UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
FACULDADE DE MEDICINA
PROGRAMA DE PÓS-GRADUAÇÃO EM PSIQUIATRIA E CIÊNCIAS DO COMPORTAMENTO

TESE DE DOUTORADO

SHORT- AND LONG-TERM ASSOCIATIONS OF ADVERSITY IN CHILDHOOD WITH DEVELOPMENTAL OUTCOMES IN CHILDREN AND YOUTH

Associações de Curto e Longo Prazo de Adversidade na Infância com Desfechos Desenvolvimentais em Crianças e Jovens

Julia Luiza Schäfer

Advisor: Prof. Dr. Giovanni Abrahão Salum Júnior

Porto Alegre, April 2022

TESE DE DOUTORADO

SHORT- AND LONG-TERM ASSOCIATIONS OF ADVERSITY IN CHILDHOOD WITH DEVELOPMENTAL OUTCOMES IN CHILDREN AND YOUTH

Associações de Curto e Longo Prazo de Adversidade na Infância com Desfechos Desenvolvimentais em Crianças e Jovens

Julia Luiza Schäfer

Advisor: Prof. Dr. Giovanni Abrahão Salum Júnior

Tese apresentada como requisito parcial para obtenção de título de Doutora em Psiquiatria e Ciências do Comportamento à Universidade Federal do Rio Grande do Sul, Programa de Pós-Graduação em Psiquiatria e Ciências do Comportamento.

Porto Alegre, April 2022

CIP - Catalogação na Publicação

Luiza Schäfer, Julia
Short- and Long-term Associations of Adversity in Childhood with Developmental Outcomes in Children and Youth / Julia Luiza Schäfer. -- 2022.
178 f.
Orientador: Giovanni Abrahão Salum.

Tese (Doutorado) -- Universidade Federal do Rio Grande do Sul, Faculdade de Medicina, Programa de Pós-Graduação em Ciências Médicas: Psiquiatria, Porto Alegre, BR-RS, 2022.

1. Childhood adversity. 2. Child development. 3. Psychopathology. 4. Cognition. I. Salum, Giovanni Abrahão, orient. II. Título.

Elaborada pelo Sistema de Geração Automática de Ficha Catalográfica da UFRGS com os dados fornecidos pelo(a) autor(a).

“The heaviest of burdens is therefore simultaneously an image of life’s most intense fulfillment. The heavier the burden, the closer our lives come to the earth, the more real and truthful they become. Conversely, the absolute absence of burden causes man to be lighter than air, to soar into heights, take leave of the earth and his earthly being, and become only half real, his movements as free as they are insignificant. What then, shall we choose? Weight or lightness?”

Milan Kundera – The Unbearable Lightness of Being

Dedicated to my grandfather, Luiz, who parted long before I gave this life meaning,
but enough after I could take an interest in people through his stories.

AGRADECIMENTOS

Eu já fui uma criança. Uma dessas crianças sobre as quais escrevi ao longo desta tese. Uma criança que, como todas as outras, precisou de estímulo, apoio emocional e estrutura material para se tornar alguma coisa “ao crescer”. Me tornei muito. Alguém de quem gosto. Alguém em quem acredito. Alguém que deseja trabalhar para que o mundo seja tão gentil com as suas crianças como foi comigo. Se hoje posso fazer isso, é pelas pessoas às quais começo agradecendo.

Aos meus pais, Fernanda Schaefer e Luiz Schäfer, por todas as escolhas e renúncias que fizeram por mim. Por me amarem incondicionalmente e suavizarem minhas dores em tantos abraços. Por me moldarem íntegra, sem que eu precisasse ser nada além do que eu sou. Existo deles. Sou por causa deles.

Ao meu padrasto, Roberto Procat, por me aceitar filha. Por me acolher com o cuidado, amor e disciplina de quem, genuinamente, se importa. À minha madrasta, Cynthia Viton Aguirre, por me acolher e olhar com olhos gentis.

Aos quatro, por acreditarem e investirem em mim.

Aos meus avós, Ieda Volpi Schäfer, Loni Schaefer e Julio Schaefer, e às minhas tias Simone Volpi Schäfer, Tina Volpi Schäfer, Natali Schaefer e Angélica Schaefer, pelo senso de unidade e amparo que me levou a edificar pertencimento. Pelas folias da infância e pelas pequenas transgressões às regras de casa. Por muitas vezes surgirem em minha defesa. Por serem presentes. Por vibrarem por mim.

Aos meus primos, Natyeli Botene, Carolina Schaefer, Guilherme Michels e Cristian Alves (em memória), e às minhas amigas de infância Jéssica Wallauer, Marcela Volkart, Vitória Galle, Marcela Teixeira e Daniela Martins, pelos encontros mais felizes da minha existência. Por serem o refúgio em que minhas risadas encontram eco e em que a ternura vem aos poros há tantos anos.

Pessoas nos transformam. Nos tocam e ensinam de um jeito duradouro e consistente. Direta, ou indiretamente. Há pessoas que imprimem tanto em nós que nos questionamos se pensaríamos das mesmas formas, ou se seríamos os mesmos, caso não as conhecêssemos. Tenho o privilégio de agradecê-las na sequência.

Ao meu orientador, Giovanni Salum, por estimular minha curiosidade. Por inspirar interesses, desacomodar verdades e provocar indagações. Por abrir caminhos de uma forma honesta e gentil. Por criar oportunidades e por acreditar naquilo que eu faço. Por, acima de tudo, dividir a visão de mundo de quem acredita e zela pelo ser humano. De quem se importa com as pessoas. De quem se compromete com a mudança.

Aos meus colegas do grupo de pesquisa da Seção de Afeto Negativo e Processos Sociais, Maurício Hoffmann, Paola Laporte, Patrícia Bado, Nathália Becker, Natan Grossman, Danielle Teixeira, Luiza Axelrud e Arthur Manfro pela parceria e incentivo ao longo dos anos. À Tauana Terra, especialmente, pela sensibilidade e leveza com a qual me empresta sua força e me eleva ao confiar na minha potência.

Aos pesquisadores da Coorte Brasileira de Alto Risco (BHRCS), em especial Gisele Gus Manfro, Pedro Mário Pan, Euripedes Constantino Miguel, Luis Augusto Rohde e Rodrigo Fonseca Bressan, por toda colaboração direta, e indireta, e por serem fonte de inspiração.

Aos amigos com quem cresço e divido os desafios e prazeres da vida adulta, Priscila Lawrenz, Fernanda Romeiro, Mateus Levandowski, Roberta Salvador, Juliana Suman e Julia Limp, pelos momentos de distração. Pelas trocas de experiências. Pelo apoio potente de, simplesmente, existirem em meu presente.

Ao parceiro que escolho há seis anos, Lucas Bandinelli, pelas tantas gargalhadas, danças desengonçadas em meio a sala e longas conversas aos fins de dia. Pela forma sútil como nosso encontro tece calma em cada banalidade do dia a dia. Por me amar de forma livre, mas segura. Por me fazer sentir valor. Pelos esforços e tentativas com as quais tentamos ser melhores, juntos, um dia de cada vez.

Às minhas crianças, Sophia, Henrique, Lucas, Arthur, Helena, Lunna, Santiago e Tereza por serem a lembrança do porquê cada esforço em construir um mundo melhor vale a pena.

Por fim, realizar pesquisa no Brasil tem sido insistir. Insistir na educação e produção de conhecimento que liberta. Que possibilita e que oportuniza. Que constrói. Portanto,

Obrigada a CAPES e CNPq pelas bolsas de financiamento que possibilitaram a realização desse trabalho.

Obrigada aos participantes de pesquisa da Coorte Brasileira de Alto Risco (BRHCS).

Obrigada aos professores da banca pela gentileza em avaliar e contribuir para este trabalho.

SUMMARY

ABBREVIATIONS

BHRC: Brazilian High-Risk Cohort.

EF: Executive functions.

SLE: Stressful life events.

DAWBA: Development and Well-Being Assessment.

CBCL: Child Behavior Checklist.

CFA: Confirmatory factor analysis.

RMSEA: Root mean square error of approximation.

CFI: Comparative fit index.

TLI: Tucker Lewis index.

ABSTRACT

Childhood adversity has been consistently associated with detrimental consequences on childhood development. Such experiences might take on different forms leading to differential influences across development. Also, their impact might remain for many years after those experiences occurred. It is unclear whether associations of childhood adversity and negative developmental outcomes vary across different forms of adversity and for how many years those experiences continue to impact development. The articles that comprise this thesis aim to investigate short-term and long-term associations of childhood adversity measured as threat and deprivation with psychopathology, emotional processing, and distinct aspects of cognition. In order to do that, data is drawn from three-time points assessments of the Brazilian High-risk Cohort (BHRC), a large school-based community cohort that takes place in the cities of São Paulo and Porto Alegre. Article #1investigate the latent constructs of threat and deprivation, following a dimensional model of adversity, while investigating their cross-sectional and longitudinal associations with psychopathology, emotional processing through attention bias towards angry faces, and executive functions (EF) during a three-year time frame. Article #2 expands findings from article #1 in the sense that it investigates associations of threat and deprivation with psychopathology and EF in a six-year time frame, at the same time it adjusts these associations for other forms of environmental inputs in the form of stressful life events (SLE). Findings support theoretical models that show threat and deprivation differentially influence development, with threat being more strongly associated with psychopathology, and deprivation with worse performance on EF tasks. Influences of threat and deprivation on the outcomes were persistent across time, and were independent of other exposure to stressful life events, suggesting its important lasting influence on mental health

across the lifespan. Such results contribute to previous knowledge on the importance of identifying developmental dimensions that are disrupted by specific early adversity events to develop better intervention strategies aimed to prevent the onset of mental disorders, as well as treat problems and difficulties of children and adolescents exposed to childhood adverse events.

Key words: Childhood adversity, threat; deprivation, child development, psychopathology, cognition, executive functions.

RESUMO

Adversidade na infância tem sido consistentemente associada a consequências prejudiciais ao desenvolvimento infantil. Tais experiências podem assumir diferentes formas, levando a influências diferentes em aspectos distintos do desenvolvimento. Não é claro se as associações de adversidade na infância e desfechos negativos no desenvolvimento variam conforme as diferentes formas e tipos de eventos adversos. Os artigos que compõem esta tese têm como objetivo investigar associações transversais e longitudinais da adversidade na infância, medida como ameaça e privação, com psicopatologia, processamento emocional e aspectos distintos da cognição. Para isso, os dados são extraídos de avaliações realizadas em três momentos da Coorte Brasileira de Alto Risco (BHRC), uma grande coorte comunitária de base escolar que ocorre nas cidades de São Paulo e Porto Alegre. O artigo #1 investiga os construtos latentes de ameaça e privação, seguindo um modelo dimensional de adversidade, enquanto investiga suas associações transversais e longitudinais com psicopatologia, processamento emocional medido como viés de atenção para faces com raiva e funções executivas (FE) durante um período de três anos. O artigo nº 2 expande as descobertas do artigo nº 1 no sentido de que investiga associações de ameaça e privação com psicopatologia e FE em um período de seis anos, ao mesmo tempo em que ajusta essas associações para outras formas de experiências ambientais medidas como eventos estressores de vida (SLE). Os resultados apoiam a ideia já presente na literatura de que a ameaça e a privação influenciam diferencialmente o desenvolvimento, com a ameaça sendo mais fortemente associada à psicopatologia e a privação com pior desempenho em tarefas de FE. As influências de ameaça e privação nos resultados foram persistentes ao longo do tempo e independentes de outras exposições a eventos estressores de vida,

sugerindo sua influência persistente na saúde mental ao longo da vida. Tais resultados contribuem para o conhecimento prévio sobre a importância de identificar dimensões do desenvolvimento que são prejudicadas por eventos específicos de adversidade na infância na direção de desenvolver melhores estratégias de intervenção visando prevenir o aparecimento de transtornos mentais, bem como tratar de forma direcionada os problemas e dificuldades de crianças e adolescentes expostos a eventos adversos na infância.

Palavras-chave: Adversidade na infância, ameaça, privação, desenvolvimento infantil, psicopatologia, cognição e funções executivas.

PRESENTATION

This present work consists of the doctoral thesis entitled “Short- and Long-term Associations of Adversity in Childhood with Developmental Outcomes in Children and Youth” presented to the Postgraduate Program of Psychiatry and Behavioral Sciences at the Federal University of Rio Grande do Sul in April 2022.

This thesis is part of the Brazilian High-Risk Cohort for Mental Conditions Study (BHRCS), one of the largest school-based community cohorts ever carried out in Brazil. The BHRCS is the result of the efforts of many researchers from the University of São Paulo (USP), Federal University of São Paulo (UNIFESP) and Federal University of Rio Grande do Sul (UFRGS) to understand the developmental trajectories of psychopathologies and mental disorders. The main aim of the BHRC is to expand knowledge about the typical and atypical development of children, adolescents, and their families through the investigation of environmental, behavioral, genetic, and neurological variables in about 2,511 children and adolescents in the cities of São Paulo and Porto Alegre.

Briefly, in the year 2010, 9937 parents of 6 to 14-year-old children from 57 schools in São Paulo and Porto Alegre were initially screened for mother, father, or siblings’ presentation of any of five disorders (e.g. Attention Deficit and Hyperactivity Disorder, anxiety disorders, Obsessive Compulsive Disorder, psychotic experiences and learning disorders). From the total screened sample, 957 children were randomly selected, while 1554 were selected based on a high-risk score procedure used to identify children with current symptoms and/or family history of psychiatric disorders. After initial screening, parents and children were assessed at three different time points (baseline, 3-year follow-up and 6-year follow-up) with retention rates of 80% (from

baseline to 3-year follow-up) and 75% (from 3-year follow-up to 6-year follow-up). Assessments were comprised of many measures, including questionnaires and interviews about life history and psychopathology directed at both, children/adolescents and parents, and neurocognitive tasks completed by children/adolescents. Currently, the BHRC is planning its fourth assessment to take place in the years 2022 and 2023.

The reasons that motivated the studies that comprise this thesis are related to the fact that childhood adversity is highly prevalent around the world, especially in low- and middle-income countries, and represents a public health problem due to its extensive costs to society and individuals, leading to poorer mental health and academic achievement. Despite the challenges there are surrounding the study of childhood adversity, determining the ways through which it can confer risk to emotional and cognitive development is critical to identify and develop novel interventions for preventing the emergence of psychopathology and developmental problems in children exposed to adversity.

This thesis is organized the following way: Introduction, Objectives, Article #1 (published in *Developmental Science*), Article #2 (submitted and currently under peer review in *Psychological Science*), Final Considerations, and Appendixes concerning other publications and collaborations of the author during the doctorate years.

1. INTRODUCTION

The maturational and interactive process of childhood development results in an ordered progression of perceptual, motor, cognitive, language, socio-emotional, and self-regulation skills that allow children to reach their full potential (1,2). Physical and mental health, security, safety, and early learning opportunities are all factors that, when negatively affected, confer a poor start in life that limits children's possibilities to success in adulthood, and posits detrimental consequences to societies and future generations (2,3). Described as experiences that compromise basic safety and support, childhood adversity encompasses a great range of negative environmental experiences, such as violence, abuse, neglect, and severe poverty, that contributes to morbidity and mortality (4) and creates enduring marks on emotional, cognitive, behavioral, and social development (5,6) . A solid body of evidence supports that children who have been exposed to childhood adversity are more likely to present with childhood and adolescent psychiatric symptoms (7), psychopathology (8–10), executive functioning deficits (11), and long-term poorer mental health outcomes later in life (12,13) thus altering typical development.

Therefore, recognized for their lasting influence on mental health across the lifespan since the earliest theoretical formulations of psychopathology etiology, adverse experiences in childhood are major preventable risk factors for poor mental and physical health (14). As a public health problem, it requires action to assure appropriate stimulation, nurturing, and nutrition for children and youth (15) across the globe, especially those living in low- and middle-income countries where higher reports of childhood maltreatment exposure are found (16). Despite the fact that most of the world's youth live in low- and middle-income countries, most research available on the association of childhood adversity with negative mental health outcomes focuses on

high-income countries (8) and fails to acknowledge the effects of geographical and economic factors on worldwide estimates of childhood exposure to adverse events (16).

1.1. Childhood adversity in the Brazilian context

Important research conducted in the Brazilian context considering exposure to adverse events in childhood has consistently reported high rates of childhood adversity. First, a study conducted with a representative sample of 5,037 adults in the city of São Paulo has found a prevalence of 53.6% of exposure to at least one lifetime childhood adverse event (17). Moreover, two Brazilian cohorts from the state of Rio Grande do Sul have reported on 85% of 3,951 adolescents reporting on at least one adverse event exposure (including physical and sexual abuse, emotional and physical neglect, domestic violence, and parental separation and death) (18), and 12.1% of 2213 children and adolescents reporting on any type of traumatic experience (including emotional, physical and sexual abuse, and physical neglect) (19).

Besides community-based studies, available current national data on violence against children and adolescents, and children living in poverty set the scene for the importance of the issue at the country level. Between the year 2019 and the first semester of 2021, a total of 129.844 official complaints were made on crimes committed against children and adolescents from 0 to 17 years old across 12 federal units. Considering underreporting problems, this number is probably even higher. Details about his data are reported in **Table 1** (20)**.** Moreover, it has been known that children and adolescents have always been more affected by poverty levels, than adults. Up to 2020, the estimate of adults in Brazil living under the poverty line was

20% against 40% of children and adolescents, whilst for under the extreme poverty line it was 6% against 12%, respectively (21).

Table 1. Violence Against Children and Adolescents in Brazil (2019-2021)

	Official complaints	% from total official complaints	% according to sex		% according to age range		
			Female	Male	0 to 4 yo	5 to 9 yo	10 to 14yo
Domestic Violence	23,494	18,1%	77%	33%	-	26%	52%
Child maltreatment	28,098	21.6%	51%	49%	26%	35%	29%
Rape	73,442	56.6%	85%	25%	-	26%	47%
Sexual Exploitation	1,093	0.8%	86%	24%	-	48%	44%
Intentional violent death	3,717	2.9%	86%	24%	-	-	82%

Extracted from the Executive Summary of Violence Against Children and Adolescents (2019-2021), Brazil (2021)

1.2. The challenges of studying childhood adversity

Despite the continuous interest and importance of the scientific investigation of childhood adverse events influences on mental health development, there are still a few important challenges to this field of research that limit a rich set of theories to produce substantial clinical gains concerning its conceptualization and definition, its measure and operationalization, its significant nature, time, and frequency variability, and the mechanisms through which it differentially confers risk to distinct aspects of development (6). Identifying the developmental processes that are disrupted by early adversity seems to be an important factor in developing better intervention strategies to either prevent or treat problems and difficulties of children who have been exposed to adversity.

1.2.1. The dimensional model to childhood adversity

Previous research on childhood adversity has largely focused on individual types of adverse experiences, such as physical and sexual abuse, poverty, or neglect. However, such an approach has led to lines of independent findings that do not account for the already known co-occurrence of multiple forms of childhood adversity

(12), therefore failing to disentangle whether the outcomes being studied are influenced by the measured event, or of other adversities children have experience (22). Moreover, investigating specific, independent childhood adversity experiences fails to provide insights into the different pathways through which different forms of childhood adversity might lead to a wide range of negative mental health outcomes (23).

One prominent approach to addressing developmental outcomes related to adverse events exposure is to distinguish core dimensions that underlie discrete adversity experiences. In that direction, the dimensional model of adversity proposed by McLaughlin and Sheridan (2016) suggests the existence of core underlying dimensions that cut across diverse forms of adversity **(Figure 1)**. It posits that childhood adversity encompasses experiences involving levels of threat and deprivation (24), defined as those experiences involving the presence of an unexpected input that represents a threat to the physical integrity or well-being of the child, and experiences characterized by the absence of expected social, cognitive, and emotional inputs that provide complex learning opportunities expected throughout development, respectively (22,25,26).

The dimensional model allows the simultaneous assessment of the frequency and severity of distinct experiences reflecting both dimensions, as well as facilitates the examination of specific mechanisms leading to psychopathology. The proposition of the model argues that experiences characterized by high levels of threat, such as physical, sexual, or emotional abuse, and exposure to violence, have particularly strong influences on emotional processing, whilst experiences characterized by higher levels of deprivation, such as physical or emotional neglect, and poverty, are more

Figure 1. The Dimensional Approach to Childhood Adversity

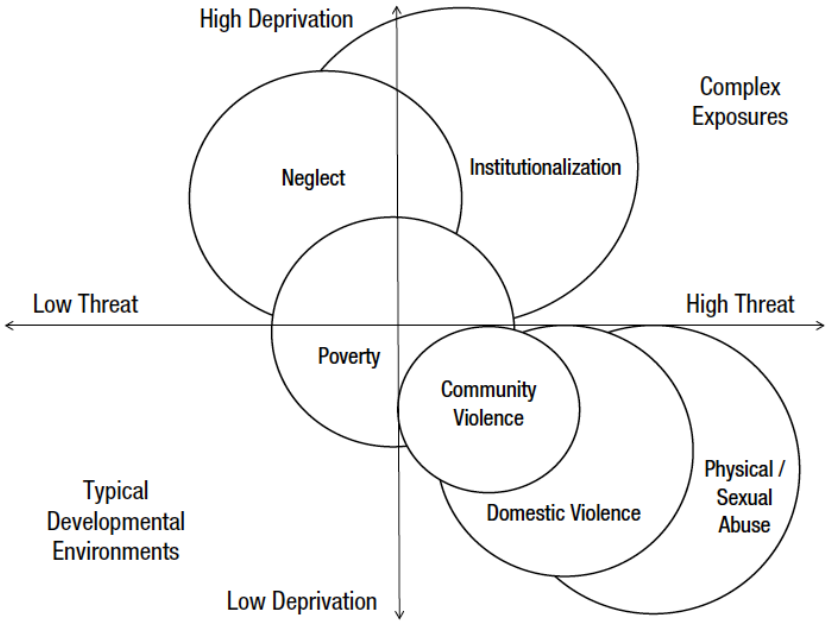


Fig. 1. A dimensional model of childhood adversity involving two central dimensions of threat and deprivation. Examples of commonly studied forms of adversity are placed along these dimensions based on the degree to which each experience typically involves threat and deprivation. Larger circles indicate greater variance in the degree to which the experience reflects the underlying dimension.

Extracted from Mclaughlin and Sheridan MA. Beyond Cumulative Risk : A Dimensional Approach to Childhood Adversity (2016).

strongly associated with poor performance on complex cognitive tasks, such as those involving executive functions (EF) (22,23).

1.3. Short- and long-term differential associations of threat and deprivation with developmental outcomes

Even though prior work examining the correlates of different forms of childhood adversity, such as threat and deprivation, on developmental outcomes can present some mixed results, they have generally supported the pattern of differential influences on developmental outcomes, such as psychopathology, emotional processing, and cognition. When it comes to psychopathology, childhood adversity has already been strongly associated with its presence throughout the lifespan across many studies.

Even though the dimensional model of threat and deprivation does not make differential predictions about how these dimensions influence psychopathology, emerging evidence from population-based longitudinal studies suggest that threat may have stronger associations with psychopathology when compared to deprivation (27,28). Moreover, childhood adversity has already been found to account for 29.8% of adult psychiatric disorders among nationally representative samples from 21 countries across the world (13), supporting the notion that its influences keep resonating through adulthood through the presence of complex (29) and recurrent mental disorders (30–32).

Moreover, there seems to be supportive evidence that children who have experienced violence, and not deprivation, present with emotional processing alterations, including requiring less perceptual information to identify anger (33,34), classifying a wider range of negative emotion as anger (35), and exhibiting attention biases to threatening social information (36). Although some studies of children raised in institutions have observed associations of some forms of deprivation with other dimensions of emotional processing (37), exposure to deprived environments have been consistently associated with poor performance on cognitive tasks particularly those encompassing language abilities and EF (38–42), as well as long-term difficulties with education and employment (43).

Important issues limiting previous literature should be taken into consideration when addressing the influences of childhood adversity on development. First, most research using the theoretical framework of threat and deprivation as underlying dimensions of childhood adversity has focused on youth living in high-income countries while most of the world's youth lives in poor countries facing adversity for which there is limited data available (16). Second, most existing research use retrospective data

and fail to adjust for pre-existing confounding factors, such as stressful life events, thus limiting conclusions about the extent to which influences on mental health outcomes measured later in life are really due to early life or current trauma exposure. Therefore, the studies present in this thesis aim to reduce these gaps by attempting to disentangle the short- and long-term associations of childhood adversity in the forms of threat and deprivation with psychopathology, emotional processing, and cognition using a school-based community sample of children and adolescents assessed at three points in time in a middle-income country (Brazil).

2. REFERENCES

1. Lo S, Das P, Horton R. A good start in life will ensure a sustainable future for all. The Lancet. 2017 Jan;389(10064):8–9.

2. Black MM, Walker SP, Fernald LCH, Andersen CT, DiGirolamo AM, Lu C, et al. Early childhood development coming of age: science through the life course. The Lancet. 2017 Jan;389(10064):77–90.

3. Daelmans B, Darmstadt GL, Lombardi J, Black MM, Britto PR, Lye S, et al. Early childhood development: the foundation of sustainable development. The Lancet. 2017 Jan;389(10064):9–11.

4. Grummitt LR, Kreski NT, Kim SG, Platt J, Keyes KM, McLaughlin KA. Association of Childhood Adversity With Morbidity and Mortality in US Adults: A Systematic Review. JAMA Pediatr. 2021 Dec 1;175(12):1269.

5. Magruder KM, McLaughlin KA, Elmore Borbon DL. Trauma is a public health issue. Eur J Psychotraumatology. 2017 Jan;8(1):1375338.

6. Danese A, Lewis SJ. New directions in research on childhood adversity. Br J Psychiatry. 2021 Oct 4;1–2.

7. Bachler E, Frühmann A, Bachler H, Aas B, Nickel M, Schiepek GK. The Effect of Childhood Adversities and Protective Factors on the Development of Child-Psychiatric Disorders and Their Treatment. Front Psychol. 2018 Nov 15;9:2226.

8. Benjet C. Childhood adversities of populations living in low-income countries: prevalence, characteristics, and mental health consequences. Curr Opin Psychiatry. 2010 Jul;23(4):356–62.

9. Lansford JE, Dodge KA, Pettit GS, Bates JE, Crozier J, Kaplow J. A 12-Year Prospective Study of the Long-term Effects of Early Child Physical Maltreatment on Psychological, Behavioral, and Academic Problems in Adolescence. Arch Pediatr Adolesc Med. 2002 Aug 1;156(8):824.

10. McLaughlin KA, Greif Green J, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC. Childhood Adversities and First Onset of Psychiatric Disorders in a National Sample of US Adolescents. Arch Gen Psychiatry. 2012 Nov 1;69(11):1151.

11. Bos KJ. Effects of early psychosocial deprivation on the development of memory and executive function. Front Behav Neurosci [Internet]. 2009 [cited 2022 Jan 16];3. Available from: http://journal.frontiersin.org/article/10.3389/neuro.08.016.2009/abstract

12. Green JG, McLaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM, et al. Childhood Adversities and Adult Psychiatric Disorders in the National Comorbidity Survey Replication I: Associations With First Onset of *DSM-IV* Disorders. Arch Gen Psychiatry. 2010 Feb 1;67(2):113.

13. Kessler RC, McLaughlin KA, Green JG, Gruber MJ, Sampson NA, Zaslavsky AM, et al. Childhood adversities and adult psychopathology in the WHO World

Mental Health Surveys. Br J Psychiatry. 2010 Nov;197(5):378–85.

14. Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health. 2017 Aug;2(8):e356–66.

15. Richter LM, Daelmans B, Lombardi J, Heymann J, Boo FL, Behrman JR, et al. Investing in the foundation of sustainable development: pathways to scale up for early childhood development. The Lancet. 2017 Jan;389(10064):103–18.

16. Viola TW, Salum GA, Kluwe-Schiavon B, Sanvicente-Vieira B, Levandowski ML, Grassi-Oliveira R. The influence of geographical and economic factors in estimates of childhood abuse and neglect using the Childhood Trauma Questionnaire: A worldwide meta-regression analysis. Child Abuse Negl. 2016;51(305141):1–11.

17. Coêlho BM, Andrade LH, Santana GL, Viana MC, Wang YP. Association between childhood adversities and psychopathology onset throughout the lifespan: Findings from a large metropolitan population. J Psychiatr Res. 2021 Mar;135:8–14.

18. Soares ALG, Howe LD, Matijasevich A, Wehrmeister FC, Menezes AMB, Gonçalves H. Adverse childhood experiences: Prevalence and related factors in adolescents of a Brazilian birth cohort. Child Abuse Negl. 2016 Jan;51:21–30.

19. Salum GA, DeSousa DA, Manfro GG, Pan PM, Gadelha A, Brietzke E, et al. Measuring child maltreatment using multi-informant survey data: a higher-order confirmatory factor analysis. Trends Psychiatry Psychother. 2016 Mar 18;38(1):23–32.

20. Violência Contra Crianças e Adolescentes (2019-2021). São Paulo, Brasil: Fórum Brasileiro de Segurança Pública e Fundação José Luiz Egydio Setúbal; 2021 Nov p. 10.

21. Bauer F, Chopitea L, Klaus M. Pobreza Infantil Monetária no Brasil: Impactos da Pandemia na Renda de Famílias com Crianças e Adolescentes. UNICEF; 2022 Mar p. 41.

22. McLaughlin KA. Future Directions in Childhood Adversity and Youth Psychopathology. J Clin Child Adolesc Psychol. 2016 May 3;45(3):361–82.

23. McLaughlin KA, Sheridan MA. Beyond Cumulative Risk: A Dimensional Approach to Childhood Adversity. Curr Dir Psychol Sci. 2016 Aug;25(4):239–45.

24. Humphreys KL, Zeanah CH. Deviations from the Expectable Environment in Early Childhood and Emerging Psychopathology. Neuropsychopharmacology. 2015 Jan;40(1):154–70.

25. McLaughlin KA, Sheridan MA, Lambert HK. Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. Neurosci Biobehav Rev. 2014 Nov;47:578–91.

26. McLaughlin KA, DeCross SN, Jovanovic T, Tottenham N. Mechanisms linking childhood adversity with psychopathology: Learning as an intervention target. Behav

Res Ther. 2019 Jul;118:101–9.

27. Platt JM, McLaughlin KA, Luedtke AR, Ahern J, Kaufman AS, Keyes KM. Targeted Estimation of the Relationship between Childhood Adversity and Fluid Intelligence in a US Population Sample of Adolescents. Am J Epidemiol. 2018;187(7):1456–66.

28. Miller AB, Machlin L, McLaughlin KA, Sheridan MA. Deprivation and psychopathology in the Fragile Families Study: A 15-year longitudinal investigation. J Child Psychol Psychiatry. 2021 Apr;62(4):382–91.

29. Schaefer JD, Moffitt TE, Arseneault L, Danese A, Fisher HL, Houts R, et al. Adolescent Victimization and Early-Adult Psychopathology: Approaching Causal Inference Using a Longitudinal Twin Study to Rule Out Noncausal Explanations. Clin Psychol Sci. 2018 May;6(3):352–71.

30. Agnew-Blais J, Danese A. Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: a systematic review and meta-analysis. Lancet Psychiatry. 2016 Apr;3(4):342–9.

31. Nanni V, Uher R, Dr MU, Danese A. Childhood M altreatm ent Predicts Unfavorable Course o f Illness and Treatm ent O utco m e in D epressio n: A M eta-A nalysis. Am J Psychiatry. :11.

32. Walsh K, McLaughlin KA, Hamilton A, Keyes KM. Trauma exposure, incident psychiatric disorders, and disorder transitions in a longitudinal population representative sample. J Psychiatr Res. 2017 Sep;92:212–8.

33. Pollak SD, Cicchetti D, Hornung K, Reed A. Recognizing emotion in faces: developmental effects of child abuse and neglect. Dev Psychol. 2000;36(5):679–88.

34. Pollak SD, Sinha P. Effects of early experience on children's recognition of facial displays of emotion. Dev Psychol. 2002;38(5):784–91.

35. Pollak SD, Kistler DJ. Early experience is associated with the development of categorical representations for facial expressions of emotion. Proc Natl Acad Sci. 2002 Jun 25;99(13):9072–6.

36. Shackman JE, Pollak SD. Impact of physical maltreatment on the regulation of negative affect and aggression. Dev Psychopathol. 2014 Nov;26(4pt1):1021–33.

37. Tottenham N, Hare TA, Quinn BT, Mccarry TW, Nurse M, Gilhooly T, et al. Prolonged institutional rearing is associated with atypically larger amygdala volume and difficulties in emotion regulation. Dev Sci. 2010;13(1):1–26.

38. Lawson GM, Hook CJ, Farah MJ. A meta-analysis of the relationship between socioeconomic status and executive function performance among children Gwendolyn. Dev Sci. 2018;21(2).

39. Sheridan MA, Peverill M, Finn AMYS, Laughlin KAMC. Dimensions of childhood adversity have distinct associations with neural systems underlying executive functioning. Dev Psychopathol. 2017;29:1777–94.

40. Rosen ML, Meltzoff AN, Sheridan MA, McLaughlin KA. Distinct aspects of the early environment contribute to associative memory, cued attention, and memory-guided attention: Implications for academic achievement. Dev Cogn Neurosci. 2019;40:100731.

41. Rosen ML, Hagen MP, Lurie LA, Miles ZE, Sheridan MA, Meltzoff AN, et al. Cognitive Stimulation as a Mechanism Linking Socioeconomic Status With Executive Function: A Longitudinal Investigation. Child Dev. 2019;00(0):1–18.

42. Lewis SJ, Koenen KC, Ambler A, Arseneault L, Caspi A, Fisher HL, et al. Unravelling the contribution of complex trauma to psychopathology and cognitive deficits: a cohort study. Br J Psychiatry. 2021 Aug;219(2):448–55.

43. Jaffee SR, Ambler A, Merrick M, Goldman-Mellor S, Odgers CL, Fisher HL, et al. Childhood Maltreatment Predicts Poor Economic and Educational Outcomes in the Transition to Adulthood. Am J Public Health. 2018 Sep;108(9):1142–7.

3. OBJECTIVES

3.1. OVERALL OBJECTIVE

Investigate cross-sectional and longitudinal associations of childhood adversity measured as threat and deprivation with psychopathology, emotional processing, and distinct aspects of cognition.

3.2. SPECIFIC OBJECTIVES

A. Threat and deprivation as a measure of childhood adversity (article #1).
    a. To evaluate the latent constructs of threat and deprivation in a large community sample from Brazil.

B. Associations of threat and deprivation with psychopathology, emotional processing, and cognition (article #1).
    a. To investigate cross-sectional associations of threat and deprivation experiences with EF, emotional processing measured by attention orienting toward angry faces, and psychopathology.
    b. To investigate longitudinal associations of threat and deprivation experiences with EF, emotional processing measured by attention orienting toward angry faces, and psychopathology three years later.

C. Long-term associations of threat and deprivation with psychopathology and cognition (article #2).
    a. To investigate whether exposure to threat and deprivation is associated with psychopathology and EF performance six years later.
    b. To test whether children exposed to higher levels of threat and deprivation are also exposed to higher levels of other forms of adversity in the form of stressful life events (SLE) three and six years later.

c. To adjust the association of threat and deprivation with psychopathology and EF six years later for previous exposure SLE.

4. ARTICLE #1

Published at ***Developmental Science***
Impact Factor (2020): 5.131
Accepted at: March 31st, 2022
doi: https://doi.org/10.1111/desc.13267

Threat and deprivation are associated with distinct aspects of cognition, emotional processing and psychopathology in children and adolescents

Julia Luiza Schäfer[1,2], Katie A. McLaughlin[3], Gisele Gus Manfro[1,2], Pedro Pan[1,4], Luis Augusto Rohde[1,2], Eurípedes Constantino Miguel[1,5], André Simioni[1,2], Maurício Scopel Hoffmann[1,6,7], Giovanni Abrahão Salum[1,2]

[1] National Institute of Developmental Psychiatry for Children and Adolescents (INCT-CNPq), São Paulo, Brazil

[2] Department of Psychiatry, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil

[3] Department of Psychology, Harvard University, Cambridge, United States

[4] Department of Psychiatry, Universidade Federal de São Paulo, São Paulo, Brazil

[5] Department & Institute of Psychiatry, University of São Paulo Medical School, São Paulo, Brazil

[6] Neuropsychiatry Departament at Universidade Federal de Santa Maria, Santa Maria, Brazil

[7] Care Policy and Evaluation Centre, London School of. Economics and Political Science, Houghton Street, London WC2A 2AE United Kingdom

Authors' Contribution

Conceptualization: Schäfer, Salum

Data curation: Hoffmann, Simioni

Formal analysis: Schäfer, Salum, Hoffmann

Funding acquisition: Rohde, Miguel, Salum

Project administration: Schäfer, Rohde, Salum, Miguel, Pan, Manfro

Supervision: Salum, McLaughling

Writing – original draft: Schäfer

Writing – review and editing: Salum, McLaughling, Pan, Rohde, Miguel, Manfro

Corresponding Author

Julia Luiza Schäfer

Hospital de Clínicas de Porto Alegre

Ramiro Barcelos, 2350 – room 2202; Porto Alegre, Brazil – 90035-003;

E-mail: julialuizaschafer@gmail.com

Funding

This work is supported by the National Institute of Developmental Psychiatry for Children and Adolescents, through research grants from the *Conselho Nacional de Desenvolvimento Científico e Tecnológico* (CNPq, Brazil; grant numbers 73974/2008-0, 465550/2014-2); the *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (CAPES, Brazil); the *Fundação de Amparo à pesquisa do Estado de São Paulo* (FAPESP, Brazil; grant

numbers 2008/57896-8, 2014/50917-0); and the *Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul* (FAPERGS, Brazil).

Conflict of Interest

Dr. Pan has received payment for the development of educational material for AstraZeneca and Janssen-Cilag. Dr. Rohde has served on speakers bureaus, on advisory boards, or as a consultant for Eli Lilly, Janssen-Cilag, Medice, Novartis, and Shire; he receives royalties from Oxford University Press and ArtMed; the ADHD and Pediatric Bipolar Disorder Outpatient Programs chaired by him have received unrestricted educational and research support from Eli Lilly, Janssen-Cilag, Novartis, and Shire; and he has received travel grants from Shire and Novartis to attend annual association meetings. Dr. Manfro received research grants from the national funding agencies FAPERGS, CAPES and CNPq. Dr. Miguel received research grants from the national funding agencies CAPES, CNPq and FAPESP. Dr. Hoffmann is supported by the research grant of the Brazilian Ministry of Health under the "Termo de Execução Descentralizada – TED 12/2019". Dr. Salum is supported by the National Institute of Mental Health (grant number R01MH120482). The other. authors no conflict interests which impact this work.

Acknowledgements

The authors thank the children and families from the Brazilian High-Risk Cohort for Psychiatric Disorders, as well as all the researchers and staff for making this study possible.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Data Availability

The data that support the findings of this study are available on request from the corresponding author, JLS. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

Research Highlights

- Exposure to threat and deprivation are associated with psychopathology longitudinally, but threat seems to play a more important role in this association;
- Exposure to deprivation, and not threat, is associated with worse performance in executive functions tasks at baseline and longitudinally;
- Exposure to threat is associated with attention orienting towards angry faces cross-sectionally, but neither form of adversity is associated with attention bias longitudinally;
- Threat and deprivation seem to have differential associations with cognitive development and psychopathology.

Abstract

Background: Exposure to childhood adversity has been consistently associated with poor developmental outcomes, but it is unclear whether these associations vary across different forms of adversity. We examined cross-sectional and longitudinal associations between threat and deprivation with cognition, emotional processing, and psychopathology in a middle-income country.

Methods: The sample consisted of 2,511 children and adolescents (6-17 years old) from the Brazilian High-Risk Cohort for Mental Conditions. Parent reports on childhood adversity were used to construct adversity latent constructs. Psychopathology was measured by the Child Behavior Checklist (CBCL) to generate a measure of general psychopathology (the "p" factor). Executive function (EF) and attention orienting toward angry faces were assessed using cognitive tasks. All measures were acquired at two time-points 3-years apart and associations were tested using general linear models.

Results: Higher levels of psychopathology were predicted by higher levels of threat cross-sectionally and longitudinally, and by deprivation longitudinally. For EF, worse performance was associated only with deprivation at baseline and follow-up. Finally, threat was associated with attention orienting towards angry faces cross-sectionally, but neither form of adversity was associated with changes over time in attention bias.

Conclusion: Our results suggest that threat and deprivation have differential associations with cognitive development and psychopathology. Exposure to adversity during childhood is a complex phenomenon with meaningful influences on child development. Because adversity can take many

forms, dimensional models might help to disentangle the specific developmental correlates of different types of early experience.

Keywords: Childhood adversity; Threat; Deprivation; Psychopathology; Executive Functions; Attention Bias; Cognition.

Introduction

Childhood adversity involves negative environmental experiences that require considerable adaptation by an average child, including physical, emotional, and sexual abuse, physical and emotional neglect, domestic violence, and parental absence (1). These experiences are highly prevalent around the world (2), especially in low and middle-income countries (3). Exposure to childhood adversity represents a public health problem due to its extensive costs to society and individuals (4), leading to poorer mental health (5,6) and academic achievement in the form of lower grades, higher school-days absence, and more frequent suspensions (7). Determining how adverse childhood experiences influence emotional and cognitive development is critical to developing novel strategies for preventing the emergence of developmental problems in children who have experienced adversity.

Distinguishing core dimensions that underlie distinct adversity experiences is a prominent strategy to address developmental outcomes related to exposure to childhood adversity (8). One relevant model, the dimensional model of adversity and psychopathology (DMAP), proposes the existence of core underlying dimensions that cut across diverse forms of adversity. It posits that childhood adversity encompasses experiences involving levels of threat and deprivation (9). Experiences of threat are defined as those involving the presence of an unexpected input that represents a threat to the physical integrity or well-being of the child, such as physical, sexual, and emotional abuse, witnessing domestic violence, and exposure to violence in the community or at school. Experiences of deprivation are those characterized by the absence of expected social, cognitive, and emotional inputs that provide complex learning opportunities expected throughout development, such as physical and emotional neglect, parental absence, poverty, and material deprivation (1,10–12). This dimensional model of adversity provides some advantages in

understanding the developmental influences of adversity. It allows the simultaneous assessment of the frequency and severity of differential experiences reflecting both dimensions, as well as facilitates the examination of specific mechanisms leading to psychopathology. It argues that experiences characterized by high levels of threat have particularly strong influences on emotional processing—particularly about cues that are negative or potentially threatening, whilst deprivation is more strongly associated with poor performance on complex cognitive tasks, such as those involving executive functions (EF) (8,10).

Even though prior work examining the correlates of different forms of childhood adversity on developmental outcomes can present some mixed results, they generally support a pattern of differential associations of threat and deprivation with important developmental outcomes. For example, threat has already been found to have a unique effect on fear conditioning (13), deficits in automatic emotion regulation (14), and physiological reactivity (15), while deprivation has already been found to have a unique effect on cognitive control (13) and to be more strongly associated with reduced executive functioning when compared to threat (16). Moreover, children who have experienced violence, one form of threat, required less perceptual information to identify anger (17,18), classified a wider range of negative emotions as anger (19), and exhibited attention biases to threatening social information (20) in previous studies. Different patterns have been observed among children exposed to deprivation. Despite relying on relatively small samples, some previous studies suggest that children exposed to deprivation had more difficulty discriminating emotional expressions than nonexposed or threat-exposed children (17) and that previously institutionalized children identified fewer emotional expressions correctly when compared to nonexposed children (21). It is important to note, however, that evidence concerning emotion recognition and deprivation might also be mixed, considering previous findings reporting

on certain areas of emotion recognition being unaffected among institutionalized children (22). Furthermore, previous data report on the association of threat with both internalizing and externalizing psychopathology (15), as well as deprivation with externalizing psychopathology through verbal abilities (23) and with internalizing and externalizing psychopathology through language ability (24).

The previous literature is limited in two important ways. First, most research investigating the correlates of childhood adversity in child development has focused on youth living in high-income countries. However, previous data have shown that estimates of trauma exposure in childhood are higher among youth living in low/middle-income countries when compared to high-income countries (3), stressing the need for more studies focusing on such populations. Second, most existing research investigating the associations between childhood adversity, psychopathology, and cognition is cross-sectional and does not examine how these experiences longitudinally influence the development of emotion, cognition, and psychopathology.

In this study, we examined the longitudinal associations of threat and deprivation with cognition, emotion, and psychopathology in children and adolescents in a large school-based community sample from a middle-income country. Specifically, we aimed (1) to evaluate the latent constructs of threat and deprivation in a large community sample from Brazil, and (2) to investigate associations of threat and deprivation experiences with EF, emotional processing measured by attention orienting toward angry faces, and psychopathology. We hypothesized that a model specifying distinctions among adversities would provide a good fit for the data. We also expected that attention orienting toward angry faces would be associated with threat, but not deprivation, that worse EF would be associated with deprivation, but not threat, and that psychopathology would be associated with both threat and deprivation.

Methods and Materials

Study design, procedures, and participants

Data for this study are drawn from the baseline and 3-year follow-up waves of the Brazilian High-Risk Cohort for Mental Conditions (BHRCS), a school-based community cohort from the cities of São Paulo and Porto Alegre. Briefly, in the year 2010, 9937 parents of 6 to 14-year-old children from 57 schools in São Paulo and Porto Alegre were screened using the Family History Survey (25). From this sample, two subgroups were recruited for further assessments. One subgroup was randomly selected (n=957), while the other was selected from a high-risk score procedure used to identify children with current symptoms and/or family history of psychiatric disorders (n=1554). The high-risk score procedure consists of the calculation of an index of family load based on the FHS considering mother, father, or siblings' presentation of any of the five disorders of interest for this study (Attention Deficit and Hyperactivity Disorder, anxiety disorders, Obsessive Compulsive Disorder, psychotic experiences, and learning disorders). This index expresses the percentage of members in the family that screened positively for each of the disorders assessed, adjusted for relatedness.

A total of 2,511 children/adolescents and their parents were assessed at two-time points through questionnaires and interviews about the history of exposure to adversities and psychopathology. Children/adolescents also completed neurocognitive tests at both time points. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects were

approved by the institutional review boards of all institutions involved in the study (CAAE: 74563817.7.1001.5237). Written, and verbal informed consent was obtained from all participants. For a detailed description of the study, its procedures, and sample see Salum et al., 2014 (26).

Measures

Adversity Experiences

Selected variables from the baseline evaluation of the BHRCS were chosen based on theoretical models of adversity (10). We examined the number and frequency of different forms of threat experiences to model the dimension of threat. Variables selected for measuring experiences of threat were drawn from two sources: the Posttraumatic Stress Disorder (PTSD) assessment of the Development and Well-Being Assessment (DAWBA)(27) and questionnaires specifically designed for the BHRCS(26). Lifetime exposure to physical and sexual abuse, attack or threat, witnessing domestic violence, and witnessing attack, were investigated from parent reports only using the first section of the PTSD assessment in the DAWBA with questions such as "*Has the child ever suffered physical violence (maltreatment) that he/she remembers?*". Some variables, such as life experiences of bullying, and frequency (never, once or twice, from time to time, and often) and experiences of physical and emotional abuse were informed by both, parents and the children, through questions such as *"Has the child (you) ever been bullied in his/her(your) life?", and* "*Has your child(you) ever been cursed by some adult, with words like 'ass', 'idiot', 'stupid', or being yelled that he/she was(you were) no good?"*(28). Sexual abuse experiences were reported only by the parents and due to its low frequency (see the Table 2 on the supplemental material) on both sources of information (DAWBA's PTSD assessment and the questionnaire), both variables were combined to form one sexual abuse exposure variable.

Deprivation measures included indicators of neglect, parental absence, and measures of material forms of deprivation that are strongly associated with cognitive forms of deprivation (e.g., reduced exposure to complex language early in development) (29,30). Deprivation was measured through the assessment of mother's educational level (adjusted into four categories ranging from higher education to no study), family income (measured in quintiles), socioeconomic classification according to Brazilian Economic Classification Criterion (A/B – the wealthiest, C, or D/E – the poorest)(31), father presence (in contact, non-contact, deceased, or unknown), and the frequency (never, once or twice, from time to time, and often) of exposure to physical neglect(28). Physical neglect was informed by both, parents, and the children, through the question "*Has it ever happened to your child(you) of not having anything to eat and/or having to wear dirty or torn clothes?"*, and father contact was assessed through the question "*What is the current contact status of the child's father?"*. (See the Supplemental Table S1 for more detailed information). Our assessment of deprivation was composed mostly of proxy measures, in a way that their presence does not necessarily indicate deprivation directly, but merely increases the likelihood of living under deprived conditions. Those types of indicators are well-suited for latent analysis, for which deprivation is a latent concept indicated by several indicators.

Psychopathology

Psychopathology was measured dimensionally at baseline and follow-up through the Child Behavior Checklist (CBCL)(32,33). The CBCL is a parent-report questionnaire that assesses the child's emotional, behavioral, and social problems yielding a total score (including all items), as well as an internalizing and externalizing score. A bifactor model with one dimension of general psychopathology (the "p" factor) was fitted to the data with two residualized dimensions of

internalizing and externalizing psychopathology. Our goal was not to estimate the structure of psychopathology in the sample, but rather to generate a dimensional measure capturing the severity of psychopathology symptoms transdiagnostically. Although debate exists about measurement models of p-factor, recent work suggests that the rank order stability of individuals is similar across these approaches, making p-factor estimation appropriate for studying individual differences in transdiagnostic psychopathology(34). Only general psychopathology scores were used for further analysis. Details on the model are in the Supplemental Material.

Cognition

Executive Functions. Three dimensions of executive functions (EF) were calculated to create a second-order model of EF. The dependent variable was a single EF standardized score encompassed by latent variables representing working memory, inhibitory control, and temporal processing dimensions. Higher scores represent better EF. At both baseline and follow-up, we performed a second-order model in which executive functions were a high-order factor informed by three lower-order factors: working memory (Digit Span Backwards and Corsi Blocks Backwards), inhibitory control (Go/No-Go task and Conflict Control Task), and temporal processing (Time Anticipation 400ms). The benefit of using a second-order model, instead of a single factor model where all tasks load on a first-order executive function latent variable, is that such first-order model resulted in an unacceptable fit. For a detailed description of the EF measure, see the Supplemental Material.

Working memory was measured by the *digit span* (a subtest of the WISC-III)(35) and Corsi *blocks* tasks (36). Both tasks involve the repetition of a given sequence. While in the *digit span task* the participants hear and repeat an increasingly difficult sequence of numbers, either forward

or backward, in the Corsi *blocks task* they repeat an increasingly difficult spatial sequence tapped by a researcher on up to nine identical blocks. Both outcomes are the level at which a correct repetition failed twice consecutively.

Inhibitory control was measured by the *conflict control task* (CCT)(37) and the *go/no-go* task (GNG)(38). Both consist of arrow-based visual stimuli with a total of 100 trials divided into two different instructions. In the *conflict control task*, participants are asked to press a button indicating the direction or opposite direction of arrows shown on the screen. Participants either press the button indicating the correct direction of a green arrow (75 congruent trials) or press the button indicating the opposite direction of a red arrow (25 incongruent trials). The *go/no-go* task requires participants to completely suppress the tendency to press the buttons indicating the direction of the green arrows (75 *go* stimuli trials) when a double-headed green arrow (25 *no-go* stimuli trials) appears on the screen. For both tasks, the intertrial interval was 1,500 ms, and the stimulus duration was 100 ms. The outcomes were the percentage of correct responses in the incongruent trials (CCT) and the percentage of successful inhibitions in the *no-go* trials (GNG).

Finally, *temporal processing* was measured by *time anticipation (TA) tasks 400 ms* (39) on baseline and follow-up. This task requires participants to anticipate when a visual stimulus will appear. In a game-like manner, the task involves an allied spaceship running out of oxygen and the participant has to give it to them to save the crew. In each task, the allied spaceship is visible for the first 10 trials, while for the remaining 16 trials the spaceship is invisible due to an invisible shield. Then, participants are asked to press a button to anticipate when it arrives. A 750-ms window of time to respond correctly and feedback after every trial are given. The anticipation interval is 400ms. The outcome is the mean percentage of the button pressed in the correct time window interval for the invisible part of the task. Tasks involving temporal delays with flexible

cognitive demands have been proposed to be a part of EF in some models (40). Temporal processing tasks used have previously been well-correlated with the other EF tasks in our sample (41,42). Results for EF model fit are reported in the Supplemental Material.

Emotional Processing

Attention orienting toward angry faces. Attention orienting toward angry faces was assessed using a dot-probe task in Eprime 2.0 (Psychology Software Tools, USA) and has been used in a previous study derived from the BHRC (43). The task consists of the presentation of paired threatening (angry) and neutral face photographs followed by a probe at the location of one of the two photographs. Each trial starts with a central fixation cross (for 500ms), followed by the face pair (for 500ms) which is replaced with the probe (for 1100ms). Participants are instructed to press one of the response keys to indicate whether the probe appeared on the left, or right side of the screen. Trials are, randomly, either congruent (16 trials), with threatening faces and probes appearing on the same side of the screen, or incongruent (16 trials), with threatening faces appearing on opposite sides of the screen. The inter-trial interval varies randomly from 750 to 1250ms. Since the neutral and the threatening stimuli are in different screen locations, they compete for attention. Therefore, attention orienting toward angry faces is measured as the difference in reaction time between the task's trials in which the probe replaces a neutral stimulus versus those in which the probe replaces a threatening stimulus. Response times were excluded as errors from trials where the response was incorrect or did not occur before probe offset. Additionally, response times less than 200ms or more than 2 standard deviations above each participant's mean were excluded as outliers, as well as attention bias scores were not calculated if more than 50% response times data were missing. Therefore, the dependent variable was a

standardized score of attention orienting toward angry faces. Scores greater than zero represent biases in attention toward threats and lower than zero biases in attention away from threats.

Data Analysis

First, we conducted factor analyses to assess the latent structure of threat and deprivation adversity experiences at baseline, and the EF and psychopathology models at baseline and follow-up. Missing data were accounted for using full information maximum likelihood estimation. Model goodness of fit was evaluated using root-mean-square error of approximation (RMSEA), comparative fit index (CFI), and Tucker-Lewis index (TLI). RMSEA equal to or below .06, and a CFI and a TLI above .95 indicate a good fit (44,45).

Second, we used the observed factor scores from the validated models to test the cross-sectional and longitudinal associations of threat and deprivation with each outcome following a series of steps. First, we tested cross-sectional associations using three linear regression models adjusted for age and sex with threat and deprivation levels at baseline as simultaneous predictors of (1) psychopathology, (2) EF, and (3) attention bias at baseline as dependent variables. Second, longitudinal associations were tested also using three models adjusted for age and sex with threat and deprivation levels at baseline as simultaneous predictors of (1) psychopathology, (2) EF, and (3) attention bias three years later as dependent variables. Longitudinal models were adjusted and controlled for the outcome variable levels at baseline. Sensitivity analyses were conducted testing the same models described above excluding the measure of family income as a marker of deprivation. No significant differences were found when comparing the results from the models with and without family incomed as a marker of deprivation. Third, to check the assumptions of linear models, interaction effects of threat and deprivation with age and sex were tested

independently for each one of the adversity measures using fully saturated models for three-way and two-way interactions (Supplemental Tables S7 – S10). If interactions were found, marginal analyses were conducted to further understand such results and are depicted in detail in the supplemental material (Supplemental Table S11 and S12). The same approach of cross-sectional and longitudinal models, followed by multiple two and three-way interaction models and marginal analyses were conducted as exploratory analyses to examine specific associations of threat and deprivation, and (1) internalizing and (2) externalizing psychopathology. Detailed results are reported in the supplemental material (Supplemental Tables S13). Two and three-way interactions between adversity, and age, and sex were conducted (Supplemental Tables S14-S17) followed by marginal analyses (Supplemental Figure S5).

Finally, further exploratory analyses were conducted examining whether executive functions and attention orienting toward angry faces could serve as mediators linking exposure to threat and deprivation to general psychopathology, as well as internalizing and externalizing specific psychopathology. Such hypothesis was tested through two similar longitudinal mediation models, both having threat and deprivation at baseline as concurrent predictors and general, internalizing and externalizing psychopathology at follow up as concurrent outcomes, and executive functions and attention orienting toward angry faces (1) at baseline and (2) at follow-up as concurrent mediators. Detailed results are presented in the Supplemental Material (Supplemental Figure S6-S7 and Supplemental Tables S18-S19). Data analysis was performed using the *Mplus* software (version 7.3) and the *lavaan* package from R (version 3.6.1).

Results

Descriptive Statistics

The total sample was comprised of 2,511 children and adolescents with a mean age of 10.42 years old at baseline and 13.71 years old on follow-up. Among those, 1375 (54.8%) were male, and 1256 (50.1%) were from the city of São Paulo. Descriptive data on variables of interest are shown in Table 1 and additional descriptive data is in the Supplemental Material (Supplemental Table S2).

(TABLE 1 HERE)

Threat and Deprivation Latent Structure

The model of threat and deprivation as latent variables (Supplemental Figure S1) was tested using the baseline measures. The model consisted of eleven indicators for the dimension of threat and six indicators of the dimension of deprivation (Supplemental Table S1). The model had acceptable fit indexes (CFI = 0.937, TLI = 0.922, RMSEA = 0.032), with all indicators presenting significant contributions to each distinct construct. Detailed information about the model is provided in Table 2.

(TABLE 2 HERE)

General psychopathology (the "p" factor)

Higher levels of threat at baseline were associated with higher levels of general psychopathology at baseline (β=0.522, p<0.001; 95% CI [0.475, 0.569]), and three years later (β=0.176, p<0.001; 95% CI [0.119, 0.232]), while higher levels of deprivation at baseline predicted higher levels of general psychopathology only three years later (β=0.072, p=0.003; 95%

CI [0.025, 0.119]), with smaller effect size (Table 3). One interaction between threat and age in predicting psychopathology at follow-up was found (β=-0.030, p=0.021; 95% CI [-0.055, -0.004]) (Supplemental Table S9), suggesting that the influence of threat on psychopathology was stronger for younger children than older children (Supplemental Table S11 and Supplemental Figure S3). The latent model that generated the general psychopathology measure fit the data well according to recommended goodness of fit statistics, as described in the Supplemental Material.

Internalizing-specific and Externalizing-specific psychopathology

Exploratory analyses indicated that higher levels of threat at baseline were associated with higher levels of both internalizing (β=0.143, p<0.001; 95% CI [0.101, 0.186]) and externalizing psychopathology (β=0.170, p<0.001; 95% CI [0.129, 0.211]) at baseline. No longitudinal associations, nor association with levels of deprivation were found (Supplemental Table S13). One significant interaction between threat and age in predicting internalizing psychopathology at baseline was found (β=0.033, p=0.002; 95% CI [0.012, 0.053]) (Supplemental Table S16), suggesting that the influence of threat on internalizing psychopathology was stronger for older children than younger children (Supplemental Figure S5). Detailed results can be found in the Supplemental Material.

Executive Functions

Higher levels of deprivation at baseline were associated with worse performance on EF tasks at both baseline (β=-0.115, p<0.001, 95% CI [-0.151, -0.079]) and follow-up (β=-0.045, p=0.038, 95% CI [-0.088, -0.003]). Exposure to threat was not associated with performance on EF tasks at baseline or follow-up. No interactions were found between either dimension of adversity

with age and sex. The latent model that generated the executive functions measure fit the data well according to recommended goodness of fit statistics, as described in the Supplemental Material.

Attention orienting toward angry faces

Biases toward angry faces at baseline were associated with higher levels of threat at baseline (β=0.079, p=0.029, 95% CI [0.008, 0.151]). One interaction between deprivation and age in predicting attention orienting toward angry faces at baseline was found (β=0.041, p=0.007; 95% CI [0.011, 0.072]) (Supplemental Table S10). For younger children, higher deprivation levels were associated with attention orienting *away* angry faces, whereas for older children higher deprivation levels were associated with attention orienting toward angry faces (Supplemental Table S12 and Supplemental Figure S4).

(TABLE 3 HERE)

Exploratory analysis: executive functions and attention orienting towards angry faces as mediators of threat and deprivation on psychopathology, internalizing and externalizing specific psychopathology

Exploratory mediation models with EF and attention orienting towards angry faces at baseline as mediators indicated significant direct associations of threat and deprivation at baseline with higher levels of psychopathology (β=0.270, p<0.001; β=0.073, p=0.002) and externalizing psychopathology (β=0.104, p<0.001) three years later. A small mediation of deprivation at baseline on psychopathology three years later via EF at baseline was significant in this model (β=0.009, p=0.005) (Supplemental Figure S6 and Supplemental Table S18). The same pattern of

results was found in the model having EF and attention towards angry faces at follow-up as mediators, showing direct effects of threat and deprivation at baseline on psychopathology (β=0.269, p<0.001; β=0.072, p=0.002) and externalizing psychopathology (β=0.099, p<0.001) three years later, as well as a mediation of deprivation at baseline with psychopathology three years later via EF at follow-up (β=0.008, p=0.006) (Supplemental Figure S7 and Supplemental Table S19). Detailed results can be found in the Supplemental Material (Supplemental Table S18-S19 and Supplemental Figure S6-S7).

Discussion

This study examined theoretical predictions of a dimensional model of childhood adversity(10). Our results suggest that threat and deprivation have differential associations with cognitive and emotional development and psychopathology. In particular, higher levels of threat were more strongly associated with psychopathology, and solely predicted higher levels of internalizing and externalizing specific psychopathology cross-sectionally when compared to deprivation. Threat was also the only adversity measure slightly associated with attention bias towards angry faces, while only higher levels of deprivation, but not threat, were associated with worse performance on EF tasks. Additionally, exploratory analyses suggest mediation of higher levels of deprivation with higher levels of psychopathology years later via worse performance on executive functions tasks.

Our results are consistent with prior work (23,24,46–48) showing that experiences of threat and deprivation are differentially associated with developmental outcomes in children. The effect sizes we found, except for associations between threat and psychopathology, were generally small. This is not surprising, given that these associations were estimated longitudinally over a 3-year

interval. The influences on emotional processing, cognition, and psychopathology are multifactorial, and many other relevant factors associated with these aspects of development were not accounted for in our models. This pattern of findings has theoretical implications for conceptual models of adversity and development, as well as clinical implications regarding potential targets for early interventions aimed at preventing the long-term consequences of adversity for mental health and academic achievement.

There is mounting evidence showing that childhood adversity is associated with high levels of psychopathology, both cross-sectionally and prospectively(49,50). This link tends to span all forms of psychopathology, including both internalizing and externalizing domains(28) – and therefore associations with general indices of psychopathology (such as the "p" factor) are expected (51) as we confirmed here. In line with previous evidence and theoretical models, we showed that associations between adversity and general psychopathology were revealed for both types of adversity domains(24). The associations with general psychopathology were stronger and present at both time points only for threat and not for deprivation, which might suggest a more prominent role of the threat domain on overall psychopathology. Prior work has already demonstrated direct effects of threat and indirect effects of deprivation on psychopathology (22,23,45), which is also supported by the mediation path of deprivation on psychopathology through worse performance on executive functions tasks that we found on our exploratory analysis.

Additionally, only threat was associated with both specific dimensions of psychopathology, which is also supported by previous evidence on direct associations of threat with internalizing and externalizing problems (22). Our interaction analyses of adversity and age on psychopathology and its domains suggested that the association of threat with psychopathology may vary with age and might follow different patterns for general and specific dimensions. Higher

levels of threat were significantly associated with higher levels of general psychopathology among younger kids, supporting previous longitudinal findings suggesting that childhood psychopathology symptoms could be primarily explained by proximal, rather than distal environmental experiences (51). Nevertheless, when it comes to specific domains of psychopathology, higher levels of threat were associated with higher levels of internalizing psychopathology among older children. Such result is in line with adolescence being a period of heightened vulnerability for the onset of internalizing psychopathology (52), as well as with documented changes in the heterogeneity and heterotypic stability of emotional and behavioral symptoms throughout development (53). Questions about age-related mechanisms involved in the associations of threat and psychopathology hold the potential to expand the field in promising ways.

Consistent with our hypotheses, higher levels of deprivation, but not threat, were associated with worse performance on EF tasks at baseline and follow-up. This pattern is consistent with previous cross-sectional studies observing that experiences characterized by deprivation, and not threat, are related to lower EF(13,47,54), and is broadly consistent with theoretical predictions arguing that deprivation may uniquely influence the development of EF in children and adolescents(10,11). Also according to our hypotheses, higher levels of threat, but not deprivation, were associated with attention orienting towards angry faces at baseline. Previous research has already shown that children and adolescents who have experienced violence have greater attention bias toward angry faces compared to those that have never experienced threat (50,55,56). Interestingly, our analysis also suggested that deprivation was associated with attention orienting *away* from angry faces in young children, and attention orienting towards angry faces in the oldest adolescents at baseline. These results are consistent with previous data reporting on age varying

associations of adversity with attention bias (57,58), supporting that these associations might depend on the developmental period of assessment. However, previous research has found different developmental patterns. Studies have shown a pattern of maltreated children exhibiting a bias towards threat and adolescents a bias away from threat (57), as well as younger anxious children presenting greater anxiety-related processing bias for angry faces when compared to older children (58). Such contradictory findings from the ones reported in this study might be related to differential influences of different types of adversities being experienced. They also raise questions concerning what age-relevant mechanisms might be involved in the association between adversity in the form of deprivation and attention bias related to threatful stimuli. Replication of these age interactions in additional samples is an important next step.

Our study has several strengths. First, by using a dimensional approach to childhood adversities, we were able to distinguish possible differential associations of distinct experiences with psychopathology, EF, and attention orienting toward angry faces. We provide supporting evidence of the pathways through which adversity influences different developmental domains in a large, longitudinal sample from a middle-income country, extending prior work that has been done almost exclusively in high-income contexts. Second, our longitudinal design allowed us to explore the associations of threat and deprivation with developmental change in these domains over time, which has rarely been done in existing studies of adversity dimensions.

Some limitations also should be noted. First, our results are mainly observational, therefore no conclusions about the causality of the associations found can be made. Second, the deprivation dimension is also characterized by emotional neglect, and an absence of cognitive stimulation, or the lack of an enriched cognitive environment (11). Our deprivation dimension was primarily a measure of physical neglect and material deprivation, and as such did not directly measure

emotional deprivation or other aspects of cognitive stimulation. The lack of assessment of emotional neglect and cognitive stimulation in this study means that inferences apply largely to the material and physical aspects of deprivation and cannot be generalized to the comprehensive experience of deprivation more broadly. Third, attention orienting toward angry faces captures only one relatively constrained domain of emotional processing. Because no other measure of emotional information processing was assessed in this study, we were not able to capture the associations of adversity with other domains of emotional processing argued to be particularly likely to be influenced by threat-related adversity, including emotional reactivity, emotional learning, and emotion regulation (59). Finally, there is no data available on children's age of adversity exposure. To understand possible associations among exposure to adversity, age, and psychopathology, the developmental period of exposure should be assessed.

Exposure to adversity, especially during childhood, is a complex phenomenon with meaningful and well-established influences on child development. Because adversity can take many forms, dimensional models—as the one investigated here—might help to disentangle the specific developmental correlates of different types of adverse early environments and the mechanisms through which they confer risk for psychopathology. Understanding these pathways is critical for developing interventions to buffer the influence of adversity experiences on children's development.

References

1. McLaughlin KA. Future Directions in Childhood Adversity and Youth Psychopathology. Journal of Clinical Child and Adolescent Psychology. 2016;45(3):361–82.
2. Costello EJ, Erkanli A, Fairbank JA, Angold A. The Prevalence of Potentially Traumatic Events in Childhood and Adolescence. 2002;15(2):99–112.
3. Viola TW, Salum GA, Kluwe-Schiavon B, Sanvicente-Vieira B, Levandowski ML, Grassi-Oliveira R. The influence of geographical and economic factors in estimates of childhood abuse and neglect using the Childhood Trauma Questionnaire: A worldwide meta-regression analysis. Child Abuse and Neglect. 2016;51(305141):1–11.
4. Magruder KM, McLaughlin KA, Elmore Borbon DL. Trauma is a public health issue. European Journal of Psychotraumatology. 2017;8(1):1375338.
5. Green JG, McLaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM, et al. Childhood adversity and adult psychopathology in the National Comorbidity Survey Replication (NCS-R)-I: Associations with first onset of DSM-IV disorders. Archives of General Psychiatry. 2010;67(2):1–21.
6. Mclaughlin KA, Green JG, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC. Childhood Adversities and First Onset of Psychiatric Disorders in a National Sample of US Adolescents. 2012;69(11):1151–60.
7. Lansford JE, Dodge KA, Pettit GS, Bates JE, Crozier J, Kaplow J. A 12-year prospective study of the long-term effects of early child physical maltreatment on psychological, behavioral, and academic problems in adolescence. Archives of Pediatrics and Adolescent Medicine. 2002;156(8):824–30.

8. Mclaughlin KA, Sheridan MA. Beyond Cumulative Risk : A Dimensional Approach to Childhood Adversity. 2016;
9. Humphreys KL, Zeanah CH. Deviations from the Expectable Environment in Early Childhood and Emerging Psychopathology. Neuropsychopharmacology. 2014;40(1):153–69.
10. McLaughlin KA, Sheridan MA, Lambert HK. Childhood adversity and neural development: deprivation and threat as distinct dimensions of early experience. Neuroscience and biobehavioral reviews. 2014;47:578–91.
11. Sheridan MA, Mclaughlin KA. Dimensions of early experience and neural development : deprivation and threat. Trends in Cognitive Sciences. 2014;18(11):580–5.
12. McLaughlin KA, DeCross SN, Jovanovic T, Tottenham N. Mechanisms linking childhood adversity with psychopathology: Learning as an intervention target. Behaviour Research and Therapy. 2019;118(March):101–9.
13. Machlin L, Miller AB, Snyder J, McLaughlin KA, Sheridan MA. Differential Associations of Deprivation and Threat With Cognitive Control and Fear Conditioning in Early Childhood. Frontiers in Behavioral Neuroscience. 2019;13(May):1–14.
14. Lambert HK, King KM, Monahan KC, McLaughlin KA. Differential associations of threat and deprivation with emotion regulation and cognitive control in adolescence. Development and Psychopathology. 2017;29(3):929–40.
15. Busso DS, McLaughlin KA, Sheridan MA. Dimensions of Adversity, Physiological Reactivity, and Externalizing Psychopathology in Adolescence: Deprivation and Threat. Psychosomatic Medicine. 2017;79(2):162–71.

16. Johnson D, Policelli J, Li M, Dharamsi A, Hu Q, Sheridan MA, et al. Associations of Early-Life Threat and Deprivation With Executive Functioning in Childhood and Adolescence A Systematic Review and Meta-analysis. 2021;
17. Pollak SD, Cicchetti D, Hornung K, Reed A. Recognizing emotion in faces: developmental effects of child abuse and neglect. Developmental psychology. 2000;36(5):679–88.
18. Pollak SD, Sinha P. Effects of early experience on children's recognition of facial displays of emotion. Developmental psychology. 2002;38(5):784–91.
19. Pollak SD, Kistler DJ. Early experience is associated with the development of categorical representations for facial expressions of emotion. Proceedings of the National Academy of Sciences. 2002;99(13):9072–6.
20. Shackman JE, Pollak SD. Impact of physical maltreatment on the regulation of negative affect and aggression. Development and Psychopathology. 2014;26(4):1021–33.
21. Wismer Fries AB, Pollak SD. Emotion understanding in postinstitutionalized Eastern European children. Development and Psychopathology. 2004;16(2):355–69.
22. Miller AB, Sheridan M, Hanson JL, Mclaughlin KA, Bates JE, Lansford JE, et al. Dimensions of Deprivation and Threat, Psychopathology, and Potential Mediators: A Multi-Year Longitudinal Analysis. Journal of abnormal psychology. 2016;127(2):160–70.
23. Miller AB, Machlin L, McLaughlin KA, Sheridan MA. Deprivation and psychopathology in the Fragile Families Study: A 15-year longitudinal investigation. Journal of Child Psychology and Psychiatry and Allied Disciplines. 2020;
24. Weissman MM, Wickramaratne P, Adams P, Wolk S, Verdeli H, Olfson M. Brief Screening for Family Psychiatric History. Archives of General Psychiatry. 2000;57.

25. Salum GA, Gadelha ARY, Pan PM, Moriyama TS, Graeff-martins ANAS, Tamanaha ANAC, et al. High risk cohort study for psychiatric disorders in childhood: rationale, design, methods, and preliminary results. Int J Methods Psychiatr Res. 2014;(March).

26. Goodman R, Ford T, Richards H, Gatward R, Meltzer H. The Development and Well-Being Assessment: Description and initial validation of an integrated assessment of child and adolescent psychopathology. Journal of Child Psychology and Psychiatry and Allied Disciplines. 2000;41(5):645–55.

27. Salum GA, DeSousa DA, Manfro GG, Pan PM, Gadelha A, Brietzke E, et al. Measuring child maltreatment using multi-informant survey data: a higher-order confirmatory factor analysis. Trends in Psychiatry and Psychotherapy. 2016;38(1):23–32.

28. Mclaughlin KA, Sheridan MA, Nelson CA. Neglect as a Violation of Species-Expectant Experience : Neurodevelopmental Consequences. Biological Psychiatry. 2017;82(7):462–71.

29. Romeo RR, Leonard JA, Robinson ST, West MR, Mackey AP, Rowe ML, et al. Beyond the 30-Million-Word Gap: Children's Conversational Exposure Is Associated With Language-Related Brain Function. Psychological Science. 2018;29(5):700–10.

30. Associação Brasileira de Empresas (ABEP). Critério de Classificação Econômica Brasil. 2010.

31. Achenbach TM, Rescola LA. Manual for the ASEBA school-age forms & profiles. Burlington; 2001.

32. Bordin IA, Rocha MM, Paula CS, Teixeira MCT V, Achenbach TM, Rescola LA, et al. Child Behavior Checklist (CBCL), Youth Self- Report (YSR) and Teacher's Report Form

(TRF): an overview of the development of the original and Brazilian versions. Cadernos de Saúde Pública. 2013;29(1):13–28.

33. Clark DA, Hicks BM, Angstadt M, Rutherford S, Taxali A, Hyde L, et al. The General Factor of Psychopathology in the Adolescent Brain Cognitive Development (ABCD) Study: A Comparison of Alternative Modeling Approaches. Clinical Psychological Science. 2021;9(2):169–82.

34. Wechsler D. WISC-III: Escala de Inteligência Wechsler para Crianças: Manual [Wechsler Intelligence Scale for Children-Third Edition]. São Paulo: Casa do Psicólogo; 2002.

35. Vandierendonck A, Kemps E, Fastame MC, Szmalec A. Working memory components of the Corsi blocks task. British Journal of Psychology. 2004;95(1):57–79.

36. Hogan AM, Vargha-Khadem F, Kirkham FJ, Baldeweg T. Maturation of action monitoring from adolescence to adulthood: An ERP study. Developmental Science. 2005;8(6):525–34.

37. Bitsakou P, Psychogiou L, Thompson M, Sonuga-Barke EJS. Inhibitory deficits in attention-deficit/hyperactivity disorder are independent of basic processing efficiency and IQ. Journal of Neural Transmission. 2008;115(2):261–8.

38. Toplak ME, Tannock R. Tapping and Anticipation Performance in Attention Deficit Hyperactivity Disorder. Perceptual and Motor Skills. 2005;100(3):659–75.

39. Barkley RA. Behavioral inhibition sustained attention, and executive functions: Constructing a unifying theory of ADHD. Psychological Bulletin. 1997;121(1):65–94.

40. Martel MM, Pan PM, Hoffmann MS, Gadelha A, Rosário MC, Jair J, et al. A General Psychopathology Factor (P Factor) in Children : Structural Model Analysis and External

Validation Through Familial Risk and Child Global Executive Function. Journal of Abnormal Psychology. 2016;

41. Manfro AG, Santoro M, Polanczyk GV, Gadelha A, Pan PM, Bressan RA, et al. Heterotypic trajectories of dimensional psychopathology across the lifespan: the case of youth-onset attention deficit/hyperactivity disorder. Journal of Child Psychology and Psychiatry and Allied Disciplines. 2019;60(5):533–44.
42. Salum GA, Mogg K, Bradley BP, Gadelha A, Pan P, Tamanaha AC, et al. Threat bias in attention orienting : evidence of specificity in a large community-based study. Psychological Medicine. 2012;1–13.
43. Hu LT, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. Structural equation modeling: a multidisciplinary journal. 1999;6(1):1–55.
44. Kline RB. Exploratory and confirmatory factor analysis. In: Petscher Y, Schatsschneider C, editors. Applied quantitative analysis in the social sciences. New York: Routledge; 2013. p. 171–207.
45. Platt JM, McLaughlin KA, Luedtke AR, Ahern J, Kaufman AS, Keyes KM. Targeted Estimation of the Relationship between Childhood Adversity and Fluid Intelligence in a US Population Sample of Adolescents. American Journal of Epidemiology. 2018;187(7):1456–66.
46. Rosen ML, Hagen MP, Lurie LA, Miles ZE, Sheridan MA, Meltzoff AN, et al. Cognitive Stimulation as a Mechanism Linking Socioeconomic Status With Executive Function: A Longitudinal Investigation. Child Development. 2019;00(0):1–18.

47. Sheridan MA, Peverill M, Finn AMYS, Laughlin KAMC. Dimensions of childhood adversity have distinct associations with neural systems underlying executive functioning. Development and Psychopathology. 2017;29:1777–94.

48. Schaefer JD, Moffitt TE, Arseneault L, Danese A, Fisher HL, Houts R, et al. Adolescent Victimization and Early-Adult Psychopathology: Approaching Causal Inference Using a Longitudinal Twin Study to Rule Out Noncausal Explanations. Clinical Psychological Science. 2018;6(3):352–71.

49. Caspi A, Houts RM, Belsky DW, Goldman-Mellor SJ, Harrington H, Israel S, et al. The p factor: One general psychopathology factor in the structure of psychiatric disorders? Clinical Psychological Science. 2014;2(2):119–37.

50. Miller LE. Perceived Threat in Childhood: A Review of Research and Implications for Children Living in Violent Households. Trauma, Violence, and Abuse. 2015;16(2):153–68.

51. Dunn EC, Soare TW, Raffeld MR, Busso DS, Crawford KM, Davis KA, et al. What life course theoretical models best explain the relationship between exposure to childhood adversity and psychopathology symptoms : recency, accumulation, or sensitive periods ? 2018;

52. Mclaughlin KA, King K. Developmental Trajectories of Anxiety and Depression in Early Adolescence. 2015;311–23.

53. Picoito J, Santos C, Nunes C. Heterogeneity and heterotypic continuity of emotional and behavioural profiles across development. Social Psychiatry and Psychiatric Epidemiology. 2021;56(5):807–19.

54. Bos KJ. Effects of early psychosocial deprivation on the development of memory and executive function. Frontiers in Behavioral Neuroscience. 2009;3(September):1–7.

55. Pollak SD, Tolley-Schell SA. Selective attention to facial emotion in physically abused children. Vol. 112, Journal of Abnormal Psychology. 2003. p. 323–38.

56. Briggs-Gowan MJ, Pollak SD, Grasso D, Voss J, Mian ND, Zobel E, et al. Attention bias and anxiety in young children exposed to family violence. Journal of Child Psychology and Psychiatry. 2015;56(11):1194–201.

57. Weissman DG, Bitran D, Miller AB, Schaefer JD, Sheridan MA, Mclaughlin KA. Difficulties with emotion regulation as a transdiagnostic mechanism linking child maltreatment with the emergence of psychopathology. 2019;(April).

58. Reinholdt-Dunne ML, Mogg K, Esbjorn BH, Bradley BP. Effects of Age and Anxiety on Processing Threat Cues in Healthy Children. Journal of Experimental Psychopathology. 2012;3(1):30–41.

59. McLaughlin KA, Lambert HK. Child trauma exposure and psychopathology: mechanisms of risk and resilience. Current Opinion in Psychology. 2017;14:29–34.

Table 1 – Sample description

	Baseline				3-year follow-up			
	N	**%**	**Valid N**					
Sex: male	1375	54.8	2511					
Site: São Paulo	1256	50	2511					
	Mean (sd)	**Range**	**Skewness/ Kurtosis**	**Valid N**	**Mean (sd)**	**Range**	**Skewness/ Kurtosis**	**Valid N**
Age (years)	10.2 (1.9)	5.83 - 14.37	0.13, -0.91	2511	13.5 (1.9)	9.2 - 17.87	0.13, -089	2010
Family income (BRL)	757.6 (536.6)	29.94 - 4910.18	2.04, 6.9	2110	783.8 (656.8)	21.65 - 8658.01	3.78, 27.83	1679
CBCL: Total CBCL scores	17.2 (16.1)	0 - 101	1.34, 1.69	2511	14.6 (15.0)	0 - 90	1.41, 1.78	2010
Working Memory								
Corsi block (backward)	4.8 (2.1)	0 - 14	0.08, -0.12	2223	5.6 (2.5)	0 - 13	-0.44, -0.06	1880
Digit span (backward)	3.5 (1.6)	0 - 12	0.45, 1.34	2249	4.1 (2.0)	0 - 13	0.15, 0.69	1880
Inhibitory Control								
CCT % Correct Inhibitions	0.6 (0.2)	0 - 1	-0.37, -0.47	2165	0.7 (0.3)	0 - 1	-1.06, 0.52	1704
Go/No-Go: Comission	0.3 (0.2)	0 - 1	0.97, 0.12	2158	0.2 (0.2)	0 - 1	1.5, 1.83	1701
Temporal Processing								
Time Anticipaion (0.4s): hits	0.6 (0.2)	0 - 1	-0.69, -0.02	2185	0.8 (0.2)	0 - 1	-1.28, 1.97	1701
Attention orienting toward angry faces (ms)	5.2 (53.0)	-357.17 - 288	0.17, 3.56	2148	2.9 (40.0)	-297.93 – 411	0.16, 13.36	1603

Note: crude scores for psychopathology, executive function tasks, and attention orienting toward angry faces are presented in order to inform about the variables' characteristics on the sample. CBCL (Child Behavior Checklist); CCT (Conflict Control Task); GNG (Go/no-go Task).

Table 2 - Factor loadings of the Threat and Deprivation Model

	Estimate	S.E.	Est./S.E.	*p*-value
Threat				
Bullying exposure (parent report)	0.483	0.033	14.650	<0.001
Bullying exposure (child report)	0.159	0.039	4.123	<0.001
DAWBA: Physical abuse	0.830	0.037	22.399	<0.001
Physical abuse (parent report)	0.658	0.038	17.383	<0.001
Physical abuse (child report)	0.245	0.044	5.589	<0.001
Emotional abuse (parent report)	0.542	0.028	19.038	<0.001
Emotional abuse (child report)	0.229	0.038	5.962	<0.001
Sexual abuse (total)	0.559	0.061	9.090	<0.001
DAWBA: Attack or threat	0.522	0.049	10.656	<0.001
DAWBA: Domestic violence witnessing	0.666	0.037	17.929	<0.001
DAWBA: Attack witnessing	0.685	0.042	16.414	<0.001
Deprivation				
Mother's educational level	0.327	0.033	10.020	<0.001
ABEP 2009: Stratified Score	0.616	0.035	17.582	<0.001
Father status	0.408	0.043	9.429	<0.001
Neglect (parent report)	0.673	0.047	14.399	<0.001
Neglect (child report)	0.201	0.057	3.554	<0.001
Family income	0.975	0.065	14.936	<0.001

Model fit baseline: CFI = 0.937, TLI= 0.922, RMSEA= 0.032
Note: all variables that were informed by the children were correlated in the model. DAWBA (Development and Well-being Assessment); ABEP (Brazilian Economic Classification).

Table 3 – Influences of threat and deprivation on psychopathology, executive functions and attention bias

	Baseline			Follow-up		
	β	***p value***	**CI 95%**	**β**	***p value***	**CI 95%**
Psychopathology						
Threat	**0.522**	**<0.001**	**0.475, 0.569**	**0.177**	**<0.001**	**0.121, 0.233**
Deprivation	0.012	0.569	-0.030, 0.054	**0.072**	**0.003**	**0.025, 0.119**
Age	0.004	0.664	-0.013, 0.020	**-0.023**	**0.013**	**-0.041, -0.005**
Sex	-0.021	0.500	-0.083, 0.041	**0.174**	**9.50e-07**	**0.105, 0.244**
Executive Function						
Threat	-0.019	0.348	-0.059, 0.021	-0.034	0.154	-0.080, 0.013
Deprivation	**-0.115**	**<0,001**	**-0.151, -0.079**	**-0.045**	**0.038**	**-0.088, -0.003**
Age	**0.188**	**<0.001**	**0.174, 0.202**	0.010	0.286	-0.008, 0.028
Sex	-0.013	0.639	-0.066, 0.040	-0.043	0.174	-0.105, 0.019
Attention bias						
Threat	**0.079**	**0.029**	**0.008, 0.151**	-0.048	0.132	-0.111, 0.014
Deprivation	-0.061	0.062	-0.025, 0.003	0.021	0.468	-0.036, 0.078
Age	-0.026	0.036	-0.051, -0.002	-0.015	0.188	-0.036, 0.007
Sex	0.075	0.117	-0.019, 0.169	-0.026	0.543	-0.109, 0.057

Note: main associations of threat and deprivation on the outcomes were adjusted for age at the outcome's assessment and sex for the baseline and follow-up models. For the longitudinal models, all effects were also adjusted and controlled for the outcome variable values at baseline.

Supplemental Material

1. Adversity

Threat and deprivation variables were selected according to documented theoretical models in order to encompass both dimensions of childhood adversity. Selected variables, their label and ranges are described below (Supplemental Table S1), as well as descriptive data for each selected variable (Supplemental Table S2).

Confirmatory factor analysis, using the full maximum likelihood to deal with missing data, were conducted and the threat and deprivation model was available for 2511 participants, and at follow up 2010 participants (Supplemental Figure S1). Both latent factors were significantly correlated ($r= 0.404$, $p <0.001$).

Supplemental Table S1 – Threat and Deprivation variable description

Variable	Label	Response options
Threat		
Bullying exposure (parent and child report)	Has the child ever been bullied in his life? Have you ever been bullied in your life?	No Yes
DAWBA: Physical abuse	Has the child ever suffered physical violence (maltreatment) that he/she remembers?	No Yes
Physical abuse (parent and child report)	Has your child been seriously picked up by an adult (including yourself), to the point of leaving marks in his body? Have you ever been seriously picked up by an adult, to the point of leaving marks in your body?	Never Yes, once or twice Yes, from time to time Yes, often happen
Emotional abuse (parent and child report)	Has your child ever been cursed by some adult, with words like 'ass', 'idiot', 'stupid', or being yelled that he/she was no good? Have you ever been cursed by some adult, with words like 'ass', 'idiot', 'stupid', or being yelled that you were no good?	Never Yes, once or twice Yes, from time to time Yes, often happen
DAWBA: Sexual abuse	Has the child ever been exposed to sexual abuse?	No Yes
Sexual abuse	Has anybody ever done sexual things with your child, or have threatened your child if he/she didn't do sexual things?	Never Yes, once or twice Yes, from time to time Yes, often happen
DAWBA: Attack or threat	Has the child ever been attacked or threatened?	No Yes
DAWBA: Domestic violence witnessing	Has the child ever witnessed serious domestic violence?	No Yes
DAWBA: Attack witnessing	Has the child ever seen a family member, or friend being seriously attacked, or threatened?	No Yes

Table continues on next page

Supplemental Table S1 – Threat and Deprivation variable description

Variable	Label	Response options
Deprivation		
Mother's educational level	Mother's educational level	Higher education (university and postgraduation) Up to High School education Up to Middle School education Without study
ABEP 2009: Stratified Score	Socio economic class	D/E (poorest) C A/B (wealthiest)
Father status	What is the current contact status of the child's father?	In contact No-contact Deceased Unknown
Neglect	Has it ever happened to your child of not having anything to eat and/or having to wear dirty or torn clothes? Has it ever happened to you of not having anything to eat and/or having to wear dirty or torn clothes?	Never Yes, once or twice Yes, from time to time Yes, often happens
Family income	What is the family total income?	Divided into quintiles

Note*:* DAWBA (Development and Well-being Assessment; ABEP (Brazilian Economic Classification).

Supplemental Table S2 – Threat and Deprivation variable frequency

	Parent Report				Child report			
	N	**%**	**Valid N**	**Missing**	**N**	**%**	**Valid N**	**Missing**
Bullying exposure: yes	950	38.7	2455	56	709	32.1	2207	304
Physical abuse (DAWBA): yes	86	3.4	2511	-				
Physical abuse								
Never	2139	85.3	2507	4	1886	85	2218	293
Yes, once or twice	293	11.7			196	0.9		
Yes, from time to time	66	2.6			105	0.5		
Yes, it often happens	9	0.4			31	0.1		
Emotional abuse								
Never	1397	55.7	2510	1	1702	76.7	2219	292
Yes, once or twice	443	17.6			254	11.9		
Yes, from time to time	524	20.9			182	0.8		
Yes, it often happens	146	5.8			71	0.3		
Sexual abuse total: yes	63	0.3	2500	11				
Attack or threat (DAWBA): yes	97	3.9	2511	-				
Domestic violence witnessing (DAWBA): yes	177	7	2511	-				
Attack witnessing (DAWBA): yes	101	4	2511	-				
Mother's educational level								
Higher education	85	0.3	2483	28				
Up to High School education	934	37.6						
Up to Middle School education	857	34.5						
Up to Elementary or no education	607	24.4						

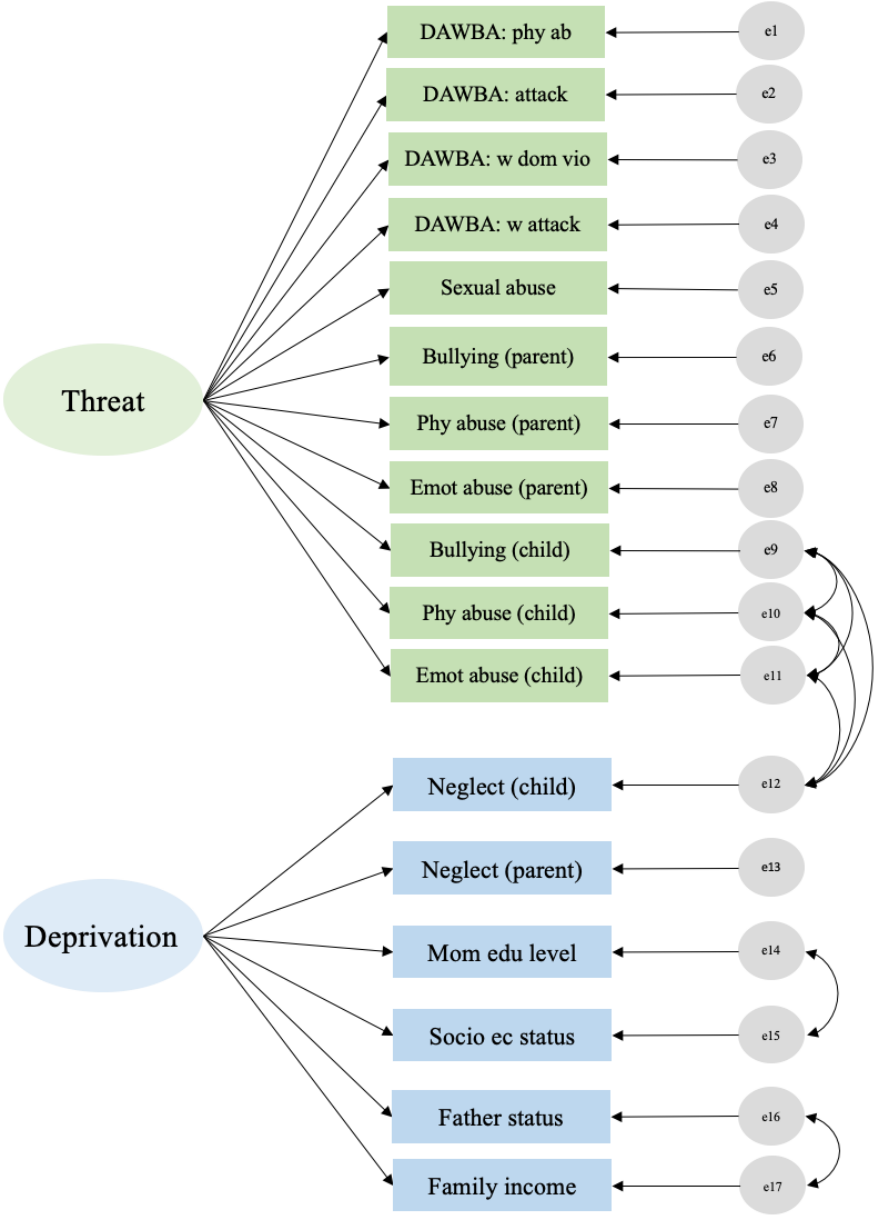
Table continues on next page

Supplemental Table S2 – Threat and Deprivation variable frequency

	Parent Report				Child report			
	N	%	Valid N	Missing	N	%	Valid N	Missing
ABEP 2009: Stratified Score								
A/B	998	39.7	2511	-				
C	1435	57.1						
D/E	78	3.1						
Father status								
In-contact	1836	73.1	2511	-				
No-contact	427	17						
Deceased	130	5.2						
Unknown	118	4.7						
Neglect								
Never	2261	90	2511	-	2082	93.9	2217	294
Yes, once or twice	176	7			90	0.4		
Yes, from time to time	61	2.4			38	0.2		
Yes, it often happens	13	0.5			7	0.03		

Note: DAWBA (Development and Well-being Assessment; ABEP (Brazilian Economic Classification).

Supplemental Figure S1 – Baseline and follow-up Threat and Deprivation model depiction



2. Psychopathology: General Psychopathology Model

Confirmatory factor analysis, using the diagonally weighted least squares (DWLS) estimator, were conducted using CBCL baseline and follow-up data using a bifactor model in which all items are loaded in a general factor (the "p" factor) and residuals variance is captured by internalizing and externalizing domains as outlined by the CBCL scoring system. The psychopathology model at baseline was available for 2511 participants and showed adequate fit indexes (CFI= 0.984, TLI= 0.983, RMSEA= 0.020, SRMR = 0.044). The psychopathology model at follow up was available for 2010 participants and also showed adequate fit indexes (CFI= 0.973, TLI= 0.972, RMSEA= 0.025, SRMR = 0.051). Additionally, both models presented good reliability with an explained common variance of the general psychopathology factor of 71% at baseline and 72% at follow-up, as well as an omega value of $\omega = 0.93$ for both time points (values indicating good reliability are those above 0.70; Lucke, 2005). Factor loadings for baseline and follow-up data are found on Supplemental Table S3-S4.

Supplemental Table S3 - Factor loadings of the General Psychopathology Model

	Baseline				Follow-up			
	Estimate	**S.E.**	***p-value***	**β**	**Estimate**	**S.E.**	***p-value***	**β**
General Psychopathology								
CBCL14 (Cries a lot)	0.293	0.006	<0.001	0.468	0.242	0.006	<0.001	0.453
CBCL29 (Fears certain animals situations, or places other than school)	0.174	0.006	<0.001	0.259	0.133	0.006	<0.001	0.223
CBCL30 (Fears going to school)	0.067	0.003	<0.001	0.212	0.051	0.003	<0.001	0.187
CBCL31 (Fears he/she might think or do something bad)	0.101	0.004	<0.001	0.201	0.054	0.005	<0.001	0.110
CBCL32 (Feels he/she has to be perfect	0.118	0.005	<0.001	0.192	0.062	0.006	<0.001	0.097
CBCL33 (Feels or complains that no one loves him/her)	0.482	0.007	<0.001	0.696	0.425	0.007	<0.001	0.641
CBCL35 (Feels worthless or inferior)	0.298	0.006	<0.001	0.579	0.264	0.006	<0.001	0.515
CBCL45 (Nervous, high strung, or tense)	0.491	0.007	<0.001	0.688	0.471	0.007	<0.001	0.660
CBCL50 (Too fearful or anxious)	0.341	0.007	<0.001	0.493	0.294	0.007	<0.001	0.434
CBCL52 (Feels too guilty)	0.148	0.004	<0.001	0.387	0.105	0.004	<0.001	0.296
CBCL71 (Self-conscious or easily embarrassed)	0.249	0.006	<0.001	0.398	0.192	0.007	<0.001	0.291
CBCL91 (Talks about killing self)	0.118	0.004	<0.001	0.356	0.099	0.004	<0.001	0.367
CBCL112 (Worries)	0.189	0.005	<0.001	0.325	0.193	0.006	<0.001	0.324
CBCL5 (There is very little he/she enjoys)	0.343	0.006	<0.001	0.559	0.344	0.007	<0.001	0.526
CBCL42 (Would rather be alone than with others)	0.184	0.005	<0.001	0.347	0.233	0.006	<0.001	0.371
CBCL65 (Refuses to talk)	0.220	0.005	<0.001	0.440	0.231	0.006	<0.001	0.425
CBCL69 (Secretive, keeps things to self)	0.251	0.006	<0.001	0.381	0.252	0.007	<0.001	0.339
CBCL75 (Too shy or timid)	0.154	0.006	<0.001	0.245	0.067	0.006	<0.001	0.100
CBCL102 (Underactive, slow moving, or lacks energy)	0.117	0.004	<0.001	0.306	0.147	0.005	<0.001	0.321
CBCL103 (Unhappy, sad, or depressed)	0.207	0.005	<0.001	0.435	0.224	0.006	<0.001	0.483
CBCL111 (Withdrawn, doesn't get involved with others)	0.134	0.004	<0.001	0.335	0.139	0.005	<0.001	0.321
CBCL47 (Nightmares)	0.249	0.006	<0.001	0.439	0.152	0.005	<0.001	0.333
CBCL49 (Constipated, doesn't move bowels)	0.123	0.005	<0.001	0.234	0.081	0.005	<0.001	0.161

Table continues on next page

Supplemental Table S3 - Factor loadings of the General Psychopathology Model

	Baseline				Follow-up			
	Estimate	**S.E.**	***p-value***	**β**	**Estimate**	**S.E.**	***p-value***	**β**
CBCL51 (Feels dizzy or lightheaded)	0.136	0.004	<0.001	0.337	0.143	0.005	<0.001	0.337
CBCL54 (overtired without any good reason)	0.341	0.006	<0.001	0.563	0.328	0.007	<0.001	0.494
CBCL56a (Physical problems without medical cause: aches or pains)	0.160	0.005	<0.001	0.344	0.143	0.005	<0.001	0.304
CBCL56b (Physical problems without medical cause: headaches)	0.280	0.006	<0.001	0.399	0.245	0.006	<0.001	0.356
CBCL56c (Physical problems without medical cause: nausea, feels sick)	0.157	0.005	<0.001	0.320	0.150	0.005	<0.001	0.311
CBCL56d (Physical problems without medical cause: problems with eyes)	0.125	0.004	<0.001	0.273	0.058	0.003	<0.001	0.174
CBCL56e (Physical problems without medical cause: rashes or other skin problems)	0.088	0.004	<0.001	0.191	0.047	0.004	<0.001	0.112
CBCL56f (Physical problems without medical cause: stomachaches)	0.212	0.005	<0.001	0.371	0.172	0.006	<0.001	0.314
CBCL56g (Physical problems without medical cause: vomiting)	0.091	0.004	<0.001	0.252	0.058	0.003	<0.001	0.196
CBCL2 (Drinks alcohol without parents' approval)	0.017	0.002	<0.001	0.098	0.063	0.004	<0.001	0.199
CBCL26 (Doesn't seem to feel guilty after misbehaving)	0.273	0.006	<0.001	0.467	0.249	0.006	<0.001	0.448
CBCL28 (Breaks rules at home, school, or elsewhere)	0.312	0.006	<0.001	0.517	0.367	0.007	<0.001	0.588
CBCL39 (Hangs around with others who get in trouble)	0.061	0.003	<0.001	0.206	0.087	0.004	<0.001	0.239
CBCL43 (Lying or cheating)	0.213	0.006	<0.001	0.366	0.245	0.007	<0.001	0.451
CBCL63 (Prefers being with older kids)	0.249	0.006	<0.001	0.378	0.262	0.007	<0.001	0.374
CBCL67 (Runs away from home)	0.040	0.002	<0.001	0.171	0.052	0.003	<0.001	0.212
CBCL72 (Sets fires)	0.064	0.003	<0.001	0.246	0.022	0.002	<0.001	0.130
CBCL73 (Sexual problems)	0.028	0.002	<0.001	0.155	0.003	0.001	<0.001	0.032
CBCL81 (Steals at home)	0.036	0.003	<0.001	0.137	0.021	0.002	<0.001	0.117
CBCL82 (Steals outside the home)	0.033	0.002	<0.001	0.141	0.006	0.002	<0.001	0.042
CBCL90 (Swearing or obscene language)	0.265	0.006	<0.001	0.469	0.325	0.007	<0.001	0.511

Table continues on next page

Supplemental Table S3 - Factor loadings of the General Psychopathology Model

	Baseline				Follow-up			
	Estimate	**S.E.**	***p-value***	**β**	**Estimate**	**S.E.**	***p-value***	**β**
CBCL96 (Thinks about sex too much)	0.056	0.003	<0.001	0.213	0.043	0.002	<0.001	0.181
CBCL99 (Smokes, chews, or sniffs tobacco)	0.008	0.001	<0.001	0.065	0.015	0.002	<0.001	0.079
CBCL101 (Truancy, skips school)	0.074	0.003	<0.001	0.258	0.114	0.005	<0.001	0.283
CBCL105 (Uses drugs for nonmedical purposes)	0.009	0.001	<0.001	0.073	0.011	0.002	<0.001	0.074
CBCL106 (Vandalism)	0.027	0.002	<0.001	0.160	0.007	0.001	<0.001	0.062
CBCL3 (Argues a lot)	0.456	0.007	<0.001	0.585	0.404	0.007	<0.001	0.534
CBCL16 (Cruelty, bullying, or meanness to others)	0.069	0.003	<0.001	0.236	0.049	0.003	<0.001	0.233
CBCL19 (Demands a lot of attention)	0.481	0.007	<0.001	0.661	0.384	0.007	<0.001	0.579
CBCL20 (Destroys his/her own things)	0.220	0.006	<0.001	0.402	0.149	0.005	<0.001	0.355
CBCL21 (Destroys things belonging to his/her family or others)	0.181	0.005	<0.001	0.387	0.117	0.005	<0.001	0.317
CBCL22 (Disobedient at home)	0.346	0.006	<0.001	0.522	0.395	0.007	<0.001	0.622
CBCL23 (Disobedient at school)	0.214	0.006	<0.001	0.372	0.230	0.007	<0.001	0.408
CBCL37 (Gets in many fights)	0.182	0.005	<0.001	0.383	0.140	0.005	<0.001	0.350
CBCL57 (Physically attacks people)	0.083	0.004	<0.001	0.258	0.078	0.004	<0.001	0.288
CBCL68 (Screams a lot)	0.338	0.006	<0.001	0.533	0.347	0.007	<0.001	0.565
CBCL86 (Stubborn, sullen, or irritable)	0.520	0.007	<0.001	0.707	0.523	0.007	<0.001	0.729
CBCL87 (Sudden changes in mood or feelings)	0.513	0.007	<0.001	0.770	0.497	0.008	<0.001	0.717
CBCL88 (Sulks a lot)	0.574	0.007	<0.001	0.773	0.552	0.008	<0.001	0.749
CBCL89 (Suspicious)	0.431	0.007	<0.001	0.677	0.397	0.007	<0.001	0.605
CBCL94 (Teases a lot)	0.274	0.006	<0.001	0.447	0.230	0.007	<0.001	0.369
CBCL95 (Temper tantrums or hot temper)	0.479	0.007	<0.001	0.681	0.528	0.008	<0.001	0.743
CBCL97 (Threatens people)	0.063	0.003	<0.001	0.250	0.049	0.003	<0.001	0.229
CBCL104 (Unusually loud)	0.301	0.006	<0.001	0.449				

Supplemental Table S4 - Factor loadings of the residual Internalizing and Externalizing factors of the General Psychopathology Model

	Baseline				Follow-up			
	Estimate	**S.E.**	***p-value***	**β**	**Estimate**	**S.E.**	***p-value***	**β**
Internalizing Psychopathology								
CBCL14 (Cries a lot)	0.113	0.013	<0.001	0.179	0.119	0.012	<0.001	0.224
CBCL29 (Fears certain animals situations, or places other than school)	0.160	0.012	<0.001	0.239	0.171	0.014	<0.001	0.288
CBCL30 (Fears going to school)	0.096	0.007	<0.001	0.302	0.059	0.006	<0.001	0.220
CBCL31 (Fears he/she might think or do something bad)	0.113	0.009	<0.001	0.224	0.122	0.012	<0.001	0.247
CBCL32 (Feels he/she has to be perfect	0.162	0.011	<0.001	0.263	0.183	0.015	<0.001	0.287
CBCL33 (Feels or complains that no one loves him/her)	0.077	0.015	<0.001	0.111	0.167	0.013	<0.001	0.251
CBCL35 (Feels worthless or inferior)	0.122	0.012	<0.001	0.236	0.169	0.011	<0.001	0.329
CBCL45 (Nervous, highstrung, or tense)	0.127	0.015	<0.001	0.178	0.172	0.014	<0.001	0.242
CBCL50 (Too fearful or anxious)	0.255	0.014	<0.001	0.369	0.284	0.014	<0.001	0.419
CBCL52 (Feels too guilty)	0.098	0.009	<0.001	0.256	0.118	0.008	<0.001	0.332
CBCL71 (Self-conscious or easily embarrassed)	0.298	0.014	<0.001	0.476	0.385	0.014	<0.001	0.585
CBCL91 (Talks about killing self)	0.002	0.008	0.784	0.006	0.026	0.006	<0.001	0.098
CBCL112 (Worries)	0.218	0.011	<0.001	0.374	0.279	0.013	<0.001	0.468
CBCL5 (There is very little he/she enjoys)	0.106	0.013	<0.001	0.172	0.196	0.014	<0.001	0.300
CBCL42 (Would rather be alone than with others)	0.200	0.012	<0.001	0.377	0.303	0.014	<0.001	0.483
CBCL65 (Refuses to talk)	0.132	0.011	<0.001	0.264	0.201	0.012	<0.001	0.370
CBCL69 (Secretive, keeps things to self)	0.271	0.014	<0.001	0.411	0.354	0.016	<0.001	0.476
CBCL75 (Too shy or timid)	0.316	0.013	<0.001	0.503	0.394	0.015	<0.001	0.584
CBCL102 (Underactive, slow moving, or lacks energy)	0.121	0.009	<0.001	0.315	0.202	0.010	<0.001	0.439
CBCL103 (Unhappy, sad, or depressed)	0.175	0.011	<0.001	0.367	0.219	0.010	<0.001	0.472
CBCL111 (Withdrawn, doesn't get involved with others)	0.153	0.010	<0.001	0.384	0.234	0.009	<0.001	0.542
CBCL47 (Nightmares)	0.104	0.012	<0.001	0.184	0.113	0.011	<0.001	0.246
CBCL49 (Constipated, doesn't move bowels)	0.101	0.010	<0.001	0.193	0.140	0.012	<0.001	0.279

Table continues on next page

Supplemental Table S4 - Factor loadings of the residual Internalizing and Externalizing factors of the General Psychopathology Model

	Baseline				Follow-up			
	Estimate	**S.E.**	***p-value***	**β**	**Estimate**	**S.E.**	***p-value***	**β**
CBCL51 (Feels dizzy or lightheaded)	0.125	0.009	<0.001	0.307	0.139	0.010	<0.001	0.326
CBCL54 (overtired without any good reason)	0.174	0.013	<0.001	0.287	0.268	0.014	<0.001	0.405
CBCL56a (Physical problems without medical cause: aches or pains)	0.146	0.010	<0.001	0.314	0.144	0.011	<0.001	0.305
CBCL56b (Physical problems without medical cause: headaches)	0.215	0.013	<0.001	0.307	0.234	0.016	<0.001	0.340
CBCL56c (Physical problems without medical cause: nausea, feels sick)	0.163	0.011	<0.001	0.331	0.32	0.011	<0.001	0.274
CBCL56d (Physical problems without medical cause: problems with eyes)	0.052	0.011	<0.001	0.114	0.33	0.008	<0.001	0.100
CBCL56e (Physical problems without medical cause: rashes or other skin problems)	0.052	0.009	<0.001	0.112	0.062	0.010	<0.001	0.148
CBCL56f (Physical problems without medical cause: stomachaches)	0.052	0.009	<0.001	0.268	0.187	0.013	<0.001	0.341
CBCL56g (Physical problems without medical cause: vomiting)	0.153	0.012	<0.001	0.273	0.065	0.007	<0.001	0.218
Externalizing Psychopathology								
CBCL2 (Drinks alcohol without parents' approval)	0.022	0.004	<0.001	0.126	0.145	0.008	<0.001	0.460
CBCL26 (Doesn't seem to feel guilty after misbehaving)	0.185	0.012	<0.001	0.316	0.085	0.013	<0.001	0.154
CBCL28 (Breaks rules at home, school, or elsewhere)	0.332	0.013	<0.001	0.550	0.139	0.014	<0.001	0.222
CBCL39 (Hangs around with others who get in trouble)	0.125	0.007	<0.001	0.423	0.171	0.009	<0.001	0.470
CBCL43 (Lying or cheating)	0.285	0.012	<0.001	0.489	0.192	0.012	<0.001	0.354
CBCL63 (Prefers being with older kids)	0.069	0.011	<0.001	0.105	0.036	0.018	0.040	0.052
CBCL67 (Runs away from home)	0.071	0.006	<0.001	0.306	0.109	0.006	<0.001	0.447
CBCL72 (Sets fires)	0.056	0.006	<0.001	0.214	0.009	0.004	0.046	0.051
CBCL73 (Sexual problems)	0.023	0.004	<0.001	0.128	0.010	0.003	<0.001	0.092
CBCL81 (Steals at home)	0.091	0.007	<0.001	0.344	0.070	0.004	<0.001	0.393
CBCL82 (Steals outside the home)	0.056	0.006	<0.001	0.240	0.047	0.004	<0.001	0.310
CBCL90 (Swearing or obscene language)	0.221	0.012	<0.001	0.392	0.071	0.015	<0.001	0.112

Table continues on next page

Supplemental Table S4 - Factor loadings of the residual Internalizing and Externalizing factors of the General Psychopathology Model

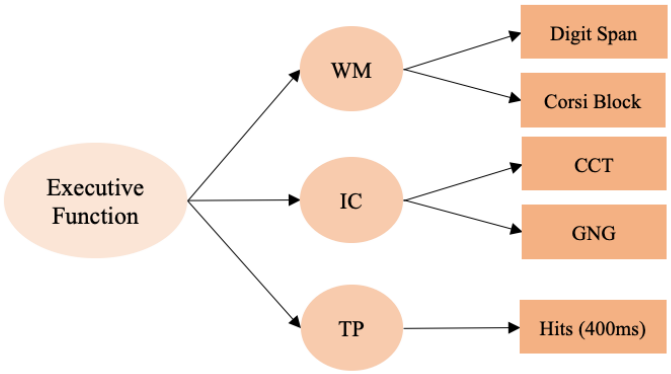
	Baseline				Follow-up			
	Estimate	**S.E.**	***p-value***	**β**	**Estimate**	**S.E.**	***p-value***	**β**
CBCL96 (Thinks about sex too much)	0.034	0.006	<0.001	0.131	0.029	0.006	<0.001	0.121
CBCL99 (Smokes, chews, or sniffs tobacco)	0.003	0.002	0.237	0.022	0.081	0.005	<0.001	0.427
CBCL101 (Truancy, skips school)	0.055	0.007	<0.001	0.192	0.129	0.010	<0.001	0.320
CBCL105 (Uses drugs for nonmedical purposes)	0.015	0.003	<0.001	0.118	0.074	0.004	<0.001	0.489
CBCL106 (Vandalism)	0.049	0.005	<0.001	0.292	0.036	0.003	<0.001	0.332
CBCL3 (Argues a lot)	0.162	0.013	<0.001	0.208	-0.002	0.018	0.912	-0.003
CBCL16 (Cruelty, bullying, or meanness to others)	0.111	0.008	<0.001	0.378	0.060	0.005	<0.001	0.282
CBCL19 (Demands a lot of attention)	0.016	0.014	0.246	0.022	-0.038	0.016	0.016	-0.058
CBCL20 (Destroys his/her own things)	0.217	0.012	<0.001	0.396	0.094	0.010	<0.001	0.225
CBCL21 (Destroys things belonging to his/her family or others)	0.210	0.011	<0.001	0.450	0.107	0.009	<0.001	0.290
CBCL22 (Disobedient at home)	0.324	0.013	<0.001	0.490	0.098	0.014	<0.001	0.154
CBCL23 (Disobedient at school)	0.326	0.012	<0.001	0.568	0.168	0.013	<0.001	0.299
CBCL37 (Gets in many fights)	0.232	0.011	<0.001	0.487	0.113	0.009	<0.001	0.282
CBCL57 (Physically attacks people)	0.148	0.008	<0.001	0.461	0.072	0.007	<0.001	0.268
CBCL68 (Screams a lot)	0.208	0.013	<0.001	0.327	0.011	0.014	0.440	0.018
CBCL86 (Stubborn, sullen, or irritable)	0.151	0.013	<0.001	0.205	-0.073	0.016	<0.001	-0.102
CBCL87 (Sudden changes in mood or feelings)	0.033	0.014	0.018	0.049	-0.070	0.016	<0.001	-0.101
CBCL88 (Sulks a lot)	0.065	0.014	<0.001	0.087	-0.126	0.017	<0.001	-0.170
CBCL89 (Suspicious)	-0.012	0.013	0.351	-0.019	-0.094	0.016	<0.001	-0.143
CBCL94 (Teases a lot)	0.221	0.012	<0.001	0.360	0.056	0.015	<0.001	0.090
CBCL95 (Temper tantrums or hot temper)	0.147	0.014	<0.001	0.208	-0.051	0.016	0.001	-0.072
CBCL97 (Threatens people)	0.081	0.006	<0.001	0.322	0.062	0.005	<0.001	0.286
CBCL104 (Unusually loud)	0.225	0.012	<0.001	0.336	0.012	0.015	0.412	0.020

3. Executive Function

Five executive function tasks were used as measures of working memory, inhibitory control and temporal processing. Missing data differs from one task to another over both time points due to assessment being performed over four sessions at baseline.

Executive function was derived from a second order model informed by three latent variables representing the dimensions of working memory, inhibitory control, and temporal processing at baseline and follow up. Working memory and inhibitory control dimensions were informed by two cognitive tasks each, while the temporal processing dimension was informed by one task (Supplemental Figure S2). The benefit of using this model, instead of a single factor model where all tasks load on a first-order executive function latent variable, is due to the fact that such model resulted in an unacceptable fit (CFI = 0.812, TLI = 0.624, RMSEA = 0.067).

Supplemental Figure S2 –Executive Function Model



Confirmatory factor analysis, using the full maximum likelihood to deal with missing data, were conducted using baseline and follow-up data. The executive function model at baseline was available for 2398 participants and showed adequate fit indexes (CFI= 0.999, TLI= 0.998, RMSEA= 0.011, SRMR = 0.007), and the follow up model was available for 1880 participants, and also showed good fit indexes (CFI= 1.000, TLI= 1.005, RMSEA= 0.000, SRMR = 0.005.). Factor loadings are shown on Supplemental Table S5.

Supplemental Table S5 – Standardized factor loadings of the baseline Executive Function Model

	Baseline			Follow-up		
	λ	**S.E.**	***p*-value**	**λ**	**S.E.**	***p*-value**
Working Memory (WM)						
Digit span (back)	0.695	0.029	<0.001	0.705	0.036	<0.001
Corsi blocks (back)	0.718	0.032	<0.001	0.787	0.042	<0.001
Inhibitory Control (IC)						
CCT (% Inhibitions, inverse)	0.920	0.052	<0.001	0.594	0.048	<0.001
GNG (% Comission)	-0.458	0.022	<0.001	-0.514	0.034	<0.001
Temporal Processing (TP)						
Time anticipation (400ms)	1.000	0.020	<0.001	1.000	0.026	<0.001
Executive Function						
WM	0.765	0.130	<0.001	0.723	0.120	<0.001
IC	0.567	0.068	<0.001	0.704	0.130	<0.001
TP	0.560	0.048	<0.001	0.636	0.075	<0.001

Note: CCT (Conflict Control Task); GNG (Go/no-go Task).

We conducted a series of Confirmatory Factor Analysis testing unidimensional models of each one of the tasks included in the study, as well as calculated the Cronbach's Alpha and Omega for each of the tasks. CFI and TLI values higher than 0.9, RMSEA lower than 0.06 and SRMR lower than 0.08 indicate adequate model fit (Hu & Bentler, 1999). For both, alpha and omega coefficients, values indicating good reliability are those above 0.70 (Lucke, 2005) Reliability information is shown on Supplemental Table S6.

Supplemental Table S6 – Executive Functions tasks reliability

	CFI	TLI	RMSEA	SRMR	α	ω
Working Memory (WM)						
Digit span (back)	0.989	0.982	0.040	0.115	0.934	0.725
Corsi blocks (back)	0.980	0.967	0.078	0.154	0.903	0.807
Inhibitory Control (IC)						
CCT (% Inhibitions, inverse)	0.992	0.991	0.011	0.019	0.812	0.813
GNG (% Comission)	0.994	0.992	0.018	0.034	0.897	0.803
Temporal Processing (TP)						
Time anticipation (400ms)	0.978	0.973	0.024	0.036	0.823	0.719

Note*:* CCT (Conflict Control Task); GNG (Go/no-go Task).

4 Interactions models

All main effect models were tested adjusting for age and sex. Therefore, in order to check for the assumptions of linear models, interaction effects between the adversity variables of threat and deprivation, and age and sex were tested through saturated models of three-way and two-way interactions. Results indicate that no three-way interactions were found among threat, age and sex, as well as deprivation, age, and sex (Supplemental Table S7 and S8). However, two-way interaction models suggested that the effect of threat on psychopathology at follow-up (β= -0.030, p=0.021, 95% CI [-0.055, -0.004]) (Supplemental Table S9) and the effect of deprivation on attention orienting towards angry faces at baseline (β= 0.041, p=0.007, 95% CI [0.011, 0.072]) (Supplemental Table S10) varies with age.

Supplemental Table S7 – Three-way interactions among threat, age and sex

	Baseline			Follow-up		
	β	***p value***	**CI 95%**	**β**	***p value***	**CI 95%**
Psychopathology						
threat	1.8745e-01	0.483	-0.336, 0.711	0.761	0.162	-0.307, 1.828
age	-1.481e-02	0.567	-0.066, 0.036	**-0.083**	**0.004**	**-0.139, -0.027**
sex	-1.467e-01	0.397	-0.486, 0.193	-0.390	0.123	-0.885, 0.106
threat*age	4.650e-03	0.898	-0.067, 0.076	-0.045	0.261	-0.122, 0.033
threat*sex	-5.795e-03	0.981	-0.495, 0.483	-0.103	0.775	-0.810, 0.604
threat*age*sex	5.422e-05	0.998	-0.046, 0.047	0.103	0.693	-0.041, 0.062
Executive Functions						
threat	-0.405	0.212	-1.043, 0.232	0.377	0.437	-1.043, 0.232
age	**0.164**	**<0.001**	**0.120, 0.207**	**0.074**	**0.004**	**0.120, 0.207**
sex	-0.188	0.205	-0.479, 0.103	**0.543**	**0.016**	**-0.479, 0.103**
threat*age	0.034	0.271	-0.027, 0.095	-0.029	0.421	-0.027, 0.095
threat*sex	0.224	0.295	-0.196, 0.644	-0.237	0.465	-0.196, 0.644
threat*age*sex	-0.023	0.259	-0.063, 0.017	0.015	0.517	-0.063, 0.017
Attention Bias						
threat	-0.720	0.204	-1.832, 0.391	0.358	0.578	-0.906. 1.622
age	0.010	0.801	-0.067, 0.086	-0.021	0.532	-0.089. 0.046
sex	0.326	0.209	-0.183, 0.835	-0.090	0.764	-0.679, 0.499
threat*age	0.057	0.297	-0.050. 0.163	-0.025	0.591	-0.118, 0.067
threat*sex	0.631	0.092	-0.103, 1.365	-0.289	0.500	-1.131, 0.552
threat*age*sex	-0.048	0.175	-0.118, 0.021	0.018	0.553	-0.043, 0.079

Supplemental Table S8 – Three-way interactions among deprivation, age and sex

	Baseline			Follow-up		
	β	*p value*	CI 95%	β	*p value*	CI 95%
Psychopathology						
deprivation	0.145	0.689	-0.568, 0.859	0.309	0.529	-0.651, 1.269
age	-0.016	0.575	-0.071, 0.039	-0.091	0.002	-0.147, -0.035
sex	-0.299	0.111	-0.667, 0.069	-0.502	0.048	-0.999, -0.005
deprivation*age	0.007	0.834	-0.061, 0.076	-0.009	0.810	-0.079, 0.062
deprivation*sex	0.024	0.176	-0.365, 0.554	-0.052	0.869	0.672, 0.568
deprivation*age*sex	-0.011	0.634	-0.055, 0.033	0.001	0.983	-0.045, 0.046
Executive Functions						
deprivation	0.172	0.544	-0.384, 0.728	0.027	0.950	-0.823, 0.876
age	**0.170**	**<0.001**	**0.127, 0.213**	**0.075**	**0.003**	**0.025, 0.`126**
sex	-0.132	0.367	-0.419, 0.155	**0.576**	**0.010**	**0.137, 1.016**
deprivation*age	-0.027	0.314	-0.081, 0.026	-0.005	0.866	-0.068, 0.057
deprivation*sex	-0.215	0.240	-0.574, 0.144	-0.174	0.537	-0.726, 0.378
deprivation*age*sex	0.020	0.251	-0.014, 0.055	0.012	0.553	-0.028, 0.053
Attention Bias						
deprivation	-0.810	0.105	-1.790, 0.170	-4.274e-02	0.941	-1.180, 1.095
age	0.011	0.780	-0.065, 0.086	-2.043e-02	0.552	-0.088, 0.047
sex	0.315	0.222	-0.191, 0.821	-6.503e-02	0.828	-0.653, 0.523
deprivation*age	0.070	0.143	-0.024, 0.165	4.510e-03	0.916	-0.079, 0.088
deprivation*sex	0.240	0.457	-0.393, 0.873	-9.730e-03	0.979	-0.749, 0.729
deprivation*age*sex	-0.020	0.525	-0.080, 0.041	-1.825e-05	0.999	-0.054, 0.054

Supplemental Table S9 – Two-way interactions among threat, age, and sex

		Baseline			Follow-up		
		β	***p value***	**CI 95%**	**β**	***p value***	**CI 95%**
Psychopathology							
	threat	**0.486**	**<0.001**	**-0.335, 0.710**	**0.559**	**0.003**	**1.193, 0.926**
	age	-0.015	0.566	-0.065, 0.036	**-0.084**	**0.004**	**-0.140, -0.028**
	sex	-0.147	0.396	-0.486, 0.192	-0.396	0.116	-0.891, 0.098
	threat*age	0.005	0.688	-0.018, 0.028	**-0.030**	**0.021**	**-0.055, -0.004**
	threat*sex	-0.005	0.906	-0.092, 0.082	0.038	0.446	-0.059, 0.135
Executive Functions							
	threat	-0.063	0.588	-0.290, 0.164	0.081	0.624	-0.244, 0.407
	age	0.166	<0.001	0.122, 0.209	**0.072**	**0.005**	**0.022, 0.123**
	sex	-0.179	0.228	-0.469, 0.112	**0.534**	**0.018**	**0.094, 0.975**
	threat*age	0.001	0.918	-0.019, 0.021	-0.007	0.558	-0.030, 0.016
	threat*sex	-0.014	0.722	-0.088, 0.061	-0.029	0.517	-0.115, 0.058
Attention Bias							
	Threat	-0.002	0.993	-0;397, 0.393	-0.001	0.997	-0.432, 0.430
	age	0.014	0.709	-0.062, 0.091	-0.023	0.498	-0.090, 0.044
	sex	0.348	0.179	-0.160, 0.856	-0.102	0.734	-0.689, 0.4483
	threat*age	-0.013	0.463	-0.048, 0.022	0.002	0.943	-0.029, 0.031
	threat*sex	0.131	0.051	-0.001, 0.263	-0.037	0.532	-0.154, 0.080

Supplemental Table S10 – Two-way interactions among deprivation, age, and sex

		Baseline			Follow-up		
		β	***p value***	**CI 95%**	**β**	***p value***	**CI 95%**
Psychopathology							
	deprivation	**0.307**	**0.019**	**0.050, 0.564**	0.299	0.080	-0.034, 0.631
	age	-0.016	0.577	-0.071, 0.039	**-0.091**	**0.002**	**-0.147, -0.035**
	sex	-0.298	0.113	-0.666, 0.071	**-0.502**	**0.048**	**-0.999, -0.005**
	deprivation*age	-0.008	0.452	-0.031, 0.014	-0.008	0.493	-0.031, 0.015
	deprivation*sex	-0.015	0.730	-0.099, 0.069	-0.05	0.312	-0.133, 0.043
Executive Functions							
	deprivation	-0.132	0.198	-0.332, 0.069	-0.214	0.154	-0.508, 0.80
	age	0.170	<0.001	0.127, 0.213	**0.076**	**0.003**	**0.026, 0.127**
	sex	-0.135	0.358	-0.422, 0.153	**0.580**	**0.010**	**0.140, 1.019**
	deprivation*age	0.002	0.802	-0.015, 0.019	0.013	0.224	-0.008, 0.033
	deprivation*sex	-0.009	0.796	-0.075, 0.057	-0.008	0.832	-0.086, 0.070
Attention Bias							
	deprivation	**-0.514**	**0.004**	**-0.867, -0.161**	-0.042	0.833	-0.436, 0.351
	age	0.011	0.772	-0.065, 0.087	-0.020	0.551	-0.088, 0.047
	sex	0.319	0.217	-0.187, 0.824	-0.065	0.828	-0.653, 0.523
	deprivation*age	**0.041**	**0.007**	**0.011, 0.072**	0.004	0.746	-0.023, 0.032
	deprivation*sex	0.039	0.517	-0.078, 0.156	-0.010	0.852	-0.115, 0.095

5 Marginal Analysis

In order to further explore both two-way interactions found, marginal analysis was conducted. Marginal effects were derived from two adjusted models. In one of them, psychopathology levels at follow-up is predicted by the interaction between levels of threat exposure at baseline and age at follow-up, while in the second one attention orienting towards angry faces at baseline is predicted by the interaction between levels of deprivation exposure and age at baseline.

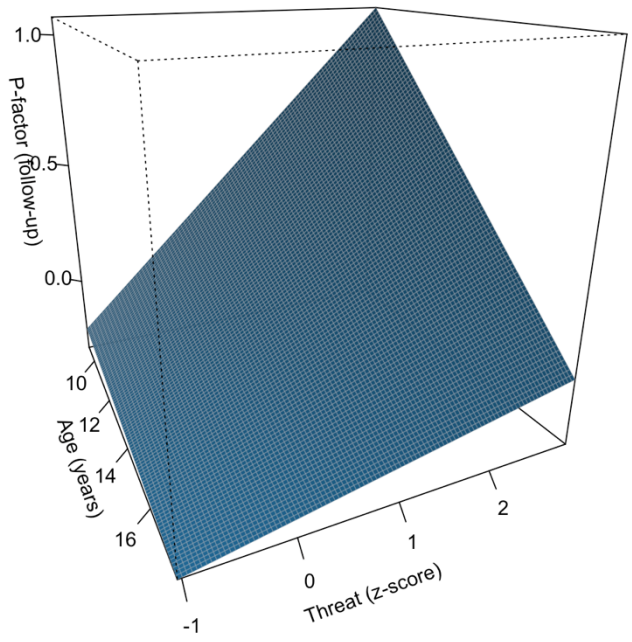
Results from the first model suggest that the effect size of threat on psychopathology three years later varies with age. It is stronger at age 9 ($\beta = 0.345$, $p<0.001$, 95% CI [0.217, 0.474]), and weaker at age 17 ($\beta = 0.107$, $p=0.040$, 95% CI [0.007, 0.207]). At age 18, the effect is no longer significant ($\beta = 0.077$, $p=218$, 95% CI [-0.046, 0.200]) (Supplemental Table S11 and Supplemental Figure S3).

Supplemental Table S11 – Marginal effects of threat for fixed values of age on psychopathology levels at follow-up

Fixed age (years)	Threat			
		95% CI		
Age	Psychopathology (beta)	LB	UB	p-value
9	0.345	0.217	0.474	**<0.001**
10	0.316	0.209	0.422	**<0.001**
11	0.286	0.201	0.371	**<0.001**
12	0.256	0.189	0.323	**<0.001**
13	0.226	0.171	0.281	**<0.001**
14	0.196	0.143	0.250	**<0.001**
15	0.167	0.104	0.230	**<0.001**
16	0.137	0.057	0.217	**0.001**
17	0.107	0.007	0.207	0.040
18	0.077	-0.046	0.200	0.218

Note: Marginal effects derived from adjusted model predicting psychopathology levels at follow-up with interactions of levels of threat exposure with age at follow-up. UB, 95% confidence interval upper bound; LB, 95% confidence interval lower bound.

Supplemental Figure S3 –Interaction of Age and Threat on Psychopathology at follow-up



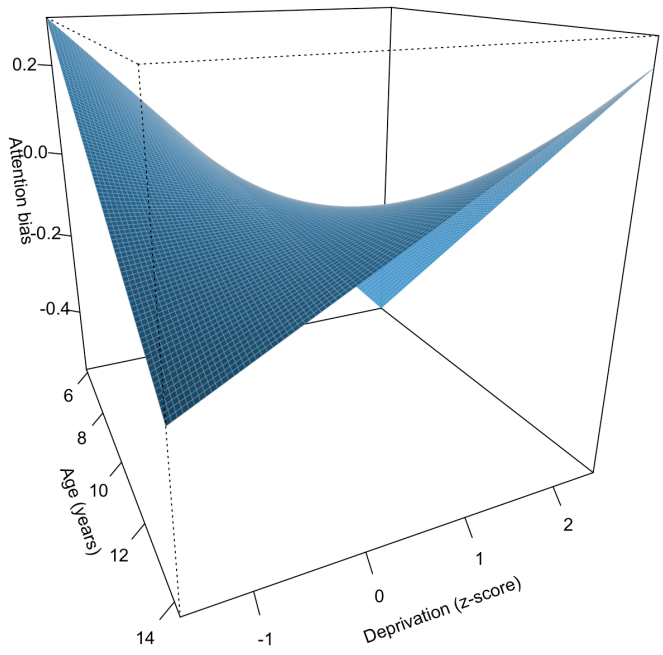
Results from the second model suggest that the effect size of deprivation on attention orienting towards angry faces at baseline varies with age. From age 6 to 9, the effect of deprivation is on attention orienting *away* from angry faces (β= -0.190, p=0.004, 95% CI [-0.317, -0.063]; β= -0.152, p=0.004, 95% CI [-0.255, -0.049]; β= -0.114, p=0.006, 95% CI [-0.195, -0.033]; β= -0.076, p=0.018, 95% CI [-0.139, -0.013]. From age 10 to 14 the effect is no longer significant, and at age 15, deprivation has a significant effect on attention orienting towards angry faces (β= 0.152, p=0.034, 95% CI [0.012, 0.293]) (Supplemental Table S12 and Supplemental Figure S4).

Supplemental Table S12 – Marginal effects of deprivation for fixed values of age on attention bias towards threat at baseline

Fixed age (years)	Deprivation			
		95% CI		
Age	Attention Bias	LB	UB	p-value
6	-0.190	-0.317	-0.063	**0.004**
7	-0.152	-0.255	-0.049	**0.004**
8	-0.114	-0.195	-0.033	**0.006**
9	-0.076	-0.139	-0.013	**0.018**
10	-0.038	-0.091	0.015	0.162
11	0.0001	-0.057	0.057	0.997
12	0.038	-0.033	0.110	0.295
13	0.076	-0.016	0.168	0.105
14	0.114	-0.001	0.230	0.053
15	0.152	0.012	0.293	**0.034**

Note: Marginal effects derived from adjusted model predicting attention bias towards threat at baseline with interactions of levels of deprivation exposure with age at baseline. UB, 95% confidence interval upper bound; LB, 95% confidence interval lower bound.

Supplemental Figure S4 –Interaction of Age and Deprivation on Attention Orienting Towards Angry Faces at baseline



6. Exploratory analysis: Threat and deprivation specific associations with internalizing and externalizing psychopathology

To assess specific associations of threat and deprivation with dimensions of psychopathology, *post.-hoc* independent linear models adjusted by age and sex with threat and deprivation at baseline as simultaneous predictors of (1) internalizing and (2) externalizing psychopathology at baseline, and (3) internalizing and (4) externalizing psychopathology at follow-up were tested. Results are shown on Supplemental Table S13.

Supplemental Table S13 – Effects of threat and deprivation on psychopathology, executive functions and attention bias

	Baseline			**Follow-up**		
	β	***p value***	**CI 95%**	**β**	***p value***	**CI 95%**
Internalizing						
Threat	**0.143**	**<0.001**	**0.101, 0.186**	-0.008	0.769	-0.059, 0.043
Deprivation	0.017	0.390	-0.021, 0.055	-0.012	0.617	-0.58, 0.034
Age	**0.028**	**<0.001**	**0.013, 0.043**	-0.008	0.368	-0.026, 0.009
Sex	**0.067**	**0.018**	**0.012, 0.122**	0.095	0.006	0.028, 0.163
Externalizing						
Threat	**0.170**	**<0.001**	**0.129, 0.211**	0.044	0.064	-0.002, 0.087
Deprivation	0.003	0.883	-0.034, 0.040	0.017	0.395	-0.023, 0.058
Age	-0.013	0.085	-0.027, 0.002	**0.020**	**0.010**	**0.005, 0.036**
Sex	**-0.218**	**<0.001**	**-0.273, -0.164**	**-0.146**	**<0.001**	**-0.205, -0.086**

Note: main effects of threat and deprivation on the outcomes were adjusted for age at the outcome's assessment and sex for the baseline and follow-up models. At the follow-up models, the effects were also adjusted by the outcome variable values at baseline.

Then, we further assessed two and three-way interactions of threat and deprivation independently with age and sex for each one of the measures at baseline and follow-up (Supplemental Table S14-S17). The only significant interaction found was one of higher levels of threat at baseline predicting higher levels of internalizing psychopathology for older children cross-sectionally (β=0.033, p=0.002; 95% CI [0.012, 0.053]; Supplemental Table S16 and Supplemental Figure S5).

Supplemental Table S14 – Three-way interactions among threat, age and sex

	Baseline			Follow-up		
	β	***p value***	**CI 95%**	**β**	***p value***	**CI 95%**
Internalizing Psychopathology						
threat	-0.374	0270	-1.040, 0.291	-0.170	0.747	-1.207, 0.866
age	**0.061**	**0.008**	**0.015, 0.106**	-0.033	0.230	-0.088, 0.021
sex	**0.310**	**0.046**	**0.006, 0.613**	-0.144	0.557	-0.626, 0.337
threat*age	0.049	0.131	-0.015, 0.113	0.011	0.767	-0.064, 0.087
threat*sex	0.130	0.560	-0.308, 0.568	-.242	0.489	-0.445, 0.929
threat*age*sex	-0.011	0.596	-0.053, 0.006	-0.018	0.487	-0.067, 0.032
Externalizing Psychopathology						
threat	0.669	0.045	0.015, 1.324	-0.495	0.283	-1.399, 0.409
age	-0.022	0.329	-0.067, 0.022	0.014	0.568	**-0.034, 0.061**
sex	-0;293	0.054	-0.592, 0.005	-0.190	0.375	**-0.610, 0.230**
threat*age	-0.046	0.152	-0.109, 0.017	0.041	0.220	-0.025, 0.107
threat*sex	-0.290	0.187	-0.721, 0.141	0.272	0.373	-0.327, 0.871
threat*age*sex	0.026	0.208	-0.015, 0.067	-0.021	0.348	-0.064, 0.023

Supplemental Table S15 – Three-way interactions among deprivation, age and sex

	Baseline			Follow-up		
	β	*p value*	CI 95%	β	*p value*	CI 95%
Internalizing Psychopathology						
deprivation	-0.399	0.187	-0.992, 0.194	0.179	0.705	-0.749, 1.107
age	**0.065**	**0.005**	**0.020, 0.111**	-0.035	0.205	-0.089, 0.019
sex	0.284	0.068	-0.021, 0.590	-0.149	0.543	-0.628, 0.331
deprivation*age	0.042	0.151	-0.015, 0.099	-0.010	0.767	-0.078, 0.058
deprivation*sex	0.306	0.116	-0.076, 0.688	-0.078	0.798	-0.678, 0.521
deprivation*age*sex	-0.027	0.145	-0.064, 0.009	0.003	0.893	-0.041, 0.047
Externalizing Psychopathology						
deprivation	0.169	0.571	-0.416, 0.754	-0.034	0.935	-0.843, 0.775
age	-0.026	0.264	-0.070, 0.019	0.020	0.415	-0.028, 0.067
sex	-0.352	0.022	-0.653, -0.051	-0.166	0.438	-0.584, 0.253
deprivation*age	-0.003	0.920	-0.059, 0.053	0.005	0.856	-0.054, 0.065
deprivation*sex	-0.092	0.631	-0.469, 0.284	-0.039	0.883	-0.562, 0.483
deprivation*age*sex	0.004	0.827	-0.032, 0.040	0.003	0.898	-0.036, 0.041

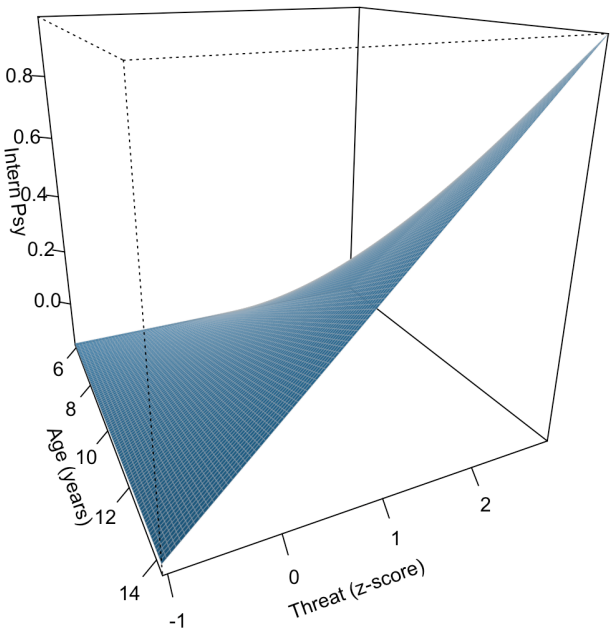
Supplemental Table S16 – Two-way interactions among threat, age, and sex

	Baseline			Follow-up		
	β	***p value***	**CI 95%**	**β**	***p value***	**CI 95%**
Internalizing Psychopathology						
threat	-0.206	0.089	-0.443, 0.031	0.175	0.336	-0.181, 0.530
age	**0.062**	**0.008**	**0.017, 0.107**	-0.032	0.252	-0.086, 0.023
sex	**0.314**	**0.042**	**0.011, 0.617**	-0.133	0.587	-0.614, 0.347
threat*age	**0.038**	**0.002**	**0.012, 0.053**	-0.014	0.269	-0.039, 0.011
threat*sex	0.013	0.734	-0.064, 0.091	0.001	0.981	-0.018, 0.052
Externalizing Psychopathology						
threat	**0.276**	**0.021**	**0.043, 0.510**	-0.089	0.575	-0.399, 0.222
age	-0.025	0.280	-0.069, 0.020	0.016	0.513	-0.032, 0.063
sex	-0.303	0.046	-0.602, -0.005	0.177	0.407	-0.596, 0.241
threat*age	-0.008	0.458	-0.028, 0.013	0.011	0.298	-0.010, 0.033
threat*sex	0.009	0.561	-0.094, 0.059	-0.012	0.772	-0.094, 0.070

Supplemental Table S17 – Two-way interactions among deprivation, age, and sex

	Baseline			Follow-up		
	β	***p value***	**CI 95%**	**β**	***p value***	**CI 95%**
Internalizing Psychopathology						
deprivation	**0.012**	**0.909**	**-0.201, 0.226**	0.120	0.465	-0.201, 0.440
age	0.066	0.005	0.020, 0.111	**-0.035**	**0.206**	**-0.089, 0.019**
sex	0.289	0.064	-0.017. 0.594	**-0.149**	**0.543**	**-0.628, 0.331**
deprivation*age	0.002	0.860	-0.017, 0.020	-0.006	0.599	-0.028, 0.016
deprivation*sex	0.027	0.455	-0.052, 0.007	-0.037	0.387	-0.122, 0.047
Externalizing Psychopathology						
deprivation	0.109	0.313	-0.102, 0.319	-0.083	0.559	-0.363, 0.196
age	-0.026	0.263	-0.071, 0.019	0.020	0.413	-0.028, 0.067
sex	-0.353	0.022	-0.654, -0.052	-0.165	0.438	-0.584, 0.253
deprivation*age	0.003	0.742	-0.015, 0.021	0.009	0.348	-0.010, 0.028
deprivation*sex	-0.051	0.147	-0.017, 0.041	-0.005	0.887	-0.029, 0.032

Supplemental Figure S5 –Interaction of Age and Threat on Internalizing Psychopathology at baseline



7 Exploratory analysis: Mediation Models

To further assess the associations among the interest variables, we conducted exploratory analyses examining whether executive functions and attention orienting toward angry faces could serve as mechanisms linking threat and deprivation exposure to general psychopathology, as well as internalizing and externalizing psychopathology. In order to test such hypothesis, two full longitudinal mediation models were tested having threat and deprivation at baseline as concurrent predictors and general, internalizing and externalizing psychopathology at follow-up as concurrent outcomes. The difference between the two models consisted on the time point assessment of the mediators. The (1) first model has executive functions and attention orienting towards angry faces assessed at baseline as concurrent mediators, while the (2) second model had the same variables assessed at the follow up as concurrent mediators.

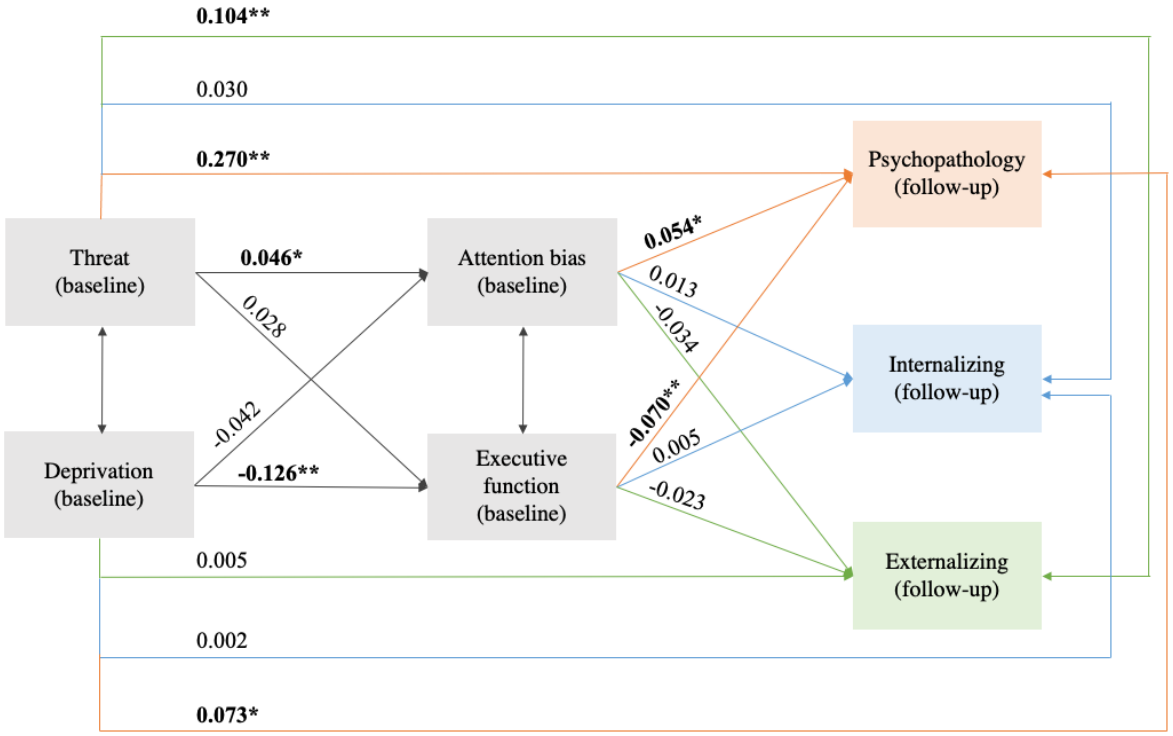
Both models yielded the same pattern of results. Direct effects were found for higher levels of threat (model 1: $\beta=0.270$, $p<0.001$; model 2: $\beta=0.269$, $p<0.001$), and higher levels of deprivation (model 1: $\beta=0.073$, $p=0.002$; model 2: $\beta=0.072$, $p=0.002$) at baseline predicting higher levels of psychopathology three years later, as well as higher levels of threat predicting higher levels of externalizing psychopathology three years later (model 1: $\beta=0.104$, $p<0.001$; model 2: $\beta=0.099$, $p<0.001$). A small mediation effect was found for higher levels of deprivation at baseline predicting higher levels of psychopathology three years later through worse performance on executive function tasks (model 1: $\beta=0.009$, $p=0.005$; model 2: $\beta=0.008$, $p=0.006$). Results for model one are presented in the Supplemental Table 18 and Supplemental Figure S6, while results for model two are presented in the Supplemental Table 19 and Supplemental Figure S7.

Supplemental Table S18 – Mediation model of the association of adversity with psychopathology with mediators (attention bias and executive functions) measured at baseline

	Psychopathology		Internalizing		Externalizing	
	β	*p value*	β	*p value*	β	*p value*
Direct effects						
Threat	**0.270**	**<0.001**	0.030	0.219	**0.104**	**<0.001**
Deprivation	**0.073**	**0.002**	0.002	0.922	0.005	0.842
Indirect effects						
Threat						
Attention bias	0.003	0.125	0.001	0.598	-0.002	0.250
Executive function	-0.002	0.245	0.000	0.821	-0.001	0.429
Deprivation						
Attention bias	-0.002	0.154	-0.001	0.601	0.001	0.264
Executive function	**0.009**	**0.005**	-0.001	0.818	0.003	0.312
Total effects						
Threat	**0.328**	**<0.001**	**0.122**	**0.010**	**0.120**	**0.004**
Deprivation	**-0.111**	**0.l018**	**-0.148**	**0.004**	**-0.221**	**<0.001**

Note: model having threat and deprivation at baseline as concurrent predictors of psychopathology, internalizing psychopathology and externalizing psychopathology at follow-up with attention orienting towards angry faces and executive functions at baseline as mediators.

Supplemental Figure S6 – Mediation model of the association of adversity with psychopathology with mediators (attention bias and executive functions) measured at baseline



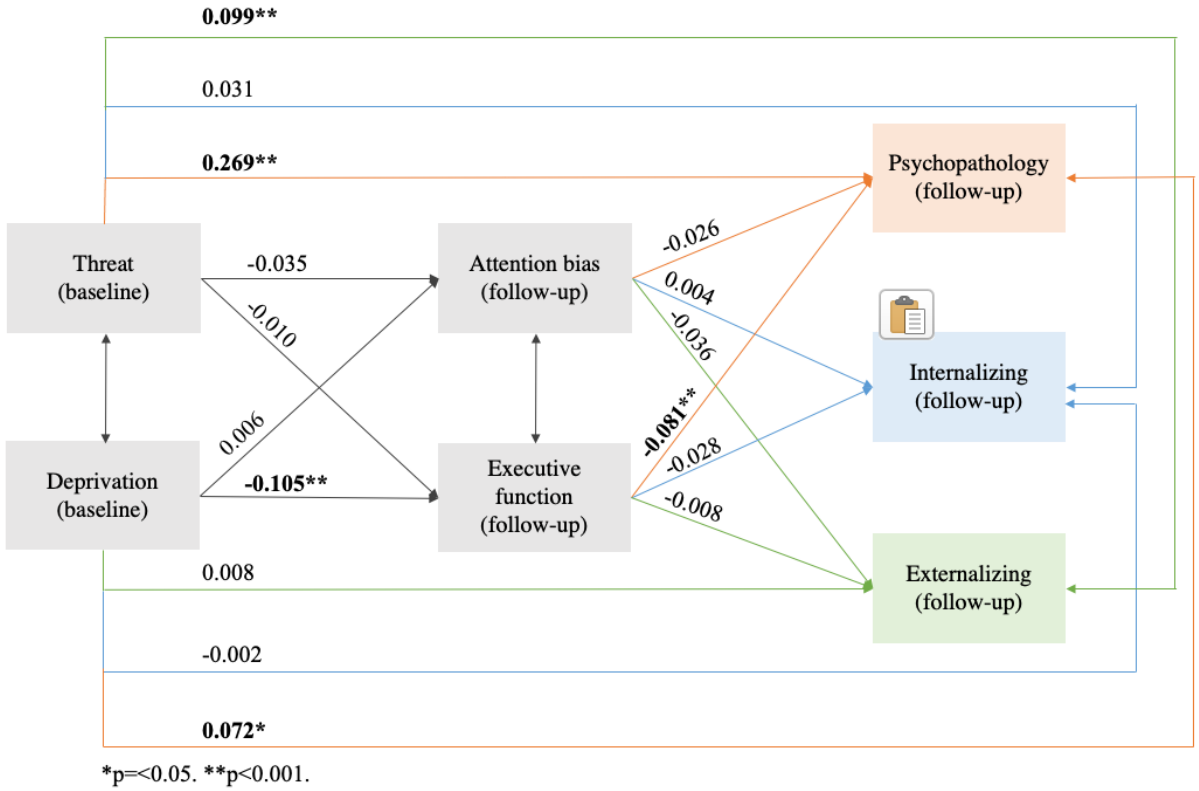
*p=<0.05. **p<0.001.

Supplemental Table S19 – Mediation model of the association of adversity with psychopathology with mediators (attention bias and executive functions) measured at baseline

	Psychopathology		Internalizing		Externalizing	
	β	*p value*	β	*p value*	β	*p value*
Direct effects						
Threat	**0.269**	**<0.001**	0.031	0.205	**0.099**	**<0.001**
Deprivation	**0.072**	**0.002**	-0.002	0.945	0.008	0.728
Indirect effects						
Threat						
Attention bias	0.001	0.399	-0.000	0.867	0.001	0.335
Executive function	0.001	0.702	0.000	0.715	0.000	0.795
Deprivation						
Attention bias	-0.000	0.823	0.000	0.892	-0.000	0.822
Executive function	**0.008**	**0.006**	0.003	0.252	0.001	0.729
Total effects						
Threat	**0.118**	**0.010**	-0.038	0.491	0.011	0.866
Deprivation	**-0.133**	**0.022**	**-0.124**	**0.035**	**-0.134**	**0.021**

Note: model having threat and deprivation at baseline as concurrent predictors of psychopathology, internalizing psychopathology and externalizing psychopathology at follow-up with attention orienting towards angry faces and executive functions at follow-up as mediators.

Supplemental Figure S7 – Mediation model of the association of adversity with psychopathology with Mediators (attention bias and executive functions) measured at follow-up



*p=<0.05. **p<0.001.

8 References

Hu, L. T., & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling: A Multidisciplinary Journal*, *6*(1), 1–55.

Lucke, J. F. (2005). The α and the ω of congeneric test theory: An extension of reliability and internal consistency to heterogeneous tests. *Applied Psychological Measurement*, *29*(1), 65–81. https://doi.org/10.1177/0146621604270882

5. ARTICLE #2

Submitted to ***Psychological Science***

Impact factor (2018): 4.902

Currently under peer-review (April 2nd, 2022)

Long-lasting associations between threat and deprivation during childhood with psychopathology and executive functions: a 6-year longitudinal study

Julia Luiza Schäfer, Ph.D, Luis Augusto Rohde, MD, Ph.D, Pedro Pan, MD, Ph.D, Rodrigo Bressan, MD, Ph.D, Ary Gadelha, MD, Ph.D, Eurípedes Constantino Miguel, MD, Ph.D, Rodrigo Grassi-Oliveira, MD, Ph.D, Edward D. Barker, Ph.D, Giovanni Abrahão Salum, MD, Ph.D

Authors' Affiliations

Drs. Schäfer, Rohde, Pan, Bressan, Gadelha, Miguel, and Salum are with the National Institute of Developmental Psychiatry (INPD, CNPq), Brazil. Drs. Schäfer, and Salum are also with the Universidade Federal do Rio Grande do Sul, Brazil. Dr. Pan, Dr. Bressan, and Dr. Gadelha are also with the Universidade Federal de São Paulo, Brazil, and Dr. Miguel is also with the Universidade de São Paulo. Dr. Grassi-Oliveira is with the Aarhus University, Denmark, and Dr. Barker is with King's College London, United Kingdom.

Corresponding Author

Julia Luiza Schäfer

Hospital de Clínicas de Porto Alegre

Ramiro Barcelos, 2350 – room 2202; Porto Alegre, Brazil – 90035-003;

E-mail: julialuizaschafer@gmail.com

Abstract

Childhood adversity is known to have significant detrimental consequences on childhood development. Such experiences might take on different forms leading to differential long-term influences. We investigated the long-lasting associations of threat and deprivation exposure during childhood, adjusting by stressful life events exposure, with psychopathology and executive functions in the transition to young adulthood. Participants were 2511 school-aged children from the Brazilian High-Risk Cohort Study (BHRC) assessed three times three years apart. Adjusted stratified general linear models by developmental periods indicated that threat exposure during childhood predicted incident psychopathology and exposure to deprivation in childhood predicted EF impairment 6 years later in participants transitioning from adolescence to early adulthood independently of other stressful life events. Our results suggest that exposure to threat and deprivation continue to confer risk after 6 years and that they might contribute to the high incidence of mental disorders during the transition from adolescence to young adulthood.

Key words: Childhood development; Environmental Effects; Life Experiences; Psychopathology; Cognitive Development.

Statement of relevance

Traumatic experiences during childhood can take on many different forms and can lead to different negative mental health consequences. In this study, we wanted to know whether going through experiences characterized by threat (to self) and deprivation (lack of basic material needs) during childhood could influence psychological difficulties and cognition (related to the ability to process information) during adolescence and young adulthood, despite going through current and stressful life events. We found that, despite current stressful life events, threat and deprivation experiences lived through childhood continue to confer risk after six years. Because we found that experiences of threat could lead to psychological difficulties and experiences of deprivation to impaired cognition in participants transitioning from adolescence to early adulthood, our results shed light on the importance of early interventions that are targeted to specific developmental domains to buffer the effects of different types of traumatic experiences.

Introduction

Exposure to childhood adversity is pervasive across societies worldwide, disproportionately affecting low- and middle-income countries (Magruder et al., 2017; Viola et al., 2016) and conferring a more important contribution to the burden of disease than all common mental disorders together (Cuijpers et al., 2011). Early life environments characterized by experiences including abuse, neglect, violence, and parental absence are often associated with persistent negative effects on mental health across the lifespan (Benjet et al., 2010a; C. Clark et al., 2010; Richards & Wadsworth, 2004), supporting the notion that exposure to such environments during childhood is particularly disruptive of numerous aspects of cognitive, emotional, and social development (Magruder et al., 2017). Because it offers a heightened risk for stress-related health disorders that may affect future adult physical and psychological health (Nelson et al., 2020), exposure to childhood adversity is of great public health importance and should encourage continuous understanding of its long-lasting consequences later in life.

There is a consistent body of research reporting short- and long-term effects of childhood adversity. Exposure to such events has been associated with childhood psychiatric symptoms (Bachler et al., 2018), childhood and adolescent psychopathology (Benjet et al., 2010a; Lansford et al., 2002; McLaughlin et al., 2012), and deficits in memory and executive functioning among school-age children (Bos, 2009). It has also been known to lead to poorer mental health outcomes later in life (Green, McLaughlin, et al., 2010; Mclaughlin et al., 2012), accounting for 29.8% of adult psychiatric disorders among nationally or regionally representative samples from 21 different countries across the world (Kessler, McLaughlin, Green, Gruber, Sampson, Zaslavsky, Aguilar-Gaxiola, Alhamzawi, Alonso, Angermeyer, Benjet, Bromet, Chatterji, De Girolamo, et al., 2010). Young adults with a history of exposure to adversity during childhood and adolescence are known

to be at heightened risk of developing a significant range of mental disorders (Norman et al., 2012) that can be complex (Schaefer et al., 2018) and recurrent (Agnew-Blais & Danese, 2016; Nanni et al., n.d.; Walsh et al., 2017), as well as presenting poorer cognitive function (Lewis et al., 2021) and difficulties with education and employment (Jaffee et al., 2018).

However, some critical issues should be taken into consideration when investigating the long-term effects of childhood adversity exposure. First, experiences that fall under the construct of childhood adversity can be considerably heterogeneous and tend to be highly correlated within individuals (McLaughlin, 2016b), positing a challenge on disentangling the differential impact that distinct types of environmental experiences might have on future negative mental health outcomes. Second, most studies use retrospective data and fail to adjust for pre-existing outcomes that might influence the associations making it more difficult to attribute emergent problems to childhood experiences. Third, most studies fail to control for other forms of exposure to adversity, such as stressful life events, and consider their potential interactions with early traumatic experience, limiting conclusions about the extent to which impacts on mental health outcomes measured later in life are really due to early-life trauma or due to traumatic events that occur later in life, given adversity also tends to cluster within individuals (Benjet et al., 2010b; Kessler, McLaughlin, Green, Gruber, Sampson, Zaslavsky, Aguilar-Gaxiola, Alhamzawi, Alonso, Angermeyer, Benjet, Bromet, Chatterji, de Girolamo, et al., 2010). Finally, most studies do not to account for possible differences in childhood adversity impacting on different age transitioning groups. This is important because late adolescence and young adulthood is a period of high incidence of mental disorders.

Using data from the Brazilian High-Risk Cohort (BHRCS) (Salum et al., 2014), cross-sectional and longitudinal associations among childhood adversity measured as threat and

deprivation (Mclaughlin & Sheridan, 2016), and psychopathology and executive functions have been demonstrated (*in press*). More specifically, even though exposure to experiences of threat and deprivation within 6 and 12 years of age predicted psychopathology at the same time of assessment and three-years later. Threat seemed to play a more important role in this association than deprivation. Meanwhile, higher levels of exposure to deprivation, and not threat, were associated with worse performance in executive functions tasks at the same time of assessment and three years later.

The present study expands on our previous analysis presenting data for our 6-year follow-up assessment. It also presents new data adjusting for stressful life events occurring during follow-up assessments. The study aims to investigate the long-term associations of childhood adversity in the form of threat and deprivation with psychopathology and executive functions at adolescence and early adult life addressing the aforementioned gaps in the literature. According to the dimensional model of adversity and psychopathology (DMAP), threat is defined as the presence of an unexpected input that represents threat to the physical integrity, or well-being of the child, (such as physical, sexual and emotional abuse, witnessing domestic violence, and exposure to violence in the community, or at school), while deprivation is described as the absence of expected social, cognitive, and emotional inputs that provide complex learning opportunities expected throughout development (such as physical and emotional neglect, parental absence, and material deprivation) (McLaughlin, 2016a; McLaughlin et al., 2014, 2019; Sheridan & Mclaughlin, 2014). Using longitudinal data from BHRCS, we tested the assumption that those children who were exposed to higher levels of threat and deprivation at baseline were also exposed to higher levels of other forms of adversity in the form of stressful life events three and six years later. Then, we investigated whether exposure to threat and deprivation at baseline was associated with

psychopathology and executive functions performance six years later while adjusting for previous outcomes, and exposure to stressful life events both occurring at baseline and 3-years after the exposure.

Open Practices

This article reports data from the Brazilian High Risk Cohort Study (BHRC) which information is available via OSF and can be accessed at https://osf.io/ktz5h/. The code repository is open to partners' review and requests for access to the data for this study should be made to (author's name) (email). The design and analysis plan for the present study were not preregistered.

Method

Sampling and Procedures

Participants were children and adolescents from a large school-based community cohort, the BHRCS (Salum et al., 2014). The BHRCS is an ongoing study since 2010 that has screened 9,937 children from 6 to 12 years old and their families and has further assessed 2,511 of those children/adolescents at three time points three years apart. Briefly, in the year 2010, 9937 parents of 6-14-years-old children from 57 schools in São Paulo and Porto Alegre were screened using the Family History Survey (Weissman et al., 2000). From this sample, two subgroups were recruited for further assessments. One subgroup was randomly selected (n=957), while the other was selected from a high-risk score procedure used to identify children with current symptoms and/or family history of psychiatric disorders (n=1554). More specifically, the high-risk score procedure consists of the calculation of an index of family load based on the FHS considering mother, father, or siblings' presentation of any of the five disorders of interest for this study (Attention Deficit and Hyperactivity Disorder, anxiety disorders, Obsessive Compulsive Disorder, psychotic experiences and learning disorders). This index expresses the

percentage of members in the family that screened positively for each of the disorders assessed, adjusted for relatedness. Sample retention rate across the three time points of the study were of 80% and 75%, respectively. Evaluation at baseline, 3- and 6-year follow-ups were comprised of several measures, including questionnaires and interviews about life history and psychopathology directed at both, children/adolescents and parents, and neurocognitive tasks completed by children/adolescents.

Procedures taken on the course of this study follow the ethical standards of the national and institutional committees in human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All participants were informed about the study's objectives and procedures and gave written, and verbal informed consent. Since procedures involved human subjects, all procedures were approved by the institutional review boards of all institutions involved in the study. For more information about the design of the study, see Salum et al., 2014.

Measures

Childhood adversity: threat and deprivation

Early adversity exposure was measured at baseline through two latent factors yielding standardized scores expressing exposure levels to threat and deprivation experiences. Variables were selected from the baseline evaluation of the BHRCS and were chosen based on the dimensional model of adversity and psychopathology (DMAP), which proposes that adversity encompasses experiences involving levels of threat and deprivation (McLaughlin et al., 2014).

Experiences comprised under the threat dimension were assessed through a semi structured interview and the Posttraumatic Stress Disorder session of the Development and Well Being Assessment (Goodman et al., 2000) and were characterized by parent report on lifetime exposure

to bullying, emotional, physical and sexual abuse, attack or threat, witnessing domestic violence, and witnessing attack. Some variables, such as lifetime experiences of bullying, and frequency of experiences of physical and emotional abuse were informed by both, parents and the children.

The deprivation dimension, assessed through a semi-structured interview, was encompassed mainly by material scarcity indicators that are strongly associated with deprived cognitive stimulation (e.g., reduced exposure to complex language early in development) (Mclaughlin et al., 2017; Romeo et al., 2018). Deprivation was measured through the assessment of mother's educational level, family income, socioeconomic classification according to Brazilian Economic Classification Criterion index (A/B – the wealthiest, C, or D/E – the poorest) (Associação Brasileira de Empresas (ABEP), 2010), having father as a present figure, and the frequency of exposure to childhood physical neglect (Salum et al., 2016). Physical neglect was informed by both, parents, and the children. More information about the development of this measure is described elsewhere (Schäfer el al., *in press*), as well as in the Supplemental Material.

Other form of adversity in adolescence and young adulthood: Stressful Life Events (SLEs)

The SLEs variable was calculated using a Life History Schedule answered by the children's parents at the 3- and 6-year follow-ups. Parents reported on the exposure to different SLEs over the three years prior to both evaluations, which reflects the time interval between the BHRCS waves. After exploration of the factor structure using Exploratory Factor Analysis and Confirmatory Factor Analysis (Supplemental Material), we used a 1-factor solution comprising nine indicators composed of experiences of family distress (parents' unemployment, divorce, or death, and family fights, or financial problems), friend or family member's illnesses or death, loss

of a pet and household loss due to a natural disaster (flood or fire). For a more detailed description of the variable creation and development, see the Supplemental Material.

Psychopathology

Psychopathology was measured dimensionally through a bifactor model with one dimension of general psychopathology (the "p" factor) and two residualized dimensions of internalizing and externalizing psychopathology. The bifactor model was drawn from data collected using the Child Behavior Checklist (CBCL)(Achenbach & Rescola, 2001; Bordin et al., 2013) at baseline, 3-year follow up, and 6-year follow-up for those children under 18 years old at the time of the evaluation, as well as using the Adolescent Behavior Checklist (ABCL) (Adams et al., 1997) at the 6-year follow-up for those participants older than 18 years old. The CBCL and ABCL are parent-report questionnaires that assess the child and adolescent's emotional, behavioral, and social problems yielding a total score (including all items), as well as an internalizing and externalizing score. Recent work suggests that the p-factor estimation is appropriate for studying individual differences in transdiagnostic psychopathology (D. A. Clark et al., 2021; Hoffmann et al., 2021), therefore our goal through this model was to generate a dimensional measure capturing the severity of psychopathology symptoms transdiagnostically. Details on the model are in the Supplemental Material.

Executive Functions

Executive Functions (EF) was measured as a single high-order standardized score comprised by three lower order factors of working memory, inhibitory control, and temporal

processing scores after regressing out effects of age and gender on the task parameters using General Additive Regression Models. Higher EF scores represent better EF.

Working memory was measured by the *digit span* (a subtest of the WISC-III) (Wechsler, 2002) and *corsi blocks* tasks (Vandierendonck et al., 2004). Both tasks involve the repetition of a given sequence. While in the *digit span task* the participants hear and repeat an increasingly difficult sequence of numbers, either forward and backward, in the *corsi blocks task* they repeat an increasingly difficult spatial sequence tapped by a researcher on up to nine identical blocks. Both outcomes are the level at which a correct repetition failed twice consecutively. Inhibitory control was measured by the *conflict control task* (CCT)(Hogan et al., 2005) and the *go/no-go* task (GNG)(Bitsakou et al., 2008). Both consist of an arrow based visual stimuli with a total 100 trials divided into two different instructions. In the *conflict control task*, participants are asked to press a button indicating the direction or opposite direction of arrows shown on the screen. Participants either press the button indicating the correct direction of a green arrow (75 congruent trials), or press the button indicating the opposite direction of a red arrow (25 incongruent trials). The *go/no-go* task requires participants to completely suppress the tendency to press the buttons indicating the direction of the green arrows (75 *go* stimuli trials) when a double-headed green arrow (25 *no-go* stimuli trials) appears on the screen. For both tasks, intertrial interval was 1,500 ms, and the stimulus duration was 100 ms. The outcomes were the percentage of correct responses in the incongruent trials (CCT) and the percentage of successful inhibitions in the *no-go* trials (GNG). Temporal processing was measured by *time anticipation (TA) tasks 400 ms*(Toplak & Tannock, 2005) on baseline and follow-up. This task requires participants to anticipate when a visual stimulus will appear. In a game-like manner, the task involves an allied spaceship running out of oxygen and the participant has to give it to them in order to save the crew. In each task, the allied

spaceship is visible for the first 10 trials, while for the remaining 16 trials the spaceship is invisible due to an invisible shield. Then, participants are asked to press a button to anticipate when it arrives. A 750-ms window of time to respond correctly and feedback after every trial are given. The anticipation interval is 400ms. The outcome is the mean percentage of button pressed in the correct time window interval for the invisible part of the task. Tasks involving temporal delays with flexible cognitive demands have been proposed to be a part of EF in some models (Barkley, 1997). For a more detailed information on this measure, see the Supplemental material.

Data Analysis

Due to our sample aging variation, the 2511 participants were grouped according to their age at baseline considering that children would be undergoing transitions to different stages of development throughout the course of the follow-ups. Group 1 was composed of children aged 6 to 10 years old at baseline, who would be transitioning from childhood to adolescence on the follow-ups, while group 2 was comprised of children who were aged 11 to 14 years old at baseline, who would be transitioning from adolescence to adulthood on the follow-ups. Age ranges for group 1 were 6 to 10 at baseline, 9 to 14 at the 3-year follow up, and 13 to 19 at the 6-year follow up, while age ranges for group 2 were 10 to 14 at baseline, 13 to 18 at the 3-year follow up, and 18 to 23 at the 6-year follow up (Figure 1). All subsequent analyses were conducted for each group independently.

First, to justify adjusting the associations of childhood adversity with the outcomes for later stressful life events, we tested the assumption that being exposed to childhood adversity in the form of threat and deprivation at baseline was a predictor of exposure to higher levels of later adversity in the form of stressful life events (SLES) three and six years later. Second, we tested

whether childhood adversity at baseline (threat and deprivation) impact levels of psychopathology and executive functions at 6-year follow up while adjusting for baseline levels from previous waves in two independent univariate analysis. Finally, we tested whether childhood adversity at baseline (threat and deprivation) impact levels of psychopathology and executive functions at 6-year follow-up, while adjusting for later adversity at 3- and 6-year follow-up assessments (SLEs), demographic factors (age, gender) and levels of the outcomes from the previous waves all in the same model including interaction terms between threat, deprivation, and SLEs (multiple model). Data analysis was performed using the *stats* package (Team, 2021) from R (version 3.6.1).

Results

Descriptive Statistics

Group 1 was comprised of 1175 children aged from 6 to 10 years old at baseline who transitioned from childhood to adolescence throughout the follow-ups. Among those, 659 (56%) were male and 661 (56%) were from the city of São Paulo. Group 2 was comprised of 1336 children aged from 11 to 14 years old at baseline who transitioned from adolescence to adulthood throughout the follow-ups. Among those, 716 (54%) were male and 595 (44%) were from the city of São Paulo. Descriptive data on variables of interest are shown on Table 1.

Threat and deprivation, and later exposure to stressful life events

Exposure to higher levels of threat at baseline predicted exposure to higher levels of SLEs three years later for both age groups (Group 1: β=0.152, p<0.001, 95% CI [0.089, 0.214]; Group 2: β=0.152, p<0.001, 95% CI [0.096, 0.208]), as well as six years later (Group 1: β=0.114, p=0.001, 95% CI [0.046, 0.182]; Group 2: β=0.179, p<0.001, 95% CI [0.118, 0.241]). Higher

levels of deprivation at baseline were predictive only of higher levels of SLEs exposure six years later for the group 2 (β=0.066, p=0.014, 95% CI [0.013, 0.118]).

Associations of threat and deprivation with psychopathology

Exposure to threat in childhood was consistent in both, univariate and multiple models. It was significantly associated with psychopathology at 6-years follow-up assessment only for group 2 (adolescence to adulthood transition), and no associations were found with deprivation (Table 2). SLEs measured at 3-year follow-up assessment predicted higher p factor at the 6-year follow-up only for group 2, while SLE measured at 6-year follow-up assessment predicted higher p factor at the 6-year follow-up in both age groups. No evidence was found for interactive associations between either form of childhood adversity and SLEs. More details are found in the Supplemental Material.

Associations of threat and deprivation with executive functions

Exposure to deprivation in childhood was significantly associated with lower performance in EF tasks above and beyond performance in previous assessments at the 6-year follow-up assessment for groups 1 and 2 in the univariate model. Also, exposure to threat in childhood was significantly associated with lower performance in EF tasks at the 6-year follow-up assessment for group 2. However, the only association that persisted in the multiple model was the one of deprivation in childhood predicting worse performance in executive functions at 6-year follow-up in the group 2, while in group 1 it only approached significance (p=0.054) (Table 3). No associations between SLEs and EF were found in multiple models and no evidence was found for

interactive associations between either form of childhood adversity and SLEs. More details are found in the Supplemental Material

Discussion

The aim of the present study was to investigate the long-term associations of childhood adversity in the form of threat and deprivation with psychopathology and executive functions at adolescence and early adult life. Our results showed that adversity cluster within individuals, with childhood exposure to threat and deprivation predicting later exposure to SLEs. Then, we showed that exposure to threat in childhood predicted long-lasting associations with indident psychopathology at 6-years follow-up, and exposure to deprivation in childhood predicted long-lasting incident lower performance in EF tasks in 6-years follow-up among adolescents transitioning into adulthood but not among children transitioning to adolescence.

Our findings support the well-established comprehension of exposure to early adversity as a consistent predictor of psychopathology later in life (Green, McLaughlin, et al., 2010; Green, Mclaughlin, et al., 2010; Mclaughlin et al., 2012), since all models that were tested yielded childhood adversity, more specifically threat, as an important predictor of overall psychopathology at 6-year follow-up for at least one age group. This result also corroborates with a range of previous findings suggesting that experiences characterized by threat have a more prominent role on child psychopathology development, than experiences characterized by deprivation (Benjet et al., 2010a; Mclaughlin & Sheridan, 2016; Miller et al., 2016, 2020). By its turn, our findings of deprivation as a consistent predictor of lower performance on executive functions at 6-year follow-up also support the previous documented association of deprivation as a stable and stronger

predictor of negative executive functions outcomes (Bos, 2009; Johnson et al., 2021; Sheridan et al., 2017) that extends until young adulthood.

Our findings point towards important directions. Early adversity, especially in the form of threat, continuously increases the risk of psychopathology development across childhood, adolescence, and adulthood and those associations could be additive or cumulative to SLEs. In contrast, deprivation continuously influenced lower cognitive functioning throughout child development, independently of SLEs exposure. Such results emphasize the continuous risk that exposure to early adversity confers to the development of psychopathology and lower cognitive performance throughout the life span, despite the exposure to new life stressors, supporting its importance as a public health issue (Nelson et al., 2020).

The pattern of findings described was only present among the group of participants that were transitioning from adolescence to adulthood at 6-year follow-up, and not among those who were transitioning from childhood to adolescence. Because these participants were older when assessed for childhood adversity exposure at baseline (10 to 14 years old), they might have had more chances of exposure due to more years of life, when compared to children who were younger at baseline (6 to 10 years old). This age-related result also corroborates with previous longitudinal (Caspi et al., 2020), as well as reviewed epidemiological data (Kessler et al., 2007; Solmi et al., 2021) indicating that the highest prevalence of onset of mental health disorders occurs around late teens (until 18 years old) and early adult life (early 20s). Incident effects of adversity might become apparent only when incidence of problems start to increase.

Our study has limitations that should be considered. First, our measures of adversity and psychopathology derive from self and parent report, and are not all observed by the interviewer. Second, it is important to note that the deprivation dimension being assessed is primarily a measure

of physical neglect and material deprivation, meaning that it does not capture the phenomenon of emotional neglect, and absence of cognitive stimulation, or the lack of an enriched cognitive environment as suggested in the literature (Sheridan & Mclaughlin, 2014). The lack of such assessment as part of the deprivation domain means that inferences apply to the material and physical aspects of deprivation and cannot be generalized to the broad and comprehensive experience of deprivation. Third, SLEs can take upon many forms, meaning that we were not able to capture every aspect of it. It should be noted that there are significant stressful exposures for the outcomes that are not being taken into account.

There are also important strengths. First, by using a dimensional approach to measure childhood adversity we were able to assess the differential influences of adversity on psychopathology and cognition development persisting until adult life. Also, since executive functions are an important aspect of human functioning, its inclusion as an outcome broadens the array of information on distal and proximal adversity associations with several dimensions of child development. Second, our longitudinal design not only allowed us to assess the associations of childhood adversity with psychopathology and executive functions over time, but it also assured the reliable assessment and control of distal and proximal adversity exposure throughout age transitions. Third, since our study expands prior work in the sense of investigating important consequences of childhood adversities using a large sample in a low-income country using.

Childhood adversity is an important predictors of mental health outcomes during child development. Therefore, elucidating and understanding the mechanisms through which environmental variables interact throughout development and impact child development is considerably important to further understand the etiology of mental disorders and related

constructs. Disentangling such relationships might support and enrich mental health prevention and overall health promotion actions.

References

Achenbach, T. M., & Rescola, L. A. (2001). *Manual for the ASEBA school-age forms & profiles*.

Adams, C. D., Kelly, M. L., & McCarthy, M. (1997). The Adolescent Behavior Checklist: Development and initial psychometric properties of a self-report measure for adolescents with ADHD. *Journal of Clinical Child Psychology*, *26*(1), 77–86. https://doi.org/10.1207/s15374424jccp2601_8

Agnew-Blais, J., & Danese, A. (2016). Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: A systematic review and meta-analysis. *The Lancet Psychiatry*, *3*(4), 342–349. https://doi.org/10.1016/S2215-0366(15)00544-1

Associação Brasileira de Empresas (ABEP). (2010). *Critério de Classificação Econômica Brasil*.

Bachler, E., Frühmann, A., Bachler, H., Aas, B., Nickel, M., & Schiepek, G. K. (2018). The Effect of Childhood Adversities and Protective Factors on the Development of Child-Psychiatric Disorders and Their Treatment. *Frontiers in Psychology*, *9*, 2226. https://doi.org/10.3389/fpsyg.2018.02226

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin*, *121*(1), 65–94. https://doi.org/10.1037/0033-2909.121.1.65

Benjet, C., Borges, G., & Medina-Mora, M. E. (2010a). Chronic childhood adversity and onset of psychopathology during three life stages: Childhood, adolescence and adulthood. *Journal of Psychiatric Research*, *44*(11), 732–740. https://doi.org/10.1016/j.jpsychires.2010.01.004

Benjet, C., Borges, G., & Medina-Mora, M. E. (2010b). Chronic childhood adversity and onset of psychopathology during three life stages: Childhood, adolescence and adulthood.

Journal of Psychiatric Research, *44*(11), 732–740. https://doi.org/10.1016/j.jpsychires.2010.01.004

Bitsakou, P., Psychogiou, L., Thompson, M., & Sonuga-Barke, E. J. S. (2008). Inhibitory deficits in attention-deficit/hyperactivity disorder are independent of basic processing efficiency and IQ. *Journal of Neural Transmission*, *115*(2), 261–268. https://doi.org/10.1007/s00702-007-0828-z

Bordin, I. A., Rocha, M. M., Paula, C. S., Teixeira, M. C. T. V, Achenbach, T. M., Rescola, L. A., Silvares, E. F. M., Bordin, I. A., Rocha, M. M., Paula, C. S., Teixeira, M. C. T. V., Achenbach, T. M., Rescorla, L. A., & Silvares, E. F. M. (2013). Child Behavior Checklist (CBCL), Youth Self- Report (YSR) and Teacher's Report Form (TRF): An overview of the development of the original and Brazilian versions. *Cadernos de Saúde Pública*, *29*(1), 13–28. https://doi.org/10.1590/S0102-311X2013000500004

Bos, K. J. (2009). Effects of early psychosocial deprivation on the development of memory and executive function. *Frontiers in Behavioral Neuroscience*, *3*(September), 1–7. https://doi.org/10.3389/neuro.08.016.2009

Caspi, A., Houts, R. M., Ambler, A., Danese, A., Elliott, M. L., Hariri, A., Harrington, H., Hogan, S., Poulton, R., Ramrakha, S., Rasmussen, L. J. H., Reuben, A., Richmond-Rakerd, L., Sugden, K., Wertz, J., Williams, B. S., & Moffitt, T. E. (2020). Longitudinal Assessment of Mental Health Disorders and Comorbidities Across 4 Decades Among Participants in the Dunedin Birth Cohort Study. *JAMA Network Open*, *3*(4), e203221. https://doi.org/10.1001/jamanetworkopen.2020.3221

Clark, C., Caldwell, T., Power, C., & Stansfeld, S. A. (2010). *Does the Influence of Childhood Adversity on Psychopathology Persist Across the Lifecourse? A 45-Year Prospective Epidemiologic Study*. https://doi.org/10.1016/j.annepidem.2010.02.008

Clark, D. A., Hicks, B. M., Angstadt, M., Rutherford, S., Taxali, A., Hyde, L., Weigard, A. S., Heitzeg, M. M., & Sripada, C. (2021). The General Factor of Psychopathology in the Adolescent Brain Cognitive Development (ABCD) Study: A Comparison of Alternative Modeling Approaches. *Clinical Psychological Science*, *9*(2), 169–182. https://doi.org/10.1177/2167702620959317

Cuijpers, P., Smit, F., Unger, F., Stikkelbroek, Y., ten Have, M., & de Graaf, R. (2011). The disease burden of childhood adversities in adults: A population-based study. *Child Abuse & Neglect*, *35*(11), 937–945. https://doi.org/10.1016/j.chiabu.2011.06.005

Goodman, R., Ford, T., Richards, H., Gatward, R., & Meltzer, H. (2000). The Development and Well-Being Assessment: Description and initial validation of an integrated assessement of child and adolescent psychopathology. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *41*(5), 645–655. https://doi.org/10.1017/S0021963099005909

Green, J. G., Mclaughlin, K. A., Berglund, P. A., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2010). Childhood Adversities and Adult Psychiatric Disorders in the National Comorbidity Survey Replication I. *Archives of General Psychiatry*, *67*(2), 113–123.

Green, J. G., McLaughlin, K. A., Berglund, P. A., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2010). Childhood adversity and adult psychopathology in the National Comorbidity Survey Replication (NCS-R)-I: Associations with first onset of

DSM-IV disorders. *Archives of General Psychiatry*, *67*(2), 1–21. https://doi.org/10.1001/archgenpsychiatry.2009.186.Childhood

Hoffmann, M. S., Moore, T. M., Axelrud, L. K., Zuo, X., Rohde, L. A., Milham, M. P., Satterthwaite, D., & Salum, G. A. (2021). Reliability and Validity of Bifactor Models of Dimensional Psychopathology in Youth from three Continents. *MedRxiv*. https://doi.org/doi.org/10.1101/2021.06.27.21259601

Hogan, A. M., Vargha-Khadem, F., Kirkham, F. J., & Baldeweg, T. (2005). Maturation of action monitoring from adolescence to adulthood: An ERP study. *Developmental Science*, *8*(6), 525–534. https://doi.org/10.1111/j.1467-7687.2005.00444.x

Jaffee, S. R., Ambler, A., Merrick, M., Goldman-Mellor, S., Odgers, C. L., Fisher, H. L., Danese, A., & Arseneault, L. (2018). Childhood Maltreatment Predicts Poor Economic and Educational Outcomes in the Transition to Adulthood. *American Journal of Public Health*, *108*(9), 1142–1147. https://doi.org/10.2105/AJPH.2018.304587

Johnson, D., Policelli, J., Li, M., Dharamsi, A., Hu, Q., Sheridan, M. A., Mclaughlin, K. A., & Wade, M. (2021). *Associations of Early-Life Threat and Deprivation With Executive Functioning in Childhood and Adolescence A Systematic Review and Meta-analysis*. https://doi.org/10.1001/jamapediatrics.2021.2511

Kessler, R. C., Amminger, G. P., Aguilar-Gaxiola, S., Alonso, J., Lee, S., & ??st??n, T. B. (2007). Age of onset of mental disorders: A review of recent literature: *Current Opinion in Psychiatry*, *20*(4), 359–364. https://doi.org/10.1097/YCO.0b013e32816ebc8c

Kessler, R. C., McLaughlin, K. A., Green, J. G., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., Aguilar-Gaxiola, S., Alhamzawi, A. O., Alonso, J., Angermeyer, M., Benjet, C., Bromet, E., Chatterji, S., De Girolamo, G., Demyttenaere, K., Fayyad, J., Florescu, S.,

Gal, G., Gureje, O., … Williams, D. R. (2010). Childhood adversities and adult psychopathology in the WHO world mental health surveys. *British Journal of Psychiatry*, *197*(5), 378–385. https://doi.org/10.1192/bjp.bp.110.080499

Kessler, R. C., McLaughlin, K. A., Green, J. G., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., Aguilar-Gaxiola, S., Alhamzawi, A. O., Alonso, J., Angermeyer, M., Benjet, C., Bromet, E., Chatterji, S., de Girolamo, G., Demyttenaere, K., Fayyad, J., Florescu, S., Gal, G., Gureje, O., … Williams, D. R. (2010). Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *British Journal of Psychiatry*, *197*(5), 378–385. https://doi.org/10.1192/bjp.bp.110.080499

Lansford, J. E., Dodge, K. A., Pettit, G. S., Bates, J. E., Crozier, J., & Kaplow, J. (2002). A 12-Year Prospective Study of the Long-term Effects of Early Child Physical Maltreatment on Psychological, Behavioral, and Academic Problems in Adolescence. *Archives of Pediatrics & Adolescent Medicine*, *156*(8), 824. https://doi.org/10.1001/archpedi.156.8.824

Lewis, S. J., Koenen, K. C., Ambler, A., Arseneault, L., Caspi, A., Fisher, H. L., Moffitt, T. E., & Danese, A. (2021). Unravelling the contribution of complex trauma to psychopathology and cognitive deficits: A cohort study. *The British Journal of Psychiatry*, *219*(2), 448–455. https://doi.org/10.1192/bjp.2021.57

Magruder, K. M., McLaughlin, K. A., & Elmore Borbon, D. L. (2017). Trauma is a public health issue. *European Journal of Psychotraumatology*, *8*(1), 1375338. https://doi.org/10.1080/20008198.2017.1375338

McLaughlin, K. A. (2016a). Future Directions in Childhood Adversity and Youth Psychopathology. *Journal of Clinical Child and Adolescent Psychology*, *45*(3), 361–382. https://doi.org/10.1080/15374416.2015.1110823

McLaughlin, K. A. (2016b). Future Directions in Childhood Adversity and Youth Psychopathology. *Journal of Clinical Child & Adolescent Psychology*, *45*(3), 361–382. https://doi.org/10.1080/15374416.2015.1110823

McLaughlin, K. A., DeCross, S. N., Jovanovic, T., & Tottenham, N. (2019). Mechanisms linking childhood adversity with psychopathology: Learning as an intervention target. *Behaviour Research and Therapy*, *118*(March), 101–109. https://doi.org/10.1016/j.brat.2019.04.008

Mclaughlin, K. A., Green, J. G., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2012). *Childhood Adversities and First Onset of Psychiatric Disorders in a National Sample of US Adolescents*. *69*(11), 1151–1160.

McLaughlin, K. A., Greif Green, J., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2012). Childhood Adversities and First Onset of Psychiatric Disorders in a National Sample of US Adolescents. *Archives of General Psychiatry*, *69*(11), 1151. https://doi.org/10.1001/archgenpsychiatry.2011.2277

Mclaughlin, K. A., & Sheridan, M. A. (2016). *Beyond Cumulative Risk: A Dimensional Approach to Childhood Adversity*. https://doi.org/10.1177/0963721416655883

McLaughlin, K. A., Sheridan, M. A., & Lambert, H. K. (2014). Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. *Neuroscience and Biobehavioral Reviews*, *47*, 578–591. https://doi.org/10.1016/j.neubiorev.2014.10.012

Mclaughlin, K. A., Sheridan, M. A., & Nelson, C. A. (2017). Neglect as a Violation of Species-Expectant Experience: Neurodevelopmental Consequences. *Biological Psychiatry*, *82*(7), 462–471. https://doi.org/10.1016/j.biopsych.2017.02.1096

Miller, A. B., Machlin, L., McLaughlin, K. A., & Sheridan, M. A. (2020). Deprivation and psychopathology in the Fragile Families Study: A 15-year longitudinal investigation. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. https://doi.org/10.1111/jcpp.13260

Miller, A. B., Sheridan, M., Hanson, J. L., Mclaughlin, K. A., Bates, J. E., Lansford, J. E., Pettit, G. S., & Dodge, K. A. (2016). Dimensions of Deprivation and Threat, Psychopathology, and Potential Mediators: A Multi-Year Longitudinal Analysis. *Journal of Abnormal Psychology*, *127*(2), 160–170. https://doi.org/10.1002/cncr.27633.Percutaneous

Nanni, V., Uher, R., Dr, M. U., & Danese, A. (n.d.). Childhood M altreatm ent Predicts Unfavorable Course o f Illness and Treatm ent O utco m e in D epressio n: A M eta-A nalysis. *Am J Psychiatry*, 11.

Nelson, C. A., Scott, R. D., Bhutta, Z. A., Harris, N. B., Danese, A., & Samara, M. (2020). Adversity in childhood is linked to mental and physical health throughout life. *The BMJ*, *371*, 1–9. https://doi.org/10.1136/bmj.m3048

Norman, R. E., Byambaa, M., De, R., Butchart, A., Scott, J., & Vos, T. (2012). The Long-Term Health Consequences of Child Physical Abuse, Emotional Abuse, and Neglect: A Systematic Review and Meta-Analysis. *PLoS Medicine*, *9*(11), e1001349. https://doi.org/10.1371/journal.pmed.1001349

Richards, M., & Wadsworth, M. E. J. (2004). Long term effects of early adversity on cognitive function. *Archives of Disease in Childhood*, *89*(10), 922–927. https://doi.org/10.1136/adc.2003.032490

Romeo, R. R., Leonard, J. A., Robinson, S. T., West, M. R., Mackey, A. P., Rowe, M. L., & Gabrieli, J. D. E. (2018). Beyond the 30-Million-Word Gap: Children's Conversational Exposure Is Associated With Language-Related Brain Function. *Psychological Science*, *29*(5), 700–710. https://doi.org/10.1177/0956797617742725

Salum, G. A., DeSousa, D. A., Manfro, G. G., Pan, P. M., Gadelha, A., Brietzke, E., Miguel, E. C., Mari, J. J., Rosário, M. C. do, & Grassi-Oliveira, R. (2016). Measuring child maltreatment using multi-informant survey data: A higher-order confirmatory factor analysis. *Trends in Psychiatry and Psychotherapy*, *38*(1), 23–32. https://doi.org/10.1590/2237-6089-2015-0036

Salum, G. A., Gadelha, A. R. Y., Pan, P. M., Moriyama, T. S., Graeff-martins, A. N. A. S., Tamanaha, A. N. A. C., Alvarenga, P., Krieger, F. V., Fleitlich-bilyk, B., Jackowski, A., Sato, J. R., Brietzke, E., Polanczyk, G. V., Brentani, H., Mari, J. D. E. J., Conceição, M., Rosário, D. O., Manfro, G. G. U. S., Bressan, R. A., … Rohde, L. A. (2014). High risk cohort study for psychiatric disorders in childhood: Rationale , design , methods and preliminary results. *Int. J. Methods Psychiatr. Res.*, *March*. https://doi.org/10.1002/mpr

Schaefer, J. D., Moffitt, T. E., Arseneault, L., Danese, A., Fisher, H. L., Houts, R., Sheridan, M. A., Wertz, J., & Caspi, A. (2018). Adolescent Victimization and Early-Adult Psychopathology: Approaching Causal Inference Using a Longitudinal Twin Study to Rule Out Noncausal Explanations. *Clinical Psychological Science*, *6*(3), 352–371. https://doi.org/10.1177/2167702617741381

Sheridan, M. A., & Mclaughlin, K. A. (2014). Dimensions of early experience and neural development: Deprivation and threat. *Trends in Cognitive Sciences*, *18*(11), 580–585. https://doi.org/10.1016/j.tics.2014.09.001

Sheridan, M. A., Peverill, M., Finn, A. M. Y. S., & Laughlin, K. A. M. C. (2017). Dimensions of childhood adversity have distinct associations with neural systems underlying executive functioning. *Development and Psychopathology*, *29*, 1777–1794. https://doi.org/10.1017/S0954579417001390

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., Il Shin, J., Kirkbride, J. B., Jones, P., Kim, J. H., Kim, J. Y., Carvalho, A. F., Seeman, M. V., Correll, C. U., & Fusar-Poli, P. (2021). Age at onset of mental disorders worldwide: Large-scale meta-analysis of 192 epidemiological studies. *Molecular Psychiatry*. https://doi.org/10.1038/s41380-021-01161-7

Team, R. C. (2021). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing.

Toplak, M. E., & Tannock, R. (2005). Tapping and Anticipation Performance in Attention Deficit Hyperactivity Disorder. *Perceptual and Motor Skills*, *100*(3), 659–675. https://doi.org/10.2466/pms.100.3.659-675

Vandierendonck, A., Kemps, E., Fastame, M. C., & Szmalec, A. (2004). Working memory components of the Corsi blocks task. *British Journal of Psychology*, *95*(1), 57–79. https://doi.org/10.1348/000712604322779460

Viola, T. W., Salum, G. A., Kluwe-Schiavon, B., Sanvicente-Vieira, B., Levandowski, M. L., & Grassi-Oliveira, R. (2016). The influence of geographical and economic factors in estimates of childhood abuse and neglect using the Childhood Trauma Questionnaire: A

worldwide meta-regression analysis. *Child Abuse & Neglect*, *51*, 1–11. https://doi.org/10.1016/j.chiabu.2015.11.019

Walsh, K., McLaughlin, K. A., Hamilton, A., & Keyes, K. M. (2017). Trauma exposure, incident psychiatric disorders, and disorder transitions in a longitudinal population representative sample. *Journal of Psychiatric Research*, *92*, 212–218. https://doi.org/10.1016/j.jpsychires.2017.05.001

Wechsler, D. (2002). *WISC-III: Escala de Inteligência Wechsler para Crianças: Manual [Wechsler Intelligence Scale for Children-Third Edition]*. Casa do Psicólogo.

Weissman, M. M., Wickramaratne, P., Adams, P., Wolk, S., Verdeli, H., & Olfson, M. (2000). Brief Screening for Family Psychiatric History. *Archives of General Psychiatry*, *57*.

Table 1 – Sample description

	Group 1: From Childhood to Adolescence			Group 2: From Adolescence to Adulthood		
	N	**%**	**Valid N**	**N**	**%**	**Valid N**
Sex: male	659	56	1175	716	54	1336
Site: São Paulo	661	56	1175	595	45	1336

	Group 1: From Childhood to Adolescence (6 to 10 years old; n = 1175)											
	Baseline				**3-year follow-up**				**6-year follow-up**			
	Mean (sd)	**Range**	**Skewness/ Kurtosis**	**Valid N**	**Mean (sd)**	**Range**	**Skewness/ Kurtosis**	**Valid N**	**Mean (sd)**	**Range**	**Skewness/ Kurtosis**	**Valid N**
Age (years)	8.51 (0.92)	5.83 - 10	-0.25, -0.96	1175	11.8 (1.23)	9.21 - 13.87	-0.15, -0.91	945	16.61 (1.06)	13.45 – 18.96	-0.06, -0.66	854
Threat (latent)	-0.01 (0.7)	-1.04 – 2.95	0.81, 0.28	1175								
Deprivation (latent)	0.01 (0.79)	-1.59 – 2.3	0.08, -0.74	1175								
Stressful Life Events					0.09 (0.64)	-0.69, 2.23	0.62, -0.32	945	0.02 (0.65)	-0.98, 1.9	0.29, -0.73	854
Psychopathology (p-factor)	-0.02 (0.88)	-1.52, 2.96	0.36, -0.28	1175	0.07 (0.84)	-1.61, 2.37	0.17, -0.38	945	0.03 (0.86)	-1.58, 3.17	0.44, 0.05	847
Executive functions (latent)	-0.01 (0.68)	-2.36, 1.78	-0.24, -0.03	1117	-0.01 (0.75)	-3.26, 1.64	-0.72, 0.57	849	0 (0.71)	-2.88, 1.73	-0.82, 1.19	760
Group 2: From Adolescence to Adulthood (11 to 14 years old; n = 1336)												
Age (years)	11.69 (1.16)	10 - 14.37	0.35, -1.11	1336	14.99 (1.17)	12.99 - 17.86	0.36, -1	1065	19.76 (1.25)	17.57 – 23.13	0.33, -0.83	947
Threat (latent)	0.12 (0.74)	-1.04 – 2.74	0.68, -0.02	1336								
Deprivation (latent)	0.04 (0.81)	-1.59 – 2.5	0.09, -0.65	1336								
Stressful Life Events					0.02 (0.65)	-0.69, 2.24	0.75, -0.33	1065	0.03 (0.68)	-0.98, 2.94	0.49, -0.01	947
Psychopathology (p-factor)	0.06 (0.92)	-1.52, 3.11	0.38, -0.27	1335	0.08 (0.87)	-1.57, 2.92	0.25, -0.32	1064	0.03 (0.89)	-1.81, 2.81	0.3, -0.22	939
Executive functions (latent)	0.01 (0.65)	-2.52, 2.36	-0.39, 0.53	1281	0.01 (0.66)	-4, 1.52	-1.23, 3.42	925	0 (0.72)	-3.32, 1.93	-0.81, 1.43	792

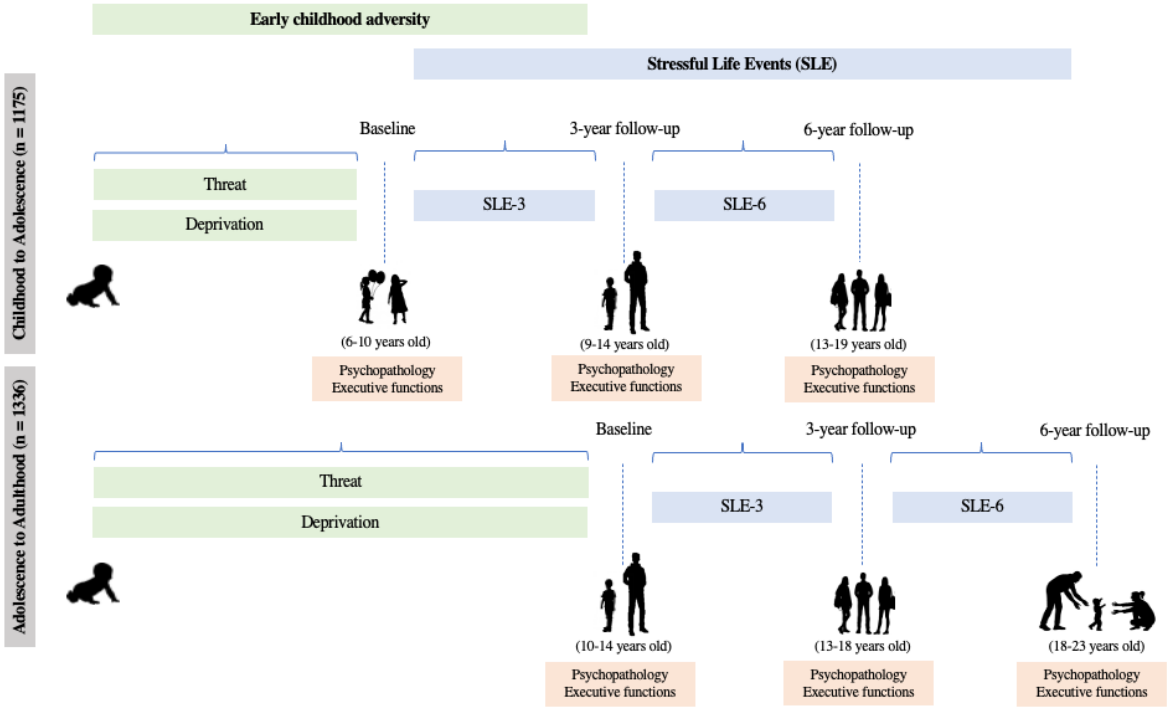
Table 2 – Univariate and Multiple models investigating the predictive effects of childhood adversity on overall levels of psychopathology as measured by the P-factor

	Group 1: Childhood to Adolescence transition (6 – 18 years old; n = 1175)		**Group 2: Adolescence to Adulthood transition (11 – 23 years old; n = 1336)**	
	β	***p value***	**β**	***p value***
Univariate models (two models, each adjusted by levels of P in previous waves)				
Childhood adversity				
Threat	0.046	0.310	**0.139**	**<0.001**
Deprivation	0.064	0.081	0.046	0.175
Multiple model (a single model with all exposures, interactions and covariates)				
Childhood adversity				
Threat	0.033	0.473	**0.101**	**0.017**
Deprivation	0.039	0.294	-0.012	0.744
Stress-full Life events				
SLEs-3	-0.041	0.369	**-0.094**	**0.038**
SLEs-6	**0.339**	**<0.001**	**0.248**	**<0.001**
Interactive effects				
SLEs-3*threat	-0.088	0.152	0.043	0.441
SLEs-3*deprivation	-0.042	0.463	-0.021	0.700
SLEs-6*threat	-0.016	0.806	-0.040	0.441
SLEs-6*deprivation	0.018	0.764	0.058	0.301
Covariates				
Age	-0.053	0.036	-0.001	0.975
Gender	**0.296**	**<0.001**	**0.228**	**<0.001**
EF-base	**0.115**	**<0.001**	**0.119**	**<0.001**
EF-3	**0.372**	**<0.001**	**0.407**	**<0.001**

Table 3 – Univariate and Multiple model investigating the predictive effects of childhood adversity on overall executive functions (EF)

	Group 1: Childhood to Adolescence transition (6 – 18 years old; n = 1175)		**Group 2: Adolescence to Adulthood transition (11 – 23 years old; n = 1336)**	
	β	***p value***	**β**	***p value***
Univariate models (two models, each adjusted by levels of EF in previous waves)				
Childhood adversity				
Threat	-0.003	0.924	**-0.074**	**0.020**
Deprivation	**-0.068**	**0.023**	**-0.104**	**<0.001**
Multiple model (a single model with all exposures, interactions and covariates)				
Childhood adversity				
Threat	0.031	0.413	-0.020	0.576
Deprivation	-0.064	0.054	**-0.081**	**0.010**
Stress-full Life events				
SLEs-3	-0.027	0.475	-0.009	0.823
SLEs-6	-0.022	0.569	-0.064	0.095
Interactive effects				
SLEs-3*threat	-0.037	0.501	0.020	0.671
SLEs-3*deprivation	-0.036	0.465	-0.074	0.105
SLEs-6*threat	0.028	0.633	-0.021	0.685
SLEs-6*deprivation	0.011	0.828	0.054	0.261
Covariates				
Age	0.025	0.262	-0.004	0.811
Gender	**-0.108**	**0.025**	-0.076	0.092
EF-base	**0.251**	**<0.001**	**0.292**	**<0.001**
EF-3	**0.373**	**<0.001**	**0.381**	**<0.001**

Figure 1: Study's sample and data collection design



Supplemental Material

1. Childhood adversity: threat and deprivation

Threat and deprivation variables were selected according to documented theoretical models in order to encompass both dimensions of childhood adversity. Selected variables, their label and ranges are described below (Supplemental Table S1), as well as descriptive data for each selected variable (Supplemental Table S2).

Confirmatory factor analysis, using the full maximum likelihood to deal with missing data, were conducted and the threat and deprivation model was available for 2511 participants, and at follow up 2010 participants (Supplemental Figure S1). Both latent factors were significantly correlated ($r= 0.404$, $p <0.001$).

Supplemental Table S1 – Threat and Deprivation variable description

Variable	Label	Response options
Threat		
Bullying exposure (parent and child report)	Has the child ever been bullied in his life? Have you ever been bullied in your life?	No Yes
DAWBA: Physical abuse	Has the child ever suffered physical violence (maltreatment) that he/she remembers?	No Yes
Physical abuse (parent and child report)	Has your child been seriously picked up by an adult (including yourself), to the point of leaving marks in his body? Have you ever been seriously picked up by an adult, to the point of leaving marks in your body?	Never Yes, once or twice Yes, from time to time Yes, often happen
Emotional abuse (parent and child report)	Has your child ever been cursed by some adult, with words like 'ass', 'idiot', 'stupid', or being yelled that he/she was no good? Have you ever been cursed by some adult, with words like 'ass', 'idiot', 'stupid', or being yelled that you were no good?	Never Yes, once or twice Yes, from time to time Yes, often happen
DAWBA: Sexual abuse	Has the child ever been exposed to sexual abuse?	No Yes
Sexual abuse	Has anybody ever done sexual things with your child, or have threatened your child if he/she didn't do sexual things?	Never Yes, once or twice Yes, from time to time Yes, often happen
DAWBA: Attack or threat	Has the child ever been attacked or threatened?	No Yes
DAWBA: Domestic violence witnessing	Has the child ever witnessed serious domestic violence?	No Yes
DAWBA: Attack witnessing	Has the child ever seen a family member, or friend being seriously attacked, or threatened?	No Yes

Table continues on next page

Supplemental Table S1 – Threat and Deprivation variable description

Variable	Label	Response options
Deprivation		
Mother's educational level	Mother's educational level	Higher education (university and postgraduation) Up to High School education Up to Middle School education Without study
ABEP 2009: Stratified Score	Socio economic class	D/E (poorest) C A/B (wealthiest)
Father status	What is the current contact status of the child's father?	In contact No-contact Deceased Unknown
Neglect	Has it ever happened to your child of not having anything to eat and/or having to wear dirty or torn clothes? Has it ever happened to you of not having anything to eat and/or having to wear dirty or torn clothes?	Never Yes, once or twice Yes, from time to time Yes, often happens
Family income	What is the family total income?	Divided into quintiles

Note*:* DAWBA (Development and Well-being Assessment; ABEP (Brazilian Economic Classification).

Supplemental Table S2 – Threat and Deprivation variable frequency

	Parent Report				Child report			
	N	**%**	**Valid N**	**Missing**	**N**	**%**	**Valid N**	**Missing**
Bullying exposure: yes	950	38.7	2455	56	709	32.1	2207	304
Physical abuse (DAWBA): yes	86	3.4	2511	-				
Physical abuse								
Never	2139	85.3	2507	4	1886	85	2218	293
Yes, once or twice	293	11.7			196	0.9		
Yes, from time to time	66	2.6			105	0.5		
Yes, it often happens	9	0.4			31	0.1		
Emotional abuse								
Never	1397	55.7	2510	1	1702	76.7	2219	292
Yes, once or twice	443	17.6			254	11.9		
Yes, from time to time	524	20.9			182	0.8		
Yes, it often happens	146	5.8			71	0.3		
Sexual abuse total: yes	63	0.3	2500	11				
Attack or threat (DAWBA): yes	97	3.9	2511	-				
Domestic violence witnessing (DAWBA): yes	177	7	2511	-				
Attack witnessing (DAWBA): yes	101	4	2511	-				
Mother's educational level								
Higher education	85	0.3	2483	28				
Up to High School education	934	37.6						
Up to Middle School education	857	34.5						
Up to Elementary or no education	607	24.4						

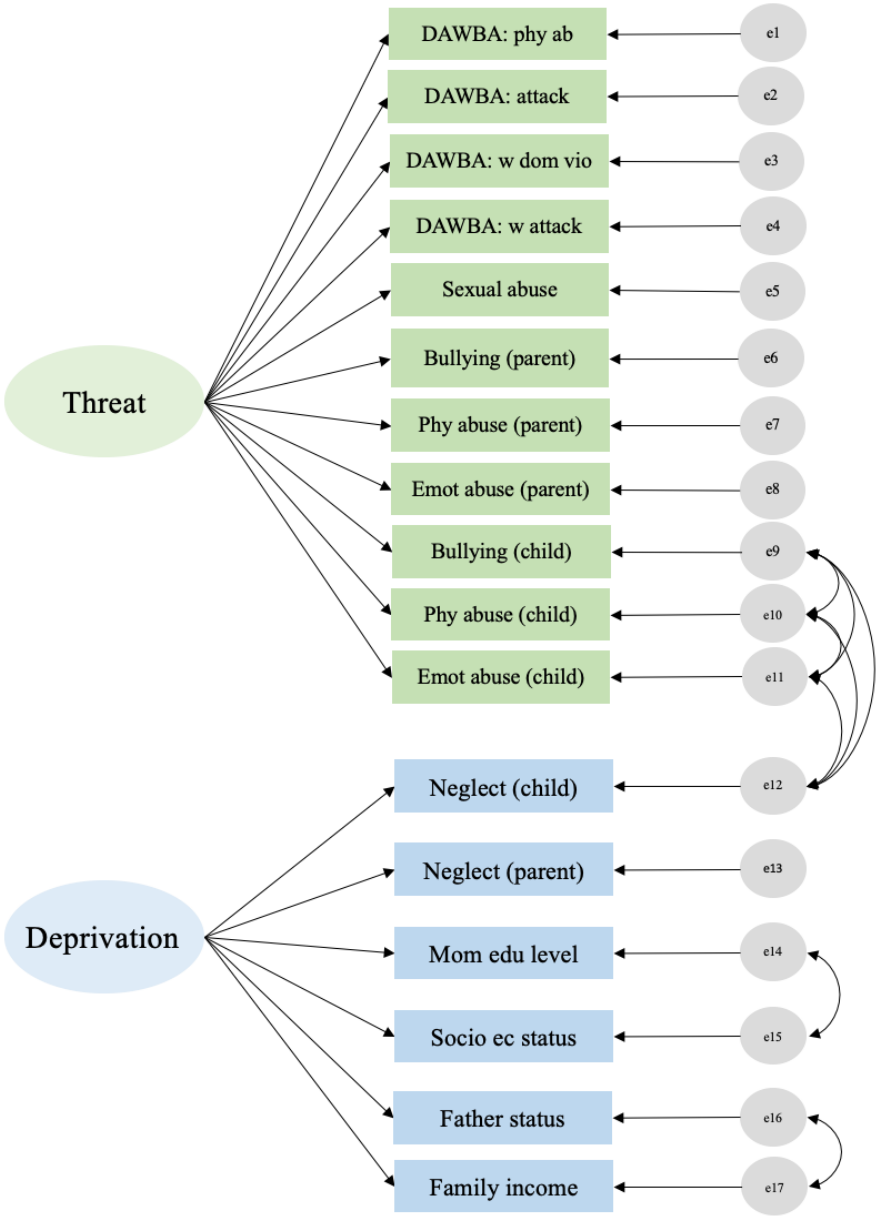
Table continues on next page

Supplemental Table S2 – Threat and Deprivation variable frequency

	Parent Report				Child report			
	N	%	Valid N	Missing	N	%	Valid N	Missing
ABEP 2009: Stratified Score								
A/B	998	39.7	2511	-				
C	1435	57.1						
D/E	78	3.1						
Father status								
In-contact	1836	73.1	2511	-				
No-contact	427	17						
Deceased	130	5.2						
Unknown	118	4.7						
Neglect								
Never	2261	90	2511	-	2082	93.9	2217	294
Yes, once or twice	176	7			90	0.4		
Yes, from time to time	61	2.4			38	0.2		
Yes, it often happens	13	0.5			7	0.03		

Note: DAWBA (Development and Well-being Assessment; ABEP (Brazilian Economic Classification).

Supplemental Figure S1 – Baseline and follow-up Threat and Deprivation model depiction



The model had acceptable fit indexes (CFI = 0.937, TLI = 0.922, RMSEA = 0.032), with all indicators presenting significant contributions to each distinct construct. Detailed information about the model is provided in Supplemental Table S3.

Supplemental Table S3 - Factor loadings of the Threat and Deprivation Model

	Estimate	S.E.	Est./S.E.	*p*-value
Threat				
Bullying exposure (parent report)	0.483	0.033	14.650	<0.001
Bullying exposure (child report)	0.159	0.039	4.123	<0.001
DAWBA: Physical abuse	0.830	0.037	22.399	<0.001
Physical abuse (parent report)	0.658	0.038	17.383	<0.001
Physical abuse (child report)	0.245	0.044	5.589	<0.001
Emotional abuse (parent report)	0.542	0.028	19.038	<0.001
Emotional abuse (child report)	0.229	0.038	5.962	<0.001
Sexual abuse (total)	0.559	0.061	9.090	<0.001
DAWBA: Attack or threat	0.522	0.049	10.656	<0.001
DAWBA: Domestic violence witnessing	0.666	0.037	17.929	<0.001
DAWBA: Attack witnessing	0.685	0.042	16.414	<0.001
Deprivation				
Mother's educational level	0.327	0.033	10.020	<0.001
ABEP 2009: Stratified Score	0.616	0.035	17.582	<0.001
Father status	0.408	0.043	9.429	<0.001
Neglect (parent report)	0.673	0.047	14.399	<0.001
Neglect (child report)	0.201	0.057	3.554	<0.001
Family income	0.975	0.065	14.936	<0.001

Model fit baseline: CFI = 0.937, TLI= 0.922, RMSEA= 0.032
Note: all variables that were informed by the children were correlated in the model. DAWBA (Development and Well-being Assessment); ABEP (Brazilian Economic Classification).

2. Other form of adversity: Stressful Life Events (SLEs)

The Stressful Life Events (SLEs) variable was calculated using a Life History Schedule answered by the children's parents at the 3- and 6-year follow-ups. Parents reported on the exposure to different SLEs (Supplemental Table S4) over the three years prior to both evaluations.

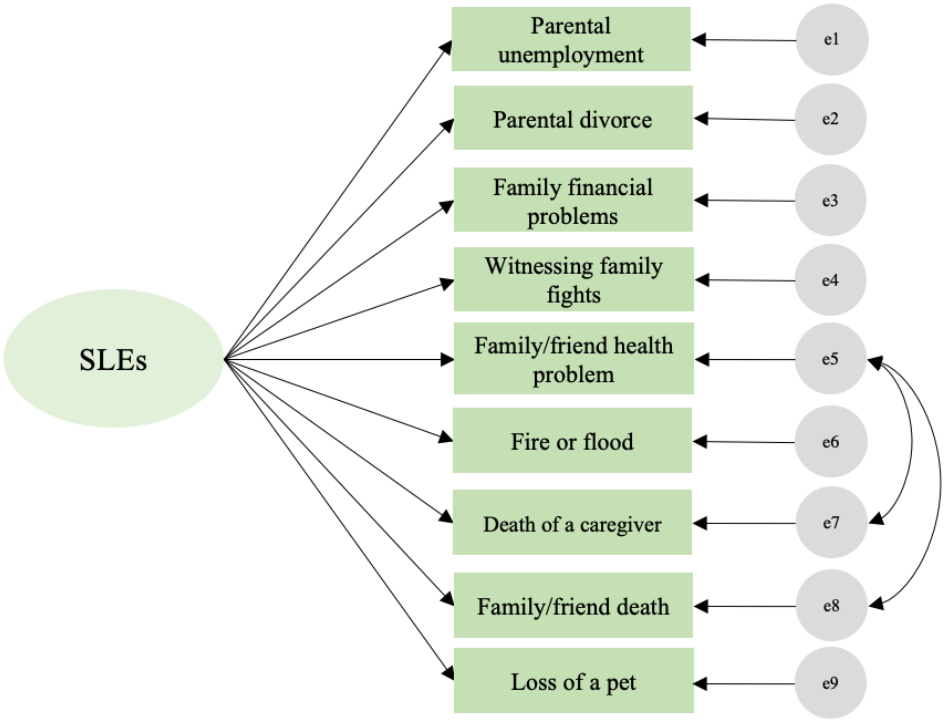
Supplemental Table S4 – SLEs indicators frequencies

	3-year follow-up (*n* = 2010)		**6-year follow-up** (*n* = 1801)	
	n	**%**	**n**	**%**
Moved homes	578	28.8	697	38
Parental unemployment	414	20.6	752	41.8
Parental divorce	179	8.9	150	8.3
Family serious financial problems	434	21.6	598	33.2
Witnessing constant fights among Family members	357	17.8	415	23
Serious health issue with family member or close friend	658	32.7	813	45.1
Being a victim of a robbery or assault	219	10.9	562	31.2
Being a victim of physical violence during a robbery or assault	19	0.9	68	3.8
Being in a car accident	52	2.6	90	5
Having the house on fire or flooded (or any other natural catastrophe)	44	2.2	56	3.1
Death of a caregivers	58	2.9	114	6.3
Death of a family member or close friend	837	41.6	1013	56.2
Loss of a pet (death/disappearance)	563	28	562	31.2

Exploratory factor analyses (EFA) were conducted using the sample from the state of Rio Grande do Sul as a discovery sample extracting four, three, two, and one factor. The one-factor solution was chosen excluding items that did not load significantly into this factor, yielding a nine-indicator model. A confirmatory factor analysis was first conducted with the sample from the state of São Paulo at the 3-year follow-up (CFI = 0.979, TLI = 0.970, RMSEA = 0.017) and then with the whole sample at the 3-year follow-up (CFI = 0.953, TLI = 0.932, RMSEA = 0.026) and at the 6-year follow-up (CFI

= 0.925, TLI = 0.892, RMSEA = 0.037). Factor loadings are presented in the Supplemental Table S5 and the final model is depicted in the Supplemental Figure S2.

Supplemental Figure S2 – Baseline and follow-up Stressful Life Events (SLEs) model depiction



Supplemental Table S5 - Factor loadings of the stressful life events (SLEs) variable

	3-year follow-up			6-year follow-up		
	Estimate	**S.E.**	***p-value***	**Estimate**	**S.E.**	***p-value***
SLEs						
Family's financial problem	0.729	0.042	<0.001	0.666	0.046	<0.001
Constant fights in the family	0.581	0.042	<0.001	0.460	0.043	<0.001
Relative or friend's health problem	0.301	0.042	<0.001	0.230	0.043	<0.001
House burned down/flooded	0.442	0.083	<0.001	0.268	0.087	<0.001
Parental job loss	0.456	0.043	<0.001	0.371	0.040	<0.001
Relative or friend's death	0.238	0.042	<0.001	0.294	0.042	<0.001
Loss of a pet	0.319	0.043	<0.001	0.445	0.042	<0.001
Parental divorce	0.323	0.057	<0.001	0.275	0.052	<0.001
Parental or caregiver death	0.157	0.083	<0.001	0.270	0.056	<0.001

3-year follow-up: CFI = 0.953, TLI = 0.932, RMSEA = 0.026; 6-year follow-up: CFI = 0.925, TLI = 0.892, RMSEA = 0.037

3. Psychopathology

Confirmatory factor analysis, using the diagonally weighted least squares (DWLS) estimator, were conducted using CBCL baseline and follow-up data using a bifactor model in which all items are loaded in a general factor (the "p" factor) and residuals variance is captured by internalizing and externalizing domains as outlined by the CBCL scoring system. The psychopathology model at baseline was available for 2511 participants and showed adequate fit indexes (CFI= 0.984, TLI= 0.983, RMSEA= 0.020, SRMR = 0.044). The psychopathology model at follow up was available for 2010 participants and also showed adequate fit indexes (CFI= 0.973, TLI= 0.972, RMSEA= 0.025, SRMR = 0.051). Factor loadings for baseline and follow-up data are found on Supplemental Table S3.

Supplemental Table S3 - Factor loadings of the General Psychopathology Model

	Baseline				Follow-up			
	Estimate	**S.E.**	***p-value***	**β**	**Estimate**	**S.E.**	***p-value***	**β**
Psychopathology								
CBCL14	0.293	0.006	<0.001	0.468	0.242	0.006	<0.001	0.453
CBCL29	0.174	0.006	<0.001	0.259	0.133	0.006	<0.001	0.223
CBCL30	0.067	0.003	<0.001	0.212	0.051	0.003	<0.001	0.187
CBCL31	0.101	0.004	<0.001	0.201	0.054	0.005	<0.001	0.110
CBCL32	0.118	0.005	<0.001	0.192	0.062	0.006	<0.001	0.097
CBCL33	0.482	0.007	<0.001	0.696	0.425	0.007	<0.001	0.641
CBCL35	0.298	0.006	<0.001	0.579	0.264	0.006	<0.001	0.515
CBCL45	0.491	0.007	<0.001	0.688	0.471	0.007	<0.001	0.660
CBCL50	0.341	0.007	<0.001	0.493	0.294	0.007	<0.001	0.434
CBCL52	0.148	0.004	<0.001	0.387	0.105	0.004	<0.001	0.296
CBCL71	0.249	0.006	<0.001	0.398	0.192	0.007	<0.001	0.291
CBCL91	0.118	0.004	<0.001	0.356	0.099	0.004	<0.001	0.367
CBCL112	0.189	0.005	<0.001	0.325	0.193	0.006	<0.001	0.324
CBCL5	0.343	0.006	<0.001	0.559	0.344	0.007	<0.001	0.526
CBCL42	0.184	0.005	<0.001	0.347	0.233	0.006	<0.001	0.371
CBCL65	0.220	0.005	<0.001	0.440	0.231	0.006	<0.001	0.425
CBCL69	0.251	0.006	<0.001	0.381	0.252	0.007	<0.001	0.339
CBCL75	0.154	0.006	<0.001	0.245	0.067	0.006	<0.001	0.100
CBCL102	0.117	0.004	<0.001	0.306	0.147	0.005	<0.001	0.321
CBCL103	0.207	0.005	<0.001	0.435	0.224	0.006	<0.001	0.483
CBCL111	0.134	0.004	<0.001	0.335	0.139	0.005	<0.001	0.321
CBCL47	0.249	0.006	<0.001	0.439	0.152	0.005	<0.001	0.333
CBCL49	0.123	0.005	<0.001	0.234	0.081	0.005	<0.001	0.161
CBCL51	0.136	0.004	<0.001	0.337	0.143	0.005	<0.001	0.337
CBCL54	0.341	0.006	<0.001	0.563	0.328	0.007	<0.001	0.494
CBCL56a	0.160	0.005	<0.001	0.344	0.143	0.005	<0.001	0.304
CBCL56b	0.280	0.006	<0.001	0.399	0.245	0.006	<0.001	0.356
CBCL56c	0.157	0.005	<0.001	0.320	0.150	0.005	<0.001	0.311
CBCL56d	0.125	0.004	<0.001	0.273	0.058	0.003	<0.001	0.174

Table continues on next page

Supplemental Table S3 - Factor loadings of the General Psychopathology Model

	Baseline				Follow-up			
	Estimate	**S.E.**	***p-value***	**β**	**Estimate**	**S.E.**	***p-value***	**β**
CBCL56e	0.088	0.004	<0.001	0.191	0.047	0.004	<0.001	0.112
CBCL56f	0.212	0.005	<0.001	0.371	0.172	0.006	<0.001	0.314
CBCL56g	0.091	0.004	<0.001	0.252	0.058	0.003	<0.001	0.196
CBCL2	0.017	0.002	<0.001	0.098	0.063	0.004	<0.001	0.199
CBCL26	0.273	0.006	<0.001	0.467	0.249	0.006	<0.001	0.448
CBCL28	0.312	0.006	<0.001	0.517	0.367	0.007	<0.001	0.588
CBCL39	0.061	0.003	<0.001	0.206	0.087	0.004	<0.001	0.239
CBCL43	0.213	0.006	<0.001	0.366	0.245	0.007	<0.001	0.451
CBCL63	0.249	0.006	<0.001	0.378	0.262	0.007	<0.001	0.374
CBCL67	0.040	0.002	<0.001	0.171	0.052	0.003	<0.001	0.212
CBCL72	0.064	0.003	<0.001	0.246	0.022	0.002	<0.001	0.130
CBCL73	0.028	0.002	<0.001	0.155	0.003	0.001	<0.001	0.032
CBCL81	0.036	0.003	<0.001	0.137	0.021	0.002	<0.001	0.117
CBCL82	0.033	0.002	<0.001	0.141	0.006	0.002	<0.001	0.042
CBCL90	0.265	0.006	<0.001	0.469	0.325	0.007	<0.001	0.511
CBCL96	0.056	0.003	<0.001	0.213	0.043	0.002	<0.001	0.181
CBCL99	0.008	0.001	<0.001	0.065	0.015	0.002	<0.001	0.079
CBCL101	0.074	0.003	<0.001	0.258	0.114	0.005	<0.001	0.283
CBCL105	0.009	0.001	<0.001	0.073	0.011	0.002	<0.001	0.074
CBCL106	0.027	0.002	<0.001	0.160	0.007	0.001	<0.001	0.062
CBCL3	0.456	0.007	<0.001	0.585	0.404	0.007	<0.001	0.534
CBCL16	0.069	0.003	<0.001	0.236	0.049	0.003	<0.001	0.233
CBCL19	0.481	0.007	<0.001	0.661	0.384	0.007	<0.001	0.579
CBCL20	0.220	0.006	<0.001	0.402	0.149	0.005	<0.001	0.355
CBCL21	0.181	0.005	<0.001	0.387	0.117	0.005	<0.001	0.317
CBCL22	0.346	0.006	<0.001	0.522	0.395	0.007	<0.001	0.622
CBCL23	0.214	0.006	<0.001	0.372	0.230	0.007	<0.001	0.408
CBCL37	0.182	0.005	<0.001	0.383	0.140	0.005	<0.001	0.350
CBCL57	0.083	0.004	<0.001	0.258	0.078	0.004	<0.001	0.288
CBCL68	0.338	0.006	<0.001	0.533	0.347	0.007	<0.001	0.565

Table continues on next page

Supplemental Table S3 - Factor loadings of the General Psychopathology Model

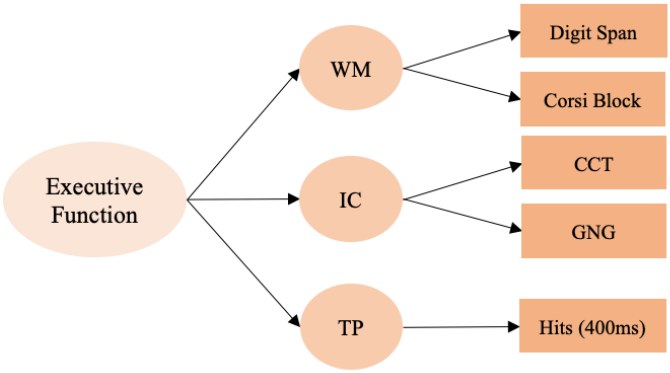
	Baseline				Follow-up			
	Estimate	**S.E.**	***p-value***	**β**	**Estimate**	**S.E.**	***p-value***	**β**
CBCL86	0.520	0.007	<0.001	0.707	0.523	0.007	<0.001	0.729
CBCL87	0.513	0.007	<0.001	0.770	0.497	0.008	<0.001	0.717
CBCL88	0.574	0.007	<0.001	0.773	0.552	0.008	<0.001	0.749
CBCL89	0.431	0.007	<0.001	0.677	0.397	0.007	<0.001	0.605
CBCL94	0.274	0.006	<0.001	0.447	0.230	0.007	<0.001	0.369
CBCL95	0.479	0.007	<0.001	0.681	0.528	0.008	<0.001	0.743
CBCL97	0.063	0.003	<0.001	0.250	0.049	0.003	<0.001	0.229
CBCL104	0.301	0.006	<0.001	0.449	0.300	0.007	<0.001	0.478

4. Executive Function

Six executive function tasks were used as measures of working memory, inhibitory control and temporal processing. Missing data differs from one task to another over both time points due to assessment being performed over four sessions at baseline.

Executive function was derived from a second order model encompassing working memory inhibitory control and temporal processing at baseline and follow up. Due to the differing variability of the executive function tasks, scores were standardized regressing using General Additive Models regressing out effects of age and gender on the task parameters. Working memory and inhibitory control dimensions were encompassed by two cognitive tasks each, while the temporal processing dimension was encompassed by one task (Supplemental Figure S2).

Supplemental Figure S2 –Executive Function Model



Confirmatory factor analysis, using the full maximum likelihood to deal with missing data, were conducted using baseline and follow-up data. The executive function model at baseline was available for 2396 participants and showed adequate fit indexes (CFI= 1.000, TLI= 0.999, RMSEA= 0.007, SRMR = 0.007), and the follow up model was available for 1880 participants and also showed good fit indexes (CFI= 1.000, TLI= 1.006, RMSEA= 0.000, SRMR = 0.004.). Factor loadings are shown on Supplemental Table S4.

Supplemental Table S4 – Standardized factor loadings of the baseline Executive Function Model

	Baseline			**Follow-up**		
	λ	**S.E.**	***p*-value**	**λ**	**S.E.**	***p*-value**
Working Memory (WM)						
Digit span (back)	0.644	0.038	<0.001	0.703	0.024	<0.001
Corsi blocks (back)	0.650	0.039	<0.001	0.787	0.025	<0.001
Inhibitory Control (IC)						
CCT (% Inhibitions, inverse)	0.935	0.082	<0.001	0.577	0.043	<0.001
GNG (% Comission)	-0.424	0.027	<0.001	-0.471	0.038	<0.001
Temporal Processing (TP)						
Hits (400ms)	1.000	0.020	<0.001	1.000	0.000	<0.001
Executive Function						
WM	0.660	0.112	<0.001	0.721	0.046	<0.001
IC	0.504	0.079	<0.001	0.652	0.053	<0.001
TP	0.459	0.049	<0.001	0.590	0.039	<0.001

We conducted a series of Confirmatory Factor Analysis testing unidimensional models of each one of the tasks included in the study, as well as calculated the Cronbach's Alpha and Omega for each of the tasks. CFI and TLI values higher than 0.9, RMSEA lower than 0.06 and SRMR lower than 0.08 indicate adequate model fit (Hu & Bentler, 1999). For both, alpha and omega coefficients, values indicating good reliability are those above 0.70 (Lucke, 2005).

Supplemental Table S5 – Executive Functions tasks reliability

	CFI	TLI	RMSEA	SRMR	α	ω
Working Memory (WM)						
Digit span (back)	0.989	0.982	0.040	0.115	0.934	0.725
Corsi blocks (back)	0.980	0.967	0.078	0.154	0.903	0.807
Inhibitory Control (IC)						
CCT (% Inhibitions, inverse)	0.992	0.991	0.011	0.019	0.812	0.813
GNG (% Comission)	0.994	0.992	0.018	0.034	0.897	0.803
Temporal Processing (TP)						
Hits (400ms)	0.978	0.973	0.024	0.036	0.823	0.719

5. Associations of threat and deprivation with psychopathology and executive functions

Supplemental Table S6 – Spearman correlations among predictors, outcomes and covariates

Group 1: From Childhood to Adolescence (6 to 18 years of age; n = 1175)										
	1. Threat	**2. Deprivation**	**3. SLEs-3**	**4. SLEs-6**	**5. P-base**	**6. P.3**	**7. P-6**	**8. EF-base**	**9. EF-3**	**10. EF-6**
2. Deprivation	**0.404*** **	**-**								
3. SLEs-3	**0.167*** **	**0.100** **	**-**							
4. SLEs-6	**0.160*** **	**0.092** **	**0.250*** **	**-**						
5. P-base	**0.411*** **	**0.191*** **	**0.149*** **	**0.130*** **	**-**					
6. P-3	**0.326*** **	**0.183*** **	**0.345*** **	**0.187*** **	**0.389*** **	**-**				
7. P-6	**0.241*** **	**0.165*** **	**0.198*** **	**0.350*** **	**0.272*** **	**0.467*** **	**-**			
8. EF-base	**-0.092** **	**-0.148*** **	**-0.065***	**-0.121*** **	**-0.078** **	**-0.103** **	**-0.147*** **	**-**		
9. EF-3	-0.056	**-0.160*** **	-0.042	-0.053	**-0.096** **	**-0.111** **	**-0.079***	**0.483*** **	**-**	
10. EF-6	-0.020	**-0.166*** **	-0.070	-0.068	-0.043	**-0.160*** **	**-0.134*** **	**0.414*** **	**0.492*** **	**-**

Continue next page

Supplemental Table S6 – Spearman correlations among predictors, outcomes and covariates

	Group 2: From Adolescence to Adulthood (11 to 23 years of age; n = 1336)									
	1. Threat	**2. Deprivation**	**3. SLEs-3**	**4. SLEs-6**	**5. P-base**	**6. P.3**	**7. P-6**	**8. EF-base**	**9. EF-3**	**10. EF-6**
2. Deprivation	**0.391*** **	**-**								
3. SLEs-3	**0.176*** **	**0.126*** **	**-**							
4. SLEs-6	**0.276*** **	**0.187*** **	**0.291*** **	**-**						
5. P-base	**0.443*** **	**0.163*** **	**144*** **	**0.144*** **	**-**					
6. P-3	**0.274*** **	**0.167*** **	**0.298*** **	**0.230*** **	**0.399*** **	**-**				
7. P-6	**0.273*** **	**0.127*** **	**0.134*** **	**0.273*** **	**0.344*** **	**0.509*** **	**-**			
8. EF-base	**-0.085** **	**-0.150*** **	-0.041	-0.007	**-0.083** **	**-0.091** **	**-0.066***	**-**		
9. EF-3	**-0.112*** **	**-0.129*** **	**-0.065***	**-0.091** **	**-0.164*** **	**-0.112** **	**-0.169*** **	**0.420*** **	**-**	
10. EF-6	**-0.105** **	**-0.172*** **	**-0.076***	**-0.118** **	**-0.120*** **	**-0.106** **	**-0.124** **	**0.413*** **	**0.435*** **	**-**

Note: *p<0.05, **p <0.01, ***p < 0.001

Table 4 – Univariate and Multiple models investigating the predictive effects of childhood adversity and Stressful Life Events on overall levels of psychopathology as measured by the P-factor

	Group 1: Childhood to Adolescence transition (6 – 18 years old; n = 1175)				**Group 2: Adolescence to Adulthood transition (11 – 23 years old; ; n = 1336)**			
	3-year follow-up (9 to 14 years)		**6-year follow-up (13 to 18 years)**		**3-year follow-up (13 to 18 years)**		**6-year follow-up (17 to 23 years)**	
	β	***p value***	**β**	***p value***	**β**	***p value***	**β**	***p value***
Univariate models (four models, each adjusted by levels of P in previous waves)								
Childhood adversity								
Threat	**0.235**	**<0.001**	0.046	0.310	**0.154**	**<0.001**	**0.139**	**<0.001**
Deprivation	**0.131**	**<0.001**	0.064	0.081	**0.110**	**<0.001**	0.046	0.175
Multiple model (a single model with all exposures, interactions and covariates)								
Childhood adversity								
Threat	**0.182**	**<0.001**	0.033	0.473	**0.089**	**0.019**	**0.101**	**0.017**
Deprivation	0.053	0.104	0.039	0.294	0.054	0.092	-0.012	0.744
Stress-full Life events								
SLEs-3	**0.355**	**<0.001**	-0.041	0.369	**0.291**	**<0.001**	**-0.094**	**0.038**
SLEs-6	.	.	**0.339**	**<0.001**	**.**	**.**	**0.248**	**<0.001**
Interactive effects								
SLEs-3*threat	-0.088	0.096	-0.088	0.152	0.016	0.751	0.043	0.441
SLEs-3*deprivation	-0.003	0.950	-0.042	0.463	-0.082	0.080	-0.021	0.700
SLEs-6*threat	.	.	-0.016	0.806	.	.	-0.040	0.441
SLEs-6*deprivation	.	.	0.018	0.764	.	.	0.058	0.301
Covariates								
Age	0.026	0.285	-0.053	0.036	**-0.046**	**0.021**	-0.001	0.975
Gender	**0.146**	**0.002**	**0.296**	**<0.001**	**0.216**	**<0.001**	**0.228**	**<0.001**
P-base	**0.287**	**<0.001**	**0.115**	**<0.001**	**0.311**	**<0.001**	**0.119**	**<0.001**
P-3	-	-	**0.372**	**<0.001**	-	-	**0.407**	**<0.001**

Table 5 – Univariate and Multiple model investigating the predictive effects of childhood adversity and Stressful Life Events on overall executive functions (EF)

	Group 1: Childhood to Adolescence transition (6 – 18 years old; n = 1175)				**Group 2: Adolescence to Adulthood transition (11 – 23 years old; ; n = 1336)**			
	3-year follow-up (9 to 14 years)		**6-year follow-up (13 to 18 years)**		**3-year follow-up (13 to 18 years)**		**6-year follow-up (17 to 23 years)**	
	β	***p value***	**β**	***p value***	**β**	***p value***	**β**	***p value***
Univariate models (four models, each adjusted by levels of EF in previous waves)								
Childhood adversity								
Threat	-0.021	0.338	-0.003	0.924	**-0.072**	**0.006**	**-0.074**	**0.020**
Deprivation	**-0.099**	**0.001**	**-0.068**	**0.023**	-0.046	0.061	**-0.104**	**<0.001**
Multiple model (a single model with all exposures, interactions and covariates)								
Childhood adversity								
Threat	0.010	0.781	0.031	0.413	**-0.058**	**0.046**	-0.020	0.576
Deprivation	**-0.106**	**0.001**	-0.064	0.054	-0.013	0.615	**-0.081**	**0.010**
Stress-full Life events								
SLEs-3	-0.050	0.167	-0.027	0.475	-0.057	0.070	-0.009	0.823
SLEs-6	.	.	-0.022	0.569	**.**	**.**	-0.064	0.095
Interactive effects								
SLEs-3*threat	0.095	0.070	-0.037	0.501	0.052	0.207	0.020	0.671
SLEs-3*deprivation	0.005	0.910	-0.036	0.465	-0.066	0.088	-0.074	0.105
SLEs-6*threat	.	.	0.028	0.633	.	.	-0.021	0.685
SLEs-6*deprivation	.	.	0.011	0.828	.	.	0.054	0.261
Covariates								
Age	0.027	0.255	0.025	0.262	-0.016	0.327	-0.004	0.811
Gender	0.040	0.379	**-0.108**	**0.025**	-0.041	0.297	-0.076	0.092
EF-base	**0.521**	**<0.001**	**0.251**	**<0.001**	**0.490**	**<0.001**	**0.292**	**<0.001**
EF-3	-	-	**0.373**	**<0.001**	-	-	**0.381**	**<0.001**

6. FINAL CONSIDERATIONS AND CONCLUSION

This thesis had the main objective to investigate cross-sectional and longitudinal associations of childhood adversity measured as threat and deprivation with psychopathology, emotional processing, and distinct aspects of cognition (measured as executive functions). Extending previous literature, this thesis was able to demonstrate differential associations of threat and deprivation with psychopathology, emotional processing, and cognitive development across childhood, adolescence, and young adulthood.

Findings from article #1 suggest that higher levels of threat are more strongly associated with psychopathology, both cross-sectionally and three years later when compared to deprivation, and only higher levels of deprivation were associated with worse performance in EF tasks. Additional exploratory analysis indicated a possible mediation effect of higher levels of deprivation with higher levels of psychopathology three years later via worse performance on executive functions tasks. Moreover, article #2 showed that adversity exposure clusters within individuals by showing that threat and deprivation exposure predicts three and six years later exposure to other stressful life events (SLE). Also, in accordance to article #1, results for article #2 showed that exposure to threat in childhood predicted long-lasting associations with incident psychopathology at 6-years follow-up, and exposure to deprivation in childhood predicted long-lasting incident lower performance in EF tasks in 6-years.

Results from these studies support the comprehension that childhood adversity is a complex phenomenon with meaningful influences across the life span. Because it can take many forms, dimensional models – as the one investigated in these studies – might help to disentangle the specific developmental correlates of different

dimensions of childhood adversity informing target specific interventions capable of buffering the negative outcomes associated with adversity experiences.

7. APPENDIX

7.1. Other articles published as a collaborator during the doctorate period

7.1.1. Appendix Article #1 (first page)

Published at ***European Child & Adolescent Psychiatry***

European Child & Adolescent Psychiatry
November 2020 – Brief Report
doi: https://doi.org/10.1007/s00787-020-01675-5

Screen time and psychopathology: investigating directionality using cross-lagged panel models

Patricia Bado, Julia Schäfer, Andre R. Simioni, Rodrigo A. Bressan, Ary Gadelha, Pedro M. Pan, Eurípedes C. Miguel, Luis A. Rohde, and Giovanni A. Salum

Introduction

Children and adolescents are likely using more digital screens during the COVID-19 pandemic, raising parental concern over digital screens effects on mental health. Previous evidence on the topic has been controversial: some studies have associated more screen time with lower well-being in children and adolescents [1], whereas other studies found no convincing evidence that spending time on digital screens might be harmful [2]. Furthermore, this effect has been found mostly in girls than in boys [3].

However, the available evidence is mostly from cross-sectional studies, preventing investigators from understanding the directionality of such associations and excluding reverse causality, i.e., that increased levels of psychopathology lead to increased screen time. Our study investigates the bidirectional associations between screen time and psychopathology (general, internalizing and externalizing), using a longitudinal design using data from a large school-based sample in both boys and girls.

7.1.2. Appendix Article #2 (abstract)

Published at ***Journal of the American Academy of Child & Adolescent Psychiatry***

Journal of the American Academy of Child & Adolescent Psychiatry
December 2020 – Volume 60 – Issue 12
doi: https://doi.org/10.1016/j.jaac.2020.11.016

Testing the Stability and Validity of an Executive Dysfunction Classification Using Task-Based Assessment in Children and Adolescents

Arthur Gus Manfro, Daniel S. Pine, Guilherme Vanoni Polanczyk, Marcos Santoro, Jordan Wassertheil Smoller, Karestan Koenen, Jari Mari, Pedro Mario Pan, André Zugman, Julia Luiza Schäfer, Sintia Belangero, Natan Pereira Grossmann, André Rafael Simioni, Marcelo Queiroz Hoexter, Euripedes Constantino Miguel, Ary Gadelha, Luis Augusto Rohde, Giovanni Abrahão Salum

Objective: It is unclear if pediatric executive dysfunction assessed only with cognitive tasks predicts clinically relevant outcomes independently of psychiatric diagnoses. This study tested the stability and validity of a task-based classification of executive function. **Method**: A total of 2,207 individuals (6–17 years old) from the Brazilian High-Risk Cohort Study participated in this study (1,930 at baseline, 1,532 at follow-up). Executive function was measured using tests of working memory and inhibitory control. Dichotomized age- and sex-standardized performances were used as input in latent class analysis and receiver operating curves to create an executive dysfunction classification (EDC). The study tested EDC's stability over time, association with symptoms, functional impairment, a polymorphism in the *CADM2* gene, polygenic risk scores (PRS), and brain structure. Analyses covaried for age, sex, social class, IQ, and psychiatric diagnoses. **Results:** EDC at baseline predicted itself at follow-up (odds ratio [OR] = 5.11; 95% CI 3.41–7.64). Participants in the EDC reported symptoms spanning several domains of psychopathology and exhibited impairment in multiple settings, including more adverse school events (OR = 2.530; 95% CI 1.838–3.483). Children in the EDC presented higher attention-deficit/hyperactivity disorder and lower educational attainment PRS at baseline; higher schizophrenia PRS at follow-up; and lower chances of presenting a polymorphism in a gene previously linked to high performance in executive function (*CADM2* gene). They also exhibited smaller intracranial volumes and smaller bilateral cortical surface areas in several brain regions. **Conclusion:** Task-based executive dysfunction is associated with several

validators, independently of psychiatric diagnoses and intelligence. Further refinement of task-based assessments might generate clinically useful tools.

Key words: Executive Function, Genetics, Neuroimage, Neuropsychology, Research Domain Criteria

7.1.3. Appendix Article #3 (abstract)

Published at ***Translational Psychiatry***

Translational Psychiatry
March 2020 – Volume 10 – Issue 1
doi: https://doi.org/10.1038/s41398-020-0772-3

Gene expression changes associated with trajectories of psychopathology in a longitudinal cohort of children and adolescents

Vanessa Kiyomi Ota, Marcos Leite Santoro, Leticia Maria Spindola, Pedro Mario Pan, Andressa Simabucuro, Gabriela Xavier, Tamiris Vieira-Fonseca, Evelin Aline Zanardo, Felipe Rodolfo Camargo dos Santos, Julia Luiza Schäfer, Leslie Domenici Kulikowski, Pedro A. F. Galante, Paula Fontes Asprino, Elisa Brietzke, Rodrigo Grassi-Oliveira, Luis Augusto Rohde, Euripedes Constantino Miguel, Ary Gadelha, Jair Jesus Mari, Rodrigo Affonseca Bressan, Giovanni Abrahao Salum & Sintia Iole Belangero

We aimed to identify blood gene expression patterns associated to psychopathological trajectories retrieved from a large community, focusing on the emergence and remission of general psychiatric symptoms. Hundred and three individuals from the Brazilian High-Risk Cohort Study (BHRCS) for mental disorders were classified in four groups according to Child Behavior Checklist (CBCL) total score at the baseline (w0) and after 3 years (w1): low–high (L–H) ($N = 27$), high–low (H–L) ($N = 12$), high–high (H–H) ($N = 34$) and low–low (L–L) groups ($N = 30$). Blood gene expression profile was measured using Illumina HT-12 Beadchips, and paired analyses comparing w0 and w1 were performed for each group. Results: 98 transcripts were differentially expressed comparing w0 and w1 in the L-H, 33 in the H–L, 177 in the H–H and 273 in the L–L. Of these, 66 transcripts were differentially expressed exclusively in the L–H; and 6 only in the H–L. Cross-Lagged Panel Models analyses revealed that RPRD2 gene expression at w1 might be influenced by the CBCL score at w0. Moreover, *COX5B, SEC62*, and *NDUFA2* were validated with another technique and were also differentially regulated in postmortem brain of subjects with mental disorders, indicating that they might be important not only to specific disorders, but also to general psychopathology and symptoms trajectories. Whereas genes related to metabolic pathways seem to be associated with the emergence of psychiatric symptoms,

mitochondrial inner membrane genes might be important over the course of normal development. These results suggest that changes in gene expression can be detected in blood in different psychopathological trajectories.

7.1.4. Appendix Article #4 (abstract)

Published at ***European Child & Adolescent Psychiatry***

European Child & Adolescent Psychiatry
December 2021
doi: https://doi.org/10.1007/s00787-021-01923-2

Childhood poverty and mental health disorders in early adulthood: evidence from a Brazilian cohort study

Carolina Ziebold, Sara Evans-Lacko, Mário César Rezende Andrade, Maurício Hoffmann, Laís Fonseca, Matheus Barbosa, Pedro Mario Pan, Euripedes Miguel, Rodrigo Bressan, Luis Augusto Rohde, Giovanni Salum, Julia Schafer, Jair de Jesus Mari & Ary Gadelha

Background: We examined the association between childhood poverty and mental health disorders (MHD) in childhood and early adulthood. We also investigated whether the association between poverty in childhood and MHD is mediated by exposure to stressful life events (SLE). **Methods:** We used data from a prospective community cohort of young people assessed at baseline (M = 9.7 years, SD = 1.9), first (M = 13.5 years, SD = 1.9), and second (M = 18.2 years, SD = 2.0) follow-ups (N = 1,590) in Brazil. Poverty was assessed using a standardized classification. Exposure to 20 different SLE was measured using the Life History instrument. Psychiatric diagnoses were evaluated using the Development and Well-Being Assessment. Latent growth models investigated the association between poverty at baseline and the growth of any MHD, externalizing, and internalizing disorders. Mediation models evaluated whether the association between childhood poverty and MHD in early adulthood was mediated by exposure to SLE. **Results:** Poverty affected 11.4% of the sample at baseline and was associated with an increased propensity for presenting externalizing disorders in adolescence or early adulthood (standardized estimate = 0.27, p = 0.016). This association was not significant for any disorder or internalizing disorders. Childhood poverty increased the likelihood of externalizing disorders in early adulthood through higher exposure to SLE (OR = 1.07, 95 CI% 1.01–1.14). Results were only replicated among females in stratified analyses. **Conclusions:** Childhood poverty had detrimental consequences on externalizing MHD in adolescence, especially among females. Poverty and SLE are preventable risk

factors that need to be tackled to reduce the burden of externalizing disorders in young people.

7.1.5. Appendix Article #5 (abstract)

Published at ***International Journal of Obesity***

International Journal of Obesity
March 2022

ADHD in childhood predicts BMI and body composition measurements over time in a population-based birth cohort

Thais Martins-Silva, Juliana dos Santos Vaz, Julia Luiza Schäfer, Giovanni Abrahão Salum, Marina Xavier Carpena, Eduardo Schneider Vitola, Vitor Breda, Eugênio Horacio Grevet, Christian Loret de Mola, Fernando Barros, Ana Maria Baptista Menezes, Helen Gonçalves, Fernando C. Wehrmeister, Luis Augusto Rohde & Luciana Tovo-Rodrigues

Background/Objectives: Obesity has been reported as an attention-deficit hyperactivity disorder (ADHD) comorbidity. So far, few studies have aimed to explore the potential causal relationship between ADHD and obesity, as well as used other measures of body composition like fat-free mass (FFM) and fat mass (FM) as measures of obesity. This study aimed to test the association between ADHD and body composition (body mass index [BMI] and others) and to evaluate the potential causal relationship with obesity. **Subjects/Methods:** Data from the 1993 Pelotas (Brazil) birth cohort at age 11-, 15-, 18-, and 22-year follow-up was used. We performed a cross-lagged panel model (CLPM) analysis between ADHD symptoms and BMI to explore the causal relationship between both traits. Finally, we tested whether ADHD, inattention, and hyperactivity symptom scales were associated with BMI, FM, and FFM at 22 years. **Results:** In the CLPM, higher ADHD scores at age 11 predicted higher BMI at age 15 (β = 0.055, 95% CI [0.037; 0.073]). ADHD symptoms at age 11 was also associated with a decrease in the FFM (β = −0.16, 95% CI [−0.28; −0.05]), and an increase in the BMI (β = 0.17, 95% CI [0.10; 0.23]) and FM (β = 0.17, 95% CI [0.06; 0.29]) at 22 years. At 22 years of age, ADHD was associated with FFM and FM. Moreover, an increase in BMI was observed with an increase in several symptoms of ADHD in general (β = 0.06, 95% CI [0.004; 0.12]), and hyperactivity symptoms (β = 0.15, 95% CI [0.05; 0.25]). **Conclusion:** ADHD at 11 years predicted a higher BMI at 15 years, and body fat composition in adulthood, suggesting higher scores on ADHD

symptoms in early life may be a critical point for body composition in early adulthood. The hyperactivity symptoms may play an important role in the BMI increase.

7.1.6. Appendix Article #6 (abstract)

Published at ***Journal of Affective Disorders***

Journal of Affective Disorders
February 2022 – Volume 298, Part A – p 190 - 193
doi: https://doi.org/10.1016/j.jad.2021.10.108

Mental health conditions in Lesbian, Gay, Bisexual, Transgender, Queer and Asexual youth in Brazil: A call for action

TauanaTerra, Julia L. Schafer, Pedro M. Pan, Angelo Brandelli Costa, Arthur Caye, Ary Gadelha, Eurípedes C.Miguel, Rodrigo A. Bressan,Luis A.Rohde, Giovanni A.Salum

Background: Lesbian, Gay, Bisexual, Transgender, Queer, and Asexual (LGBTQA+) youth have a greater chance of experiencing stressful life events when compared to cisgender heterosexual peers, which can lead to mental health problems. We aimed to estimate the prevalence of mental disorders among LGBTQA+ youths from two large cities in Brazil. **Methods:** Participants were 13–22 years old youths from the 3rd wave of the Brazilian High-Risk Cohort for Psychiatric Disorders (n = 1475). Mental disorders were assessed using the Development and Well-Being Behavior Assessment. Sexual orientation and gender identity were assessed using a self-report confidential questionnaire. Data were analyzed through logistic regressions (adjusting for sociodemographic) using sampling weights to account for attrition and our oversampling high-risk design. **Results**: 15.18% of the sample described themselves as LGBTQA+. The LGBTQA+ group presented higher rates of anxiety disorders (30.14% vs. 13.37%; OR = 3.37; 95%CI:2.51–4.50), depressive disorders (27.75% vs. 15.34%; OR = 2.17; 95%CI:1.60–2.93) and post-traumatic stress disorder (4.98% vs. 2.25%; OR = 4.20; 95%CI:2.24–7.82), if compared with the cisgender heterosexual group. No difference was found for conduct disorders (2.97% vs. 5.21%; OR = 0.82; 95%CI:0.35–1.65) or attention deficit hyperactivity disorder (5.92% vs. 3.28%; OR = 1.56; 95%CI:0.83–2.79). **Limitations:** Although recruitment was performed at 57 schools in the two cities, sampling was non-probabilistic and included only urban areas, which might bias prevalence estimates and group comparisons. **Conclusions:** Our results elucidate the mental health disparities between LGBTQA+ people and cisgender heterosexuals in Brazil. It highlights the need to promote the inclusion of this

population in policy formulation and support actions to mitigate the suffering related to sexual orientation and gender identity.