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## Distinct domains of childhood disadvantage and cognitive performance among older Brazilians: Evidence from ELSI-Brazil

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### ABSTRACT

Objective: To investigate the relationship between of distinct domains of childhood disadvantage and cognitive performance among older adults within the context of a middle-income country. Methods: This study used baseline data (2015/2016) from the Brazilian Longitudinal Study of Aging (ELSI), a nationally representative cohort of 9412 adults aged 50 and over. Nine childhood exposure variables were grouped into three domains (family SES, childhood health, and cultural capital), for which scores were created. Survey-weighted Ordinary Least Squares (OLS) regressions estimated the association childhood disadvantage with cognitive performance as measured by immediate memory, late memory and semantic verbal fluency. Mediation analysis assessed whether adulthood socioeconomic status (SES) mediated this relationship of interest. Results: Important disparities in cognitive performance were observed, particularly in terms of age, education, income, occupational status. Before controlling for adulthood SES in the multivariable analysis, all domains of childhood disadvantage were found to be associated with lower cognitive performance across all three measures. After inclusion of adulthood SES variables, the observed associations only remained for semantic verbal fluency. Formal mediation analysis indicated that adulthood SES mediates 47.9% (95% CI: 34.3%-78.6%) of the association between later-life verbal fluency and poor childhood health, and 49.9% (95% CI: 43.6%-57.8%) of the association between later-life verbal fluency and low childhood cultural capital. Conclusions: We found that childhood disadvantage is associated with low performance in memory tests and

semantic verbal fluency tests among older Brazilians. Adulthood SES fully mediated the association between all domains of childhood disadvantage and memory performance and only partially mediated its association with verbal fluency. Our findings support policy efforts to enhance early childhood development and improve adulthood SES, and guide additional research to better the mechanisms driving these relationships.

## 1. Introduction

The socioeconomic conditions in which individuals are born and raised have been shown to strongly influence health later in life (Sachs-Ericsson et al., 2016; Slopen et al., 2014; Vanhoutte & Nazroo, 2016; Wise, 2016). Previous research (Demakakos et al., 2018; Holman et al., 2016; Ports et al., 2019) has also shown that different childhood circumstances, such as poor parenting, inadequate nutrition, disadvantaged socioeconomic position may increase the risk of chronic conditions, such as cancer, in adult life. Stringhini et al. (Stringhini et al., 2016) found that being in the lowest socioeconomic status (SES) groups during early stages of life was associated with increased risk of diabetes in later life. Similarly, childhood social disadvantage has been found to be associated with increased risk for cardiovascular diseases in adulthood (Camelo et al., 2015; Crump & Howell, 2020). Evidence on the impact of early life stressors on a variety of health outcomes have been increasingly observed among older adults leading to a burgeoning literature, especially among higher-income countries (Black et al., 2017; Cui et al., 2020; Lam et al., 2019; Pavela & Latham, 2016; Pikhartova et al., 2014; Vikström et al., 2011).

The ways through which the socioeconomic environment "gets under our skin" (a process known as biological embedding (Hertzman, 2012; Nelson, 2017)) seem to be numerous and are not thoroughly understood, despite the considerable growth of the literature around this

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topic. To date, several conceptual models have been proposed to explain the relationship between early life conditions and the health of older adults. These include the pathway model (which contends that childhood conditions put people on distinct life routes with important stressors for the health of individuals), the model of risk accumulation (which establishes that previous noxious exposures generate adverse effects that accumulate over time), and the social mobility model (which assumes that early life exposures may be modified by other socioeconomic environments throughout the life course) (Ben-Shlomo & Kuh, 2002; Carmeli et al., 2020; Liu et al., 2010; Yang et al., 2017). Another explanation, known as the sensitive period model, suggests that experiences during sensitive periods of development (such as gestation, birth, childhood, and adolescence) produce far-reaching and long-lasting biological effects that may not be reversable and condition disease risks in later life (Black et al., 2017). Some researchers have additionally suggested that immune responses, stress-related endocrine pathways, neural processes and epigenetic transformations may be key biological drivers of this process (Barker, 1999; Berens et al., 2017).

While the models discussed above provide clues to understanding different pathways linking childhood experiences with later life health, there is currently insufficient empirical evidence about which childhood adverse events could be expected to affect which health outcomes in older adults. Results from aging cohort studies based in high-income countries have suggested that certain childhood disadvantage circumstances tend to be associated with lower cognitive performance and/or cognitive decline in later life (Brandt et al., 2012; Cermakova et al., 2018; Faul et al., 2021; Tsang et al., 2022; Walsemann & Ailshire, 2020; Wehrle et al., 2020). But there have been fewer studies examining how these processes might unfold in low- and middle-income countries (LMICs) (Kobayashi et al., 2017; Maharani, 2020; Torres et al., 2021). The need for such evidence is particularly relevant in LMICs, given the rapid increase in the size of their older populations and their still developing economies and institutional capacities in terms of providing social protections for their aging citizens (Bloom et al., 2015). For example, Ye et al. found associations between low childhood socioeconomic status and poorer cognitive performance among older Chinese (Ye et al., 2022) while Lin et al. (Lin & Chen, 2021) found that adverse childhood circumstances are also associated with faster cognitive decline among the same population. In India, deprivations in childhood were found to be associated with later-life cognitive impairment (Muhammad et al., 2022).

Understanding determinants of the aging process is particularly relevant in Brazil, which has the world's sixth largest population with 17.8 million adults (8.5%) aged 65 and over (Lima-Costa et al., 2023). In 2020, life expectancy was estimated at 76 years, placing it squarely within the median for the Latin America and the Caribbean region, but healthy life expectancy was only 65, suggesting considerable burden of morbidity within the population (Wang et al., 2020). Hallmark features of Brazil's social and economic context include its high level of income inequality (Gini Index of 48.9 in 2020), making the country the 16th most unequal in the world in terms of income distribution (GINI index, 2019). Brazil is also known as a leader in innovative social policies, including a universal health system, a large conditional cash transfer program, and a national pension program, among others, although the impact of these programs on older adults as well as their long-term sustainability are largely unknown.

Given this context, the current study sought to address the following question: Is there an association between childhood disadvantage and cognitive performance in older adults in Brazil? More specifically, are there particular domains of childhood disadvantage that are more impactful on later-life cognition? Our hypothesis is that circumstances in early life related to disadvantaged socioeconomic status, poor quality parenting, lack of access to adequate nutrition and health care, late or inadequate schooling, among other variables, increase the risk of low cognitive performance later in life. Further, we aimed to address whether this relationship is potentially reversible by testing whether early adulthood experiences may mediate or moderate the relationship between early life disadvantage and cognitive performance in later life.

## 2. Analytical conceptual framework

This study explores two main means by which childhood disadvantage may affect health in later life (see Fig. 1). The graphical portrayal of this conceptual framework is intended to make a theory-informed analysis of the association in question and to aid in choosing essential covariates. We note that the graphic is not a formal Directed Acyclic Graph (DAG), so the lack of arrows between some nodes should not be interpreted as evidence of no relationship. The most fundamental idea is that adversity events or disadvantageous circumstances that take place during childhood can have a direct impact on the health of older people, which is represented by arrow *a*. This sole arrow would be enough to represent the entire phenomenon by which childhood disadvantage affect later life health if intermediary stages of life had no relevance. A more reasonable approach, however, is to hypothesize that events in early and mid-adult life may actually alter the relationship of interest. And in this case, adult life variables can affect that relationship in two possible ways.

First, childhood disadvantage may lead to certain events or pathways in early adulthood that ultimately have direct impacts later in life. In other words, these intermediary stages of life may mediate the relationship of interest (represented by arrows b and c in Fig. 1). For instance, dropping out of school can have a direct impact on cognition in later life because there may be cognitive abilities that can only be developed during a critical period of childhood (arrow *a*) as suggested by the pathway model or can impact cognition in advanced age because finishing school tends to provide better work and economic conditions throughout adult life and these better life conditions may lead to better cognitive performance in later life (arrows b and c) as suggested by the risk accumulation model. It is possible that some circumstances or domains of childhood disadvantage are fully mediated by adult life conditions, which means that such impacts could potentially be reversed with appropriate measures. If there is no evidence of mediation (either full or partial), that would be evidence that there may be domains of childhood disadvantage that have irreversible long-lasting effects as suggested by sensitive period hypothesis (Godfrey & Barker, 2001).

Second, the relationship between childhood disadvantage in later life health might be moderated by early and mid-adulthood circumstances (represented by arrow d). It suggests that the causal mechanisms by which the explanatory variable affects the outcome does not include intermediary stages of life but can be modified by them.

Although we show these effects in different diagrams for illustrative purposes, both effects could happen at the same time. Nonetheless, disentangling these effects is vital for a deeper understanding of the drivers of healthy aging. In addition, many other variables may confound the relationship of interest and therefore these factors must be controlled for in statistical models.

## 3. Methods

## 3.1. Data

We used baseline data from the Brazilian Longitudinal Study of Aging (ELSI – *Estudo Longidutinal de Saúde do Idoso*). This ongoing study, part of the larger family of global Health and Retirement Surveys, aims to understand the social and biological aspects of aging in a middle-income country setting and to inform health and social policies in the country. Participants aged 50 and over were drawn from a multi-stage cluster sample, stratified by municipality, census tract and residence. The baseline assessment took place in 2015–2016 and included an extensive in-person interview and collection of biological materials and other measures. The baseline sample had a total of 9412 people from 70 municipalities and is designed to be statistically representative of Brazil



Fig. 1. Conceptual framework for different possible relationships between childhood disadvantage and later life health.

as a whole as well as all five of the country's major geographic region. A detailed methodological description of the study, its data collection procedures and strategy, and its preliminary results has been published elsewhere (Lima-Costa et al., 2018, 2023). Further information can also be found in the official ELSI website (Fiocruz. ELSI, 2015), where all baseline data are made publicly available. The ELSI-Brazil study was approved by the Research Ethics Committee of the Oswaldo Cruz Foundation, Minas Gerais (CAAE 34649814.3.0000.509).

### 3.2. Measures

Measures of childhood disadvantage. Nine variables representing possible harmful exposures in childhood were available in the survey data. Some of these were already categorized as binary variables due to the survey question wording itself, while others variables required decisions on how best to operationalize their categorization, as described below. Given the shared nature of these variables, and the fact that no single measure would encompass the multidimensional concept of childhood disadvantage, we combined them into three domains of childhood disadvantage (family SES, childhood health, and cultural capital). The binary variables for (i) poor family SES in childhood (selfdeclared as poor from birth to fifteen years of age), (ii) both parents are illiterate and (iii) overcrowded home (defined as having four or more people per bedroom when the survey participant was ten years old) were grouped into the family SES domain. The binary variables for (i) poor self-rated childhood health status (coded as "yes" for average, poor and very poor, and "no" for good or very good), (ii) lack of tap water (defined as having water supply with plumbing at age 10) and (iii) hunger experience (defined as having experienced lack of food at home and going to bed feeling hungry in the period from birth to fifteen years of age) were grouped into the childhood health domain. The binary variables for (i) out of school at age 10, (ii) no books at home and (iii) lived in rural setting until age 15 were grouped into the cultural capital

domain. Examination of results from factor analysis (based on inspection of the resulting Eigenvalues and scree plots) confirmed that the variables composing each of the three scores were part of a single latent variable. In order to facilitate interpretation, we chose to operationalize each of these measures as a categorical variable with values representing 0, 1 or two or more 2 events within each domain.

*Measures of cognitive abilities in later life.* Two competencies were included in our study: memory and semantic verbal fluency. For assessing memory, survey respondents were asked to listen to a list of 10 random words and recall them immediately and then later in the interview. Thus, numerical variables (0-10) for immediate memory and late memory were generated. For semantical verbal fluency, each participant was asked to say as many animal names as possible in 1 min, generating another numerical variable for cognition. These validated measures have been used widely in the aging and cognition literature (Castro-Costa et al., 2018; Demakakos et al., 2012; Kang et al., 2016; Tsimpida et al., 2022; Zhang et al., 2020).

*Measures of early and mid-adulthood socioeconomic status.* Three variables were operationalized for this purpose: 1) educational attainment (categories: no study, some or complete elementary school, some or complete middle school, some or complete high school, some college study or degree); 2) occupational status (categories: intense physical effort, some physical effort, standing or walking most of the time, seated most of the time); and 3) household income (expressed in terms of Brazilian monthly minimum wages). Due to their high correlation, we combined these three variables into a single score using polychoric factor analysis for the mediation analysis. Similar and/or identical measures have been widely used in studies relying on data from sister aging surveys, such as SHARE and ELSA (Angelini et al., 2019; Arpino et al., 2018; Börsch-Supan et al., 2013).

For the construction of our multivariable models, we selected covariates based on insights from the existing literature and confirmed these choices using forward stepwise selection. These covariates include: age group (50–59, 60–69, 70–79, and 80 and over as an overall measure of risk); birth sex – given evidence of gender differences in cognitive outcomes, self-reported skin color (white; black; brown or other as a measure of exposure to racism and life chances).

## 3.3. Statistical analysis

Univariate and bivariate analysis were used to describe the sample and descriptive statistics are presented as weighted proportions. The

#### Table 1

Sociodemographic and health characteristics by cognitive performance.

bivariate relationships between each exposure and each outcome variable were calculated and portrayed in a figure. Statistical significance for the bivariate analyses was obtained through the design-based F test (Heeringa et al., 2010, p. 487). For multivariable analysis, ordinary least squares (OLS) regression models were applied and nested models (Hutcheson, 2011; Vittinghoff et al., 2012, p. 526) were used to study whether the addition of subsequent blocks of covariates improved model fit or provided evidence of possible mediation effects. Statistical significance of the OLS coefficients was obtained through the adjusted

	Immediate memory				Late memory (Words recalled from a list of 10)			Verbal flu	iency			
	(Words recalled from a list of 10)			a list of 10)				(Animal names said		l min)		
	0-3 words	4-5 words	6+ words	_	0-3 words	4-5 words	6+ words		<9 names	9-15 names	16+ names	
	%	%	%		%	%	%		%	%	%	
Age groups												
50–59	18.49	51.44	30.07	***	53.14	35.54	11.32	***	16.39	57.90	25.71	***
60–69	28.59	48.17	23.23		62.84	30.08	7.08		19.51	60.71	19.78	
70–79	48.59	40.27	11.14		77.82	19.30	2.88		26.10	55.40	18.50	
80+	69.10	25.90	5.00		92.46	6.22	1.32		31.63	43.10	25.27	
Sex												
Female	29.13	46.47	24.39		61.13	30.21	8.66		22.12	57.07	20.81	***
Male	29.14	48.12	22.74		63.36	29.06	7.58		17.32	57.56	25.12	
Race				_				_				
White	23.50	48.82	27.68	***	56.61	32.59	10.79	***	15.25	57.66	27.09	***
Black	32.88	45.11	22.01		68.16	24.41	7.43		26.39	53.71	19.89	
Brown	31.83	47.10	21.07		64.86	28.77	6.37		21.23	58.40	20.37	
Others	34.31	44.82	20.87		65.69	27.85	6.46		25.78	51.78	22.44	
Education (Years of schooling)				_				_				
Less than 5	50.48	40.53	8.99	***	80.83	17.34	1.84	***	31.64	53.90	14.46	***
Between 5 and 8	26.54	53.37	20.09		65.39	29.09	5.53		20.50	62.09	17.41	
9 or more	12.68	47.71	39.61		42.98	41.00	16.03		8.56	56.42	35.03	
Occupational status												
Intense physical effort	39.70	46.01	14.29	***	72.26	23.54	4.20	***	24.12	57.21	18.67	***
Some physical effort	33.94	46.69	19.37		68.09	25.45	6.46		23.04	57.50	19.46	
Standing or walking most of the	23.49	48.19	28.32		55.35	35.01	9.64		17.52	57.97	24.51	
time												
Seated most of the time	18.51	47.86	33.63		52.00	34.46	13.54		13.20	55.80	31.00	
Household income												
Less than 2 Minimum Wages	37.27	46.88	15.85	***	70.89	24.37	4.74	***	28.10	55.58	16.31	***
2–5 Minimum Wages	29.25	47.83	22.92		62.90	29.41	7.69		18.77	58.78	22.46	
5–9 Minimum Wages	18.82	46.25	34.93		50.45	36.99	12.56		11.41	59.70	28.89	
9+ Minimum Wages	14.39	45.78	39.83		43.93	38.67	17.40		9.34	51.19	39.48	
Living with partner												
No partner	34.55	44.03	21.42	***	66.13	27.11	6.76	***	22.26	54.85	22.89	**
Living with partner	26.15	49.00	24.84		59.98	31.09	8.93		18.56	58.70	22.74	
Residence in urban area												
No	41.61	44.65	13.73	***	73.81	22.22	3.98	***	27.20	57.14	15.66	***
Yes	26.89	47.70	25.40		60.07	31.02	8.91		18.59	57.32	24.08	
Region		· · · · · · · · · · · · · · · · · · ·					· <u> </u>					
North	33.37	45.11	21.52	***	63.58	29.56	6.85	***	20.62	60.62	18.76	***
Northeast	41.36	44.48	14.16		71.98	23.42	4.61		27.73	55.41	16.86	
Southeast	25.62	47.27	27.11		58.87	31.82	9.31		17.63	57.92	24.45	
South	22.70	48.99	28.30		59.13	30.93	9.94		16.41	57.49	26.10	
Midwest	22.90	54.27	22.83		56.90	33.79	9.31		15.88	56.42	27.71	
Chronic conditions							·					
None	24.28	47.74	27.99	***	58.40	31.10	10.50	***	17.91	55.46	26.64	**
One	29.18	47.75	23.06		62.45	30.04	7.51		19.71	59.20	21.09	
Two	31.38	46.65	21.98		63.26	29.91	6.83		21.37	56.06	22.57	
Three or more	33.10	46.37	20.53		65.55	26.88	7.58		21.25	58.00	20.75	
Poor self-rated health												
			00 4 4									
No	25.52	45.84	28.64	***	57.78	31.27	10.96	***	17.32	55.40	27.29	***

Weighted and survey-adjusted proportions.

Design-corrected F-test \* = p < 0.05; \*\* = p < 0.01; \*\*\*p < 0.001.

Data source: Brazilian Longitudinal Study of Aging (ELSI-Brazil), baseline assessment (2015-2016).

version of the Wald test (given the weighted, complex survey data) (Heeringa et al., 2010, p. 487). To formally assess our hypotheses regarding mediation, a formal analysis based on the Baron and Kenny approach was conducted using a system of seemingly unrelated regressions (SUR) and 1000 bootstrap samples to calculate confidence intervals of indirect and direct effects (Hayes, 2013). Missing data were generally low (about 4%) and were not concentrated in any specific individual type of variable. As a sensitivity test, we estimated our main regressions both with complete cases using listwise deletion and with imputed values using multiple imputation by chained equations (MICE) and found no clinically or statistically significant differences in results (data not shown). For simplicity, we report results of the complete case analysis.

All analyses were conducted in Stata 15 using the 'svy' command to account for the complex survey design and survey weights. Any not shown exploratory analysis is available under request.

#### 4. Results

Table 1 presents descriptive statistics for individual characteristics stratified by the three measures of cognitive performance (classified into three levels). The mean immediate memory score was 4.4 (standard deviation: 0.05), mean late memory score was 2.9 (standard deviation: 0.06) and mean score in verbal fluency was 12.0 (standard deviation: 0.16). Statistically significant bivariate associations were found for all covariates, except sex in regard to memory. A clear gradient of cognitive performance was observed for age, educational attainment, occupational status and income. In terms of age, the older a person is, the lower is their performance in the memory test (both immediate and late memory). The percentage of individuals aged 50–59 achieving the highest level of memory performance is approximately 6 times larger

than the one observed among those aged 80 and over. For verbal fluency, however, the age gradient is much less pronounced. For race/ skin color, we observe that those who self-identify as white have better performance across all cognitive measures while the other groups perform similarly. Regarding educational attainment, there is a sharp gradient indicating that the more educated a person is, the higher performance in cognitive tests. In the test of immediate memory, the percentage of people with less than five years of schooling in highest level of performance (8%) is around five times lower than among those with nine or more years of schooling (40%). For late memory, that gap goes to over 8 times. And for verbal fluency, the disparities are smaller, but still quite important. When it comes to occupational status, there is a gradient showing that the more physically intense is the work a person does/did, the lower their performance in these cognitive tests. For current household income, the pattern observed is that the higher the income the higher performance across all cognition measures. A statistically significant positive bivariate association was found for living with a partner in all three cognition tests, but its size is relatively small. Another relevant disparity in cognitive performance observed here was between rural and urban settings, as those living in rural settings perform substantially below those living in urban areas. In terms of macrogeographical regions in the country, those living in the South have the highest performances across all cognitive measures. Those living in the Northeast had consistently low performances. particularly in immediate and late memory tests, in which only 14% and 5% achieved the highest level of performance, representing about half of the performance observed in the South region. Another bivariate association was between the number of chronic conditions and the measures of cognitive performance. The higher the number of chronic conditions, the lower the cognitive performance. Lastly, those who in the poor current self-rated health category performed consistently lower in all three cognition tests.



Fig. 2. Bivariate relationships between cognitive performance and measures of childhood disadvantage. The numbers represent the percentage in the sample that experienced the exposure in question. The \* symbol represents that the difference is statistically significant at p-value <0.05.

Fig. 2 depicts the bivariate relationships between the nine individual exposure variables in childhood and the three measures of cognitive performance. It also shows the percentage of individuals in the sample that experienced each exposure in childhood. The green bars show the mean performance in the cognitive test among those who experience each one of the nine childhood exposures. The orange bars show the mean performance in the cognitive test among those who did not experience each one of the nine childhood exposures. The individual exposure variables are shown within their grouped domain (family SES, childhood health, or cultural capital. First, in regard to the domain 'family SES', we observed that being in poor financial status in childhood and have illiterate parents are associated with lower performance in all three tests, but no average association is observed for being raised in an overcrowded home. Second, among the exposure variables composing the domain 'childhood health', the only average association observed with lower cognitive performance was for those who grew up in homes with no access to tap water. Third, for the domain 'cultural capital', we found statistically significant associations between all their exposure variables and lower performance in all three tests. Being out of school of age 10, having no books at home and living in a rural setting until age 15 were also associated with lower performances in immediate memory, late memory and verbal fluency tests.

Table 2 shows the multivariable analysis based on OLS regression for all three outcome measures. Model 1 refers to regression including all explanatory variables (scores for each domain of childhood

disadvantage) and the following relevant covariates: age, birth sex, race/skin color, geographic region. Model 2 contains all these regressors as well as the adulthood SES variables (educational attainment, occupational status and household income) hypothesized as possible mediators and/or moderators. In other model specifications (data now shown), interaction terms were added (each childhood disadvantage score interacted with the adulthood SES variable), but they were not statistically significant neither they changed the size of coefficient of the explanatory variables. That ruled out the hypothesis of moderation effect by these adulthood SES variables. When interpreting the coefficients described below, it is important to highlight the additional complexity created by our model specification that includes all exposure variables. For example, while exposure variable A may be a confounder for the relationship between exposure variable B and the outcome variable Y, by definition, exposure variable B is a mediator of the relationship between A and the outcome variable. These results should therefore be interpreted as the association of exposure A with outcome Y after controlling for appropriate covariates and independent of exposures B and C (Westreich & Greenland, 2013).

All domains of childhood disadvantage exhibited negative associations with memory measures (both immediate and late). On average, having 2 or more negative family SES exposures is associated with recalling 0.26 (95% CI: 0.12; 0.40) and 0.25 (95% CI: 0.07; 0.43) fewer words in the immediate and late memory tests, respectively, compared to not having any of these exposures in childhood. In comparison to not

#### Table 2

#### OLS estimates for childhood disadvantage domains.

	Immediate Memory		Late Memory		Verbal Fluency		
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	
Childhood Disadvantage Scores (0, 1 or 2+ events)	1						
Family SES Domain (ref: 0)							
1	-0.06	0.03	0.03	0.13	-0.03	0.25	
	(-0.07)	(0.06)	(0.07)	(0.07)	(0.25)	(0.25)	
2+	-0.26***	-0.04	-0.25**	-0.024	-0.32	0.27	
	(-0.07)	(0.06)	(0.09)	(0.08)	(0.22)	(0.22)	
Child Health Domain (ref: 0)							
1	-0.31***	-0.15*	-0.29***	-0.14	-1.45***	-0.96***	
	(-0.07)	(0.06)	(0.09)	(0.09)	(0.20)	(0.22)	
2+	-0.32***	-0.11	-0.23*	-0.03	-1.51***	-0.95***	
	(-0.07)	(0.07)	(0.09)	(0.09)	(0.23)	(0.25)	
Cultural Capital Domain (ref: 0)							
1	-0.22**	-0.04	-0.35***	-0.14	-1.39***	-0.87***	
	(-0.07)	(0.07)	(0.09)	(0.09)	(0.25)	(0.22)	
2+	-0.51***	-0.03	-0.64***	-0.17	-2.05***	-0.98***	
	(-0.08)	(0.09)	(0.09)	(0.11)	(0.23)	(0.23)	
Education (ref: less than 5 years of schooling)							
Between 5 and 8 years		0.58***		0.41***		0.78***	
		(0.07)		(0.08)		(0.18)	
9 or more years		1.04***		1.07***		2.39***	
		(0.08)		(0.08)		(0.23)	
	<u> </u>						
Occupational status (ref: intense physical effort)							
Some physical effort		0.12		-0.03		-0.20	
		(0.08)		(0.08)		(0.21)	
Standing or walking most of the time		0.31***		0.08		-0.07	
		(0.08)		(0.08)		(0.19)	
Seated most of the time		0.36***		0.13		0.27	
		(0.09)		(0.10)		(0.28)	
Household income (ref: <2 Minimum Wages)							
2–5 Minimum Wages		0.067		0.02		0.29*	
0		(0.06)		(0.06)		(0.13)	
5–9 Minimum Wages		0.26***		0.32***		0.77**	
		(0.06)		(0.07)		(0.23)	
9+ Minimum Wages		0.25*		0.27*		1.16***	
		(0.11)		(0.12)		(0.29)	
Observations	9084	<u> </u>	9084		9069		

Coefficients from survey-adjusted OLS regression. Standard errors in parentheses. \*\*\*p < 0.001, \*\*p < 0.01, \*p < 0.05.

Other covariates include age, sex, race, macrogeographic region. Data source: ELSI-Brazil, 2015–2016

Differences in the number of observations across models refer to listwise deletion for missing data.

having any of the negative exposures of childhood health domain, having had one exposure is associated on average with 0.32 (95% CI: 0.18; 0.46) fewer words recalled in the immediate memory test and 0.29 (95% CI: 0.11; 0.47) fewer words in the late memory test. In terms of harmful exposures within the cultural capital domain, one score is associated on average with 0.22 (95% CI: 0.06; 0.36) and 0.35 (95% CI: 0.17; 0.53) fewer words recalled in the immediate and late memory tests, respectively, while having a score of 2+ is associated with 0.51 (95% CI: 0.35; 0.67) and 0.64 (95% CI: 0.46; 0; 82) fewer words recalled in the immediate and late memory tests. Yet, these effects disappear when we control for variables of adulthood SES. The multivariable analysis for the memory outcomes further reinforced the positive impact of schooling and the higher income.

In regard to semantic verbal fluency, we found significant associations only for the childhood health and the cultural capital domains. Before controlling for the possible mediation effect of adulthood SES variables, having at least one of three negative exposures of the childhood health domain is associated with 1.45 (95% CI: 1.06; 1.84) fewer animal names recalled in the verbal fluency test, which represents about 12% of the average performance in this population. This effect size is reduced to 0.96 (95% CI: 0.53; 1.39) after controlling for possible mediators. Without controlling for the possible mediation effect of adulthood SES variables, having one of three negative exposures of the cultural capital domain is associated on average with 1.39 (95% CI: 0.90; 10.88) fewer animal names recalled in the verbal fluency test in comparison to not having any of these childhood exposures. Similarly, having two or more of these exposures is associated on average with 2.05 (95% CI: 1.60; 2.50) fewer animal names recalled in the verbal fluency test. After controlling for possible adulthood SES mediation, these last two coefficients decreased to 0.98 (95% CI: 0.; 1.15) and 0.93 (95% CI: 0.53; 1.43), respectively.

The decrease in the OLS coefficients of the explanatory variables after the inclusion of adulthood SES variables suggest a mediation effect (as generally hypothesized in the analytical conceptual framework). To further investigate it, we conducted a formal mediation analysis using a single variable constructed through polychoric factor analysis using the three adulthood SES variables available: educational attainment, occupational status and income. It indicated that adulthood SES mediates 47.9% (95% CI: 34.3%–78.6%) of the association between later-life verbal fluency and the harmful exposures of the childhood health domain, and 49.9% (95% CI: 43.6%–57.8%) of the association between later-life verbal fluency and the harmful exposures of cultural capital domain in childhood.

## 5. Discussion

Our study sheds light on the relationship between childhood disadvantage and cognitive performance in later life within the context of a large middle-income country. We investigated the influence of nine potentially harmful exposure variables grouped within three domains of childhood disadvantage on three validated and widely used measures of cognition among older adults. Overall, our findings suggest that childhood disadvantage is associated with lower cognitive performance among older Brazilians. In the multivariable analysis, we found statistically significant associations between the scores for all domains of childhood disadvantage and all outcome measures of cognition. In particular, we observed that the associations between harmful exposures both of the 'family SES' domain and of the 'childhood health' domain with later-life memory performance may be fully mediated by adulthood SES. Yet, for verbal fluency, we observed no consistent association with the family SES domain, but important ones with the childhood health domain and the cultural capital domain. These last two associations were found to be partially mediated by adulthood SES. All that said, it is important to highlight that due to the fact that the final regression models contain multiple exposure variables, all these associations should be interpreted as "after controlling for appropriate covariates and

independent of other exposures".

This work has several strengths. First, based on our scoping review of the literature, particularly those from existing aging cohorts, this study is unique in its investigation of the relationship between multiple measures of childhood disadvantage and later-life cognition in Latin America using nationally-representative data. Second, unlike other studies in the field that investigate the relationship between a single childhood exposure variable and/or a single health outcome in later life, we studied a variety of exposures, both individually and grouped within domains of childhood disadvantage. The existence of these distinct domains was informed by theory and confirmed by factor analysis, allowing us not only to have a more nuanced view of the relationships between harmful childhood experiences and health outcomes across the life course, but also to obtain further insights on the possible underlying mechanisms. Third, by using a variety of model specifications in the multivariable analysis, we were able to disentangle different pathways that may exist (mediation) and those that seem to be weak or nonexistent (such as the lack of evidence for a moderation effect by latent variables representing mid-adulthood SES).

Although not the main focus of the present work, we found important socioeconomic disparities in cognitive performance. The gradients of cognitive performance in relation to education, income and occupational status are particularly salient. Macrogeographical disparities are also present, as has been previously documented by Castro-Costa et al. (Castro-Costa et al., 2018).

Our findings suggest that the specific circumstances of childhood disadvantage may affect different aspects of cognition through different mechanisms. For example, while the results for memory point out directly to mechanisms related to the social mobility model, the findings around semantic verbal fluency suggest a mix of mechanisms related to social mobility but also to the sensitive period paradigm, given that there is a substantial portion of the observed that is direct.

While studies of this type are common in the high-income world, little evidence is available from LMICs. In a study of older rural South Africans (Kobayashi et al., 2017), poor childhood health was found to be associated with lower cognitive scores while having had a father in a formal job was associated with better cognitive scores, but only the latter association was partially mediated by educational attainment. Another study using the same sample of older adults from South Africa found that most adverse childhood events (ACEs) were not associated with cognitive performance in older adults, except for having a parent who had a drug abuse problem (Kobayashi et al., 2020). A study based on an aging cohort study in India found that older adults who had poor health status and/or poor financial status in childhood were more likely to suffer from cognitive impairment in later life (Muhammad et al., 2022). Low childhood SES has been found to be associated with cognitive impairment in China (Ma et al., 2021; Ye et al., 2022) and this relationship was partially mediated by educational attainment. Cognitive decline has also been found to be associated with childhood disadvantage in China (Lin & Chen, 2021) and in this case education was also found to be an important mediator. Unlike what we saw in the Brazilian population of older adults, the study on Chinese older adults also found an important gender gap in cognitive performance. It is important to highlight the difficulty in directly comparing findings from these other studies because each has operationalized outcome measures in slightly different ways. Some studies, for example. combine memory tests with arithmetic tests into a cognitive score, some do not consider semantic verbal fluency, and others focus solely on the rate of cognitive decline. Nevertheless, taken together, these studies indicate the importance of early childhood on older adult health in LMICs.

Investigating the ways through which specific circumstances of childhood disadvantage affect health later in life is vital not only for expansion of scientific knowledge about the ways biological mechanisms underly these statistical associations, but also to aid in the development of tailored interventions to promote health among aging populations and tackle health disparities. Nonetheless, childhood disadvantage is a not phenomenon that manifests in single event or realm and may have an overall combined or cumulative impact via stress, biological underdevelopment, and more rapid decline of health functions.

Some limitations of this study must be taken into account when interpreting its findings. Because we relied on cross-sectional data, no longitudinal aspect involved in the phenomenon of interest could be investigated and therefore we are unable to determine for how long childhood stressors affected these individuals neither could we assess whether their cognitive performances relate to a late decline in life or are linked to some unobserved factor. While the problem of reverse causality is less of a concern, the issue of omitted variable bias cannot be completely ruled out, although the careful work of theory-driven and statistically tested model specification provides some confidence in the results presented here. There is also a possible limitation related to a threat of recall bias, given that individuals were asked to recall conditions that occurred many decades in their past. Given that the cognitive performance (particularly memory) is the outcome, the exposure reporting is likely differential and may indeed have led to bias in our results. Another concern is that there might be sample selection (survival bias, which is typical of aging surveys), because only individuals who survived at least to age 50 when the survey baseline assessment occurred could be included in the study. This might be relevant for Brazil given that infant mortality was very high before the 1970s when survey participants were growing up (, 2020World Population Prospects -Population Division - United Nations). It is reasonable to hypothesize that survival bias could lead to an underestimate our coefficients, given the relationship between being older and cognitive decline. An additional limitation is that the health behaviors included as covariates could be also operating as mediators. It is unclear whether or not their inclusion is biasing the association estimate, even though they improve our statistical models' goodness of fit. A last possible concern is that of missing data, which was quite small at only 4%. Sensitivity tests that used multiple imputation by chained equations (MICE) provided virtually identical results to the ones obtained with listwise deletion suggesting that missing data did not overly affect our results.

## 6. Conclusion

Overall, our study found that multiple dimensions of childhood disadvantage are associated with lower performance in memory tests and semantic verbal fluency tests among older Brazilians. Breaking down childhood disadvantage into three different domains (family SES, childhood health, and cultural capital) helped us better understand the phenomenon and its possible mechanisms. In regard to memory tests, all domains of childhood disadvantage were found to be associated with lower performance in the multivariable analysis when excluding adulthood SES, indicating a total mediation pathway. For semantic verbal fluency, the childhood health domain and the cultural domain had more pronounced negative associations and were found to be mediated by adulthood SES (around half of the effect was indirect in both cases). These findings should inform efforts to develop interventions targeting early childhood development as well as fostering other key factors (such as education and poverty alleviation efforts sch a conditional cash transfers) to strengthen adulthood SES and thus lessen the impact of early life stressors on the health of older adults.

### Author statement

Brayan V. Seixas carried out the study design, literature review, data analysis and draft the first manuscript. James Macinko participated in the study design, writing and supervised the work. All authors reviewed and approved the final manuscript.

#### **Ethics statement**

The current paper relied on publicly available data from the Brazilian Longitudinal Study on Aging (ELSI – Estudo Longitudinal de Saúde do Idoso). The ELSI-Brazil study was approved by the Research Ethics Committee of the Oswaldo Cruz Foundation, Minas Gerais (CAAE 34649814.3.0000.509). Participants signed separate informed consent forms for each aspect of the survey. The consent fully clarifies and ensures all the rights and obligations of the participant. All interviewers were trained to answer and explain any potential doubts or queries raised by the participant who is entitled to consult a third party before signing the consent.

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### Declaration of competing interest

The authors declare that there is no conflict of interest.

### Data availability

The data used here is publicly available at https://elsi.cpqrr.fiocruz.br/.

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#### B.V. Seixas and J. Macinko

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