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Family instability in childhood affects language and memory in adulthood: results from the *Pró-Saúde* Study, Brazil

Instabilidade familiar na infância afeta a linguagem e memória na vida adulta: resultados do Estudo Pró-Saúde

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Abstract *The study aims to investigate associations between adverse childhood psychosocial exposures and declarative memory, language, and executive function in adults with secondary schooling or more and without dementia. In 361 participants from the Pró-Saúde Study, we estimated associations between maternal educational attainment, principal source of the family´s income, food insecurity, and childhood family structure and performance in learning, word recall, and semantic and phonemic verbal fluency tests using multiple linear regression models. Individuals whose mother was the family breadwinner (mean difference: -1.97, 95%CI: -3.27; -0.72) and head-of-household (mean difference: -1.62, 95%CI: -2.89; -0.35) or who lived with a non-parental caregiver or in institutions in childhood (mean difference: -2.19, 95%CI: -4.29; -0.09) showed a reduction in the mean number of words in language and memory in adulthood. The results provide further evidence of the effect of adverse exposures in childhood. Without effective interventions, such exposures are likely to have far-reaching impacts on cognition.*

Key words *Pró-Saúde Study, Cognitive function, Childhood adversities*

Resumo *Nosso objetivo é investigar as associações de exposições psicossociais adversas na infância com memória declarativa, linguagem e função executiva em adultos livres de demência com ensino médio completo ou mais. Em 361 participantes do Estudo Pró-Saúde estimamos as associações entre escolaridade materna, principal apoio financeiro familiar, insegurança alimentar e estrutura familiar na infância com o desempenho no teste de aprendizagem e evocação de palavras, e fluência verbal semântica e fonêmica usando modelos de regressão linear múltipla. Ter a mãe como principal suporte financeiro familiar (diferença média: -1,97, IC95%: -3,27; -0,72) e ter morado apenas com ela (diferença média: -1,62, IC95%: -2,89; -0,35) ou outra pessoa/ser institucionalizado (diferença média: -2,19, IC95%: -4,29; -0,09) na infância permaneceu associada à uma redução na média de palavras nos testes de linguagem e memória na vida adulta. Nossos achados adicionam mais evidências sobre o efeito de exposições na infância que, sem intervenções apropriadas, provavelmente terão legados de longo alcance na cognição.*

Palavras-chave *Estudo Pró-Saúde, Função cognitiva, Adversidades precoces*

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Introduction

The brain is a major locus of integration and influence for a multitude of environmental factors that shape human life, ranging from physical factors (e.g., nutrition) to psychosocial factors (e.g., family stability)[1]. Given the effects of stress on the development of brain structures and areas, exposure to single-parent households in early life may compromise cognitive health, since people growing up in these environments are more likely to experience perceived stress and emotional insecurity due to changes in family structure[2]. On average, single motherhood is also associated with lower income, greater risk of poverty, worse maternal mental health, poor parenting practices, and a range of other disruptions such as home and school moves and multiple family transitions[3]. Still, it is not known whether different types of childhood family structure shape cognition over time or result in experiences in adulthood that may largely explain early onset of cognitive decline.

Family structures have evolved since the 1960s due to changes in marriage, divorce, and fertility, leading to a marked increase in single parent families[2]. Traditionally, fathers tended to provide material assets while mothers´ contributions to their children´s upbringing were based on maternal educational attainment. However, measurement of these characteristics can be affected by gender bias due to heteropatriarchal values. For example, paternal socioeconomic status has been considered the most stable way to measure family social class (traditionally, men spent more time in the labor market than women)[4,5]. A gender perspective on family income could thus help shed light on differential patterns of maternal and paternal socioeconomic indicators within the family and compare their relative contributions to the children´s development.

In addition, more than two billion people worldwide, mainly in low- and middle-income countries, lack regular access to safe, nutritious, and sufficient food[6]. However, most research on the relationship between those conditions and cognitive function has been conducted in Europe and North America (and more recently in China). Much less is known about the effects of early life circumstances on cognitive function in middle-aged adults in low- and middle-income countries (LMIC)[7].

Emerging data indicate that early-life socioeconomic status (SES)[1] predicts late-life level of cognitive function. Meanwhile, higher lifetime education, a marker for high SES, consistently predicts lower risk of cognitive impairment or dementia in late life[8,9]. Previous evidence reinforce the importance of studies that contribute to disentangle the understanding about how nutritional and psychosocial factors during childhood influence different domains of cognition in healthy adults with higher lifetime education.

In adults without dementia, with secondary schooling or greater, the current study thus aims to investigate if still the effect of exposures in childhood, such as maternal educational attainment, childhood family structure, principal family breadwinner, and food insecurity, on declarative memory, language, and executive function in adulthood.

Methods

The study is part of the longitudinal *Pró-Saúde* Study[10], a research project with a longitudinal, multidimensional design in a working-age population living in the second largest metropolitan area in Brazil. The larger study´s overall objective is to investigate the role of socioeconomic and sociocultural determinants of health patterns among civil servants at university campuses in the state of Rio de Janeiro, Brazil. The current analyses include data obtained in waves 1 (1999) and 4 (2012-2013). In all waves, questionnaires were self-administered at the workplace, with the support of trained and certified research assistants.

In wave 4, cognitive performance tests were applied to a subsample of 520 participants 35-79 years of age, stratified by age and education. For purposes of the current analyses, we excluded participants with incomplete secondary schooling or less (n=32), with a history of stroke (n=4), over 64 years of age (to avoid age-related changes in cognitive performance) (n=31), and in use of medications that potentially interfere with cognition such as anticonvulsant, antipsychotic, antiparkinsonian, and anticholinesterase drugs (n=40). Participants were instructed to bring their prescriptions and packages of any medications used in the previous two weeks. We also excluded individuals with missing data on personal educational attainment (n=1), cognitive function tests (n=1), maternal educational attainment (n=21), food insecurity (n=21), main source of family´s income (n=6), and parental structure in childhood (n=2). The current analyses thus included 361 participants (Figure 1).

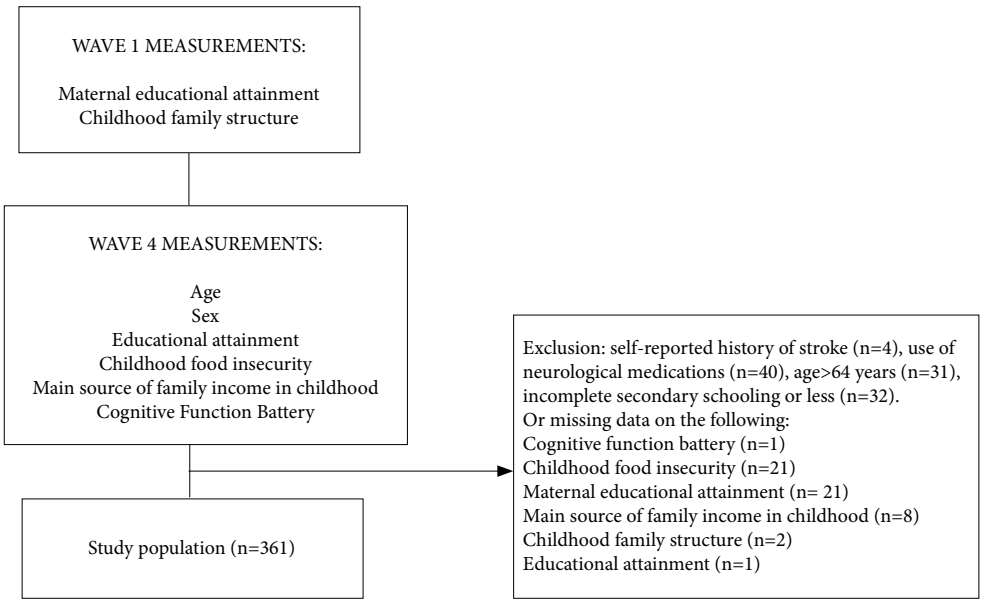

Figure 1. Flowchart of study population.

Source: Authors.

The study protocol was approved by the Institutional Review Board of the Institute of Social Medicine, Rio de Janeiro State University (CAAE: 04452412.0.0000.5260). All participants signed written informed consent.

The response variables were the final scores obtained at wave 4 in the following cognitive function tests:

• Learning and word recall tests, validated for the elderly Brazilian population[11,12], used to evaluate declarative memory by asking the participant to repeat ten unrelated words presented three times, each time for two seconds and in different order. Recall was tested by asking for the same ten words after completing other tests. We used the sum of the scores from these two tests (0 to 40 words).

• Semantic[13], and phonemic[11,12] verbal fluency tests were used to assess executive function and language, respectively, by asking participants to say as many names of animals as possible (semantic test) or words starting with the letter F (phonemic test) in one minute. The score corresponds to the total number of correct animal names and words beginning with the letter "F" provided by the participant.

The target exploratory variables were maternal educational attainment, principal source of the family´s income, food insecurity, and childhood parental structure. Maternal educational attainment and childhood family structure at 12 years of age were assessed at wave 1. Maternal educational attainment was assessed with the question, "What was the last grade of school your mother completed?", and the answers were grouped in three categories: secondary or more (≥11 years of schooling), primary (≥8 and <11 years of schooling), and incomplete primary or less (<8 years of schooling). Childhood family structure (two-parent, maternal, paternal, or lived with a non-parental caregiver or in an orphanage or shelter) was assessed with the question, "When you were 12 years old, which parents or other adults or guardians did you live with most of the time?".

The family´s main source of income (father, mother, other) and food insecurity (no; yes) in childhood were measured in wave 4. Family income was accessed with the question, "When you were 12 years old, who was considered the head of the family or the main breadwinner in the house where you lived?". Childhood food insecurity was measured by the modified version[14] derived from the Brazilian Household Food Insecurity Scale[15]. The scale includes six questions "When you were 12 years old, how often was

there not enough money at home for food?", "How often did you not have a healthy and varied diet?", "Did you eat only a few types of food?", "Did you eat less than you felt you should?", "Did you have to skip meals?", and "How often did you go a whole day without eating or have only one meal a day?". All questions had four response options (frequently, sometimes, rarely, never). Individuals who responded "frequently", "sometimes", or "rarely" to at least one of the items were considered to have experienced household food insecurity at age 12. The scale presented test-retest reliability, kappa coefficients were considered moderate (0.65), Cronbach's alpha showed satisfactory internal consistency (0.84), and factor loadings were above 0.800[14]. Other childhood information on living parents (father and mother living, father living, mother living, and father and mother deceased), family economic status (wealthy, middle-class, poor, very poor), place of residence (state capital, large city, small city, countryside), physical abuse by parents (no; yes), and age when the person worked for the first time. However, these other data were not associated with any test of cognition and were not presented.

The following variables measured at wave 4 were investigated as potential confounders in the analyses: sex (male; female), age (continuous in the multivariate analyses), and current educational attainment (university or higher and secondary schooling).

The study population´s characteristics were described as relative frequencies for categorical variables and as means and standard deviations (SD) for continuous variables (Table 1). Crude means (SD) of the outcomes according to each exposure were presented, and the associations were tested using analysis of variance (ANOVA) for normal distribution with multiple comparison tests (Bonferroni) (Table 2).

Multiple linear regression models were used to estimate the magnitude of the associations through mean differences and 95% confidence intervals (95%CI) (Table 3). We first estimated the crude associations between each putative explanatory variable (maternal educational attainment, principal source of family´s income, food insecurity, and childhood family structure) and performance in each cognitive function test (learning and word recall tests, semantic and phonemic verbal fluency tests) (Model 1). We then included adjustment for age, sex, and participants´ educational attainment (Model 2). Regression diagnostics were run to verify whether the full models violated the assumptions for linear regression (i.e., normality of error distribution, linearity, homoscedasticity). Analyses were performed with Stata 15.0 (Stata Corporation, College Station, USA).

Table 1. Characteristics of study population, adults without dementia, with secondary schooling or greater. *Pró-Saúde* Study, Rio de Janeiro, Brazil (n=361).

Variable	Number of observations (%)
Sex	
Male	181 (50.1)
Female	180 (49.9)
Age (years)	
<45	84 (23.3)
45-54	193 (53.4)
55-64	84 (23.3)
Educational attainment	
University or greater	229 (63.5)
Secondary schooling	132 (36.5)
Maternal educational attainment	
Secondary schooling or greater	119 (33.0)
Primary schooling	95 (26.3)
Incomplete primary schooling or less	147 (40.7)
Main source of family income in childhood	
Father	296 (82.0)
Mother	54 (15.0)
Other	11 (3.0)
Childhood family structure	
Two-parent	283 (78.4)
Maternal	52 (14.4)
Paternal	7 (1.9)
Other caregiver or lived in institution	19 (5.3)
Childhood food insecurity	
No	175 (48.5)
Yes	186 (51.5)
Learning and word recall (words), mean (SD)	29.0 (4.8)
Semantic verbal fluency (words), mean (SD)	20.7 (5.7)
Phonemic verbal fluency (words), mean (SD)	13.7 (4.4)

SD=standard deviation; n=number of observations; cm=centimeters.

Source: Authors.

Table 2. Mean number of words (SD)in learning and word recall tests and semantic and phonemic verbal fluency tests according to adverse childhood exposures. *Pró-Saúde* Study, Rio de Janeiro, Brazil.

Exposures	Mean number of words (SD)		
	Learning and word recall tests	Semantic verbal fluency test	Phonemic verbal fluency test
Maternal educational attainment			
Secondary schooling or greater	29.3 (4.9)	22.0 (5.6)	14.0 (3.7)
Primary schooling	29.2 (4.7)	20.8 (6.1)	13.9 (4.9)
Incomplete primary schooling or less	28.6 (4.7)	19.7 (5.2)**	13.4 (4.5)
Main source of family income in childhood			
Father	28.9 (4.8)	20.9 (5.7)	14.1 (4.3)
Mother	29.4 (4.7)	19.6 (5.8)	11.8 (4.6)**
Other	27.7 (5.1)	20.6 (4.1)	14.0 (2.7)
Childhood family structure			
Two-parent	29.2 (4.7)	28.9 (5.5)	14.1 (4.2)
Maternal	29.0 (4.4)	20.7 (6.0)	12.3 (4.7)*
Paternal	25.5 (4.7)	16.5 (4.0)	11.7 (5.7)
Other caregiver or lived in institution	26.4 (6.3)	19.8 (7.4)	13.4 (4.6)
Childhood food insecurity			
No	29.7 (4.7)	21.6 (5.4)	13.7 (3.9)
Yes	28.3 (4.7)**	19.9 (5.8)**	13.7 (4.8)

Analysis of variance performed for normal distribution with multiple comparison tests (Bonferroni). *0.01<p<0.05 and **p<0.01. SD=standard deviation.

Source: Authors.

Results

Among the 361 participants, 50.1% were men, 53.4% were 45-54 years of age, and 63.43% had university degrees or greater. For most of the participants, at 12 years of age, the mother had not completed primary school (40.7%), the father was the main source of family income (81.9%), they were living with both the father and mother (78.3%), and the household was experiencing food insecurity (51.5%). The mean number of words spoken in the learning and word recall test was 29.0 (SD=4.8), mean score on the semantic verbal fluency test was 20.7 (SD=5.7), and mean score on the phonemic verbal fluency test was 13.7 (SD=4.4) (Table 1).

Participants whose mothers had incomplete primary schooling or less performed worse on average in the semantic verbal fluency test. Participants whose mothers were the main source of family income and in households headed by the mother spoke fewer words in the phonemic verbal fluency test. And participants who experienced food insecurity in childhood performed worse in learning, word recall, and semantic verbal fluency tests (Table 2).

In the linear regression analysis (Table 3), participants whose mothers had incomplete primary schooling or less were associated with a mean reduction of 0.73 words (95%CI -1.89; -0.43) in the learning and word recall tests and 2.38 words (95%CI -3.74; -1.01) in the semantic verbal fluency test compared to those whose mothers had secondary schooling or greater. Those whose mothers were the main source of family income in childhood showed 2.28 fewer words (95%CI: -3.54; -1.01) in the phonemic verbal fluency test compared to those whose fathers were the main breadwinner. Adults that had lived in households headed by the mother alone in childhood showed 3.69 fewer words (95%CI: -7.27; -0.10) and those who had lived in families headed by the father alone showed 2.78 fewer words (95%CI: -5.01; -0.56) in the learning and word recall tests compared to those who had lived in two-parent households. Adults who had lived only with the mother in childhood also showed 4.37 fewer words (95%CI: -8.62; -0.12) in the semantic verbal fluency test compared to those who had lived with both the father and mother. In addition, those who had experienced childhood food insecurity spoke 1.35 fewer words on

Table 3. Associations between adverse childhood exposures and learning and word recall tests and semantic and phonemic verbal fluency tests among adults without dementia with secondary schooling or greater. *Pró-Saúde* Study, Rio de Janeiro, Brazil.

	Learning and word recall		Semantic verbal fluency		Phonemic verbal fluency	
	Model 1 Mean difference (95%CI)	Model 2 Mean difference (95%CI)	Model 1 Mean difference (95%CI)	Model 2 Mean difference (95%CI)	Model 1 Mean difference (95%CI)	Model 2 Mean difference (95%CI)
Maternal educational attainment						
Secondary schooling or greater	1.00	1.00	1.00	1.00	1.00	1.00
Primary schooling	-0.10 (-1.40; 1.19)	0.69 (-0.53; 1.92)	-1.27 (-2.79; 0.24)	-0.52 (-2.00; 0.95)	-0.15 (-1.34; 1.94)	0.43 (-0.74; 1.61)
Incomplete primary schooling or less	-0.73 (-1.89; -0.43)	0.14 (-0.98; 1.27)	-2.38 (-3.74; -1.01)	-1.32 (-2.67; 0.03)	-0.57 (-1.64; 0.49)	0.16 (-0.90; 1.24)
Main source of family income in childhood						
Father	1.00	1.00	1.00	1.00	1.00	1.00
Mother	0.44 (-0.95; 1.84)	0.65 (-0.66; 1.97)	-1.36 (-3.02; 0.29)	-0.74 (-2.34; 0.84)	-2.28 (-3.54; -1.01)	-1.97 (-3.21; -0.72)
Other	-1.25 (-4.16; 1.65)	-1.44 (-4.17; 1.27)	-0.35 (-3.79; 3.08)	0.16 (-3.12; 3.45)	-0.04 (-2.67; 2.58)	0.15 (-2.41; 2.72)
Childhood family structure						
Two-parent	1.00	1.00	1.00	1.00	1.00	1.00
Maternal	-0.22 (-1.63; 1.19)	-0.21 (-1.54; 1.12)	-0.17 (-1.85; 1.49)	0.18 (-1.41; 1.78)	-1.83 (-3.13; -0.53)	-1.62 (-2.89; -0.35)
Paternal	-3.69 (-7.27; -0.10)	-1.62 (-5.05; 1.81)	-4.37 (-8.62; -0.12)	-2.39 (-6.50; 1.71)	-2.42 (-5.71; 0.86)	-0.74 (-4.00; 2.51)
Other caregiver or lived in institution	-2.78 (-5.01; -0.56)	-2.19 (-4.29; -0.09)	-1.10 (-3.75; 1.54)	-0.14 (-2.68; 2.39)	-0.72 (-2.75; 1.31)	-0.14 (-2.13; 1.84)
Childhood food insecurity						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	-1.35 (-2.34; -0.36)	-0.80 (-1.74; 0.13)	-1.69 (-2.86; -0.52)	-1.08 (-2.21; 0.04)	-0.00 (-0.91; 0.91)	0.39 (-0.49; 1.29)

Linear regressions were performed. Model 1: crude model. Model 2: variables adjusted for participants´ gender, age, and educational attainment. 95%CI=95% confidence interval; cm=centimeters.

Source: Authors.

average (95%CI: -2.34; -0.36) in the learning and word recall tests and 1.69 fewer words (95%CI: -2.86; -0.52) in the semantic verbal fluency test compared to those who had not experienced hunger in childhood.

However, after adjusting for gender, age, and the participant´s educational attainment (Model 2), only those whose mother was the main source of family income (1.97 fewer words spoken, 95%CI: -3.27; -0.72) and those who had lived only with the mother in childhood (1.62 fewer words spoken, 95%CI: -2.89; -0.35) remained associated with the phonemic verbal fluency test. Also, those who had lived with another caregiver or in institutions in childhood (2.19 fewer words spoken on average, 95%CI: -4.29; -0.09) remained associated with the results of learning and word recall tests (Table 3). However, maternal educational attainment and childhood food insecurity were not associated statistically with any cognitive domain in adulthood.

Discussion

In adults without dementia with secondary schooling or greater, after adjustment, individuals who had lived in single-parent households

headed by their mothers and whose mothers were the main source of income used fewer words and performed worse on the phonemic verbal fluency test. In addition, living in households headed by other caregivers or in institutions (e.g., orphanages) also reduced the number of words used in learning and word recall tests in adulthood. Family structure reflects material, psychosocial, and emotional resources of caregivers and quality of learning environment, critical for early development.

Studies report that single motherhood is associated with poorer home environments and parenting behaviors, including lack of routine, harsh discipline, and lower levels of parental supervision[16,17]. Single mothers are also at higher risk of poor mental health[16], e.g., maternal depression is associated with lower levels of children´s cognitive and emotional well-being[18]. Meanwhile, exposure to a socially enriched family environment in two-parent households appears to benefit cognitive development by stimulating learning through language and reasoning while fostering opportunities for interaction and socialization[19].

Previous evidence from three British birth cohorts[20] found that single motherhood has become much more common and still presents, on average, negative consequences for children's cognitive attainment, because it reduces the resources available to them. Over time, the effects of parental separation on children´s outcomes become increasingly affected by the age at which parents separate. Individuals whose parents separated when they were already school age experienced smaller deficits, largely because mothers who separated when their children were older suffered smaller reductions in their financial status. In our study, exposures were measured at age 12, when there would supposedly be less long-term impact. Still, the study provides new insights on adverse effects on cognition that persist into adulthood.

On average, women have lower levels of employment and lower occupational status than men[8] and are more likely to be heads of single-parent households. Mothers are the primary teachers of small children, and their language input can vary[21,22]. However, growing evidence indicates that early-life SES disproportionately affects language ability and neurolinguistic systems compared to other neurocognitive domains[1]. In addition, previous evidence suggests that the home language environment underlies the link between SES and the structure and function of canonical language-related brain regions[23,24]. Structurally, lower SES is associated with reduced gray matter in left Perisylvian regions underlying phonological, semantic, and syntactic components of language comprehension and production[23,25], as well as with bilateral occipitotemporal regions involved in reading[26,27].

Previous evidence[28] shows that low maternal educational level had independent negative effects on semantic memory, learning, attention, executive control, and language. Maternal education is associated with better health and nutritional throughout life[29]. Higher maternal education may provide to better learning environments in childhood, more intellectual stimulation, and greater mentorship quality, which, in turn, can lead to higher personal educational attainment, better cognitive performance[30] and greater resistance to Alzheimer's disease (AD)[8,9]. Also, a systematic review and meta-analysis of 37 studies (n=46,727) found significant associations between dementia and food deprivation and low educational level[31].

In our study, maternal educational attainment and childhood food insecurity were not associated with any cognitive domains. However, in individuals whose mothers were the main source of family income and who lived only with their mothers or with other caregivers or in institutions, there was a negative impact on language and memory in adulthood. Almost two fewer words spoken from a mean word around twelve on each cognitive test. It is important to highlight that this effect was observed even in those who eventually reached secondary schooling or more, and in general population of Brazil can be much stronger considering that 46.6% of the population aged 25 and over still concentrated in education levels up to primary schooling or equivalent[32]. Our results add on understanding of dementia predictors since the effects of family structure in childhood on fewer words spoken in healthy adults may be an indicative of worse progression of cognition throughout life.

The latent causal model suggests that adversities in early life can affect brain maturation during childhood and adolescence and impair cognitive performance in adulthood by reducing myelin, dendritic branching, and development of connectivity patterns[7]. Early-life adversity would thus be associated with poor cognitive function even after controlling for factors in adulthood because some negative effects on cognition from childhood adversity can be irreversible.

This study has some limitations. Although the cognitive battery assessed several domains,

it was brief by necessity. Multiple tests within a domain provide better sensitivity and specificity for detecting differences in specific cognitive domains. We intentionally used minimally adjusted models for sociodemographic characteristics and thus cannot speculate on other factors that may have influenced cognition. Our measures of childhood conditions were based on retrospective self-reports, so there was a potential recall bias, possibly resulting in underestimation of the association between childhood conditions and cognition. Finally, we lacked information on the conditions leading to the childhood family structure (e.g., divorce versus death of one or both parents).

Despite these limitations, the study has several strengths, including analysis of adults without dementia, with complete secondary schooling or greater, with multiple exposures in childhood, and in effects across more than one cognitive domain in adulthood. Although the cognitive function tests performed do not have cutoff points to dementia to adults, in our study we aim to investigate the determinants of cognitive function of healthy adults. Although our reduced sample size from *Pró-Saúde* study, we observed similar characteristics, especially considering the exposures of interest, of participants included compared to those excluded in the present analyses (data not-shown). The study adds to a growing body of literature indicating long-term impacts from adverse psychosocial conditions in childhood on cognitive function in mid-life, especially because most studies focus on this relationship in childhood outcomes[2,20]. We found that individuals whose mother had been the main breadwinner and head-of-household or who had lived with other caregivers or in institutions at 12 years of age performed worse in language and memory in adulthood. Overall, the findings suggest two policy responses: 1) income support for single-parent families or for children living with other adults or in institutions and 2) measures to address the growing gap in adult attainment for individuals whose parents or guardians experienced adverse economic conditions.

Collaborations

LF Araújo: conceptualization, formal analysis, writing of original draft, and revision and editing. E Faerstein: conceptualization, data curation, fundraising, investigation, methodology, and revision and editing.

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