FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2022

LOWER SOCIOECONOMIC STATUS IN CHILDHOOD, PERSISTENT LOW WAGES LINKED TO RISK FOR DEMENTIA AND FASTER MEMORY DECLINE

SAN DIEGO, AUGUST 2, 2022 — Socioeconomic deprivation, including neighborhood disadvantages and persistent low wages, are associated with higher dementia risk, lower cognitive performance and faster memory decline, according to several studies reported today at the Alzheimer's Association International Conference® (AAIC®) 2022 in San Diego and virtually.

Socioeconomic status (SES) — reflecting both social and economic measures of a person's work experience, and of an individual's or family's economic access to resources and social position — has been linked to both physical and psychological health and well-being. Research examining its impact on cognition is growing, and key findings presented at AAIC 2022 include:
- Individuals who experience high socioeconomic deprivation — measured using income/wealth, unemployment rates, car/home ownership and household overcrowding — are significantly more likely to develop dementia compared to individuals of better socioeconomic status, even at high genetic risk.
- Lower-quality neighborhood resources and difficulty paying for basic needs were associated with lower scores on cognitive tests among Black and Latino individuals.
- Higher parental socioeconomic status was associated with increased resilience to the negative effects of Alzheimer's marker ptau-181, better baseline executive function and slower cognitive decline in older age.
- Compared with workers earning higher wages, sustained low-wage earners experienced significantly faster memory decline in older age.

"It's vital we continue to study social determinants of health related to cognition, including socioeconomic status, so we can implement public health policies and create community environments that can improve the health and well-being of all," said Matthew Baumgart, vice president of health policy at the Alzheimer's Association.

At the recent Alzheimer's Association Promoting Diverse Perspectives: Addressing Health Disparities Related to Alzheimer's and All Dementias conference, researchers gathered to share knowledge and drive collaboration on vital health equity issues, including social determinants of dementia risk like socioeconomic status.

Socioeconomic deprivation associated with increased dementia risk

Researchers are beginning to understand that risk of cognitive impairment and dementia are, to a significant degree, determined by the conditions in which people are born, grow, live, work and age. To better understand how socioeconomic conditions and genetic risk for developing dementia may interact, Matthias Klee, a Ph.D. student in psychology at the University of Luxembourg, and team, collaborated with researchers from universities of Exeter and Oxford to examine data from 196,368 participants' records in the U.K. Biobank whose genetic risk for developing dementia was assessed through risk scores.

With this sample, the researchers investigated the contribution of individual socioeconomic deprivation — such as low income and low wealth — and area-level socioeconomic deprivation — such as employment rates and car/home ownership — to the risk of developing dementia, and compared it with genetic risk for dementia.

Klee and team reported at AAIC 2022 that:
- Both individual socioeconomic and area-level socioeconomic deprivation contribute to risk of dementia; area-level socioeconomic deprivation was associated with increased risk of dementia for those in very disadvantaged neighborhoods.
- For participants with moderate or high genetic risk, greater area-level deprivation is associated with even higher risk for developing dementia, after adjusting for individual-level socioeconomic conditions.
- Analyses with imaging markers indicated that socioeconomic deprivation both on the individual and the area level were linked to higher burden of white-matter lesions, a marker indicating brain aging and damage.

"Our findings point to the importance of the conditions in which people live, work and age for their risk of developing dementia, particularly those who are already genetically more vulnerable," said Klee. "Both individual health behaviors and non-influenceable living conditions are relevant to explain risk of dementia, particularly for individuals with increased genetic vulnerability. This knowledge opens new opportunities to reduce the number of people affected by dementia not only through public health interventions but also by improving socioeconomic conditions through policymaking."

Economic adversity and neighborhood disadvantage related to lower cognitive testing scores

A large body of research has shown that SES can influence the risk of dementia later in life. SES is often studied using years of education and income level as general factors in health research; however, it is not yet understood how subjective indicators, such as perceived neighborhood environment and access to resources, might also play a role in cognitive health.

To understand this relationship better, Anthony Longoria, M.S., clinical psychology doctoral candidate at University of Texas Southwestern, examined perceptions of neighborhood physical environment and perceived SES alongside a measure of cognition (Montreal Cognitive Assessment scores) in 3,858 diverse individuals from the Dallas Heart Study.

The researchers found that lower quality neighborhood resources, poorer access to food/heating and medical care, and exposure to violence were related to lower scores on a commonly used test of cognitive function in Black and Hispanic, but not White participants.

"This is important given that minority groups disproportionately experience economic adversity and neighborhood disadvantage, in addition to being more likely to be diagnosed with dementia and receive less timely care," said Longoria.

Additional data analyses show perceived neighborhood disadvantage and economic status also may affect white matter volume (WMV) and hyperintensities (WMH) in the brain, both of which are associated with dementia risk and vascular factors. Reported lower income and education were associated with higher WMH in the overall sample, and lower trust, access to health care, income, and education were significantly associated with lower cerebral WMV. "Violence" was associated with more WMH in Black women, lower "trust" was associated with lower WMV in Hispanic men, and lower "access to medical care" was associated with lower WMV in White women.

"Scientists and policymakers should emphasize improving neighborhood resources — including safety, access to high-quality food, clean outdoor spaces and health care — when developing public health policies to help reduce community risk of Alzheimer's and related dementias," said Longoria.

Parental socioeconomic status associated with reduced impact of Alzheimer's pathology later in life

Little research to date has examined the impact of socioeconomic conditions on cognitive resilience, including biological markers of neurodegeneration. To study this, Jennifer Manly, Ph.D., professor of neuropsychology at Columbia University Irving Medical Center, and team, partnered with participants in a population-representative intergenerational study in New York City to determine whether parental socioeconomic status, as measured by years of education, buffers the association with levels of plasma ptau-181 (a marker of brain aging and Alzheimer's disease). They also studied whether there was an association with changes in memory among middle-aged adults, and whether moderation of Alzheimer's disease and related brain changes is similar across racialized and ethnic groups.

As reported at AAIC 2022, Manly and team found that higher parental socioeconomic status was associated with reduced impact of Alzheimer's marker ptau-181 on memory, language and executive function in their children as they age.

"Evidence from our multiethnic, intergenerational study suggests that early life socioeconomic conditions may promote cognitive reserve against Alzheimer's-related brain changes," said Manly. "These data show how structural and policy-driven investments, such as access to high quality education, have generational implications. Interventions that reduce childhood poverty could narrow Alzheimer's-related disparities."

Low hourly wages associated with faster memory decline in older age

Research into the effects of lower income on health is rapidly expanding. To study whether earning low hourly wages over a long period of time is associated with memory decline, Katrina Kezios, Ph.D., postdoctoral researcher at Columbia University Mailman School of Public Health, and team, used data from a national longitudinal study of American adults who were working for pay in midlife.

Kezios and team categorized study participants' history of low wages into those who (a) never earned low wages, (b) intermittently earned low wages or (c) always earned low wages, and then examined the relationship with memory decline over 12 years.

The researchers found that, compared with workers never earning low wages, sustained low-wage earners experienced significantly faster memory decline in older age. They experienced approximately one excess year of cognitive aging per 10-year period; in other words, the level of cognitive aging experienced over a 10-year period by sustained low-wage earners would be what those who never earned low wages experienced in 11 years.

"Our findings suggest that social policies that enhance the financial well-being of low-wage workers, including increasing the minimum wage, may be especially beneficial for cognitive health," said Kezios.

About the Alzheimer's Association International Conference® (AAIC®)
The Alzheimer's Association International Conference (AAIC) is the world's largest gathering of researchers from around the world focused on Alzheimer's and other dementias. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.
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- Matthias Klee, M.Sc., et al. Socioeconomic Deprivation, Genetics and Risk of Dementia (Funder: European Research Council)
- Anthony Longoria, M.S., et al. Allostatic load and the influence of economic adversity and neighborhood disadvantage on cognitive function in a multiethnic cohort (Funder: Moss Heart Trust)
- Jennifer Manly, Ph.D., et al. Parental SES buffers the effect of plasma pTau181 on memory among non-Latinx White, Latinx, and non-Latinx Black middle-aged adults (Funder: National Institute on Aging)
- Katrina Kezios, Ph.D., et al. Low Hourly Wages in Middle-Age are Associated with Faster Memory Decline in Older Age: Evidence from the Health and Retirement Study

*** AAIC 2022 news releases may contain updated data that does not match what is reported in the following abstracts.

Proposal ID: 66803

Title: Socioeconomic Deprivation, Genetics and Risk of Dementia

Background: The risk of Alzheimer's disease and other subtypes of dementia is determined by multiple pathways including genetic, environmental and lifestyle factors. With higher risk in socioeconomically deprived individuals, it remains unclear whether associations of genetic risk with dementia incidence may be modified by individual- or area-level socioeconomic deprivation.

Method: Participants of the UK Biobank study attended baseline assessments at 22 assessment centers between 2006 and 2010 and were followed-up until 2016 or 2017. Cox proportional-hazards regressions with area-level socioeconomic deprivation based on the Townsend Deprivation Index and individual-level socioeconomic deprivation based on car and home ownership, housing type, and income were run. A comprehensive polygenic risk score was employed and potential mediation through lifestyle and depressive symptoms was assessed. In an imaging substudy, associations of socioeconomic deprivation with six imaging-derived phenotypes including white matter hyperintensities were examined.

Result: 196,368 participants (mean [standard deviation] age, 64.1 [2.9] years, 52.7% female) aged 60 years and older, of European ancestry, without dementia diagnosis or cognitive impairment at baseline were followed-up for 1,545,316 person-years (median [interquartile range] follow-up, 8.0 [7.4-8.6] years). In high genetic risk and high area-level deprivation 1.71% (95% confidence interval, 1.44% to 2.01%) developed dementia compared to 0.56% (95% confidence interval, 0.48% to 0.65%) in low genetic risk and low-to-moderate area-level deprivation (hazard ratio, 2.31; 95% confidence interval, 1.84 to 2.91). In high genetic risk and high individual-level deprivation 1.78% (95% confidence interval, 1.50% to 2.09%) developed dementia compared to 0.31% (95% confidence interval, 0.20% to 0.45%) in low genetic risk and low individual-level deprivation (hazard ratio, 4.06; 95% confidence interval, 2.63 to 6.26). There was no significant interaction between genetic risk and area-level ($P = .77$) or individual-level ($P = .07$) deprivation. An imaging substudy including 11,083 participants found greater burden of white matter hyperintensities associated with higher socioeconomic deprivation.

Conclusion: In older adults without dementia area-level and individual-level socioeconomic deprivation and genetic risk were significantly and independently associated with a higher risk of dementia. Dementia prevention interventions may be particularly effective if targeted to people living in deprived households and areas, regardless of genetic vulnerability.

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# Figure 1. Risk of Incident Dementia for A Area-level and B Individual-level Socioeconomic Deprivation with Genetic Risk

A Area-level Socioeconomic Deprivation

Subgroup	Total No.	No. Dementia Cases / Person-Years	HR (95% CI)	P Value
Low Genetic Risk				
Low-to-Moderate Deprivation	31,648	177 / 249,647	1 [Reference]	
High Deprivation	7,626	70 / 59,124	1.30 (0.99-1.73)	.06
Intermediate Genetic Risk				
Low-to-Moderate Deprivation	94,316	744 / 744,724	1.39 (1.18-1.64)	<.001
High Deprivation	23,505	294 / 182,389	1.72 (1.41-2.08)	<.001
High Genetic Risk				
Low-to-Moderate Deprivation	31,131	345 / 246,144	1.96 (1.63-2.35)	<.001
High Deprivation	8,142	139 / 63,285	2.31 (1.84-2.91)	<.001
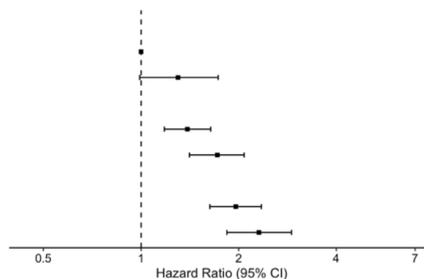
Hazard Ratio (95% CI): 0.5 1 2 4 7

B Individual-level Socioeconomic Deprivation

Subgroup	Total No.	No. Dementia Cases / Person-Years	HR (95% CI)	P Value
Low Genetic Risk				
Low Deprivation	8,110	25 / 63,790	1 [Reference]	
Intermediate Deprivation	23,624	134 / 186,093	1.50 (0.97-2.30)	.07
High Deprivation	7,540	88 / 58,887	2.69 (1.71-4.24)	<.001
Intermediate Genetic Risk				
Low Deprivation	23,417	103 / 184,307	1.42 (0.92-2.20)	.12
Intermediate Deprivation	70,774	614 / 558,529	2.24 (1.50-3.36)	<.001
High Deprivation	23,630	321 / 184,276	3.12 (2.06-4.74)	<.001
High Genetic Risk				
Low Deprivation	7,747	46 / 61,124	1.95 (1.20-3.17)	.01
Intermediate Deprivation	23,423	294 / 184,928	3.24 (2.14-4.89)	<.001
High Deprivation	8,103	144 / 63,377	4.06 (2.63-6.26)	<.001

Hazard Ratio (95% CI): 0.5 1 2 4 7
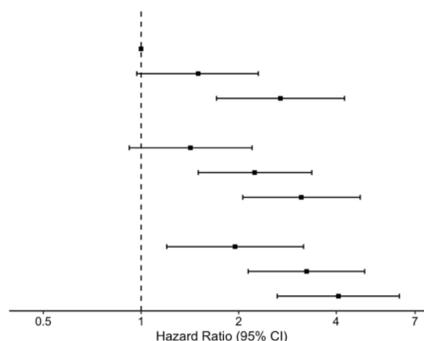
Note. All Cox proportional-hazards regressions were adjusted for the 20 first principal components of ancestry, 3rd degree relatedness, number of alleles used to compute polygenic risk, age, sex, education, marital status, healthy lifestyle, and depressive symptoms in last two weeks. Additionally, adjustments for individual-level (A) and area-level socioeconomic deprivation (B) were included. The total number and number of dementia cases per person-years are based on the first imputed data set.

Figure 2. Relative Difference in Imaging-derived Phenotype Volumes Between Higher and Lower Socioeconomic Deprivation Categories

A Area-level Socioeconomic Deprivation (High vs Low-to-Moderate)
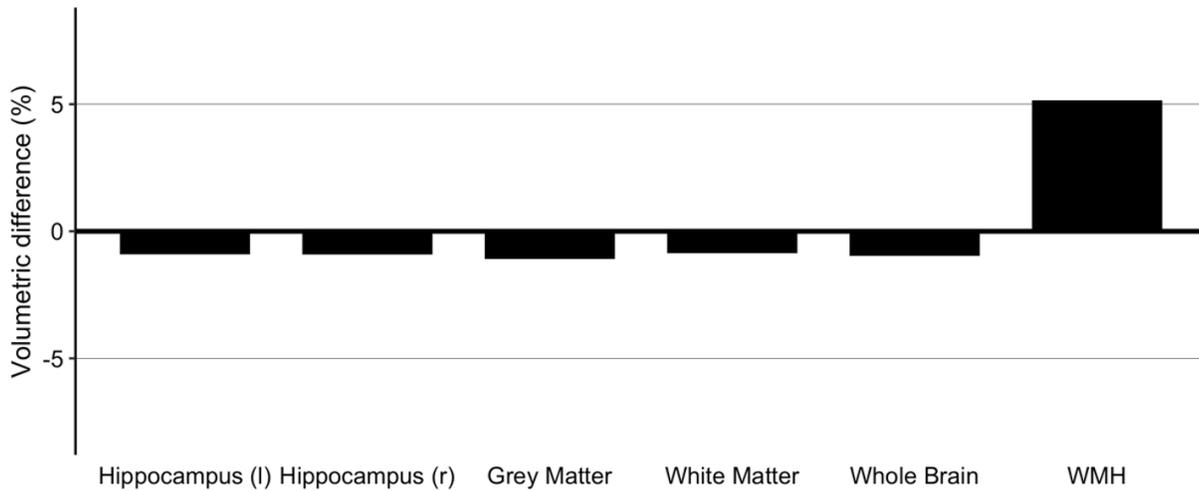
B Individual-level Socioeconomic Deprivation (High vs Low)
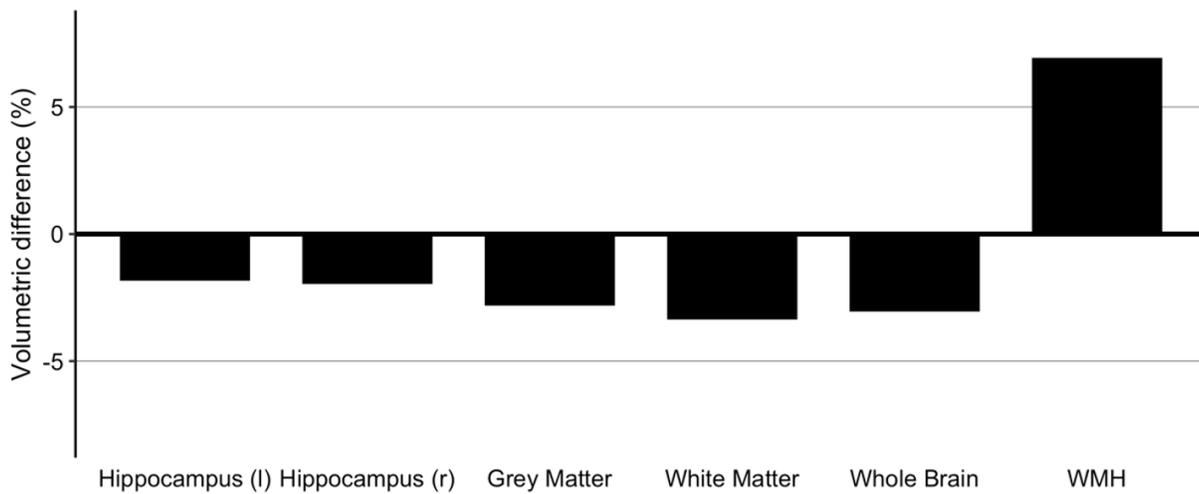
Note. Descriptive volumetric differences for volumes of grey and white matter, whole brain, hippocampus (l: left, r: right) and total burden of white matter hyperintensities (WMH) in between (A) high vs low-to-moderate area-level and (B) high vs low individual-level socioeconomic deprivation in the first imputed data set. Volumetric differences are computed as a descriptive ratio of mean volumes in higher deprivation compared to mean volumes in lower deprivation and are provided in percent.

Table 1. Baseline Characteristics of Participants

Characteristic	Total No. (%)[a]	
	Incident Dementia (n = 1,769)	No Incident Dementia (n = 194,599)
Age in years, mean (SD)	65.8 (2.7)	64.1 (2.8)
Sex		
Female	790 (44.7)	102,644 (52.8)
Male	979 (55.3)	91,955 (47.2)
Education[b,c]		
High	317 (17.9)	49,493 (25.4)
Medium	472 (26.7)	59,160 (30.4)
Low	255 (14.4)	30,939 (15.9)
Other[d]	725 (41.0)	55,007 (28.3)
Married or in a Relationship[c]	1,586 (89.7)	179,256 (92.1)
Depressive Symptoms in last 2 Weeks[c]	411 (23.2)	32,942 (16.9)
Healthy Lifestyle[c,e]		
5 (Favorable)	251 (14.2)	39,022 (20.1)
2-4 (Intermediate)	1,049 (59.3)	116,772 (60.0)
1 (Unfavorable)	469 (26.5)	38,805 (19.9)
Individual-level Socioeconomic Deprivation[c,e,f]		
1 (Low)	174 (9.8)	39,100 (20.1)
2-4 (Intermediate)	1,037 (58.6)	116,784 (60.0)
5 (High)	558 (31.6)	38,715 (19.9)
Area-level Socioeconomic Deprivation[c,e,g]		
1-4 (Low-to-Moderate)	1,266 (71.6)	155,829 (80.1)
5 (High)	503 (28.4)	38,770 (19.9)
Genetic Risk Group[e,h]		
1 (Low)	247 (14.0)	39,027 (20.1)
2-4 (Intermediate)	1,038 (58.7)	116,783 (60.0)
5 (High Genetic)	484 (27.4)	38,789 (19.9)

[a]Percentages may not sum to 100 because of rounding.

[b]Education was grouped based on the UNESCO ISCED 2011 classification system [5].

[c]Missing values have been imputed. Reported values are averaged across 5 imputed datasets.

[d]The response level other summarised options prefer not to answer and none of the above.

[e]Categories based on continuous scores. Numbers indicate quintiles from lowest (1) to highest (5).

[f]Individual-level socioeconomic deprivation summarises information on home and car ownership, housing type and income.

[g]Area-level socioeconomic deprivation based on the Townsend deprivation index [3].

[g]Genetic Risk based on a polygenic risk score for dementia [4].

multiethnic cohort

Background: Previous research has demonstrated a link between objective socio-economic indicators and cognitive test performance. Although some studies include subjective indicators, such as perceived neighborhood environment, little is known about which specific factors are most strongly associated with cognitive performance and whether these measures are useful beyond traditional SES proxies. Further, in addition to being disproportionately at risk of experiencing neighborhood disadvantage and lower SES, racial/ethnic minorities are more likely to be diagnosed with dementia and receive less timely care compared with White individuals. This study aims to investigate how perceived neighborhood environment and neighborhood disadvantage are related to cognitive performance within a large diverse sample.

Method: A probability-based sample of participants (N=3858; Female=59%; Black=51%; Hispanic=14%) from the Dallas Heart Study Phase 2 (DHS-2; Mean: Age=50, Education=13) were administered the Montreal Cognitive Assessment (MoCA), in addition to measures of perceptions of neighborhood physical environment and violence, and perceived SES. Multiple regression was used to determine associations of these variables with MoCA scores relative to traditional SES measures (i.e., income, education), controlling for demographic and relevant health factors. Post-hoc analyses stratified by racial/ethnic group were conducted to determine whether indicators differentially influenced test scores.

Result: After controlling for socio-demographic and health factors, reporting lower quality neighborhood resources and difficulty paying for "very basics like food and heating" and "medical care" were associated with lower MoCA scores in the overall sample. Post-hoc analyses revealed significant relationships between MoCA scores and quality of neighborhood resources, "food and heating," and "medical care" only in Black participants, while "violence" was significantly associated with lower MoCA scores in Hispanics. There were no significant relationships found in Whites. Overall, subjective measures of SES and neighborhood environment contributed modest variance in the overall model, specifically for Black and Hispanic participants (R^2=3% to 5%).

Conclusion: Experiencing neighborhood and economic adversity was associated with lower scores on a cognitive screening measure and accounted for more variance than income or education in Black individuals and income in Hispanic individuals, while no relationship was seen in White participants. Future research is needed to determine whether these allostatic stressors influence cognitive impairment or dementia later in life.

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Proposal ID: 66616

Title: Parental SES buffers the effect of plasma pTau181 on memory among non-Latinx White, Latinx, and non-Latinx Black middle-aged adults

Background: Inclusive ADRD research should consider social and structural forces as potential sources of cognitive reserve and resilience. Characterization of neuropathology is critical for cognitive reserve research, but few cohorts have AD biomarker data in concert with sufficient sample size, population representativeness, and multi-level, lifecourse measurement of determinants that is necessary to contribute substantial or novel evidence for when and where to intervene. We partnered with participants in a population-representative intergenerational study in NYC to determine whether parental socioeconomic status (PSES) buffers the association of plasma pTau181 concentrations with memory among middle aged adults, and whether moderation of neuropathology is similar across racialized and ethnic groups.

Method: Offspring participants were 1038 adult children (56±11-years-old range: 28-88, 68% women, 12.6±4 years education, 48% Latinx tested in Spanish, 24% Latinx tested in English, 21% non-Latinx Black, 7% non-Latinx White) of 694 parents in a longitudinal community-based study of Northern Manhattan residents age 65+. Blood collected from Offspring determined pTau181 concentration (Quanterix Simoa) and APOE genotype, and memory was tested with the Selective Reminding Test. PSES was measured with years of school collected directly from parents. Regression models examined associations of pTau181 concentration with memory, tested PSES as an effect modifier, and determined whether relationships differed by racial and ethnic group.

Result: In an unadjusted model, higher pTau181 concentrations predicted lower delayed recall (β=-0.438, 95% CI:-0.662,-0.214,p<0.001), and this was robust to addition of offspring age, sex/gender, years of education, racial and ethnic classification, APOE status, parental age, and PSES into the model (β=-0.332, 95% CI:-0.542,-0.122,p<0.001). pTau181 concentrations had a weaker relationship to delayed recall among offspring with higher PSES (β=-0.291, 95% CI: -0.540,-0.043,p<0.022) than among those with lower PSES (β=-0.477, 95% CI:-0.875,-0.078,p=0.019), and this effect modification was similar in all race and ethnicity groups.

Conclusion: Evidence from a multiethnic intergenerational study suggests that early life socioeconomic conditions promote cognitive reserve against AD neuropathology. The buffering effect of parental SES was present in all groups, but because racial and ethnic minoritized groups have disproportionate exposure to low SES in childhood, interventions that reduce childhood poverty could narrow ADRD disparities.

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Proposal ID: 61298
Title: Low Hourly Wages in Middle-Age are Associated with Faster Memory Decline in Older Age: Evidence from the Health and Retirement Study
Background: Little research has investigated the long-term relationship between low wages and memory decline, despite the growing share of low-wage workers in the US labor market. We examined whether cumulative exposure to low wages over 12 years in midlife is associated with memory decline in later life.
Method: We used 1992-2016 data from the Health and Retirement Study, a biennial longitudinal survey of nationally representative samples of Americans aged 50+. We analyzed data from 3,803 individuals born 1936-1941 using confounder-adjusted linear mixed-effects models. Low-wage was defined as hourly wage lower than two-thirds of the federal median wage for the corresponding year. Low-wage exposure history was categorized into 'never', 'intermittent', and 'sustained' based on wages earned from 1992 to 2004. Memory function was measured at each visit from 2004 to 2016 by a memory composite score; on average, participants completed 4.8 memory assessments from 2004-2016. Estimates were obtained in the total sample and within strata of sex (N_{males}=1,913, $N_{females}$=1,890).
Result: At the beginning of cognitive follow-up (2004) our sample was on average 65 years old with a mean memory score of 1.15 standard units. The confounder-adjusted annual rate of memory decline among workers who never earned low wages was -0.12 standard units, 95% CI: [-0.14, -0.10]. Compared with this, memory decline among workers with sustained earning of low midlife wages was significantly faster ($\beta_{time*sustained}$:-0.012, 95% CI: [-0.02, -0.01]), corresponding to an annual rate of -0.13 standard units for this group. Put into terms of "excess cognitive aging", the cognitive aging experienced by workers with sustained exposure to low midlife wages over a 10-year period is what workers never earning low-wages would experience in 11 years. Similar associations were found among males and females. No significant association between intermittent earning of low wages and memory decline was observed.
Conclusion: Sustained earning of low wages in midlife was significantly associated with a downward trajectory of memory performance in older age. Enhancing social policies to protect low-wage workers (e.g., increasing minimum wage) may be especially beneficial for the cognitive health of individuals with sustained low-wage employment in midlife.

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