education, additional adjustment for race (Model 1b), and cognitive status through consensus diagnosis (Model 2b).

Adjusted regression analyses of ADI scores with Cardiometabolic factors and cognitive measures								
	Model 1b: Adjusted for age, sex, education, and race						Model 2b: Adjusted for age, sex, education, race, and diagnosis	
	MCI		CU		Combined		Combined	
Cardiometabolic factors and cognitive measures	Estimate (S.E.)	*p*-value	Estimate (S.E.)	*p*-value	Estimate (S.E.)	*p*-value	Estimate (S.E.)	*p*-value
Systolic blood pressure	−0.015 (0.0602)	0.800	0.071 (0.0472)	0.132	0.045 (0.0369)	0.226	0.042 (0.0372)	0.258
HDL cholesterol	−0.076 (0.0843)	0.370	−0.100 (0.0631)	0.113	−0.100 (0.0500)	**0.047**	−0.095 (0.0502)	0.059
LDL cholesterol	−0.089 (0.1582)	0.575	−0.038 (0.1225)	0.757	−0.065 (0.0956)	0.499	−0.049 (0.0959)	0.611
HbA1c	0.003 (0.0022)	0.119	0.001 (0.0018)	0.684*	0.002 (0.0014)	0.213	0.002 (0.0014)	0.222
CMI	0.001 (0.0014)	0.517	0.002 (0.0011)	0.135	0.002 (0.0008)	0.064	0.001 (0.0008)	0.085
MMSE	0.0001 (0.0070)	0.990	−0.002 (0.0030)	0.509	−0.005 (0.0035)	0.169	−0.001 (0.0032)	0.741
MoCA	−0.002 (0.0108)	0.888	−0.016 (0.0059)	**0.006**	−0.021 (0.0067)	**0.002**	−0.010 (0.0055)	0.056
PACC5	−0.0002 (0.0030)	0.955	−0.003 (0.0014)	**0.033**	−0.005 (0.0018)	**0.005**	−0.002 (0.0014)	0.145

Note: Results with statistical significance ($p < 0.05$) are highlighted. Cardiometabolic and cognitive measures were collected as described in the footnotes of Table 1 and methods. Bolded values indicate statistically significant *p*-values.

Abbreviations: ADI, Area Deprivation Index; CMI, cardiometabolic index; CU, cognitively unimpaired; HbA1c, hemoglobin A1c; HDL cholesterol, high-density lipoprotein cholesterol; LDL cholesterol, low-density lipoprotein cholesterol; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; PACC5, Preclinical Alzheimer's Cognitive Composite.

*Indicates a significant probability of interaction of ADI with sex.

5 | CONCLUSIONS

Neighborhood disadvantage is associated with poorer cardiometabolic health and poorer cognitive performance among CU individuals, but not those with MCI, in unadjusted analyses and analyses adjusting for age, sex, and education. When additionally adjusting for race or diagnosis, neighborhood disadvantage was still associated with cognitive measures, but not cardiometabolic measures. Neighborhood disadvantage is a measure of numerous social determinants of health that permeate through various existing systems and structures, and reflect the effects of these structures on individuals. Such structural inequities in the availability of resources and opportunities require structural interventions that may further help to mitigate ADRD risk. There is an urgent need for the implementation of public policy that must function hand-in-hand with grassroots organizing efforts, as interventions to rebuild existing structures with equity and justice in mind, and target social and structural determinants of health that impact ADRD risk for those who have been historically disenfranchised.

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CONFLICT OF INTEREST STATEMENT

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CONSENT STATEMENT

Written informed consent was obtained from all participants and/or their legally authorized representatives.

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