HHS Public Access

Author manuscript

J Mood Anxiety Disord. Author manuscript; available in PMC 2024 October 10.

Published in final edited form as:

J Mood Anxiety Disord. 2024 September ; 7: . doi:10.1016/j.xjmad.2024.100065.

Smaller hippocampal volume is associated with anxiety symptoms in high-risk Black youth

Rebecca Lipschutz[a], **Abigail Powers**[a], **Sean T. Minton**[a], **Anais F. Stenson**[b], **Timothy D. Ely**[a], **Jennifer S. Stevens**[a], **Tanja Jovanovic**[b], **Sanne J.H. van Rooij**[a,*]

[a]Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA

[b]Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, USA

Abstract

Although there is an established link between smaller hippocampal volume and anxiety, the longitudinal relations between hippocampus structure and anxiety in diverse youth are not well understood. The present longitudinal study investigated hippocampal volumes related to anxiety symptoms in a sample of Black 8–14-year-old youth (N = 64), a population historically underrepresented in neuroimaging research. Smaller hippocampal volumes were associated with greater anxiety symptoms independent of age, sex, intracranial volume and trauma exposure. Exploratory longitudinal analyses showed smaller hippocampal volume as a predictor for anxiety symptoms (n = 37) and not a consequence of anxiety symptoms (n = 32), however results were inconclusive as this finding was no longer significant after correcting for baseline anxiety symptoms. Overall, this data increases our understanding of potential neurobiological mechanisms for anxiety in a high-risk sample of Black youth and suggests future directions into studying trajectories of developmental risk.

Keywords

Anxiety; Youth; Hippocampus; Neuroimaging; Trauma

*Correspondence to: Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, 69 Jesse Hill Jr Dr SE, Atlanta, GA 30303, USA. sanne.van.rooij@emory.edu (S.J.H. van Rooij).

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Anais Stenson reports a relationship with National Institutes of Health that includes: employment. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.xjmad.2024.100065.

1. Introduction

Anxiety disorders are common across childhood and adolescence, affecting approximately 30% of youth [1]. Importantly, childhood anxiety disorders are linked to increased risk for adult anxiety disorders and other psychopathology across the lifespan. Understanding neurobiological mechanisms underlying anxiety in youth will inform trajectories of risk and potential treatment targets.

Identifying alterations in brain structure may elucidate mechanisms and vulnerability factors for the development of anxiety disorders. Limbic regions including the hippocampus and amygdala are implicated in anxiety through emotional processes related to threat and fear learning. These regions are critical for stress regulation and are vulnerable to environmental stressors during development through increased levels of stress hormones [2,3]. Multiple cross-sectional studies in primarily white youth demonstrated associations between lower hippocampal volume and anxiety disorders [4–6] or symptoms [7], while several smaller studies ($n < 40$) showed no associations [8–12]. Structural findings for the amygdala are mixed, showing both larger [8] and smaller [6,10,11] volumes in anxious youth. To our knowledge, associations between pediatric anxiety and hippocampal and amygdala volume have not been investigated in a predominately Black sample of youth. It is important to understand neurobiological mechanisms of psychopathology and investigate these relations in diverse samples to increase generalizability of findings and reduce health disparities across underrepresented populations (Garcini et al., 2022). Although limbic structures have been implicated in anxiety disorders, the temporal relations between hippocampus structure and anxiety are not well understood. The majority of existing studies examined cross-sectional relations- thus limiting understanding of longitudinal and developmental structural alterations in the context of anxiety.

The present study investigated hippocampal and amygdala volumes related to anxiety symptoms in a sample of Black youth. In line with existing structural neuroimaging studies, we hypothesized that smaller hippocampal volume would be associated with higher risk for anxiety symptoms. To examine the temporal direction of the results, exploratory longitudinal analyses followed up on associations between brain structure and anxiety symptoms. Specifically, we tested 1) if brain structure volume prospectively predicted anxiety symptoms at follow-up assessments and 2) if anxiety symptoms at baseline predicted later brain structure volume.

2. Methods

2.1. Participants and procedures

A sample of Black children and adolescents aged 8–14 years (N = 69; M_{age} = 10.8 years, SD = 1.6; 52% female) underwent magnetic resonance imaging (MRI). Participants were recruited through the Grady Trauma Project as part of two NIH-funded studies examining intergenerational effects of trauma (R01 HD071982) and critical periods in fear processing (R01 MH111682) in Black children (see [13,14] for more details regarding recruitment and study design). Exclusion criteria for children were a history of bipolar disorder or schizophrenia, active psychotic symptoms, cognitive disability, previous head injury with

loss of consciousness, history of stroke, epilepsy, neurological disorder, autism spectrum disorder, or brain tumor, metal in the body, hearing, or vision impairment unable to be corrected by glasses.

Children participated in research visits at the laboratory and an MRI scan at Emory University. Children and caregivers completed a baseline assessment (n = 67) and at least one follow-up assessment 9- and 18-months following baseline (n = 54 and n = 43, respectively). Children completed a MRI scan at one of the three assessments, 50% (n = 34) completed their MRI at baseline, 30% (n = 20) at 9-month follow-up, and 20% (n = 15) at 18-month follow up. The protocol was approved by the Institutional Review Boards of Emory University and Grady Research Oversight Committee. Written consent was obtained from the child's legal guardian and oral (younger than 11) or written (ages 11 and older) consent was obtained from child participants. Children and caregivers were compensated for their time.

2.2. Measures

2.2.1. Anxiety symptoms—Caregivers reported on child anxiety symptoms using the Behavioral Assessment System for Children (BASC-2 [15]). The anxiety subscale includes 14 items for the child version and 11 items on the adolescent version [16], rated on a four-point Likert Scale from 0 (*never*) to 4 (*almost always*). Age and sex-normed *T* scores were generated using scoring software and ranged from 29 to 89. T scores of 50 indicate the mean; scores between 60–69 indicate at-risk and above 70 were considered clinically significant. The BASC was collected at baseline assessment (α = .84), and follow-up visits (84% completed at 9-month follow up, and 67% completed at 18-month follow up).

2.2.2. Trauma exposure—Children reported on trauma exposure with the Traumatic Events Screening Inventory (TESI) for children[17] at baseline. This 19-item questionnaire assessed potentially traumatic events, including disasters, accidents, injuries, violence, and abuse, with *Yes* or *No* to each item. The summed child trauma exposure score was used as a covariate in analyses.

2.3. MRI

Before their actual scan, participants completed a separate mock scan visit during which they were acclimated to the scanner. Structural MRI scans were acquired on 3.0-T Siemens Tim Trio (whole-body) MR scanners using a 32-channel head coil. MRI data for five participants were collected using a separate 3.0-T Siemens Tim Trio (whole-body) MR scanner; however, the same parameters and sequences were used for all participants. A T1-weighted image (176 slices, repetition time [TR] = 2250 ms, echo time [TE] = 4.18 ms, and voxel size 1 × 1 × 1 mm) was used for within-subject registration and to measure left and right hippocampal volumes. Structural T1-weighted MRI scans were analyzed using Freesurfer v6.0. Quality control and processing were performed in conjunction with standardized ENIGMA protocols (http://enigma.ini.usc.edu). Left and right hippocampal and amygdala and intracranial volumes (ICV) were extracted and exported to SPSS 26.0 (IBM SPSS Statistics 26.0). Structural data that failed extraction with Freesurfer due to motion were excluded, resulting in N = 64 for analyses.

2.4. Statistical analyses

IBM SPSS Statistics, Version 26 (IBM Corp., Armonk, NY) was used for all statistical analyses. Data was checked for normality, skewness, and kurtosis. Missing data was handled using listwise deletion. Power analyses conducted in SPSS indicated a sample size of 61 was needed to achieve 80% power for detecting a moderate effect (.35) at $\alpha = .05$ in correlation analyses. Caregiver report of anxiety symptoms and child report of trauma exposure were used in primary analyses to minimize bias from using the same reporter for both anxiety symptoms and trauma exposure. Results using child report of anxiety symptoms are included as supplementary results in Supplementary Table 1.

2.4.1. Cross-sectional analyses—We performed correlation analyses between hippocampus and amygdala volumes and anxiety symptoms reported at the visit concurrent with the MRI scan. Partial correlations correcting for age, sex, and ICV were performed. Based on prior studies with this sample illustrating significant associations between trauma exposure and hippocampus volume [18], partial correlations also corrected for trauma exposure.

2.4.2. Exploratory longitudinal analyses—To examine the temporal direction of the results, exploratory longitudinal analyses followed up on potential significant cross-sectional correlations between brain structure (hippocampus or amygdala volume) and anxiety symptoms collected at different timepoints. As children completed their MRI scan at only one of three visits, subsamples of the overall sample were used to examine correlations between brain structure volume and anxiety symptoms reported at visits 9–18 months before or after their MRI scan. Thirty-two children had baseline anxiety data and completed their MRI scan at a follow-up visit and 37 children had follow-up anxiety data 9–18 months after their MRI scan. Correlation and partial correlation analyses correcting for ICV, age, sex, and baseline anxiety symptoms were performed. Based on power analyses described above, follow-up analyses with subgroups may be underpowered and should be considered exploratory.

3. Results

Children reported exposure to an average of 5.6 potentially traumatic events ($SD = 3.5$, range = 0–18) at the baseline assessment. The mean levels of anxiety at baseline in this sample were 48.4 ($SD = 11.8$) with 20.6% (n = 13) of children in the at-risk category for anxiety and 4.8% (n = 3) with clinically significant scores. At follow up, mean anxiety levels were 47.1 ($SD = 11.8$) with 7% (n = 4) of children in the at-risk category and 5% (n = 3) with clinically significant scores. There were no significant differences in anxiety symptoms ($p = .99$) or hippocampal volume ($p = .72$) between children with MRI at baseline versus follow-up.

3.1. Cross-sectional analyses

3.1.1. Hippocampal volume and concurrent anxiety symptoms—Smaller left and right hippocampal volume correlated with higher levels of anxiety symptoms (Table 1.1, Fig. 1a,b). Partial correlations between left and right hippocampus volume with anxiety

symptoms were significant ($r = -.29$, $p = .02$, and $r = -.26$, $p = .04$, respectively) after correcting for ICV. After controlling for ICV, age, sex, and trauma exposure, the correlations between anxiety and both left and right hippocampus volume remained significant (Table 1.1).

3.1.2. Amygdala volume and concurrent anxiety symptoms—Anxiety symptoms were not correlated with right or left amygdala volume, $r = -.10$, $p = .44$, and $r = -.13$, $p = .30$, respectively. All partial correlations correcting for ICV, age, sex, and trauma were non-significant (ps = .51–.95).

3.2. Longitudinal analyses

Exploratory longitudinal analyses followed up on significant correlations between anxiety and hippocampal volume. Baseline anxiety symptoms did not significantly predict right or left hippocampus volume at follow-up assessments 9–18 months later (Table 1.2 (top); Fig. 1c). However, smaller left hippocampus volume significantly predicted increased anxiety symptoms at follow-up assessments (Table 1.2 (bottom); Fig. 1d). The negative correlation between left hippocampus and follow up anxiety symptoms remained significant after correction for ICV, $r = -.42$, $p = .01$ but not when additional covariates age, sex, trauma, and baseline anxiety were included (Table 1.2 (bottom)). Right hippocampus volume was not significantly correlated with later anxiety symptoms (Table 1.2 (bottom)).

4. Discussion

In this study, we demonstrated that smaller bilateral hippocampal volume was associated with higher levels of anxiety symptoms in a sample of highly-trauma exposed Black youth. The cross-sectional results are consistent with our hypothesis and prior studies that observed associations between smaller hippocampus with anxiety diagnoses or symptoms in adult and pediatric samples[4–7]. The association between hippocampus and anxiety symptoms remained after controlling for age, sex, ICV, and child trauma exposure, highlighting the relationship between anxiety and hippocampal volume independent of trauma exposure. This is notable as trauma exposure has been linked with reduced hippocampal volume [18] and risk for anxiety problems in youth [21]. This finding adds to prior work demonstrating reduced hippocampal volume as a potential mechanism between early adversity and stress regulation [19] and internalizing outcomes across the lifespan [20–22]. Taken together, existing research suggests that smaller hippocampal volumes in the context of early adversity and high-risk environments may increase sensitivity to later exposure to stressful life events and confer vulnerability for the development of psychopathology.

One possible explanation may be that lower hippocampal volume serves as a risk factor increasing vulnerability for anxiety disorders [20,23]. Alternatively, smaller hippocampal volume may be a consequence of anxiety disorders such that increased anxiety symptoms and related levels of stress hormones reduce hippocampal volume. Exploratory analyses examined the direction of this effect, however, were limited by the small sample size and attrition across data collection. Associations between baseline anxiety symptoms and later hippocampal volume were not observed. Smaller hippocampal volume was associated with

later anxiety problems; however, this association did not survive correction for baseline levels of anxiety symptoms.

The lack of prospective findings emphasizes the observed cross-sectional association between hippocampal volume and anxiety symptoms and requires replication of prospective analyses in larger samples. Existing longitudinal neuroimaging studies have examined bidirectional relationships between psychopathology and brain structure with mixed findings[25,26]. Early internalizing symptoms at age 5–6 predicted altered patterns of brain development 2.5 years and decreased bilateral hippocampal volume predicted later internalizing symptoms without accounting for earlier levels of internalizing symptoms. However, in a cohort of healthy adolescents no associations were observed between limbic volumes and internalizing symptoms in either direction. Notably, prior studies included primarily white, healthy samples with low trauma exposure. It is possible that other social and environmental factors may influence hippocampal development and be contributing to the lack of prospective findings in our sample of urban high-risk Black youth, including high levels of trauma exposure, socioeconomic status, or discrimination.

Additionally, the lack of prospective findings and inconsistencies in the directions of effects between our results and prior studies may be related to the participant ages and time between assessment periods. Age specific effects have been observed in this cohort and prior longitudinal studies showing differences in brain structure and function between youth below and above age 10 [18,26] related to trauma and psychopathology risk. As children in this study were first assessed at age 8–12 years of age, it is possible that anxiety symptoms had already developed for many youths, thus limiting the capacity to fully detect causal directions. Muetzel [25] included youth as young as 5 to 6 years old, highlighting the importance of capturing these developmental trajectories at earlier timepoints when the brain is rapidly developing, and behavioral problems may first emerge. Due to the sample size, we could not explore the moderating effects of age, but further exploration of these developmental sensitive periods is warranted. Lastly, the present study did not include repeated measurements of hippocampal volume; thus, we were not able to fully test the bidirectional relationships while accounting for prior hippocampal volume.

Our overall finding that smaller hippocampal volumes is associated with anxiety problems in childhood has important clinical implications. Smaller hippocampal volumes may reflect altered capacity for stress regulation and emotional processing, contributing to higher levels of symptoms. The levels of anxiety symptoms in this sample were mainly below clinical significance, suggesting that hippocampal volume may be a potential biomarker of subclinical anxiety levels. Existing mechanisms found to increase hippocampal volume could help mitigate risk for anxiety, including physical exercise, meditation/mindfulness-based interventions, and cognitive stimulation [27–29]. Early caregiving experiences and maternal behavior may also influence hippocampal growth at sensitive periods of brain development [19,30], suggesting early windows of opportunity for interventions.

Several strengths and limitations of this study should be noted. Our findings build on prior work by showing associations between smaller hippocampal volume and anxiety in a nonclinical sample of Black youth. This was a longitudinal study with a minoritized and

socioeconomically under-resourced sample that is largely understudied in neuroimaging research. Additionally, majority of prior studies examined cross-sectional associations limiting interpretation of longitudinal and developmental effects. Although the study was adequately powered to detect moderate effects in the full sample, the longitudinal analyses were likely underpowered due to reduced sample size, thus replication in larger longitudinal samples is necessary. This study focused on anxiety, however prior research has shown associations with depression and broader internalizing symptoms [24–26,31,32], thus conclusions regarding the specificity of these findings with anxiety symptoms are limited. Additional research should examine transdiagnostic mechanisms underlying internalizing psychopathology. While our findings are in line with prior studies, findings from this high-risk Black population from urban Atlanta may not generalize to other populations. Research has also demonstrated deleterious effects of poverty on hippocampus and amygdala structure [33], thus it is possible that brain structure in this sample may have been influenced by growing up in poverty. Although we did not examine unique effects of poverty in the sample, there was little variation in socioeconomic status among families as most of the families were from a low-resourced sample [34].

In this study, we demonstrate that smaller hippocampal volume is associated with greater anxiety symptoms in a high-risk sample of trauma-exposed Black youth that is underrepresented in neuroimaging research. Additional longitudinal research in larger samples is needed to examine if lower hippocampal volume is a risk factor for the development of anxiety symptoms or a consequence of experiencing anxiety and further understand these developmental adaptations even earlier in childhood. These results increase our understanding of neurobiological mechanisms for anxiety, which is important for identification of trajectories of risk and intervention opportunities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

This work was supported by the National Institutes of Health [grant numbers R01HD071982 and R01MH111682].

References

[1]. Merikangas KR, He J, Burstein M, Swanson SA, Avenevoli S, Cui L, et al. Lifetime prevalence of mental disorders in U.S. adolescents: results from the National Comorbidity Survey Replication–Adolescent Supplement (NCS-A). J Am Acad Child Adolesc Psychiatry 2010;49:980–9. 10.1016/j.jaac.2010.05.017. [PubMed: 20855043]

[2]. Sapolsky RM, Uno H, Rebert CS, Finch CE. Hippocampal damage associated with prolonged glucocorticoid exposure in primates. J Neurosci J Soc Neurosci 1990;10:2897–902. 10.1523/jneurosci.10-09-02897.1990.

[3]. McEwen BS. The neurobiology of stress: from serendipity to clinical relevance. Brain Res 2000;886:172–89. 10.1016/s0006-8993(00)02950-4. [PubMed: 11119695]

[4]. Bashford-Largo J, Zhang R, Mathur A, Elowsky J, Schwartz A, Dobbertin M, et al. Reduced cortical volume of the default mode network in adolescents with generalized anxiety disorder. Depress Anxiety 2022;39:485–95. 10.1002/da.23252. [PubMed: 35312127]

[5]. Gold AL, Steuber ER, White LK, Pacheco J, Sachs JF, Pagliaccio D, et al. Cortical thickness and subcortical gray matter volume in pediatric anxiety disorders. Neuropsychopharmacol 2017;42:2423–33. 10.1038/npp.2017.83.

[6]. Mueller SC, Aouidad A, Gorodetsky E, Goldman D, Pine DS, Ernst M. Gray matter volume in adolescent anxiety: an impact of the brain-derived neurotrophic factor Val66Met polymorphism? J Am Acad Child Adolesc Psychiatry 2013;52:184–95. 10.1016/j.jaac.2012.11.016. [PubMed: 23357445]

[7]. Koolschijn PCMP, van IJzendoorn MH, Bakermans-Kranenburg MJ, Crone EA Hippocampal volume and internalizing behavior problems in adolescence. Eur Neuropsychopharmacol 2013;23:622–8. 10.1016/j.euroneuro.2012.07.001. [PubMed: 22824414]

[8]. Bellis De, Casey MD Dahl BJ, Birmaher RE, Williamson DEB, Thomas KM, et al. A pilot study of amygdala volumes in pediatric generalized anxiety disorder. Biol Psychiatry 2000;48:51–7. 10.1016/s0006-3223(00)00835-0. [PubMed: 10913507]

[9]. Liao M, Yang F, Zhang Y, He Z, Su L, Li L. White matter abnormalities in adolescents with generalized anxiety disorder: a diffusion tensor imaging study. BMC Psychiatry 2014;14:41. 10.1186/1471-244x-14-41. [PubMed: 24528558]

[10]. Milham MP, Nugent AC, Drevets WC, Dickstein DS, Leibenluft E, Ernst M, et al. Selective reduction in amygdala volume in pediatric anxiety disorders: a voxel-based morphometry investigation. Biol Psychiatry 2005;57:961–6. [PubMed: 15860335]

[11]. Strawn JR, Hamm L, Fitzgerald DA, Fitzgerald KD, Monk CS, Phan KL. Neurostructural abnormalities in pediatric anxiety disorders. J Anxiety Disord 2015;32:81–8. 10.1016/j.biopsych.2005.01.038. [PubMed: 25890287]

[12]. Merz EC, He X, Noble KG. Anxiety, depression, impulsivity, and brain structure in children and adolescents. NeuroImage Clin 2018;20:243–51. 10.1016/j.nicl.2018.07.020. [PubMed: 30094172]

[13]. Stevens JS, Van Rooij SJH, Stenson AF, Ely TD, Powers A, Clifford A, et al. Amygdala responses to threat in violence-exposed children depend on trauma context and maternal caregiving. Dev Psychopathol 2023;35:1159–70. 10.1017/s0954579421001085. [PubMed: 34689856]

[14]. Powers A, Stevens JS, O'Banion D, Stenson AF, Kaslow N, Jovanovic T, et al. Intergenerational transmission of risk for PTSD symptoms in African American children: The roles of maternal and child emotion dysregulation. Psychol Trauma Theory Res Pr Policy 2022;14:1099–106. 10.1037/tra0000543.

[15]. Reynolds CR, Kamphaus RW, Vannest KJ. Behavior Assessment System for Children (BASC). In: Kreutzer JS, DeLuca J, Caplan B, editors. Encyclopedia of Clinical Neuropsychology. New York, NY: Springer; 2011. p. 366–71.

[16]. Cecil R. Reynolds, Kamphaus RW The Behavior Assessment System for Children (2nd ed.). 2004.

[17]. Ribbe D Psychometric review of traumatic event screening instrument for children (TESI-C). Measurement of stress, trauma, and adaptation. Lutherville, MD: Sidran Press; 1996. p. 386–7.

[18]. van Rooij R.D SJH. Smith AF. Stenson TD. Ely X. Tottenham Yang N. et al.. Increased Activation of the Fear Neurocircuitry in Children Exposed to Violence Depress Anxiety, 2020, p. 303–312, 10.1002/da.22994. [PubMed: 31951308]

[19]. VanTieghem M, Korom M, Flannery J, Choy T, Caldera C, Humphreys KL, et al. Longitudinal changes in amygdala, hippocampus and cortisol development following early caregiving adversity. Dev Cogn Neurosci 2021;48:100916. 10.1016/j.dcn.2021.100916. [PubMed: 33517107]

[20]. Gorka AX, Hanson JL, Radtke SR, Hariri AR. Reduced hippocampal and medial prefrontal gray matter mediate the association between reported childhood maltreatment and trait anxiety in adulthood and predict sensitivity to future life stress. Biol Mood Anxiety Disord 2014;4:12. 10.1186/2045-5380-4-12. [PubMed: 25408863]

[21]. Rao U, Chen L-A, Bidesi AS, Shad MU, Thomas MA, Hammen CL. Hippocampal changes associated with early-life adversity and vulnerability to depression. Biol Psychiatry 2010;67:357–64. 10.1016/j.biopsych.2009.10.017. [PubMed: 20015483]

[22]. Weissman DG, Lambert HK, Rodman AM, Peverill M, Sheridan MA, McLaughlin KA. Reduced hippocampal and amygdala volume as a mechanism underlying stress sensitization to depression following childhood trauma. Depress Anxiety 2020;37:916. 10.1002/da.23062. [PubMed: 32579793]

[23]. Schwartz CE, Kunwar PS, Hirshfeld-Becker DR, Henin A, Vangel MG, Rauch SL, et al. Behavioral inhibition in childhood predicts smaller hippocampal volume in adolescent offspring of parents with panic disorder. e605–e605 Transl Psychiatry 2015;5. 10.1038/tp.2015.95.

[24]. Picci G, Taylor BK, Killanin AD, Eastman JA, Frenzel MR, Wang Y, et al. Left amygdala structure mediates longitudinal associations between exposure to threat and long-term psychiatric symptomatology in youth. Hum Brain Mapp 2022;43:4091–102. 10.1002/hbm.25904. [PubMed: 35583310]

[25]. Muetzel RL, Blanken LME, van der Ende J, El Marroun H, Shaw P, Sudre G, et al. Tracking brain development and dimensional psychiatric symptoms in children: a longitudinal population-based neuroimaging study. Am J Psychiatry 2018;175:54–62. 10.1176/appi.ajp.2017.16070813. [PubMed: 28817944]

[26]. Jarvers I, Kandsperger S, Schleicher D, Ando A, Resch F, Koenig J, et al. The relationship between adolescents' externalizing and internalizing symptoms and brain development over a period of three years. NeuroImage Clin 2022;36:103195. 10.1016/j.nicl.2022.103195. [PubMed: 36137498]

[27]. Fotuhi M, Do D, Jack C. Modifiable factors that alter the size of the hippocampus with ageing. Nat Rev Neurol 2012;8:189–202. 10.1038/nrneurol.2012.27. [PubMed: 22410582]

[28]. Joss D, Lazar SW, Teicher MH. Effects of a mindfulness based behavioral intervention for young adults with childhood maltreatment history on hippocampal morphometry: a pilot MRI study with voxel-based morphometry. Psychiatry Res Neuroimaging 2020;301:111087. 10.1016/j.pscychresns.2020.111087. [PubMed: 32413812]

[29]. Hölzel BK, Carmody J, Vangel M, Congleton C, Yerramsetti SM, Gard T, et al. Mindfulness practice leads to increases in regional brain gray matter density. Psychiatry Res Neuroimaging 2011;191:36–43. 10.1016/j.pscychresns.2010.08.006.

[30]. Luby JL, Barch DM, Belden A, Gaffrey MS, Tillman R, Babb C, et al. Maternal support in early childhood predicts larger hippocampal volumes at school age. Proc Natl Acad Sci USA 2012;109:2854–9. 10.1073/pnas.1118003109. [PubMed: 22308421]

[31]. Albaugh MD, Nguyen T-V, Ducharme S, Collins DL, Botteron KN, D'Alberto N, et al. Age-related volumetric change of limbic structures and subclinical anxious/depressed symptomatology in typically developing children and adolescents. Biol Psychol 2017;124:133–40. 10.1016/j.biopsycho.2017.02.002. [PubMed: 28185945]

[32]. Snyder HR, Hankin BL, Sandman CA, Head K, Davis EP. Distinct patterns of reduced prefrontal and limbic gray matter volume in childhood general and internalizing psychopathology. Clin Psychol Sci 2017;5:1001–13. 10.1177/2167702617714563. [PubMed: 29399423]

[33]. Luby J, Belden A, Botteron K, Marrus N, Harms MP, Babb C, et al. The effects of poverty on childhood brain development: the mediating effect of caregiving and stressful life events. JAMA Pedia 2013;167:1135–42. 10.1001/jamapediatrics.2013.3139.

[34]. Gluck RL, Hartzell GE, Dixon HD, Michopoulos V, Powers A, Stevens JS, et al. Trauma exposure and stress-related disorders in a large, urban, predominantly African-American, female sample. Arch Women's Ment Health 2021;24:893–901. 10.1007/s00737-021-01141-4. [PubMed: 33990847]

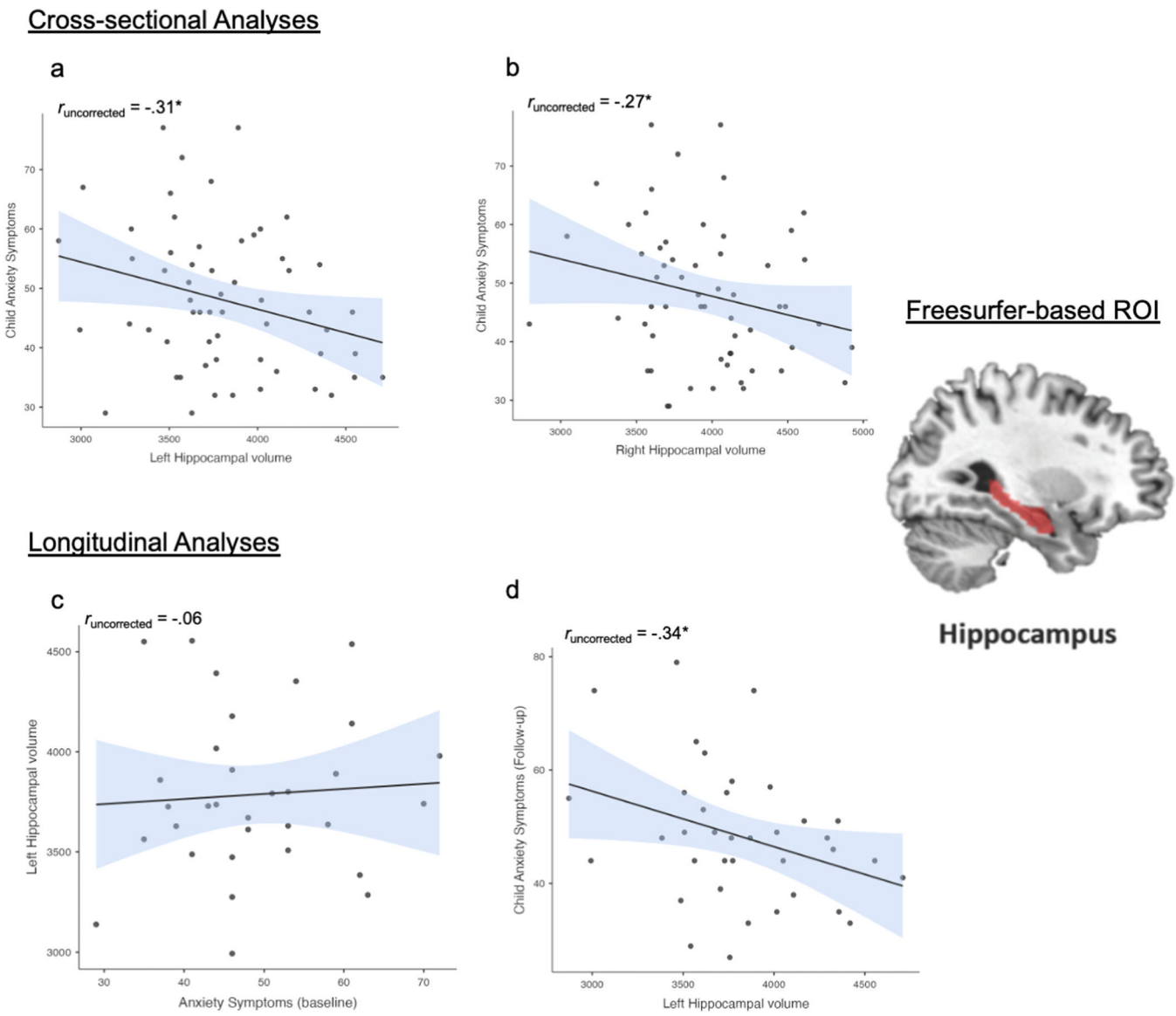

Fig. 1.

Correlation analyses of Hippocampal volume with anxiety symptoms. Results show the uncorrected analyses, the results from corrected analyses (corrected for ICV, age, sex, trauma) can be found in Table 1. (a) and (b) correlations between concurrent anxiety symptoms and hippocampus volume (N = 64). (c) correlation between baseline anxiety symptoms and follow up left hippocampus volume(n = 32) (d) correlation between left hippocampus volume and follow up anxiety symptoms (n = 37). ROI = region of interest.

Table 1

Correlations between Anxiety symptoms and Hippocampus volume.

1.1 Cross-sectional analyses		**L Hippo**		**R Hippo**	
(N = 64)		***r***	***p***	***r***	***p***
a) Uncorrected	Anxiety*1*	−.31 *	0.01	−.27 *	.03
b) Corrected for ICV		−.30 *	0.02	−.26 *	.04
c) Corrected for ICV, age, sex, and trauma		−.35 * *	0.01	−.27 *	.04
1.2 Longitudinal analyses		**L Hippo**		**R Hippo**	
(n = 32)		***r***	***p***	***r***	***p***
a) Uncorrected	$Anxiety_{bas} \rightarrow Hippo_{FU}$	.06	.72	.00	.98
b) Corrected for ICV	$Anxiety_{bas} \rightarrow Hippo_{FU}$	.04	.84	−.05	.79
c) Corrected for age, sex, ICV and trauma	$Anxiety_{bas} \rightarrow Hippo_{FU}$	−.01	.94	−.05	.80
(n = 37)					
a) Uncorrected	$Hippo \rightarrow Anxiety_{FU}$	−.34 *	.03	−.25	.14
b) Corrected for ICV	$Hippo \rightarrow Anxiety_{FU}$	−.42 *	.01	−.26	.12
c) Corrected for ICV, sex, ICV and trauma baseline anxiety	$Hippo \rightarrow Anxiety_{FU}$	−.15	.41	−.20	.28

Note.

*1*Anxiety symptoms assessed at the same timepoint as the MRI scan. L Hippo = Left Hippocampal volume. R Hippo = Right Hippocampal volume. ICV = intracranial volume. Bas = baseline assessment. FU = follow up assessment.