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ORIGINAL ARTICLE

Childhood family adversity and recurrent depression in adulthood: the findings of three ELSA-Brasil follow-up visits

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Objective: This study investigated the association between childhood family adversity and depression in a cohort of Brazilian adults over three visits.
Methods: A total of 12,636 participants from the Longitudinal Study of Adult Health (ELSA-Brasil), baseline (2008-2010) and followed up in 2012-2014 and 2017-2019, were included. Five types of family dysfunction and the childhood family dysfunction score (0, 1, and $\geqslant$ 2 dysfunctions) were used. The Clinical Interview Schedule-Revised was used to assess depression in visits 1 and 2 or 3. Multinomial logistic regression models estimated crude and adjusted OR and 95%CI.
Results: The mean age of the sample was 59.6 (SD, 8.8) years, 7.4% presented depression in one visit, and 2.2% presented it in two or three visits. After adjustment, compared to no family dysfunction, mental disorder (OR = 3.91; 95%%CI 2.94-5.21), substance abuse (OR = 2.14; 95%CI 1.65-2.77), and parental separation/divorce (OR = 1.55; 95%CI 1.12-2.15) increased the odds of depression in two or three visits. Exposure to $\geqslant$ 2 types of family dysfunction increased the odds of depression in one, and two or three visits in a dose-response gradient.
Conclusion: Exposure to childhood family dysfunction contributes to the occurrence and recurrence of depression in adults. Interventions to prevent dysfunctional family environments and their repercussions on children can reduce the burden of depression.

Keywords: Adverse childhood experiences; childhood trauma; depression; cohort study

Introduction

Adverse childhood experiences (ACEs) are stressful and/or traumatic events experienced between birth and 18 years of age. They include different types of violence, neglect, separation/loss of parents, and exposure to dysfunctional family environments.[1] ACEs are a major public health problem, with high prevalence rates worldwide, especially in low- and middle-income countries,[2] where more than half of the studied populations reported at least one ACE.[3] Brazilian studies have found high rates of at least one ACE, reaching 58-70% between 2015 and 2017.[4,5]

Childhood and adolescence are sensitive periods of emotional and cognitive development involving increased susceptibility to adverse exposures.[6] Such experiences can hyperactivate the hypothalamic-pituitary-adrenal axis and alter sympathetic autonomic response to stress, weakening the ability to respond to challenges and adverse conditions throughout life, which affects physical and mental health over the short and long term.[7] Many children experience multiple ACEs, and exposure to more than one or to certain combinations can increase their deleterious health effects.[8]

Depression is among the most frequent mental disorders associated with ACEs. In 2019, the worldwide prevalence of depression reached 279.6 per 100,000 people (95%CI 251.6-310.3), making it one of the leading causes of global disease burden.[9] In a representative sample of the Brazilian population, self-reported depression increased from 7.6% in 2013 to 10.2% in 2019.[10] Furthermore, the COVID-19 pandemic appears to have increased the global prevalence by 30%.[11]

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Depression is usually a recurrent mood disorder, with multiple episodes occurring throughout life, resulting in a significant burden of suffering and additional effects. It is estimated that 85% of all people who have experienced a depressive episode have already experienced one or will experience another in their lifetime.[12] One meta-analysis of 13 cohorts (n=217,929) found that the risk of adult depression is almost three times higher in children who experience an ACE than those who do not.[13] Few studies have investigated the impact of ACEs on adult mental health in low- and middle-income countries,[14] such as Brazil. Its high prevalence of ACEs and large socially vulnerable population[15] reinforce the importance of such research. The present study investigated the association between childhood family adversities and depression and depression in three follow-up visits of a multicenter cohort of Brazilian adults born between 1934 and 1975, in addition to the existence of a dose-response gradient between the number of childhood family adversities and depression.

Methods

Study design

This longitudinal study is based on data from the Longitudinal Study of Adult Health (Estudo Longitudinal de Saúde do Adulto [ELSA]-Brasil), in which exposure to ACEs was retrospectively measured. ELSA-Brasil investigated a multicenter and multiracial cohort of public servants regarding the incidence and progression of chronic noncommunicable diseases and associated biopsychosocial, behavioral, social, and occupational factors. Visit 1 (baseline: 2008-2010) included 15,105 active and retired civil servants (aged 35 to 75 years) from public education and research institutions in six state capitals in the northeastern, southern, and southeastern regions of the country.[16] New examinations and interviews took place in 2012-2014 (visit 2) and 2017-2019 (visit 3). In all three visits, trained and certified examiners collected data through standardized questionnaires, face-to-face interviews, and clinical and laboratory examinations.

Study population

Of the 15,105 participants, 550 died and 1,964 did not attend visit 3, resulting in 12,636 eligible participants (an 86.8% retention rate across all three visits, excluding deaths). Due to missing data on each family dysfunction, the analytic sample varied for each exposure type.

Study variables

Depression assessment in the three visits

The presence of depression was assessed with the Clinical Interview Schedule-Revised, a structured interview translated and adapted to Brazilian Portuguese,[17] which enables the diagnosis of a depressive episode in the last 7 days according to ICD-10 criteria. The depression variable, assessed at visit 1 and follow-up visits 2 and 3, was categorized as no visits, one visit, and two or three visits.

Explanatory variables

This study focuses on childhood family adversities that were retrospectively assessed using five items selected from the Adverse Childhood Experiences International Questionnaire[18] in visit 3 (Table 1). The scale's original reference evaluation period, 18 years, was lowered to 14 years. Five binary variables were created, with a value of 1 indicating the presence of family dysfunction.

The accumulation of childhood family adversities was measured by a childhood family dysfunction score that corresponded to the sum of all positive responses for each dysfunction type. Scores ranged from 0 to 5 and were categorized as: 0, 1, or $\geqslant$ 2 family dysfunctions. Three, four, and five dysfunctions were aggregated due to low numbers.

Covariables

The covariates were obtained in visit 3. Potential confounding factors were defined according to an operational model which considered that exposure to family dysfunction temporally preceded the investigated outcomes, since they occurred by 14 years of age, thus assuming a longitudinal and potentially causal relationship. The selected variables were sex; age (categorized as 41-49, 50-59, 60-69, and $\geqslant$ 70) to represent different birth cohorts, which was included as a continuous variable in the regression models; self-reported race (White, Brown, Black, Asian, or Indigenous), and maternal education

Table 1 Explanatory variables and selected items from the ACE-IQ related to family dysfunction[†] measured at follow-up visit 3 of the ELSA-Brasil study, 2017-2019

Family dysfunction	Questionnaire item
Substance abuse	Before you turned 14, did you live with someone who drank too much or was an alcoholic, or who abused illegal drugs or prescription drugs?
Mental disorder	Did you live with someone who had depression, mental illness, or wanted to kill themselves?
Incarceration/conviction	Did you live with someone who was ever arrested or convicted?
Parental[†] separation	Did your parents separate or divorce?
Parental[†] death	Did your mother, father, or guardian die before you turned 14?

ACE-IQ = Adverse Childhood Experiences International Questionnaire; ELSA-Brasil = Estudo Longitudinal de Saúde do Adulto.
[†] The ACE-IQ considers biological and non-biological parents.

(none/incomplete elementary school high school, complete elementary school/incomplete high school, complete high school/incomplete higher education, complete higher education), since it has been associated with family dysfunction and depression.[19]

Data analysis

The population was described according to covariates and childhood family dysfunction score using absolute and relative frequencies; distribution differences were estimated with Pearson's chi-square test. Multinomial logistic regression models estimated the magnitude of the association of each family dysfunction and the childhood family dysfunction score with depression in the three visits. The reference category was no depression in any follow-up visit. The odds ratios and 95%CI were estimated from the crude and adjusted models for each explanatory variable. The analyses were performed in Stata 14.0.

Ethics statement

The research ethics committees of the Instituto de Saúde Coletiva, Universidade Federal da Bahia (0017.1.069.000-06), Fundação Oswaldo Cruz (0058.0.011.000-07), Hospital Universitário, Universidade de São Paulo (University Hospital/USP 0016.1.198.000-06), Universidade Federal de Minas Gerais (0186.1.203.000-06), Centro de Ciências da Saúde, Universidade Federal do Espírito Santo (08109612.7.2003.5060), and Hospital das Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul (0017.1.069.000-06) approved the study. All participants provided written informed consent prior to inclusion.

Results

The mean participant age in visit 3 was 59.6 years (SD, 8.8). As shown in Table 2, the majority of participants were female (55.5%), White (53.7%) and their maternal education level was none/incomplete elementary school (64.1%). In total, the prevalence of depression was 7.9 in one visit and 2.2% in two or three visits. The following variables were more associated with having $\geqslant$ 2 dysfunctions than having none: age group 50-59 years (46.2% vs. 38.7%), Black race (24.5% vs. 11.9%), and a maternal education level of none/incomplete elementary school (71.8% vs. 61.2%). The prevalence of depression in one visit was higher among participants exposed to $\geqslant$ 2 family dysfunctions than among those exposed to none (12.7 vs. 6.2), as was the presence of depression in two or three visits (5.9% vs 1.4%) (Table 2).

Table 2 Characteristics of the study population according to the childhood family dysfunction score, ELSA-Brasil, 2017-2019

		Childhood family dysfunction score %		
		0	1	$\geqslant$ 2
Total	11,762 (100.0)	7,035 (59.8)	3,357 (28.5)	1,369 (11.8)
Sex				
Male	5,233 (44.5)	46.7	43.2	36.2
Female	6,529 (55.5)	53.3	56.8	63.8
			$p < 0.0001$	
Age group (years)				
41-49	1,506 (12.8)	11.6	13.5	17.3
50-59	4,824 (41.0)	38.7	43.7	46.2
60-69	3,800 (32.3)	33.5	31.7	27.8
$\geqslant$ 70	1,632 (13.9)	16.2	11.1	8.7
			$p < 0.0001$	
Race				
White	6,252 (53.7)	59.4	46.8	41.7
Mixed	3,161 (27.2)	25.0	30.2	30.9
Black	1,805 (15.5)	11.9	19.4	24.5
Asian	306 (2.6)	3.0	2.3	1.5
Indigenous	109 (0.9)	0.7	1.3	1.4
			$p < 0.0001$	
Maternal education				
None/incomplete elementary school high school	7,436 (64.1)	61.2	67.4	71.8
Complete elementary school/incomplete high school	1,630 (14.1)	14.7	13.5	11.9
Complete high school/incomplete higher education	1,957 (16.9)	18.6	14.7	12.9
Complete higher education	568 (4.9)	5.5	4.3	3.4
			$p < 0.0001$	
Depression in three visits[†]				
No visits	10,416 (90.3)	92.4	89.6	81.4
1 visit	857 (7.4)	6.2	7.9	12.7
2 or 3 visits	258 (2.2)	1.4	2.5	5.9
			$p < 0.0001$	

Data presented as n (%), unless otherwise specified.
ELSA-Brasil = Estudo Longitudinal de Saúde do Adulto.
p-value estimated with Pearson's chi-square test.
[†] Depressive episode in the last 7 days according to Clinical Interview Schedule-Revised results.

In total, 40.3% of the participants reported at least one childhood family adversity. Substance abuse was the most prevalent family dysfunction (41.1%), followed by parental separation (24.6%). Almost 17% reported a mental disorder in the family environment, 12.4% reported the death of a parent, and 3.4% reported the incarceration/conviction of a family member.

Multivariate analysis showed that, compared to no depression in three visits, the odds of depression in one visit were increased by the following dysfunction types: incarceration/conviction of a family member, 118% (95% CI 1.44-3.31); mental disorder, 113% (95%CI 1.75-2.60); substance abuse, 37% (95%CI 1.17-1.61); and parental separation, 32% (95%CI 1.08-1.61). The odds of depression in two or three visits were increased by the following dysfunction types: mental disorder, 291% (95%CI 2.94-5.21); substance abuse, 114% (95%CI 1.65-2.77); and parental separation, 55% (95%CI 1.12-2.15). Incarceration/conviction only increased the odds of depression in one visit, and parental death was not associated with depression (Table 3).

In the adjusted models, exposure to one family dysfunction type increased the odds of depression by 22% (95%CI 1.03-1.43) in one visit and by 58% (95%CI 1.17-2.14) in two or three visits. Exposure to $\geqslant$ 2 types of family dysfunction increased the odds of depression by 98% (95%CI 1.63-2.41) in one visit and by 288% (95% CI 2.83-5.31) in two or three visits, suggesting a dose-response effect between exposure and the outcome (Table 4).

Discussion

The present study found that exposure to family dysfunction in childhood, specifically substance abuse, mental disorders, and parental separation, were associated with the recurrence of depression in two or three visits of the ELSA-Brasil cohort. The presence of substance abuse, mental disorders, incarceration/conviction, and parental separation were also associated, to a lesser degree, with depression in a single follow-up visit. A dose-response gradient was found between the number of dysfunctions and depression, i.e., that the higher the number of adversities indicative of family dysfunction experienced by 14 years of age, the greater the odds and severity of depression, which was expressed by the persistence of depression in multiple assessments. It is important to note that adjustment for age, sex, race, and maternal education only marginally changed the magnitude of the association.

The association between family dysfunction (except incarceration/conviction and parental death) and the recurrence of depression in the study's three visits was consistent with previous results from cross-sectional studies that retrospectively measured ACEs[20] and from longitudinal studies that measured them prospectively.[21] Interestingly, the 1958 British Birth Cohort also found no association between parental death (between 7 and 16 years of age) and the occurrence of psychiatric disorders at age 45, although a positive association was found with these disorders in adolescence (16 years of age) and early adulthood (23 years of age).[22] The authors considered that having at least one adult to assume parental roles may have had a protective effect in adulthood, but not at younger ages. Considering the longitudinal evidence above, it is possible that exposure to the types of family dysfunction examined in this study had a variable effect on the occurrence of mental disorders in adults, and some of these effects may be

Table 3 Association between selected family dysfunctions in childhood and depression[†] in three visits, ELSA-Brasil, 2017-2019

	Depression in three visits[†]	
Family dysfunction	1 visit	2 or 3 visits
Substance abuse (n=12,047)		
Crude model	**1.59 (1.36-1.85)**	**2.48 (1.93-3.19)**
Adjusted model	**1.37 (1.17-1.61)**	**2.14 (1.65-2.77)**
Mental disorder (n=12,041)		
Crude model	**2.40 (1.98-2.91)**	**4.36 (3.30-5.77)**
Adjusted model	**2.13 (1.75-2.60)**	**3.91 (2.94-5.21)**
Incarceration/conviction (n=12,053)		
Crude model	**2.45 (1.66-3.63)**	**2.08 (1.01-4.27)**
Adjusted model	**2.18 (1.44-3.31)**	**1.95 (0.94-4.04)**
Parental separation (n=11,738)		
Crude model	**1.47 (1.21-1.78)**	**1.84 (1.35-2.52)**
Adjusted model	**1.32 (1.08-1.61)**	**1.55 (1.12-2.15)**
Parental death (n=12,044)		
Crude model	1.09 (0.89-1.34)	1.29 (0.92-1.80)
Adjusted model	1.10 (0.88-1.36)	1.32 (0.93-1.86)

Data presented as odds ratio (95%CI).
Odds ratio estimated by multinomial logistic regression. Reference category: no visits.
Model adjusted for age, sex, race, and maternal education.
Bold type denotes significant associations ($p < 0.05$).
ELSA-Brasil = Estudo Longitudinal de Saúde do Adulto.
[†] Depressive episode in the last 7 days according to Clinical Interview Schedule-Revised results.

Table 4 Association between childhood family dysfunction score and depression† assessed in three visits, ELSA-Brasil, 2017-2019

	Childhood family dysfunction score		
	0	1	⩾ 2
Depression† in three visits (n=11,531)			
1 visit			
Crude model	1.00	**1.32 (1.13-1.55)**	**2.34 (1.94-2.83)**
Adjusted model	1.00	**1.22 (1.03-1.43)**	**1.98 (1.63-2.41)**
2 or 3 visits			
Crude model	1.00	**1.77 (1.31-2.38)**	**4.63 (3.42-6.27)**
Adjusted model	1.00	**1.58 (1.17-2.14)**	**3.88 (2.83-5.31)**

Data presented as odds ratio (95%CI).
Childhood family dysfunction score: substance abuse, mental disorder, incarceration/conviction, parental separation, and parental death.
The odds ratio was estimated by multinomial logistic regression. Reference category: no visits
Model adjusted for age, sex, race, and maternal education.
Bold type denotes significant associations ($p < 0.05$)
ELSA-Brasil = Estudo Longitudinal de Saúde do Adulto.
† Depressive episode in the last 7 days assessed by Clinical Interview Schedule-Revised.

totally or partially attenuated throughout life, as appears to be the case with parental death.

Individually, except for parental death and incarceration/conviction, the childhood family dysfunctions analyzed here contributed to the burden of depression in adulthood, especially exposure to mental disorders, which almost tripled the odds of depression in two or three visits, as well as substance abuse, which doubled the odds. Analyzing data from the 1958 British Birth Cohort, Selous et al.[22] found an association between family dysfunction, other prospectively measured ACEs, and depression at 23, 33, 42, and 50 years of age. They concluded that these experiences influence multiple depressive episodes, although the magnitude of the associations was attenuated over time. Although our results add to recent evidence,[23] they contradict studies from the 1990s, such as Kessler et al.,[24] who found an association between family dysfunction, other ACEs, and the initial manifestation of mood disorders (but not recurrence) in a subsample of the U.S. National Comorbidity Survey 1990-1992.

Dysfunctions and other ACEs commonly co-occur in the same family environment,[5] increasing the risk of depression and other mental disorders in adulthood due to the cumulative effect of multiple ACEs, as demonstrated in a meta-analysis.[25] Our findings also show that the greater the number of family dysfunctions, the greater the odds of mental disorders in adulthood, indicating that exposure to multiple dysfunctions is more harmful to mental health than exposure to individual dysfunctions.[25] We highlight the fact that the family dysfunctions we investigated may co-occur with other unmeasured ACEs, such as domestic violence, sexual abuse, and neglect.[26] For example, both mental disorders and the abuse of and/or dependence on alcohol and other drugs are associated with a higher risk of domestic violence and neglect in childcare.[27] Therefore, we cannot rule out that the impact of family adversities on mental health in adulthood in the present study also reflect the effect of other experiences we did not measure. That is, it is possible that the reference category in our analysis includes individuals exposed to unassessed adversities. Likewise, we cannot rule out that the exposed individuals were misclassified, since they might also have been exposed to unmeasured adversities. As we know, misclassifying exposure can lead to underestimating the magnitude of the association.[28]

Evidence shows that ACEs experienced early in life leave a lasting mark on emerging brain architecture, affecting mental health in both the short and long term.[29,30] Such experiences indirectly contribute to depression in adulthood through psychobiological mechanisms; they act as stressors that disrupt the hypothalamic-pituitary-adrenal axis,[31] inducing chronic inflammation,[6] or even lead to behavioral, cognitive, and socio-emotional changes.[6] Childhood family dysfunction also indirectly influences the emergence of depressive symptoms via socioeconomic conditions in adulthood, as reported in a cohort of older Japanese adults, in which 10% of the total association between ACEs and depressive symptoms was mediated by socioeconomic status.[32]

Imaging studies have shown the potentially negative effect of exposure to ACEs on brain structure, function, and connectivity in adults with and without mental disorders.[33] These experiences appear to affect not only brain volume, but also the sensory systems and circuits involved in threat detection, emotional regulation, and reward anticipation. Another study demonstrated that even mild ACEs could damage neural circuits in healthy young individuals.[34]

Epigenetic processes, including DNA methylation, are recognized as biological mechanisms that link ACEs to long-term health effects.[35] For example, findings from the Health and Retirement Study indicated that epigenetic aging explained about 9%-14% of the association between ACE and depression.[36] Another potential mechanism linking ACEs and depression is systemic inflammation. A recent meta-analysis has suggested that the relationship between ACEs and depressive symptoms is at least partially mediated by inflammatory markers.[37]

A consistent relationship has also been found between childhood socioeconomic disadvantage and family dysfunction.[38] Childhood socioeconomic disadvantage, i.e., deprivation of material and other resources, is in itself a stressful condition that can affect health throughout life.[39] However, we point out that the associations we observed persisted after adjusting for maternal education, an indicator of childhood socioeconomic disadvantage. Finally, despite adjusting for age, it is possible that the subjective experience of adversity varied between birth cohorts, being more pronounced in younger cohorts, which could be partly due to recall bias, given that these events are chronologically more distant in older people. A Canadian cohort also found that the prevalence of ACEs, including family dysfunctions, was higher in younger adults than older adults.[40] According to the results of the South African Birth to Twenty Plus cohort, ACE prevalence varied with age, with adolescents reporting much higher rates of exposure to violence and physical and sexual abuse than those reported retrospectively by their caregivers.[41] It is important to consider that the increased frequency of reported ACEs in younger birth cohorts reflects, in part, social recognition of these problems, which were often ignored in the past. Such recognition is an important step towards preventing exposure or protecting those who have been exposed.

Recognizing the influence of the family environment on mental health makes it possible to detect and prevent family dysfunctions and develop early interventions for exposed children. Resilience appears to be an important mediator in the relationship between ACEs and depression.[42] It is estimated that a 10%-25% reduction in exposure to ACEs could prevent 31.4-80.3 million cases of depression and anxiety worldwide.[43] However, it is important to recognize that family structures have changed and the frequency of parental separation, single-parent households, and other family arrangements has increased,[44] as has the burden of mental disorders and substance abuse.[9] In other words, the possibility of exposure to family problems is high and may be increasing. Therefore, interventions aimed at promoting healthy family environments and detecting and providing psychosocial support in crisis situations should be prioritized in health and social welfare policies.

Our findings help expand the evidence from low- and middle-income countries on the relationship between family dysfunction in childhood and depression in adulthood. The large sample size, the use of validated scales, and data collection with rigorous quality control are strong points of this study. Its limitations include the measurement of depression over the previous 7 days, which may have led to classifying participants with previous depressive episodes as not depressed, leading to underestimation of the magnitude of the associations. Retrospectively measuring family dysfunction may have led to underestimation due to embarrassment, potential memory bias, or low problem recognition, especially among older generations.[45] Survival bias, i.e., the non-participation of those most exposed to family dysfunctions and depression due to death or absence in the three visits, could also have contributed to underestimation. In the 1958 British Birth Cohort, children exposed to two or more ACEs, including family dysfunction, had almost twice the risk of premature mortality by middle age than unexposed children.[22] Including parental death in the family dysfunction score may have led to underestimating the score's association with depression. Finally, evidence suggests that family dysfunction in childhood can impair educational attainment and socioeconomic status in adulthood. Considering that socioeconomic status is also an established risk factor for depression, it is possible that both the prevalence of ACEs and the magnitude of the associations observed in ELSA-Brasil are underestimated in relation to the general population, since the cohort consisted of public servants (who have a higher education level), thus excluding the extremes of the social hierarchy.

Thus, it can be concluded that exposure to family dysfunction in childhood increases the risk of depression in adulthood in a dose-response gradient. Promoting healthy family environments and providing adequate support to exposed children would seem to be a strategic measure for reducing the global burden of depression and promoting emotional well-being throughout life.

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Disclosure

The authors report no conflicts of interest.

Author contributions

MBL: Conceptualization, Methodology, Formal analysis, Writing – original draft.
SMB: Investigation, Project administration, Funding acquisition, Conceptualization, Methodology, Writing – review and editing.
RHG: Investigation, Project administration, Funding acquisition, Writing – review & editing.
ALP: Writing – review & editing.
LVC: Writing – review & editing.
MCV: Writing – review & editing.
LG: Investigation, Project administration, Conceptualization, Methodology, Formal analysis, Writing – review & editing.

All authors have read and approved of the final version to be published.

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