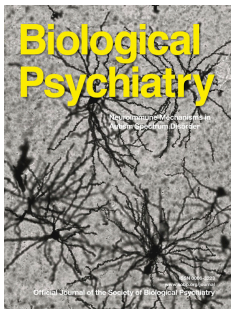
Journal Pre-proof



Childhood Maltreatment and Deviations from Normative Brain Structure: A Mega-Analysis of 3,711 Individuals from the ENIGMA MDD and ENIGMA PTSD Working Groups

Haley R. Wang, Zhen-Qi Liu, Elena Pozzi, Ahmed Hussain, Priyanka Sigar, Chadi Abdallah, Nina Alexander, Justin Baker, Jochen Bauer, Jennifer Urbano Blackford, Josh Cisler, Colm G. Connolly, Andrew Cotton, Judith Daniels, Udo Dannlowski, Maria Densmore, Terri deRoon-Cassini, Danai Dima, Stefan Du Plessis, Amit Etkin, Negar Fani, Lukas Fisch, Jacklynn Fitzgerald, Thomas Frodl, Cynthia H.Y. Fu, Ali Saffet Gonul, Evan M. Gordon, Ian Gotlib, Roberto Goya-Maldonado, Nynke A. Groenewold, Dominik Grotegerd, Tim Hahn, J. Paul Hamilton, Laura Han, Ilan Harpaz-Rotem, Courtney C. Haswell, Ryan Herringa, Julia Herzog, Jonathan Ipser, Neda Jahanshad, Tanja Jovanovic, Milissa Kaufman, Tilo Kircher, Maximilian Konowski, Sheri-Michelle Koopowitz, Axel Krug, John Krystal, Ruth Lanius, Christine Larson, Amit Lazarov, Lauren Lebois, Elisabeth Leehr, Ifat Levy, Meng Li, Antje Manthey, Adi Maron-Katz, Andrew McIntosh, Katie McLaughlin, Susanne Meinert, Benson Mwangi, Steven M. Nelson, Igor Nenadić, Yuval Neria, Richard Neufeld, Amar Ojha, Bunmi Olatunji, Elizabeth A. Olson, Nils Opel, Matthew Peverill, Kerry Ressler, Marisa Ross, Isabelle Rosso, Matthew Sacchet, Kelly Sambrook, Christian Schmahl, Soraya Seedat, Martha E. Shenton, Maurizio Sicorello, Anika Sierk, Jair C. Soares, Dan J. Stein, Frederike Stein, Murray B. Stein, Benjamin Suarez-Jimenez, Jean Théberge, Sophia I. Thomopoulos, Carissa Tomas, Paula Usemann, Leigh L. van den Heuvel, Sanne van Rooij, Henrik Walter, Martin Walter, Xin Wang, Heather Whalley, Nils R. Winter, Mon-Ju Wu, Hong Xie, Tony Yang, Xi Zhu, Sigal Zilcha-Mano, Giovana B. Zunta-Soares, Sophia Frangou, Paul M. Thompson, Lauren Salminen, Delin Sun, Rajendra Morey, Jennifer S. Stevens, Lianne Schmaal, Tiffany C. Ho

PII: S0006-3223(26)00093-4

DOI: https://doi.org/10.1016/j.biopsych.2026.02.016

Reference: BPS 16052

To appear in: *Biological Psychiatry*

Received Date: 22 September 2025

Revised Date: 2 February 2026

Accepted Date: 23 February 2026

Please cite this article as: Wang H.R., Liu Z.-Q., Pozzi E., Hussain A., Sigar P., Abdallah C., Alexander N., Baker J., Bauer J., Blackford J.U., Cisler J., Connolly C.G., Cotton A., Daniels J., Dannlowski U., Densmore M., deRoon-Cassini T., Dima D., Du Plessis S., Etkin A., Fani N., Fisch L., Fitzgerald J., Frodl T., Fu C.H.Y., Gonul A.S., Gordon E.M., Gotlib I., Goya-Maldonado R., Groenewold N.A., Grotegerd D., Hahn T., Hamilton J.P., Han L., Harpaz-Rotem I., Haswell C.C., Herringa R., Herzog J., Ipser J., Jahanshad N., Jovanovic T., Kaufman M., Kircher T., Konowski M., Koopowitz S.-M., Krug A., Krystal J., Lanius R., Larson C., Lazarov A., Lebois L., Leehr E., Levy I., Li M., Manthey A., Maron-Katz A., McIntosh A., McLaughlin K., Meinert S., Mwangi B., Nelson S.M., Nenadić I., Neria Y., Neufeld R., Ojha A., Olatunji B., Olson E.A., Opel N., Peverill M., Ressler K., Ross M., Rosso I., Sacchet M., Sambrook K., Schmahl C., Seedat S., Shenton M.E., Sicorello M., Sierk A., Soares J.C., Stein D.J., Stein F., Stein M.B., Suarez-Jimenez B., Théberge J., Thomopoulos S.I., Tomas C., Usemann P., van den Heuvel L.L., van Rooij S., Walter H., Walter M., Wang X., Whalley H., Winter N.R., Wu M.-J., Xie H., Yang T., Zhu X., Zilcha-Mano S., Zunta-Soares G.B., Frangou S., Thompson P.M., Salminen L., Sun D., Morey R., Stevens J.S., Schmaal L. & Ho T.C., Childhood Maltreatment and Deviations from Normative Brain Structure: A Mega-Analysis of 3,711 Individuals from the ENIGMA MDD and ENIGMA PTSD Working Groups *Biological Psychiatry* (2026), doi: https://doi.org/10.1016/j.biopsych.2026.02.016.

Childhood Maltreatment and Deviations from Normative Brain Structure: A Mega-Analysis of 3,711 Individuals from the ENIGMA MDD and ENIGMA PTSD Working Groups

Haley R. Wang[1,2], Zhen-Qi Liu[3], Elena Pozzi[4,5], Ahmed Hussain[6], Priyanka Sigar[7], Chadi Abdallah[8,9], Nina Alexander[10], Justin Baker[11,12], Jochen Bauer[13], Jennifer Urbano Blackford[14,15], Josh Cisler[16], Colm G. Connolly[17], Andrew Cotton[18], Judith Daniels[19,20], Udo Dannlowski[21], Maria Densmore[22,23], Terri deRoon-Cassini[24,25], Danai Dima[26,27], Stefan Du Plessis[28,29], Amit Etkin[30], Negar Fani[31], Lukas Fisch[21], Jacklynn Fitzgerald[32], Thomas Frodl[33], Cynthia H.Y. Fu[34,35], Ali Saffet Gonul[36], Evan M. Gordon[37], Ian Gotlib[38], Roberto Goya-Maldonado[39], Nynke A. Groenewold[40], Dominik Grotegerd[21], Tim Hahn[21], J. Paul Hamilton[41], Laura Han[42,43,44], Ilan Harpaz-Rotem[45], Courtney C. Haswell[6,46], Ryan Herringa[47], Julia Herzog[48], Jonathan Ipser[40], Neda Jahanshad[49], Tanja Jovanovic[50], Milissa Kaufman[11,12], Tilo Kircher[10], Maximilian Konowski[21], Sheri-Michelle Koopowitz[40], Axel Krug[51], John Krystal[46,52], Ruth Lanius[53], Christine Larson[54], Amit Lazarov[55,56], Lauren Lebois[11,12], Elisabeth Leehr[21], Ifat Levy[57], Meng Li[58], Antje Manthey[59,60], Adi Maron-Katz[61], Andrew McIntosh[62], Katie McLaughlin[63,64], Susanne Meinert[21,65], Benson Mwangi[66,67], Steven M. Nelson[68,69], Igor Nenadić[10], Yuval Neria[56], Richard Neufeld[70,71], Amar Ojha[72,73], Bunmi Olatunji[74], Elizabeth A. Olson[75], Nils Opel[21,58,76], Matthew Peverill[77], Kerry Ressler[78,79], Marisa Ross[80], Isabelle Rosso[78,79], Matthew Sacchet[81], Kelly Sambrook[82], Christian Schmahl[48,83], Soraya Seedat[84,85], Martha E. Shenton[86], Maurizio Sicorello[48,83], Anika Sierk[60], Jair C. Soares[66,67], Dan J. Stein[87], Frederike Stein[10], Murray B. Stein[88], Benjamin Suarez-Jimenez[89], Jean Théberge[22,23], Sophia I. Thomopoulos[90], Carissa Tomas[25,91], Paula Usemann[10], Leigh L. van den Heuvel[84,85], Sanne van Rooij[31], Henrik Walter[92], Martin Walter[58,93], Xin Wang[94], Heather Whalley[62], Nils R. Winter[21], Mon-Ju Wu[66,67], Hong Xie[94], Tony Yang[95], Xi Zhu[96], Sigal Zilcha-Mano[97], Giovana B. Zunta-Soares[66,67], Sophia Frangou[98,99], Paul M. Thompson[90], Lauren Salminen[90], Delin Sun[100,101,102], Rajendra Morey[103], Jennifer S. Stevens[104,105], Lianne Schmaal[4,5], Tiffany C. Ho[1,7]

1. Department of Psychology, University of California, Los Angeles, Los Angeles, CA, USA
2. Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, Los Angeles, CA, USA
3. Montréal Neurological Institute, McGill University, Montréal, QC, Canada
4. Centre for Youth Mental Health, The University of Melbourne, Melbourne, Australia
5. Orygen, The National Centre of Excellence in Youth Mental Health, Parkville, Australia
6. Brain Imaging and Analysis Center, Duke University, Durham, NC, USA
7. Department of Psychiatry and Behavioral Sciences, University of California, Los Angeles, Los Angeles, CA, USA
8. Department of Psychiatry, Baylor College of Medicine, Houston, TX, USA
9. Department of Psychiatry, Yale University, New Haven, CT, USA
10. Department of Psychiatry, University of Marburg, Marburg, Germany
11. McLean Hospital, Belmont, MA, USA
12. Harvard Medical School, Boston, MA, USA
13. Clinic for Radiology, University of Münster, Münster, Germany
14. Munroe-Meyer Institute, University of Nebraska Medical Center, Omaha, NE, USA
15. Department of Psychiatry and Behavioral Sciences, Vanderbilt University Medical Center, Nashville, TN, USA
16. University of Texas at Austin, Austin, TX, USA
17. Department of Biomedical Sciences, Florida State University, Tallahassee, FL, USA
18. Department of Neurology, Division of Cognitive Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, USA
19. Department of Clinical Psychology, University of Groningen, The Netherlands
20. Trauma Centrum Beilen, GGZ Drenthe, Beilen, The Netherlands
21. Institute for Translational Psychiatry, University of Münster, Münster, Germany

22. Department of Psychiatry, Western University, London, ON, Canada

23. Imaging Division, Lawson Research Institute, London, ON, Canada

24. Division of Trauma and Acute Care Surgery, Department of Surgery, Medical College of Wisconsin, WI, USA

25. Comprehensive Injury Center, Medical College of Wisconsin, WI, USA

26. Department of Psychology, City St George's, University of London, London, UK

27. Department of Neuroimaging, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

28. Department Psychiatry, FMHS, Stellenbosch University, Tygerberg, Cape Town, South Africa

29. Genomics of Brain Disorders Research Unit, South African Medical Research Council/Stellenbosch University, Cape Town, South Africa

30. Stanford University, Stanford, CA, USA

31. Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA, USA

32. Department of Psychology, Marquette University, Milwaukee, WI, USA

33. Department of Psychiatry, Psychotherapy and Psychosomatics, University Hospital Aachen, Aachen, Germany

34. Centre for Affective Disorders, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

35. Department of Psychology, University of East London, London, UK

36. Department of Psychiatry, Ege University School of Medicine, Izmir, Turkey

37. Department of Radiology, Washington University School of Medicine, St. Louis, MO, USA

38. Department of Psychology, Stanford University, Stanford, CA, USA

39. Department of Psychiatry and Psychotherapy, University Medical Center Göttingen, Göttingen, Germany

40. Department of Psychiatry & Neuroscience Institute, University of Cape Town, Cape Town, South Africa

41. Department of Biological and Medical Psychology, University of Bergen, Bergen, Norway

42. Department of Psychiatry, Amsterdam UMC location Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

43. Amsterdam Neuroscience, Mood, Anxiety, Psychosis, Sleep & Stress program, Amsterdam, The Netherlands

44. Amsterdam Public Health, Mental Health program, Amsterdam, The Netherlands

45. Departments of Psychiatry and of Psychology, Yale University, New Haven, CT, USA

46. Clinical Neuroscience Division, National Center for PTSD, VA Connecticut Healthcare System, West Haven, CT, USA

47. Department of Psychiatry, University of Wisconsin School of Medicine & Public Health, Madison, WI, USA

48. Department of Psychosomatic Medicine and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Heidelberg, Germany

49. Mark and Mary Stevens Neuroimaging and Informatics Institute, Keck School of Medicine of USC, University of Southern California, Marina del Rey, CA, USA

50. Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, USA

51. Department of Psychiatry and Psychotherapy, University Hospital Bonn, Bonn, Germany

52. Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA

53. Department of Neuroscience, Western University, London, ON, Canada

54. Department of Psychology, University of Wisconsin-Milwaukee, Milwaukee, WI, USA

55. School of Psychological Sciences, Tel Aviv University, Tel Aviv, Israel

56. Irving Medical Center, Columbia University, New York, NY, USA

57. Departments of Comparative Medicine, Neuroscience, and Psychology, Yale University, New Haven, CT, USA

58. Department of Psychiatry and Psychotherapy, University Hospital Jena, Jena, Germany

59. Health and Medical University Potsdam, Potsdam, Germany

60. Charité Universitätsmedizin Berlin Campus Charite Mitte: Charité Universitätsmedizin Berlin, Berlin, Germany

61. Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA

62. Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, Scotland, UK

63. Department of Psychology, Harvard University, Cambridge, MA, USA

64. Ballmer Institute for Children's Behavioral Health, University of Oregon, Eugene, OR, USA

65. Institute for Translational Neuroscience, University of Münster, Münster, Germany

66. Center of Excellence on Mood Disorders, Louis A. Faillace, MD, Department of Psychiatry and Behavioral Sciences, The University of Texas Health Science Center at Houston, Houston, TX, USA

67. School of Behavioral Health Sciences, The University of Texas Health Science Center at Houston, Houston, TX, USA

68. Department of Pediatrics, University of Minnesota, Minneapolis, MN, USA

69. Masonic Institute for the Developing Brain, University of Minnesota, Minneapolis, MN, USA

70. Departments of Psychology and Psychiatry, Neuroscience Program, Western University, London, ON, Canada

71. Department of Psychology, University of British Columbia, Okanagan, Kelowna, BC, Canada

72. Center for Neuroscience, University of Pittsburgh, Pittsburgh, PA, USA

73. Center for the Neural Basis of Cognition, University of Pittsburgh, Pittsburgh, PA, USA

74. Department of Psychology, Nashville, TN, USA

75. Crisis Text Line, New York, NY, USA

76. German Center for Mental Health (DZPG), Berlin, Germany

77. Department of Psychiatry, University of Wisconsin-Madison, Madison, WI, USA

78. Division of Depression and Anxiety Disorders, McLean Hospital, Belmont, MA, USA

79. Department of Psychiatry, Harvard Medical School, Boston, MA, USA

80. Northwestern University, Evanston, IL, USA

81. Meditation Research Program, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

82. University of Washington, Seattle, WA, USA

83. German Center for Mental Health (DZPG), Partner Site Mannheim-Heidelberg-Ulm, Mannheim, Germany

84. Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

85. South African Medical Council Unit on the Genomics of Brain Disorders, Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch University, Stellenbosch, South Africa

86. Department of Psychiatry, Mass General Brigham (MGB), Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA

87. SAMRC Unit on Risk & Resilience in Mental Disorders, Department of Psychiatry & Neuroscience Institute, University of Cape Town, Cape Town, South Africa

88. Department of Psychiatry, University of California, San Diego, San Diego, CA, USA

89. The Del Monte Institute for Neuroscience, Department of Neuroscience, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

90. Imaging Genetics Center, Mark and Mary Stevens Neuroimaging and Informatics Institute, Keck School of Medicine, University of Southern California, Marina del Rey, CA, USA

91. Division of Epidemiology and Social Sciences, Institute of Health and Humanity, Medical College of Wisconsin, WI, USA

92. Division of Mind and Brain Research, Department for Psychiatry, Charité– Universitätsmedizin Berlin, Berlin, Germany

93. German Center for Mental Health (DZPG), Mannheim, Germany

94. Department of Neuroscience and Psychiatry, University of Toledo, Toledo, OH, USA

95. Department of Psychiatry, Division of Child and Adolescent Psychiatry, School of Medicine, University of California, San Francisco, San Francisco, CA, USA

96. Department of Bioengineering, The University of Texas at Arlington, Arlington, TX, USA

97. School of Psychological Sciences, University of Haifa, Haifa, Israel

98. Djavad Mowafaghian Centre for Brain Health, University of British Columbia, Vancouver, BC, Canada

99. Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, USA

100. Department of Psychiatry and Behavioral Sciences, School of Medicine, Duke University, Durham, NC, USA

101. Brain Imaging Analysis Center, Duke University, Durham, NC, USA

102. Department of Veteran Affairs Mid-Atlantic Mental Illness Research, Education and Clinical Center, Durham, NC, USADuke University, Durham, NC, USA

103. Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA

104. Atlanta VA Medical Center, Atlanta, GA, USA

***Corresponding author:** Tiffany C. Ho, PhD (tiffanycho@ucla.edu)

Running title: Childhood Maltreatment and Normative Brain Deviations

Keywords: Childhood maltreatment; brain morphometry; normative modeling; sex differences, major depressive disorder; PTSD

Abstract word count: 248 words

Main text word count: 3,987 words

Number of Figures: 3

Number of Tables: 3

Number of Supplemental Files: 1

Abstract

Background: Childhood maltreatment (CM), encompassing abuse and neglect, is highly prevalent and associated with elevated risk for Major Depressive Disorder (MDD), Posttraumatic Stress Disorder (PTSD), and other related conditions. The extent to which neuroanatomical alterations in MDD and PTSD are attributable to CM, however, is uncertain.

Methods: Here, we analyzed CM and whole-brain MRI data from 3,711 participants in the ENIGMA MDD and PTSD Working Groups (25 sites; 33.3±13.0 years; 59.9% female). Normative modeling estimated deviation z-scores for 14 subcortical volumes (SV), 68 cortical thickness (CT), and 68 surface area (SA) measures. To identify transdiagnostic effects, associations between CM and brain deviation scores were evaluated across all participants (patients and healthy controls) stratified by sex and three age bins (pediatric, young adult, older adult).

Results: In young adults (ages 18-35), abuse was associated with larger volumes in thalamus and pallidum, thinner isthmus cingulate and middle frontal regions, and thicker medial orbitofrontal cortex; there were no significant effects in pediatric (≤18 years) participants. The strongest effects were observed in young female adults ($|\beta|$=.07-.22, q<.05): greater abuse and neglect were correlated with smaller hippocampus and putamen volumes, thinner entorhinal cortex, and smaller SA in fusiform/inferior parietal regions, and with larger SA in orbitofrontal and occipital cortices. In males, abuse had widespread effects on CT and SA ($|\beta|$=.1-.18, q<.05); effects for neglect were minimal.

Conclusions: Our findings of age- and sex-specific instantiations of CM on brain morphometry highlight the importance of developmental context in understanding how adverse experiences shape neurobiological vulnerability to MDD and PTSD.

Introduction

Early life adversity (ELA), particularly childhood maltreatment (CM) such as abuse and neglect, is common, affecting more than two-thirds of the general population (1, 2). Although not all individuals who experience CM develop mental disorders, experiences of CM remain one of the most potent risk factors for stress-related psychopathologies, including major depressive disorder (MDD) and posttraumatic stress disorder (PTSD) (3-5). Importantly, individuals who are diagnosed with such disorders and have a history of CM tend to experience an earlier age of onset, poorer clinical outcomes, and greater treatment resistance than those with these disorders but no history of CM (6). Despite the clear link between CM experience and subsequent risk for psychiatric disorders, the neuroanatomical consequences of CM that occur transdiagnostically, and independently of psychiatric disease, is not well documented. This knowledge gap is notable as the neurobiological consequences of a psychiatric disorder may in fact be driven by CM. For instance, in prior studies from ENIGMA MDD and ENIGMA PTSD, the associations between subcortical gray matter volumes and psychiatric diagnosis were attenuated or non-significant once CM was included as a statistical covariate (7, 8). Understanding the extent to which CM impacts brain morphometry transdiagnostically (and independently of psychiatric disease) may have the potential to influence conceptualization of symptom presentation and guide treatment selection and clinical decision making.

Specifically, many studies examining the effects of CM on brain morphometry have not adequately accounted for the inter-individual variation across regions (9), despite evidence of regional differences in deviations from normative neurodevelopment (10). Brain regions exhibit diverse developmental courses, with some following inverted U-shaped trajectories that reach their peak in childhood or adolescence, with notable sex differences (11-14). Consequently, interpreting adversity-related effects necessitates consideration of age- and sex-specific variation (15, 16). Two example regions are thalamus and amygdala, which are consistently implicated in stress and trauma-related processes and show robust associations with CM in previous research (17, 18). Larger thalamic volumes during childhood may suggest accelerated maturation, but the same pattern observed in adulthood may reflect delayed or

atypical development (11, 19). Additionally, while both male and female brains show inverted U-shaped age-related changes in amygdala volume, males demonstrate a more rapid increase in amygdala size during childhood compared to females, leading to sexual dimorphism and inter-individual variation. To address this, investigators have recently charted normative brain growth, akin to pediatric growth charts, to quantify individual variation with respect to age-stratified norms (12, 20). Unlike traditional group-average comparisons that treat inter-individual differences as noise (21), this approach models the full range of normal variation and converts raw brain measures into "deviation" scores showing how much individuals differ from expected age- and sex-specific patterns. This is crucial for parsing biological heterogeneity in psychiatric research and detecting subtle, individual-specific abnormalities often missed by case-control designs (20, 22, 23).

In addition, the effect of CM exposure on brain phenotypes may depend on developmental stage (24). Germane to this idea is the concept of *sensitive periods*, which are periods of heightened plasticity during which environmental influences have outsized effects on developing systems (10). Rather than standing in strict opposition to an accumulation model—which posits that effects scale with the number of exposures that typically increase with age (25)—these perspectives may be complementary, as adversity experienced during a sensitive window could confer a large initial impact that is compounded later in life with further exposures. Indeed, childhood maltreatment has been associated with an increased risk of psychiatric disorders that persist well into adulthood. To date, however, few studies have addressed this issue using samples from across the lifespan. Within a sensitive period, the neurobiological sequelae of adverse experiences may be most prominent immediately after exposure (as described in *recency* models (26)), or they may not be manifested or measurable at the phenotypic level until later in development (27) (as described in *incubation* models (28, 29)). For example, several empirical studies have documented this delayed manifestation pattern, finding minimal structural brain differences in children exposed to ELA, but more pronounced effects emerging in adolescence and early adulthood (24, 30). To distinguish among these possibilities, a lifespan approach is critically needed (25).

Prior research on the structural brain correlates of CM have also not fully captured the nuanced effects of different experience types (31, 32) or potential sex differences in these associations (33). Recent data-driven approaches have identified distinct co-occurring dimensions of ELA that may have differential neural correlates (34), though these dimensional patterns have not yet been examined in relation to normative brain development. Prominent theoretical frameworks distinguish between adversity characterized by threat versus deprivation and also highlight the impact of fragmented care—defined as inconsistent, unpredictable, or disrupted caregiving—on neurodevelopment (35). Various forms of childhood maltreatment—such as emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse—may lead to distinct cognitive and behavioral adaptations or maladaptive coping strategies (36, 37). For example, sexual abuse, which typically involves high levels of threat, has been associated with structural deficits in reward circuits and altered amygdala reactivity (18, 38, 39), whereas emotional maltreatment, often linked to deprivation, has been connected with abnormalities in fronto-limbic socioemotional networks (40). Finally, the impact of childhood maltreatment likely interacts with hormonal factors and gender-specific social environments, potentially resulting in differing outcomes for males and females. For example, women are more than twice as likely as men to develop MDD or PTSD following exposures to all types of abuse and neglect (41, 42). Despite this, many studies have relied on mixed-sex samples, often due to limited sample sizes, missing opportunities to detect sex differences in the neurobiological sequelae of ELA.

Taken together, there is a clear need to examine the enduring effects of CM on brain morphometry across the lifespan. In this study, we employed a *normative modeling approach* that quantifies individual deviations from expected neuroanatomical variation by generating continuous z-scores, which indicate the direction of normative deviation (with lower scores reflecting values below the normative range, and higher scores reflecting values above the normative range) (43, 44). Normative modeling uniquely addresses methodological challenges of accounting for developmental heterogeneity by providing age- and sex-adjusted reference standards analogous to pediatric growth charts, thus offering advantages over traditional approaches that rely on group-average comparisons. Our aim was to explore the extent to

which the pattern of brain deviations is correlated with continuous measures of childhood trauma severity in a way that aligns with dimensional models of ELA. In our framework, different types of maltreatment—such as abuse and neglect—are expected to differentially impact distinct neural circuits in parallel. For instance, whereas threat-related abuse may predominantly affect regions involved in stress regulation and fear learning (e.g., the hippocampus and amygdala), deprivation-related neglect may influence circuits underpinning reward processing and socioemotional function (e.g., the striatum, medial orbitofrontal cortex, and association cortices). Recognizing that brain development and the neurobiological sequelae of CM vary by age and sex, we analyzed cortical thickness, surface area, and subcortical volumes separately for different age cohorts and for males and females. Our large, trauma-enriched sample (N=3,711), spanning ages 8 to 69 from 25 international sites via the ENIGMA MDD and PTSD Working Groups (45-47), allowed us to correlate continuous measures of trauma severity with these continuous deviation scores. This approach aims to determine the extent to which our findings support a dimensional model of CM that captures differential neural alterations associated with different forms of adversity, and how these associations vary as a function of age and sex.

Methods

ENIGMA Data

Data from 25 independent sites (Fig. S1) across eight countries were obtained through the ENIGMA Consortium Major Depressive Disorder (MDD) and Posttraumatic Stress Disorder (PTSD) Working Groups. The overall sample consisted of 1,389 patients (872 MDD, 517 PTSD), and 2,322 healthy controls. Cortical thickness and cortical surface area measures were extracted based on the Desikan-Killiany (aparc) atlas (48), while subcortical volumes were segmented using the Aseg atlas in FreeSurfer (49). All neuroimaging data were processed with FreeSurfer according to the standardized processing pipelines and quality assurance procedures stipulated by the ENIGMA Consortium (https://enigma.ini.usc.edu/protocols/imaging-protocols/). Detailed information on participant recruitment, data collection procedures, and MRI acquisition and preprocessing for each site is provided in Supplemental Methods S1-S2.

Childhood Maltreatment Assessment

Childhood Maltreatment (CM) was assessed in all samples via self-report using the Childhood Trauma Questionnaire-Short Form (CTQ-SF) (50), a widely validated retrospective measure of childhood maltreatment. The CTQ-SF comprises five subscales: physical abuse, emotional abuse, sexual abuse, physical neglect, and emotional neglect. Two composite scores were derived: (1) total severity of childhood abuse, calculated as the sum of the three abuse subscales, and (2) total severity of childhood neglect, calculated as the sum of the two neglect subscales. We separated abuse from neglect to facilitate the detection of distinct neurobiological correlates associated with each type of maltreatment.

Normative Modeling of Brain Morphometry

Sex-specific normative models for each FreeSurfer-derived regional subcortical volume, cortical thickness, and surface area measure were generated using the CentileBrain normative modeling tools

(Methods S3) developed by the ENIGMA Lifespan Group (51) and are freely available (https://centilebrain.org/). These models were developed using data from an independent multi-site sample of 37,407 healthy individuals (53.3% female; ages 3-90 years and provide separate standards for females and males. CentileBrain generated z-scores for each morphometric measure in each participant, reflecting deviations from age- and sex-specific population means. Z-scores were calculated by subtracting the brain measure estimated by CentileBrain from the raw value, then dividing by the model's root mean square error. While the CentileBrain algorithms include site harmonization based on Combat-GAM (52), we did not use this feature for reasons discussed under *Harmonization Effects* in the Sensitivity Analyses section, below.

Statistical Analyses

Main Analyses. We pooled extracted subcortical volumes, cortical thickness, and cortical surface area measures from individual subjects across all sites from the ENIGMA MDD and PTSD Working Groups into a single database. General linear models examined associations between CTQ scores (total abuse and neglect) and z-scores for each regional morphometric measure (14 subcortical volumes, 68 cortical thickness, 68 surface area measures; separately for left and right hemispheres). Separate analyses were conducted for males and females to allow detection of potentially different associations between CM and brain deviations. As z-scores already account for age and intracranial volume in the normative model, we did not further adjust for these variables. CTQ scores were not associated with age, age-squared, or sex.

Age-Dependent Effects. While normative modeling inherently accounts for age by generating deviation scores relative to a population-derived reference for each specific age (akin to pediatric growth charts), we stratified our sample into pediatric (≤18 years, n=349), young adult (>18 and <35 years, n=1,908), and older adult (≥35 years, n=1,454) cohorts to examine developmental stages that correspond to distinct phases of neurodevelopment and plasticity. Categorizing participants into these broadly defined age cohorts allows us to investigate potential differences in the magnitude and specificity of ELA-

associated brain deviations during critical developmental windows, such as adolescence versus early and later adulthood. Moreover, this stratification approach is consistent with methods used in prior ENIGMA Consortium studies (53-56), allowing for comparability across large-scale neuroimaging investigations.

Multiple Comparisons Correction. To adjust for multiple comparisons, we applied false discovery rate (FDR) correction using the Benjamini-Hochberg procedure, with *p*-values adjusted separately for each age cohort and sex and for each metric (subcortical volumes, cortical thickness, cortical surface area). Results were considered significant if FDR-corrected *p*-value (q) ≤ 0.05. The number of comparisons was 68 for cortical thickness analyses, 68 for surface area analyses, and 14 for subcortical volume analyses. To obtain comparable standardized regression coefficients, z-scores for each region served as outcome measures.

Sex and Age Differences in Brain-CM Associations. To statistically compare the strength of associations between sexes and age cohorts, we employed Fisher's exact transformation tests (Methods S4). This method allowed us to determine whether standardized regression coefficients (β) from our general linear models differed significantly between males and females (within the same age cohort) and between each pair of age cohorts with significant CM associations (within the same sex).

Sensitivity Analysis

We conducted several sensitivity analyses to evaluate the robustness of our findings. 1) We adjusted for diagnostic status ("patients" versus "controls") as a covariate in our models (Methods S5). 2) We tested whether effects persisted within specific diagnostic groups by re-running analyses separately for MDD and PTSD cohorts (Methods S5B). 3) Leave-one-out cross-validation assessed site-specific influences by sequentially excluding each site and re-running our models (Methods S6). 4) We tested the effect of harmonization on our dataset using ComBat-GAM (Methods S7). 5) Bootstrap sampling analysis determined whether null findings in the pediatric cohort (n=349) stemmed from limited statistical power rather than developmental differences (Methods S8). 6) Given the high correlation between abuse and neglect in our sample ($r=.73$, $p<.001$; Figure S5), we conducted a two-covariate analysis including both

Total Abuse and Total Neglect as simultaneous predictors to disentangle their overlapping effects (Methods S9). 7) We examined the specific effects of sexual abuse by re-running our GLMs using the CTQ Sexual Abuse subscale score (Methods S10). 8) Finally, we conducted a sensitivity analysis adjusting for years of education as a proxy for socioeconomic status in the subset of participants with available data (n=1,235; Methods S11).

Results

Participant Characteristics and Childhood Trauma

The final sample demographics and clinical characteristics, stratified by age cohorts, are presented in Table S1. Sample measures are further broken down by diagnostic group, age, and sex respectively (Tables S2-S3, Fig. S1-3).

Associations Between CM and Subcortical Volume Deviation Scores

Our analyses revealed significant associations between CM and deviations from normative subcortical volume (SV) in adults, with distinct patterns observed across age cohorts, sexes, and CM types (Fig. 1; Table 1). Notably, there were no significant associations between CM and deviations in normative SV in the pediatric cohort.

Childhood Abuse. In young adult males, more severe childhood abuse was associated with *larger* volumes in the bilateral thalamus and pallidum, which partially persisted in older adult males. Older adult males with more severe experiences of abuse exhibited *smaller* amygdala volumes. In young adult females, more severe childhood abuse was associated with *larger* volumes in the bilateral thalamus and pallidum; as well as *smaller* volumes of the bilateral hippocampus and putamen. This pattern persisted primarily in the right-hemisphere structures in the older adult females (Fig. 1A; Table 1).

Childhood Neglect. No significant associations were observed between childhood neglect and SV deviations in males across all age cohorts. In contrast, young adult females showed positive associations between more severe childhood neglect and *larger* bilateral pallidum volumes. Consistent with our analyses with childhood abuse, greater severity of neglect in young adult females was also associated with *smaller* volumes in the right hippocampus and left putamen. In older adult females, greater severity of neglect was associated with *smaller* volumes in the left putamen, *smaller* bilateral caudate volumes, and *larger* right thalamic volumes (Fig. 1B; Table 1).

Associations Between Cortical Thickness Deviation Scores and ELA

Our analyses revealed significant associations between CM and deviations from normative cortical thickness (CT) in adults, with distinct patterns observed across age cohorts, sexes, and CM types (Fig. 2; Table 2). No significant associations were observed between CM and deviations from normative CT in the pediatric cohort.

Childhood Abuse. In young adult males, greater childhood abuse severity was significantly associated with *thinner* cortical regions in the bilateral isthmus cingulate, right banks of the superior temporal sulcus, right middle temporal, left lateral occipital, and right supramarginal areas and, conversely, *thicker* bilateral medial and lateral orbitofrontal cortices. No associations between CM and CT deviations were found in older adult males (Fig. 2A; Table 2). In young adult females, greater childhood abuse severity was associated with *thinner* bilateral caudal anterior cingulate, left inferior parietal, left isthmus cingulate, left posterior cingulate, left insula, right entorhinal, and right middle temporal regions, but *thicker* right medial orbitofrontal cortex. Older adult females showed partially similar results, with greater childhood abuse severity associated with *thinner* bilateral isthmus, posterior, and caudal anterior cingulate regions, left lateral occipital, lingual, and supramarginal areas, but *thicker* bilateral medial orbitofrontal cortices and left inferior temporal cortex (Fig. 2A; Table 2).

Childhood Neglect. The effects of childhood neglect on CT deviation scores were not as pronounced or as widespread compared to those observed with abuse. In young adult males, more severe childhood neglect was associated with *thinner* right middle temporal cortex. No significant associations were found in older adult males. In young adult females, more severe childhood neglect was associated with *thinner* right entorhinal cortex. In older adult females, more severe childhood neglect was associated with *thinner* left posterior cingulate and lingual gyrus (Fig. 2B; Table 2).

Associations Between Surface Area Deviation Scores and ELA

Our analyses revealed significant associations between CM and deviations from normative surface area (SA) in adults, with patterns varying by age, sex, and CM type (Fig. 3; Table 3). Consistent with our previous analyses, no significant associations were found between CM and SA deviation scores in the pediatric cohort.

Childhood Abuse. In young adult males, more severe childhood abuse was associated with *smaller* SA in the right banks of the superior temporal sulcus and right superior parietal region but *larger* SA in the bilateral frontal pole. In older adult males, more severe childhood abuse was associated with *smaller* SA of the temporal pole (Fig. 3A; Table 3). In young adult females, more severe childhood abuse was associated with *larger* SA in several regions, including the banks of the left superior temporal sulcus, left isthmus of the cingulate, and bilateral fusiform, inferior parietal, and parahippocampal areas, but *larger* SA in bilateral occipital regions, medial orbitofrontal cortex, pars orbitalis, and the frontal and temporal poles. This pattern persisted in older adult females, although to a lesser extent (Fig. 3A; Table 3).

Childhood Neglect. The SA deviations associated with childhood neglect were not as pronounced or as widespread as the effects that we observed with abuse. In males, no significant associations between childhood neglect and SA deviation were detected. In females, associations were only found in young adults: greater severity of childhood neglect was associated with *smaller* SA in bilateral cingulate cortex, parietal lobes, and fusiform regions, as well as *larger* SA in lateral occipital regions, orbitofrontal cortices, and the temporal pole (Fig. 3B; Table 3).

Sex and Age Differences in Brain-CM Associations

Fisher's exact tests revealed young adults demonstrated stronger associations than older adults across all three morphometric phenotypes and both types of CM exposure. Additionally, females generally showed stronger associations with CM than males, particularly for SA measures (Table S5).

Sensitivity Analyses

Sensitivity analyses confirmed the robustness of our primary findings. Results remained consistent after adjusting for diagnostic status, across leave-one-out cross-validation, with ComBat-GAM harmonization, and when analyzing MDD and PTSD cohorts separately (Tables S6–S7; Fig. S4). Additional sensitivity analyses examining the specificity of abuse versus neglect, effects of sexual abuse specifically, and adjustment for years of education are reported (Tables S8–S10; Fig. S5). Bootstrap analysis indicated limited statistical power in the pediatric cohort (Results S1).

Discussion

In this large-scale transdiagnostic investigation, we leveraged normative modeling to characterize the neuroanatomical alterations of childhood maltreatment (CM) across the lifespan. Our findings demonstrate that the structural associations with early-life adversity (ELA) are not uniform; rather, they appear deeply intertwined with developmental timing and biological sex. Widespread deviations in cortical thickness, surface area, and subcortical volume were most pronounced during young adulthood, with females exhibiting significantly more extensive structural alterations than males. These cross-sectional results challenge the notion of one static trauma signature, suggesting instead that the observable neuroanatomical impact of CM is shaped by the types and severity of ELA as well as sex-specific neurodevelopmental trajectories.

Childhood abuse showed the most extensive effects across subcortical and cortical regions, particularly among young adult females, with many patterns persisting at reduced magnitude in older adult females. Neglect effects were more circumscribed: in young adult females, they were limited to surface area deviations primarily in cingulate regions, while in young adult males, effects were restricted to smaller right middle temporal cortex. Notably, both abuse and neglect in young adult females were associated with overlapping alterations, including smaller right entorhinal cortex, reduced surface area in fusiform and inferior parietal regions, and larger surface area in lateral occipital, medial orbitofrontal cortices, and temporal poles. Across sexes, young adults exposed to abuse exhibited larger bilateral thalamus and pallidum volumes, smaller isthmus cingulate cortex, and larger medial orbitofrontal cortex.

Broadly, these distinct patterns support longstanding theories and emerging evidence that different forms of CM differentially shape neurocircuits implicated in affective, cognitive, and socioemotional processing (18, 39) and that many of these effects are sex-specific (33, 57) and transdiagnostic (58-60). Our findings revealed nuanced associations between CM and brain morphometry, with some regions showing larger structural deviations and others showing smaller (i.e., more negative) deviations within the same age cohort. These opposing patterns likely reflect complex reorganizational changes across neural circuits rather than uniform effects, potentially resulting from compensatory

adaptation and learning during development (61-63). Although we did not detect significant associations in the pediatric cohort (n=349), this null finding is likely attributable to limited statistical power, based on our power analysis.

The more pronounced effects in females, particularly during young adulthood and potentially as a consequence of sexual trauma, suggest that there are important sex-specific neural vulnerabilities to CM to consider within a *sensitive period* framework (25). This may reflect interactions between CM and sex-specific neurodevelopmental trajectories, potentially mediated by gonadal hormones and their organizational effects on brain development. Sociocultural factors and potential "normalizing" effects of treatment in older individuals may also contribute to these. The effects of CM on brain morphometry were observed primarily in association cortices, which undergo protracted development and may be particularly vulnerable to ELA during adolescence and young adulthood. Additionally, although we found no significant associations among the pediatric cohort, our power analysis suggests this likely reflects limited statistical power rather than ta rue absence of effects. The implications of these findings for sensitive period and incubation models are discussed in the Supplemental Discussion.

Our study is not without limitations. First, cross-sectional data preclude causal inferences about CM effects on neurodevelopmental trajectories. Second, as a measure of CM, the CTQ does not capture all forms of ELA (e.g., housing instability, toxicant exposure). Third, although the sample size in our pediatric cohort is among the largest in the literature, we likely had limited statistical power to detect subtle effects. Fourth, we could not fully account for confounders including socioeconomic status, symptom severity, and medication use, which could not be harmonized across sites. Additionally, sample heterogeneity in CM timing, chronicity, and co-occurrence of abuse/neglect may obscure nuanced associations. Our sensitivity analyses suggest stronger unique effects of abuse, with neglect effects largely attenuated after adjusting for abuse severity. Future longitudinal research with comprehensive ELA assessments and consideration of genetic, epigenetic, and resilience factors is needed. Full limitations are discussed in the Supplemental Discussion.

Despite these limitations, our investigation reveals that ELA in the form of childhood maltreatment has widespread effects on brain structure, with particularly pronounced effects on association cortices in young adult females. The distinct patterns observed for abuse versus neglect, along with sex-specific effects, underscore the complexity of how ELA shapes brain development during periods of heightened susceptibility. While future longitudinal research in at-risk samples is needed to determine whether these neurobiological pathways mediate the associations between CM and emergence of stress-based psychopathologies, our results are broadly consistent with this hypothesis. Specifically, individuals with MDD or PTSD who experienced childhood maltreatment also exhibit distinct brain morphometry patterns compared to those without such exposures, suggesting potentially different neurobiological pathways to these disorders. This heterogeneity may partially explain mixed treatment responses often observed clinically. While our results do not directly address treatment resistance, they suggest value in assessing ELA history when developing treatment plans, as recognizing these distinct patterns may inform more comprehensive care for trauma-exposed individuals. Future research should determine whether these distinct brain morphometric patterns predict differential responses to pharmacological and psychological interventions. Finally, our results highlight the importance of early intervention and that adolescence and young adulthood may represent vital intervention points, particularly for females with a history of childhood maltreatment.

Acknowledgements

ZQL is supported by Fonds de Recherche du Québec – Nature et Technologies (FRQNT); AH is supported by R01 MH111671 and VISN6 MIRECC; CA is supported by the Beth K and Stuart Yudofsky Chair in the Neuropsychiatry of Military Post Traumatic Stress Syndrome; NA is supported by the Deutsche Forschungsgemeinschaft (DFG, grant to SFB/TRR 393 – Project-ID 521379614).
JUB is supported by NIMH MH106998; UD is supported by the German Research Foundation (DFG) grant FOR2107 DA1151/5-1, DA1151/5-2, DA1151/9-1, DA1151/10-1, DA1151/11-1 to UD; SFB/TRR 393, project grant no 521379614) and the Interdisciplinary Center for Clinical Research (IZKF) of the medical faculty of Münster; TdC is supported by R01 MH106574; DD is supported by the National Institute for Health and Care Research (NIHR) Maudsley Biomedical Research Centre, South London and Maudsley NHS Trust; NF is supported by MH101380 and MH111671-01A1; CHF is supported by the National Institute for Health and Care Research (NIHR) Maudsley Biomedical Research Centre (Grant JR 4), and the International Psychoanalytical Association (IPA 158102845); EMG is supported by R01 NS140256; IG is supported by NIMH R37 101495; RGM is supported by the German Federal Ministry of Education and Research (BMBF: 01 ZX 1507, “PreNeSt – e:Med”); NAG is supported by the Bill & Melinda Gates Foundation [OPP 1017641]; IHR is supported by MH102634 and the U.S. National Center for PTSD; RH is supported by NIMH R01 MH132221 and R01 MH128371; SLB is supported by R01 MH126814 and U01 MH121737; AB is supported by JDRF (3-SRA-2019-836-M-B) and the Department of Defense (W81XWH-18-1-0230); LG is supported by R01 MH117229, R01 MH118181, R61 AT009864-01A1, R33 AT009864, and the Beckman Foundation; JCS is supported by partial grants from NIMH (R01 MH12345), SUNOVION (Research Grant), and Mind Medicine (Research Grant); DJS is supported by the South African Medical Research Council (SAMRC); FS is supported by the German Research Foundation (DFG, SFB/TRR 393, project grant no. 521379614); BSJ is supported by NIMH R01 MH131532; JT is supported by the Canadian Institutes of Health Research (CIHR) and the Canadian

Institute for Military and Veteran Health Research (CIMVHR); SIT is supported by R01 MH121806, R01 MH129742, and R01 AG058854 (to PMT); LLvdH is supported by the South African Medical Research Council (SAMRC) MRC-RFA-IFSP-01-2013/SHARED ROOTS; XW is supported by R21 MH098198-01 and the ProMedica Translational Research Stimulation Award; HW is supported by Wellcome Trust funding (220857/Z/20/Z); TY is supported by the National Center for Complementary and Integrative Health (1R61 AT009864-01A1 and R33 AT009864); XZ is supported by K01 MH122774; PMT is supported by R01 MH121806, R01 MH129742, and R01 AG058854; LH is supported by a Veni Award (grant number 09150162210201) from the Dutch Research Council (NWO); LS is supported by NIH R01 MH129742 and by a Dame Kate Campbell Fellowship at the University of Melbourne; TCH is supported by K01 MH117442 (TIGER), the Klingenstein Third Generation Foundation (Child and Adolescent Depression Fellow Award), the Stanford Maternal Child and Health Institute (Early Career Award and K Support Award), the Stanford Center for Cognitive and Neurobiological Imaging (Seed Grant), the Ray and Dagmar Dolby Family Fund, and NIH (R01 MH127176, R21 MH130817). We thank Erin O'Leary, Geoffrey May, Orren Ravid, and Julia Herzog for their contributions to data collection. Finally, an earlier version of this manuscript (prior to peer-review and the extensive revisions made in response to reviewer feedback) has been posted on bioRxiv.

Disclosures

CA served as a consultant and on advisory boards for Douglas Pharmaceutical, Freedom Biosciences, Aptinyx, Genentech, Janssen, Psilocybin Labs, Lundbeck, Guidepoint, and FSV7. He also received royalties from a patent for using mTORC1 inhibitors to augment the effects of antidepressants. IHR reports research funding from BI Pharma on precision psychiatry.

RH is a consultant for Jazz Pharmaceuticals.

LL reports unpaid membership on the Scientific Committee for the International Society for the Study of Trauma and Dissociation (ISSTD) and spousal IP payments from Vanderbilt University for

technology licensed to Acadia Pharmaceuticals and spousal private equity in Violet Therapeutics unrelated to the present work.

EAO reports employment at Crisis Text Line.

KR has performed scientific consultation for Bioxcel, Bionomics, Acer, and Jazz Pharma; serves on Scientific Advisory Boards for Sage, Boehringer Ingelheim, Senseye, and the Brain Research Foundation, and he has received sponsored research support from Alto Neuroscience.

AE reports salary and equity from Alto Neuroscience, equity from Mindstrong Health and Akili Interactive.

TTY reports a clinical trials agreement that provides funds to UCSF by NeuroQore, and a portion of these funds to UCSF have supported TTY's effort on paper(s) with NeuroQore. None of the funds from NeuroQore supported TTY's efforts on this current paper.

All other authors report no biomedical financial interests or potential conflicts of interest.

Data Sharing Statement

The datasets analyzed during the current study are not publicly available due to site restrictions, but data may be available from the corresponding sites on reasonable requests.

Supplement Description:

Supplement Methods, Results, Discussion, Figures S1-S5, Tables S1-S10

References

1. Swedo EA, Aslam MV, Dahlberg LL, Niolon PH, Guinn AS, Simon TR, et al. Prevalence of Adverse Childhood Experiences Among U.S. Adults — Behavioral Risk Factor Surveillance System, 2011–2020. MMWR Morb Mortal Wkly Rep. 2023;72(26):707-15.

2. 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;67(2):113-23.

3. 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. Archives of general psychiatry. 2012;69(11):1151-60.

4. Cuijpers P, Smit F, Unger F, Stikkelbroek Y, Ten Have M, de Graaf R. The disease burden of childhood adversities in adults: a population-based study. Child Abuse Negl. 2011;35(11):937-45.

5. LeMoult J, Humphreys KL, Tracy A, Hoffmeister J-A, Ip E, Gotlib IH. Meta-analysis: Exposure to early life stress and risk for depression in childhood and adolescence. J Am Acad Child Adolesc Psychiatry. 2020;59(7):842-55.

6. Teicher MH, Samson JA. Childhood maltreatment and psychopathology: A case for ecophenotypic variants as clinically and neurobiologically distinct subtypes. Am J Psychiatry. 2013;170(10):1114-33.

7. Frodl T, Janowitz D, Schmaal L, Tozzi L, Dobrowolny H, Stein DJ, et al. Childhood adversity impacts on brain subcortical structures relevant to depression. J Psychiatr Res. 2017;86:58-65.

8. Logue MW, van Rooij SJH, Dennis EL, Davis SL, Hayes JP, Stevens JS, et al. Smaller hippocampal volume in posttraumatic stress disorder: A multisite ENIGMA-PGC study: Subcortical volumetry results from posttraumatic stress disorder consortia. Biol Psychiatry. 2018;83(3):244-53.

9. Nemeroff CB. Paradise lost: The neurobiological and clinical consequences of child abuse and neglect. Neuron. 2016;89(5):892-909.

10. Gee DG, Casey BJ. The impact of developmental timing for stress and recovery. Neurobiol Stress. 2015;1:184-94.

11. Rutherford S, Fraza C, Dinga R, Kia SM, Wolfers T, Zabihi M, et al. Charting brain growth and aging at high spatial precision. Elife. 2022;11.

12. Ge R, Yu Y, Qi YX, Fan Y-N, Chen S, Gao C, et al. Normative modelling of brain morphometry across the lifespan with CentileBrain: algorithm benchmarking and model optimisation. Lancet Digit Health. 2024;6(3):e211-e21.

13. Wierenga LM, Doucet GE, Dima D, Agartz I, Aghajani M, Akudjedu TN, et al. Greater male than female variability in regional brain structure across the lifespan. Hum Brain Mapp. 2022;43(1):470-99.

14. Frangou S, Modabbernia A, Williams SCR, Papachristou E, Doucet GE, Agartz I, et al. Cortical thickness across the lifespan: Data from 17,075 healthy individuals aged 3-90 years. Hum Brain Mapp. 2022;43(1):431-51.

15. Rutherford S, Kia SM, Wolfers T, Fraza C, Zabihi M, Dinga R, et al. The Normative Modeling Framework for Computational Psychiatry. bioRxiv. 2022.

16. Lenroot RK, Giedd JN. Sex differences in the adolescent brain. Brain and cognition. 2010;72(1):46-55.

17. McCrory E, De Brito SA, Viding E. The impact of childhood maltreatment: a review of neurobiological and genetic factors. Front Psychiatry. 2011;2:48.

18. Teicher MH, Samson JA. Annual Research Review: Enduring neurobiological effects of childhood abuse and neglect. Child Psychology Psychiatry. 2016;57(3):241-66.

19. Bethlehem RAI, Seidlitz J, White SR, Vogel JW, Anderson KM, Adamson C, et al. Brain charts for the human lifespan. Nature. 2022;604(7906):525-33.

20. Marquand AF, Kia SM, Zabihi M, Wolfers T, Buitelaar JK, Beckmann CF. Conceptualizing mental disorders as deviations from normative functioning. Mol Psychiatry. 2019;24(10):1415-24.

21. Marquand AF, Rezek I, Buitelaar J, Beckmann CF. Understanding Heterogeneity in Clinical Cohorts Using Normative Models: Beyond Case-Control Studies. Biol Psychiatry. 2016;80(7):552-61.

22. Wolfers T, Doan NT, Kaufmann T, Alnæs D, Moberget T, Agartz I, et al. Mapping the Heterogeneous Phenotype of Schizophrenia and Bipolar Disorder Using Normative Models. JAMA psychiatry. 2018;75(11):1146-55.

23. Lupien SJ, McEwen BS, Gunnar MR, Heim C. Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nat Rev Neurosci. 2009;10(6):434-45.

24. Dannlowski U, Stuhrmann A, Beutelmann V, Zwanzger P, Lenzen T, Grotegerd D, et al. Limbic scars: long-term consequences of childhood maltreatment revealed by functional and structural magnetic resonance imaging. Biological psychiatry. 2012;71(4):286-93.

25. Gabard-Durnam LJ, McLaughlin KA. Do sensitive periods exist for exposure to adversity? Biol Psychiatry. 2019;85(10):789-91.

26. 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? Psychol Med. 2018;48(15):2562-72.

27. Baumeister D, Akhtar R, Ciufolini S, Pariante CM, Mondelli V. Childhood trauma and adulthood inflammation: a meta-analysis of peripheral C-reactive protein, interleukin-6 and tumour necrosis factor-α. Mol Psychiatry. 2016;21(5):642-9.

28. Gunnar MR, Quevedo KM. Early care experiences and HPA axis regulation in children: a mechanism for later trauma vulnerability. Prog Brain Res. 2008;167:137-49.

29. Andersen SL, Teicher MH. Desperately driven and no brakes: developmental stress exposure and subsequent risk for substance abuse. Neurosci Biobehav Rev. 2009;33(4):516-24.

30. Dannlowski U, Kugel H, Huber F, Stuhrmann A, Redlich R, Grotegerd D, et al. Childhood maltreatment is associated with an automatic negative emotion processing bias in the amygdala: Amygdalar Emotion Processing Bias. Hum Brain Mapp. 2013;34(11):2899-909.

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

32. Cohodes EM, Chen SH, Lieberman AF, Bush NR. Examination of the associations between young children's trauma exposure, trauma-symptomatology, and executive function. Child Abuse Negl. 2020;108(104635):104635.

33. Teicher MH, Anderson CM, Ohashi K, Khan A, McGreenery CE, Bolger EA, et al. Differential effects of childhood neglect and abuse during sensitive exposure periods on male and female hippocampus. NeuroImage. 2018;169:443-52.

34. Beck D, Whitmore L, MacSweeney N, Brieant A, Karl V, de Lange A-MG, et al. Dimensions of early-life adversity are differentially associated with patterns of delayed and accelerated brain maturation. Biol Psychiatry. 2025;97(1):64-72.

35. Baram TZ, Davis EP, Obenaus A, Sandman CA, Small SL, Solodkin A, et al. Fragmentation and unpredictability of early-life experience in mental disorders. Am J Psychiatry. 2012;169(9):907-15.

36. Pechtel P, Pizzagalli DA. Effects of early life stress on cognitive and affective function: An integrated review of human literature. Psychopharmacology. 2011;214(1):55-70.

37. Callaghan BL, Tottenham N. The Stress Acceleration Hypothesis: Effects of early-life adversity on emotion circuits and behavior. Curr Opin Behav Sci. 2016;7:76-81.

38. Teicher MH, Samson JA, Anderson CM, Ohashi K. The effects of childhood maltreatment on brain structure, function and connectivity. Nat Rev Neurosci. 2016;17(10):652-66.

39. Sheridan MA, McLaughlin KA. Dimensions of early experience and neural development: deprivation and threat. Trends Cogn Sci. 2014;18(11):580-5.

40. Cassiers LLM, Sabbe BGC, Schmaal L, Veltman DJ, Penninx BWJH, Van Den Eede F. Structural and Functional Brain Abnormalities Associated With Exposure to Different Childhood Trauma Subtypes: A Systematic Review of Neuroimaging Findings. Front Psychiatry. 2018;9.

41. Garcia M, Montalvo I, Creus M, Cabezas Á, Solé M, Algora MJ, et al. Sex differences in the effect of childhood trauma on the clinical expression of early psychosis. Compr Psychiatry. 2016;68:86-96.

42. Molnar BE, Buka SL, Kessler RC. Child sexual abuse and subsequent psychopathology: results from the National Comorbidity Survey. Am J Public Health. 2001;91(5):753-60.

43. Group ECHRfPW, Haas SS, Ge R, Agartz I, Amminger GP, Andreassen OA, et al. Normative Modeling of Brain Morphometry in Clinical High Risk for Psychosis. JAMA psychiatry. 2023.

44. Haas SS, Ge R, Agartz I, Paul Amminger G, Andreassen OA, Bachman P, et al. Normative modeling of brain morphometry in Clinical High-Risk for Psychosis. bioRxiv. 2023.

45. Schmaal L, Pozzi E, C Ho T, van Velzen LS, Veer IM, Opel N, et al. ENIGMA MDD: seven years of global neuroimaging studies of major depression through worldwide data sharing. Transl Psychiatry. 2020;10(1):172.

46. Huggins AA, Baird CL, Briggs M, Laskowitz S, Hussain A, Fouda S, et al. Smaller total and subregional cerebellar volumes in posttraumatic stress disorder: a mega-analysis by the ENIGMA-PGC PTSD workgroup. Mol Psychiatry. 2024;29(3):611-23.

47. Thompson PM, Jahanshad N, Ching CRK, Salminen LE, Thomopoulos SI, Bright J, et al. ENIGMA and global neuroscience: A decade of large-scale studies of the brain in health and disease across more than 40 countries. Transl Psychiatry. 2020;10(1):100.

48. Desikan RS, Segonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. NeuroImage. 2006;31(3):968-80.

49. Fischl B. FreeSurfer. NeuroImage. 2012;62(2):774-81.

50. Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl. 2003;27(2):169-90.

51. Ge R, Yu Y, Qi YX, Fan YV, Chen S, Gao C, et al. Normative modeling of brain morphometry across the lifespan using CentileBrain: Algorithm benchmarking and model optimization. bioRxivorg. 2023.

52. Pomponio R, Erus G, Habes M, Doshi J, Srinivasan D, Mamourian E, et al. Harmonization of large MRI datasets for the analysis of brain imaging patterns throughout the lifespan. NeuroImage. 2020;208:116450.

53. Writing Committee for the E-CNVWG, van der Meer D, Sønderby IE, Kaufmann T, Walters GB, Abdellaoui A, et al. Association of Copy Number Variation of the 15q11.2 BP1-BP2 Region With Cortical and Subcortical Morphology and Cognition. JAMA psychiatry. 2020;77(4):420-30.

54. Boedhoe PSW, van Rooij D, Hoogman M, Twisk JWR, Schmaal L, Abe Y, et al. Subcortical Brain Volume, Regional Cortical Thickness, and Cortical Surface Area Across Disorders: Findings From the ENIGMA ADHD, ASD, and OCD Working Groups. Am J Psychiatry. 2020;177(9):834-43.

55. Quidé Y, Watkeys OJ, Tonini E, Grotegerd D, Dannlowski U, Nenadić I, et al. Childhood trauma moderates schizotypy-related brain morphology: analyses of 1182 healthy individuals from the ENIGMA schizotypy working group. Psychol Med. 2023:1-13.

56. Sharkey RJ, Bacon C, Peterson Z, Rootes-Murdy K, Salvador R, Pomarol-Clotet E, et al. Differences in the neural correlates of schizophrenia with positive and negative formal thought disorder in patients with schizophrenia in the ENIGMA dataset. Mol Psychiatry. 2024.

57. Keding TJ, Heyn SA, Russell JD, Zhu X, Cisler J, McLaughlin KA, et al. Differential Patterns of Delayed Emotion Circuit Maturation in Abused Girls With and Without Internalizing Psychopathology. Am J Psychiatry. 2021;178(11):1026-36.

58. McLaughlin KA, Peverill M, Gold AL, Alves S, Sheridan MA. Child maltreatment and neural systems underlying emotion regulation. J Am Acad Child Adolesc Psychiatry. 2015;54(9):753-62.

59. Heleniak C, Jenness JL, Stoep AV, McCauley E, McLaughlin KA. Childhood maltreatment exposure and disruptions in emotion regulation: A transdiagnostic pathway to adolescent internalizing and externalizing psychopathology. Cognit Ther Res. 2016;40(3):394-415.

60. 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;197(5):378-85.

61. Draganski B, Gaser C, Busch V, Schuierer G, Bogdahn U, May A. Neuroplasticity: changes in grey matter induced by training: Neuroplasticity. Nature. 2004;427(6972):311-2.

62. May A. Experience-dependent structural plasticity in the adult human brain. Trends Cogn Sci. 2011;15(10):475-82.

63. Zatorre RJ, Fields RD, Johansen-Berg H. Plasticity in gray and white: neuroimaging changes in brain structure during learning. Nat Neurosci. 2012;15(4):528-36.

Figures

Figure 1. Deviations from Normative Subcortical Volume Associated with Childhood Trauma. **(A).** Normative deviations in subcortical volumes associated with abuse in males and females; **(B).** Normative deviations in subcortical volumes associated with neglect in males and females. β represents the standardized effect size from the general linear model (GLM, FDR corrected $q<.05$)**.** Results from the pediatric cohort are not displayed as there were no significant associations between CTQ and subcortical volumes in this age cohort.

Figure 2. Deviations from Normative Cortical Thickness Associated with Childhood Trauma. **(A).** Normative deviations in cortical thickness associated with abuse in males and females; **(B).** Normative deviations in cortical thickness associated with neglect in males and females. β represents the standardized effect size from the GLM (FDR corrected $q<.05$). Results from the pediatric cohort are not displayed as there were no significant associations between CTQ and subcortical volumes in this age cohort.

Figure 3. Deviations from Normative Surface Area Associated with Childhood Trauma. **(A).** Normative deviations in surface area associated with abuse in males and females; **(B).** Normative deviations in surface area associated with neglect in males and females. β represents the standardized effect size from the GLM (FDR corrected $q<.05$). Results from the pediatric cohort are not displayed as there were no significant associations between CTQ and subcortical volumes in this age cohort.

Tables

Childhood Trauma	Sex	Region	Young Adult (n=1908)		Older Adult (n=1454)	
			β (SE)	***p* value**	**β (SE)**	***p* value**
Abuse	**Male**	Left Thalamus	**0.126 (0.036)**	**5.56e-04**	-0.026 (0.041)	5.37e-01
		Right Thalamus	**0.1 (0.037)**	**6.32e-03**	-0.034 (0.041)	4.16e-01
		Left Pallidum	**0.143 (0.036)**	**9.40e-05**	**0.117 (0.041)**	**4.51e-03**
		Right Pallidum	**0.171 (0.036)**	**2.76e-06**	**0.114 (0.041)**	**5.74e-03**
		Left Amygdala	-0.043 (0.037)	2.46e-01	**-0.104 (0.041)**	**1.21e-02**
		Right Amygdala	0.007 (0.037)	8.56e-01	**-0.12 (0.041)**	**3.54e-03**
	Female	Right Thalamus	**0.11 (0.029)**	**1.62e-04**	**0.141 (0.034)**	**3.01e-05**
		Left Caudate	**-0.065 (0.029)**	**2.69e-02**	-0.07 (0.034)	3.93e-02
		Left Putamen	**-0.139 (0.029)**	**2.05e-06**	**-0.155 (0.034)**	**4.27e-06**
		Right Putamen	**-0.106 (0.029)**	**2.74e-04**	-0.05 (0.034)	1.45e-01
		Left Pallidum	**0.164 (0.029)**	**1.79e-08**	**0.146 (0.034)**	**1.55e-05**
		Right Pallidum	**0.169 (0.029)**	**6.17e-09**	**0.115 (0.034)**	**7.29e-04**
		Left Hippocampus	**-0.08 (0.029)**	**6.53e-03**	-0.019 (0.034)	5.68e-01
		Right Hippocampus	**-0.129 (0.029)**	**1.09e-05**	-0.038 (0.034)	2.69e-01
Neglect	**Male**	-	-		-	
	Female	Right Thalamus	0.064 (0.029)	2.96e-02	**0.096 (0.034)**	**4.64e-03**
		Left Caudate	-0.032 (0.029)	2.71e-01	**-0.087 (0.034)**	**1.06e-02**
		Right Caudate	-0.039 (0.029)	1.78e-01	**-0.086 (0.034)**	**1.08e-02**
		Left Putamen	**-0.073 (0.029)**	**1.28e-02**	**-0.102 (0.034)**	**2.55e-03**
		Left Pallidum	**0.114 (0.029)**	**9.09e-05**	0.057 (0.034)	9.41e-02
		Right Pallidum	**0.124 (0.029)**	**2.22e-05**	0.032 (0.034)	3.43e-01
		Right Hippocampus	**-0.092 (0.029)**	**1.68e-03**	0.013 (0.034)	6.98e-01

Table 1. Deviations from Normative Subcortical Volume Associated with Childhood Trauma. P-values are **t**hresholded to show regions with normative values significantly associated with childhood trauma in at least one age cohort. See the full results table of all regions and cohorts in Table S4. Significant regions

(q<.05) are indicated by bolded effect sizes and p values. β represents the standardized effect size from the GLM. Results from the pediatric cohort are not displayed as there were no significant associations between CTQ and subcortical volumes in this age cohort.

Childhood Trauma	Sex	Region	Young Adult (n=1905)		Older Adult (n=1449)	
			β (SE)	*p* value	β (SE)	*p* value
Abuse	Male	Left Isthmus cingulate	**-0.13 (0.036)**	**3.68e-04**	-0.017 (0.041)	6.83e-01
		Left Lateral occipital	**-0.114 (0.037)**	**1.94e-03**	-0.066 (0.041)	1.10e-01
		Left Lateral orbitofrontal	**0.152 (0.036)**	**3.40e-05**	-0.016 (0.041)	7.07e-01
		Left Medial orbitofrontal	**0.132 (0.036)**	**3.15e-04**	0.107 (0.041)	9.40e-03
		Right Bankssts	**-0.153 (0.036)**	**2.83e-05**	-0.117 (0.041)	4.65e-03
		Right Isthmus cingulate	**-0.118 (0.037)**	**1.25e-03**	-0.029 (0.041)	4.84e-01
		Right Lateral orbitofrontal	**0.142 (0.036)**	**1.01e-04**	0.013 (0.041)	7.47e-01
		Right Medial orbitofrontal	**0.184 (0.036)**	**4.78e-07**	0.102 (0.041)	1.36e-02
		Right Middle temporal	**-0.164 (0.036)**	**6.85e-06**	-0.016 (0.041)	6.99e-01
		Right Supramarginal	**-0.123 (0.036)**	**7.56e-04**	-0.061 (0.041)	1.44e-01
	Female	Left Caudal anterior cingulate	**-0.116 (0.029)**	**7.59e-05**	**-0.132 (0.034)**	**9.95e-05**
		Left Inferior parietal	**-0.095 (0.029)**	**1.15e-03**	-0.075 (0.034)	2.83e-02
		Left Inferior temporal	0.005 (0.029)	8.69e-01	**0.098 (0.034)**	**3.99e-03**
		Left Isthmus cingulate	**-0.103 (0.029)**	**4.26e-04**	**-0.127 (0.034)**	**1.81e-04**
		Left Lateral occipital	-0.076 (0.029)	9.51e-03	**-0.108 (0.034)**	**1.53e-03**
		Left Lingual	-0.004 (0.029)	8.96e-01	**-0.099 (0.034)**	**3.61e-03**
		Left Medial orbitofrontal	0.057 (0.029)	5.39e-02	**0.107 (0.034)**	**1.68e-03**
		Left Posterior cingulate	**-0.124 (0.029)**	**2.28e-05**	**-0.166 (0.034)**	**9.57e-07**
		Left Supramarginal	-0.01 (0.029)	7.27e-01	**-0.097 (0.034)**	**4.50e-03**
		Left Insula	**-0.083 (0.029)**	**4.67e-03**	0.015 (0.034)	6.62e-01
		Right Caudal anterior cingulate	**-0.09 (0.029)**	**2.02e-03**	-0.035 (0.034)	3.09e-01
		Right Caudal middle frontal	-0.044 (0.029)	1.37e-01	**-0.107 (0.034)**	**1.71e-03**
		Right Entorhinal	**-0.114 (0.029)**	**9.69e-05**	-0.054 (0.034)	1.14e-01
		Right Isthmus cingulate	-0.058 (0.029)	4.88e-02	**-0.091 (0.034)**	**7.40e-03**
		Right Medial orbitofrontal	**0.087 (0.029)**	**2.95e-03**	**0.104 (0.034)**	**2.19e-03**
		Right Middle temporal	**-0.1 (0.029)**	**6.34e-04**	-0.023 (0.034)	4.92e-01
		Right Posterior cingulate	-0.049 (0.029)	9.75e-02	**-0.103 (0.034)**	**2.39e-03**
Neglect	Male	Right Middle temporal	**-0.146 (0.036)**	**6.82e-05**	0.018 (0.041)	6.65e-01
	Female	Left Lingual	-0.027 (0.029)	3.64e-01	**-0.124 (0.034)**	**2.49e-04**
		Left Posterior cingulate	-0.057 (0.029)	5.07e-02	**-0.111 (0.034)**	**1.04e-03**
		Right Entorhinal	**-0.1 (0.029)**	**6.55e-04**	-0.002 (0.034)	9.54e-01

Table 2. Deviations from Normative Cortical Thickness Associated with Childhood Trauma. P-values are thresholded to show regions with normative values significantly associated with childhood trauma in at least one age cohort. See the full results table of all regions and cohorts in Table S4. Significant regions (q<.05) are indicated by bolded effect sizes and p values. β represents the standardized effect size from the GLM. Results from the pediatric cohort are not displayed as there were no significant associations between CTQ and subcortical volumes in this age cohort.

Childhood Trauma	Sex	Region	Young Adult (n=1905)		Older Adult (n=1449)	
			β (SE)	*p* value	β (SE)	*p* value
Abuse	Male	Left Pars orbitalis	**0.156 (0.036) ***	**1.92e-05**	0.066 (0.041)	1.10e-01
		Left Frontal pole	**0.133 (0.036) ***	**2.89e-04**	0.06 (0.041)	1.45e-01
		Right Bankssts	**-0.12 (0.036) ***	**1.07e-03**	-0.077 (0.041)	6.30e-02
		Right Superior parietal	**-0.117 (0.037) ***	**1.44e-03**	0.006 (0.041)	8.82e-01
		Right Frontal pole	**0.144 (0.036) ***	**8.52e-05**	0.083 (0.041)	4.52e-02
		Right Temporal pole	0.103 (0.037)	4.86e-03	**0.18 (0.041) ***	**1.22e-05**
	Female	Left Bankssts	**-0.085 (0.029) ***	**3.68e-03**	-0.022 (0.034)	5.11e-01
		Left Entorhinal	0.026 (0.029)	3.80e-01	**0.104 (0.034) ***	**2.13e-03**
		Left Fusiform	**-0.101 (0.029) ***	**5.92e-04**	-0.026 (0.034)	4.51e-01
		Left Inferior parietal	**-0.079 (0.029) ***	**7.37e-03**	-0.048 (0.034)	1.56e-01
		Left Inferior temporal	**0.075 (0.029) ***	**1.00e-02**	0.071 (0.034)	3.70e-02
		Left Isthmus cingulate	**-0.07 (0.029) ***	**1.73e-02**	-0.021 (0.034)	5.32e-01
		Left Lateral occipital	**0.089 (0.029) ***	**2.30e-03**	0.072 (0.034)	3.52e-02
		Left Medial orbitofrontal	**0.096 (0.029) ***	**1.07e-03**	0.066 (0.034)	5.14e-02
		Left Middle temporal	**0.082 (0.029) ***	**4.92e-03**	**0.121 (0.034) ***	**3.53e-04**
		Left Parahippocampal	**-0.109 (0.029) ***	**1.85e-04**	-0.036 (0.034)	2.97e-01
		Left Pars opercularis	**-0.093 (0.029) ***	**1.56e-03**	**-0.086 (0.034) ***	**1.16e-02**
		Left Pars orbitalis	**0.114 (0.029) ***	**9.75e-05**	**0.113 (0.034) ***	**8.48e-04**
		Left Precuneus	-0.042 (0.029)	1.57e-01	**-0.086 (0.034) ***	**1.13e-02**
		Left Superior temporal	**0.071 (0.029) ***	**1.60e-02**	0.078 (0.034)	2.18e-02
		Left Frontal pole	**0.219 (0.029) ***	**4.50e-14**	**0.199 (0.033) ***	**3.32e-09**
		Left Temporal pole	**0.101 (0.029) ***	**5.92e-04**	**0.16 (0.034) ***	**2.44e-06**
		Right Bankssts	**-0.085 (0.029) ***	**3.65e-03**	-0.013 (0.034)	7.09e-01
		Right Caudal anterior cingulate	**-0.096 (0.029) ***	**1.09e-03**	0.017 (0.034)	6.15e-01
		Right Entorhinal	**0.138 (0.029) ***	**2.19e-06**	**0.097 (0.034) ***	**4.16e-03**
		Right Fusiform	**-0.116 (0.029) ***	**7.60e-05**	-0.025 (0.034)	4.65e-01
		Right Inferior parietal	**-0.073 (0.029) ***	**1.22e-02**	-0.024 (0.034)	4.76e-01
		Right Inferior temporal	**0.1 (0.029) ***	**6.00e-04**	0.082 (0.034)	1.65e-02
		Right Lateral occipital	**0.15 (0.029) ***	**2.98e-07**	**0.094 (0.034) ***	**5.47e-03**
		Right Lingual	**0.084 (0.029) ***	**4.26e-03**	0.04 (0.034)	2.41e-01
		Right Medial orbitofrontal	**0.171 (0.029) ***	**4.12e-09**	**0.213 (0.033) ***	**2.74e-10**
		Right Middle temporal	**0.073 (0.029) ***	**1.33e-02**	**0.101 (0.034) ***	**2.92e-03**

		Right Parahippocampal	**-0.07 (0.029) ***	**1.68e-02**	-0.062 (0.034)	6.83e-02
		Right Pars opercularis	**-0.067 (0.029) ***	**2.14e-02**	-0.049 (0.034)	1.48e-01
		Right Pars orbitalis	**0.099 (0.029) ***	**7.19e-04**	0.066 (0.034)	5.39e-02
		Right Postcentral	**-0.079 (0.029) ***	**7.20e-03**	-0.029 (0.034)	4.01e-01
		Right Precentral gyrus	**-0.094 (0.029) ***	**1.38e-03**	-0.026 (0.034)	4.52e-01
		Right Precuneus	-0.049 (0.029)	9.80e-02	**-0.115 (0.034) ***	**7.22e-04**
		Right Rostral anterior cingulate	**-0.154 (0.029) ***	**1.30e-07**	**-0.095 (0.034) ***	**5.11e-03**
		Right Rostral middle frontal	-0.003 (0.029)	9.29e-01	**-0.092 (0.034) ***	**7.08e-03**
		Right Superior parietal	-0.038 (0.029)	2.00e-01	**-0.123 (0.034) ***	**2.91e-04**
		Right Supramarginal	**-0.085 (0.029) ***	**3.72e-03**	**-0.096 (0.034) ***	**4.63e-03**
		Right Frontal pole	**0.187 (0.029) ***	**1.25e-10**	**0.153 (0.034) ***	**6.31e-06**
		Right Temporal pole	**0.199 (0.029) ***	**7.66e-12**	**0.138 (0.034) ***	**4.88e-05**
		Right Transverse temporal	**-0.074 (0.029) ***	**1.17e-02**	-0.012 (0.034)	7.30e-01
Neglect	**Male**	-	-		-	
	Female	Left Caudal anterior cingulate	**-0.07 (0.029) ***	**1.72e-02**	-0.012 (0.034)	7.18e-01
		Left Fusiform	**-0.077 (0.029) ***	**8.91e-03**	-0.017 (0.034)	6.25e-01
		Left Inferior parietal	**-0.078 (0.029) ***	**8.13e-03**	-0.073 (0.034)	3.22e-02
		Left Lateral occipital	**0.095 (0.029) ***	**1.20e-03**	0.018 (0.034)	5.91e-01
		Left Parahippocampal	**-0.101 (0.029) ***	**5.42e-04**	-0.049 (0.034)	1.47e-01
		Left Pars orbitalis	**0.09 (0.029) ***	**2.08e-03**	0.053 (0.034)	1.19e-01
		Left Frontal pole	**0.138 (0.029) ***	**2.22e-06**	0.103 (0.034)	2.50e-03
		Right Bankssts	**-0.094 (0.029) ***	**1.37e-03**	-0.011 (0.034)	7.48e-01
		Right Cuneus	**0.072 (0.029) ***	**1.44e-02**	-0.04 (0.034)	2.39e-01
		Right Entorhinal	**0.107 (0.029) ***	**2.49e-04**	0.01 (0.034)	7.74e-01
		Right Fusiform	**-0.075 (0.029) ***	**1.06e-02**	-0.038 (0.034)	2.66e-01
		Right Inferior parietal	**-0.088 (0.029) ***	**2.72e-03**	-0.02 (0.034)	5.55e-01
		Right Inferior temporal	**0.091 (0.029) ***	**1.93e-03**	0.051 (0.034)	1.30e-01
		Right Lateral occipital	**0.156 (0.029) ***	**8.42e-08**	0.025 (0.034)	4.70e-01
		Right Lingual	**0.082 (0.029) ***	**5.07e-03**	0.006 (0.034)	8.56e-01
		Right Medial orbitofrontal	**0.133 (0.029) ***	**5.16e-06**	0.11 (0.034)	1.23e-03
		Right Parahippocampal	**-0.077 (0.029) ***	**8.31e-03**	-0.047 (0.034)	1.65e-01
		Right Pars orbitalis	**0.071 (0.029) ***	**1.61e-02**	0.012 (0.034)	7.22e-01
		Right Pars triangularis	**0.079 (0.029) ***	**7.00e-03**	-0.042 (0.034)	2.20e-01
		Right Postcentral	**-0.097 (0.029) ***	**9.14e-04**	0.035 (0.034)	3.01e-01
		Right Precentral gyrus	**-0.11 (0.029) ***	**1.68e-04**	-0.003 (0.034)	9.36e-01
		Right Rostral anterior cingulate	**-0.106 (0.029) ***	**2.84e-04**	-0.029 (0.034)	3.87e-01
		Right Supramarginal	**-0.092 (0.029) ***	**1.72e-03**	-0.046 (0.034)	1.79e-01
		Right Frontal pole	**0.145 (0.029) ***	**6.81e-07**	0.09 (0.034)	8.36e-03
		Right Temporal pole	**0.14 (0.029) ***	**1.69e-06**	0.047 (0.034)	1.64e-01

Table 3. Deviations from Normative Surface Area Associated with Childhood Trauma. P-values are **t**hresholded to show regions with normative values significantly associated with childhood trauma in at least one age cohort. See the full results table of all regions and cohorts in Table S4. Significant regions (q<.05) are indicated by bolded effect sizes and p values. β represents the standardized effect size from

the GLM. Results from the pediatric cohort are not displayed as there were no significant associations between CTQ and subcortical volumes in this age cohort.