Meta-Analysis of Structural Magnetic Resonance Imaging Studies in Pediatric Posttraumatic Stress Disorder and Comparison with Related Conditions

SUPPLEMENTAL INFORMATION

Supplemental Methods

Database of Imaging Studies in Pediatric Posttraumatic Stress Disorder

Our additional comprehensive MEDLINE search identified five studies that were eligible for our database per inclusion criteria (Figure 1). Inclusion criteria are as follows: studies were performed in a pediatric population (i.e., included participants less than 18 years of age), included structural MRI region-of-interest (ROI) analyses with volumetric data accessible as principal summary measures of group means and standard deviations, and included participants diagnosed with PTSD. Of the additional five studies that were added to the database, three were included in the ROI meta-analysis (1-3), one only reported on the insula (4), which was a region that did not meet the threshold of having three studies to conduct a meta-analysis, and one was excluded because summary measures were not available (5). Thus, a total of 15 studies were included in the ROI meta-analysis (Figure 1, Table 1).

Pediatric PTSD Region-of-Interest Meta-Regression

In addition to age and sex, we aimed to investigate the association between the age of PTSD onset and heterogeneity in hippocampal and amygdala effect sizes. Given that only a limited number of studies included in the hippocampal (4 studies) and amygdala (3 studies) meta-analyses provided the age at diagnosis, we were unable to test this as a moderator variable (Table S2).

Comparison to Related Clinical Groups

Exact search terms for comparison studies in anxiety, depression, and trauma exposure without PTSD are as follows, respectively: "(child OR adolescent OR pediatric OR youth) AND (anxiety) AND (gray matter)", "(child OR adolescent OR pediatric OR youth) AND (depression OR depressed OR MDD OR depressive) AND (gray matter)", "(child OR adolescent OR pediatric OR youth) AND (maltreatment OR adversity OR "childhood trauma") AND (gray matter OR MRI).

Pediatric PTSD Region-of-Interest Meta-Analysis

For a given ROI, some studies separately reported left and right measures while others included only the combined total measure. For studies that only reported left and right measurements, we used a previously described method (6) to calculate the mean and standard deviation for the total volume. The method requires an estimate of the correlation coefficient between the left and right volumes. This coefficient was set to 0.8.

Supplemental Results

Meta-Analysis (Tracing Studies Only)

We conducted a secondary meta-analysis based on whether studies used hand tracing or automated delineation of ROIs. Out of the 15 studies, one study (7) used FreeSurfer image analysis suite for volumetric segmentation with an independent manual hand tracing analysis for validation. Two studies (3,8) used FreeSurfer image analysis suite for volumetric segmentation without an additional manual hand tracing confirmation (Table 1). Thus, we carried out a secondary meta-analysis for the hippocampus and amygdala in which we removed studies that used automated segmentation without a manual validation. Specifically, we removed Ahmed et al., 2012 and Weems et al., 2015 from amygdala analyses and Ahmed et al., 2012 from hippocampal analyses. Ahmed et al., 2012 was also removed from the corpus callosum meta-analysis, which resulted in only two studies remaining for this ROI. Thus, no corpus callosum results are reported here for this secondary analysis. Results from this analysis are summarized in Table S3 and Figure S1 and are consistent with the primary analyses performed including all studies. Specifically, total, right, and left hippocampal volume is smaller in the pediatric PTSD group relative to the no PTSD (without trauma exposure) group. Notably, total and left, but not right, amygdala volumes are significantly different between the PTSD and no PTSD group after the two studies are removed. Specifically, pediatric PTSD is associated with smaller total ($p=0.02$) and left ($p=0.02$) amygdala volume relative to the no PTSD group. Results from the primary analysis including all studies indicated a trend-level difference in total, right, and left amygdala volumes in pediatric PTSD relative to no PTSD, suggesting that pediatric PTSD might be associated with smaller total amygdala volume, which is consistent with the results from the secondary analysis (Table S3, Figure S1).

Meta-Regressions (Tracing Studies Only)

There was significant heterogeneity across studies for total, right, and left hippocampal as well as total and left amygdala meta-analyses (Table S3). Meta-regression results revealed that age was a significant moderator of heterogeneity for total, right, and left hippocampal regions as well as for total and left amygdala regions accounting for more than 70% of the heterogeneity across effect sizes from studies included in the regional meta-analysis (Table S4). Specifically, older age was associated with larger negative effect sizes, such that pediatric PTSD is associated with smaller hippocampal and amygdala volumes relative to no PTSD to a greater degree than in studies with younger participants (Figure S4). Sex was also a significant moderator of variability across effect sizes for total, right, and left hippocampal regions as well as total and left amygdala, accounting for more than 60% of heterogeneity across studies' effect sizes (Table S4). Specifically, a higher percentage of female participants was associated with larger negative effect sizes for total hippocampal and total amygdala volume (Figure S6).

Comparison Analyses (Tracing Studies Only)

Pediatric PTSD versus adult PTSD. There were no significant differences between effect sizes in pediatric versus adult PTSD for any hippocampal or amygdala regions (Table S6).

Pediatric PTSD versus Pediatric Exposure to Trauma without PTSD Diagnosis. Similar to the findings including all studies in the meta-analysis database, our qualitative comparison in this additional analysis revealed a difference between pediatric PTSD and pediatric exposure to trauma without PTSD. Specifically, whereas there was a medium negative effect size and small negative effect size for total hippocampal (ES=-0.58) and amygdala (ES=-0.30) volumes, respectively, in pediatric PTSD, there was a small positive and small to medium positive effect size for total hippocampal (ES=0.24) and amygdala (ES=0.42) volumes in pediatric trauma exposure without PTSD (Table S7). Thus, these findings are similar to the pediatric PTSD comparison to pediatric trauma without PTSD in which the full pediatric PTSD database was used.

Pediatric PTSD versus Pediatric Depression. Our qualitative comparison showed that pediatric PTSD was associated with medium negative effect sizes for total (ES=-.58) and right (ES=-0.52) hippocampal volumes and small negative effect size for total amygdala volume (ES=-0.30). Pediatric depression, however, was associated with small positive effect sizes for both total hippocampal (ES=0.2) and amygdala (ES=0.2) volumes (Table S8). Thus, these findings are similar to the pediatric PTSD comparison to pediatric depression in which the full pediatric PTSD database was used.

Pediatric PTSD versus Pediatric Anxiety. Paralleling findings described in the main text, our qualitative comparison in this secondary analysis revealed that both pediatric PTSD (ES=-0.58) and pediatric anxiety (ES=-0.38) were associated with a smaller total hippocampal volume (Table S9). Pediatric anxiety (ES=-0.38) and PTSD (ES=-0.52) were both also associated with smaller right hippocampal volume. Finally, whereas pediatric PTSD was associated with a small negative effect size for total amygdala volume (ES=-0.30), smaller total amygdala volume was not associated with pediatric anxiety (ES=-0.17) (Table S9).

Supplemental Figures and Tables

Study	Average Participant Age[b]	Included or Excluded	Exclusion Reason
Ahmed et al., 2012	**15.3**	**Included**	
Carrion et al., 2001	**11.0**	**Included**	
Carrion et al., 2009	**11.0**	**Included**	
Carrion et al., 2010	13.2	Excluded	Regions reported in this study were not common to three or more studies.
De Bellis et al., 1999	**12.1**	**Included**	
De Bellis et al., 2001	**10.5**	**Included**	
De Bellis et al., 2002	**11.5**	**Included**	
De Bellis et al., 2002	**12.1**	**Included**	
De Bellis et al., 2003	**11.7**	**Included**	
De Bellis et al., 2006	**12.0**	**Included**	
De Bellis et al., 2015	**10.5**	**Included**	
Keding et al., 2015	13.9	Excluded	This study used voxel-based morphometry and did not include region-of-interest data.
Klabunde et al., 2017[a]	13.9	Excluded	Regions reported in this study were not common to three or more studies.
Morey et al., 2016	**10.4**	**Included**	
Mutluer et al., 2018[a]	**15.4**	**Included**	
Postel et al., 2019[a]	**16.0**	**Included**	
Richert et al., 2006	11.0	Excluded	Regions reported in this study were not common to three or more studies.
Rinne-Albers et al., 2017[a]	16.4	Excluded	The primary summary statistics we not provided or obtainable for this study.
Thomas et al., 2004	11.7	Excluded	This study reported pituitary volume, which was a region not common to that of any other studies included in the meta-analysis.
Tupler et al., 2006	11.7	Excluded	For all regions, the sample in this study overlapped with the sample in the De Bellis et al. studies.
Weems et al., 2013	**11.0**	**Included**	
Weems et al., 2015[a]	**13.9**	**Included**	

Table S1. Database of 22 studies considered; 15 studies in the meta-analytic database are listed in boldface text. Exclusion reasons are listed for the 7 out of 22 studies that were not included in final meta-analytic database.

[a] Studies added from MEDLINE search to update database from Bromis et al., 2018 to present time (2019).

[b] Indicates average age of all participants in the study (PTSD and comparison groups).

Study	Year	Most common types of trauma exposures	Age of PTSD Onset	Time since trauma exposure	Duration of illness
Ahmed F	2012	Sexual abuse, witnessing violence, direct physical assault, motor vehicle accidents	not stated	not stated	not stated
Carrion VG	2001	Witnessing violence, physical abuse, separation and loss sexual abuse, physical neglect, emotional abuse	not stated	not stated	not stated
Carrion VG	2009	Specific exposures not stated; PTSD Reaction Index	not stated	not stated	not stated
De_Bellis MD	2015	Physical abuse or neglect, sexual abuse	6.95	not stated	3.18
De_Bellis MD	2001	Specific exposures not stated; Childhood maltreatment	4.11	3.8	6.49
De_Bellis MD	2002	Physical abuse, sexual abuse, emotional abuse, or neglect	3.9	not stated	7.18
De_Bellis MD	2003	Physical abuse, sexual abuse, emotional abuse, or neglect	3.86	not stated	7.88
De_Bellis MD	2006	Sexual abuse, witnessing domestic violence	not stated	not stated	not stated
De_Bellis MD	1999	Physical abuse, sexual abuse, emotional abuse, or neglect	4.5	not stated	7.7
De_Bellis MD	2002	Physical abuse, sexual abuse, emotional abuse, or neglect	not stated	not stated	not stated
Morey RA	2016	Witnessing domestic violence, experiencing physical, sexual, or emotional abuse and/or neglect	not stated	not stated	2.89
Mutluer T	2018	Sexual abuse	not stated	not stated	not stated
Postel C	2019	Sexual abuse, witness of suicide, car accident, loss of loved one	13.33	not stated	2.11
Weems CA	2013	Witnessing violence, physical abuse, separation and loss sexual abuse, physical neglect, emotional abuse	not stated	not stated	not stated
Weems CF	2015	Physical abuse, witnessing interpersonal violence, sexual abuse	not stated	not stated	not stated

Table S2. Supplemental demographic and clinical data from participants in database of 15 MRI studies comparing participants with PTSD to participants without PTSD.

		Sample Size		Comparison of participants with and without PTSD			Heterogeneity		
Region	Studies (n)	PTSD Group (n)	Comparison Group (n)	Effect Size	95% CI	p	I^2 (%)	p	Small-Study Bias
Gray Matter (total)	**3**	**123**	**205**	**-0.56**	**-0.83, -0.28**	**<0.001**	**25.24**	**0.26**	**0.28**
Cerebral Volume (total)	**3**	**123**	**205**	**-0.56**	**-0.79, -0.33**	**<0.001**	**0.00**	**0.59**	**0.04**
Temporal Lobe (total)	**4**	**105**	**160**	**-0.60**	**-0.86, -0.35**	**<0.001**	**0.00**	**0.79**	**0.57**
Temporal Lobe (right)	**3**	**96**	**151**	**-0.58**	**-0.85, -0.32**	**<0.001**	**0.00**	**0.60**	**0.43**
Temporal Lobe (left)	**3**	**96**	**151**	**-0.54**	**-0.80, -0.27**	**<0.001**	**0.00**	**0.50**	**0.75**
Hippocampus (total)	**6**	**150**	**238**	**-0.58**	**-0.99, -0.14**	**0.009**	**75.45**	**0.00**	**0.25**
Hippocampus (right)	**6**	**150**	**238**	**-0.52**	**-1.07, -0.09**	**0.019**	**78.56**	**0.00**	**0.27**
Hippocampus (left)	**6**	**159**	**238**	**-0.39**	**-1.00, -0.04**	**0.032**	**77.93**	**0.00**	**0.36**
Amygdala (total)	**6**	**159**	**238**	**-0.30**	**-0.73, -0.05**	**0.024**	**58.81**	**0.03**	**0.39**
Amygdala (right)	6	159	238	-0.43	-0.61, 0.01	0.054	51.71	0.07	0.47
Amygdala (left)	**6**	**150**	**238**	**-0.58**	**-0.80, -0.06**	**0.024**	**65.57**	**0.01**	**0.35**
Vermis (total)	**3**	**120**	**181**	**-0.46**	**-0.88, -0.04**	**0.033**	**64.51**	**0.06**	**0.18**

Table S3. Meta-analysis results of comparison between pediatric participants with PTSD and all participants without PTSD only including studies that use only hand tracing methods. For the meta-analytic comparison between participants with and without PTSD, significant differences are noted in boldface text. Effect sizes are reported as Hedges' g values. Negative effect sizes indicate that the region is smaller in pediatric participants with PTSD, whereas positive effect sizes indicate that the region is larger in pediatric participants with PTSD compared to participants without PTSD.

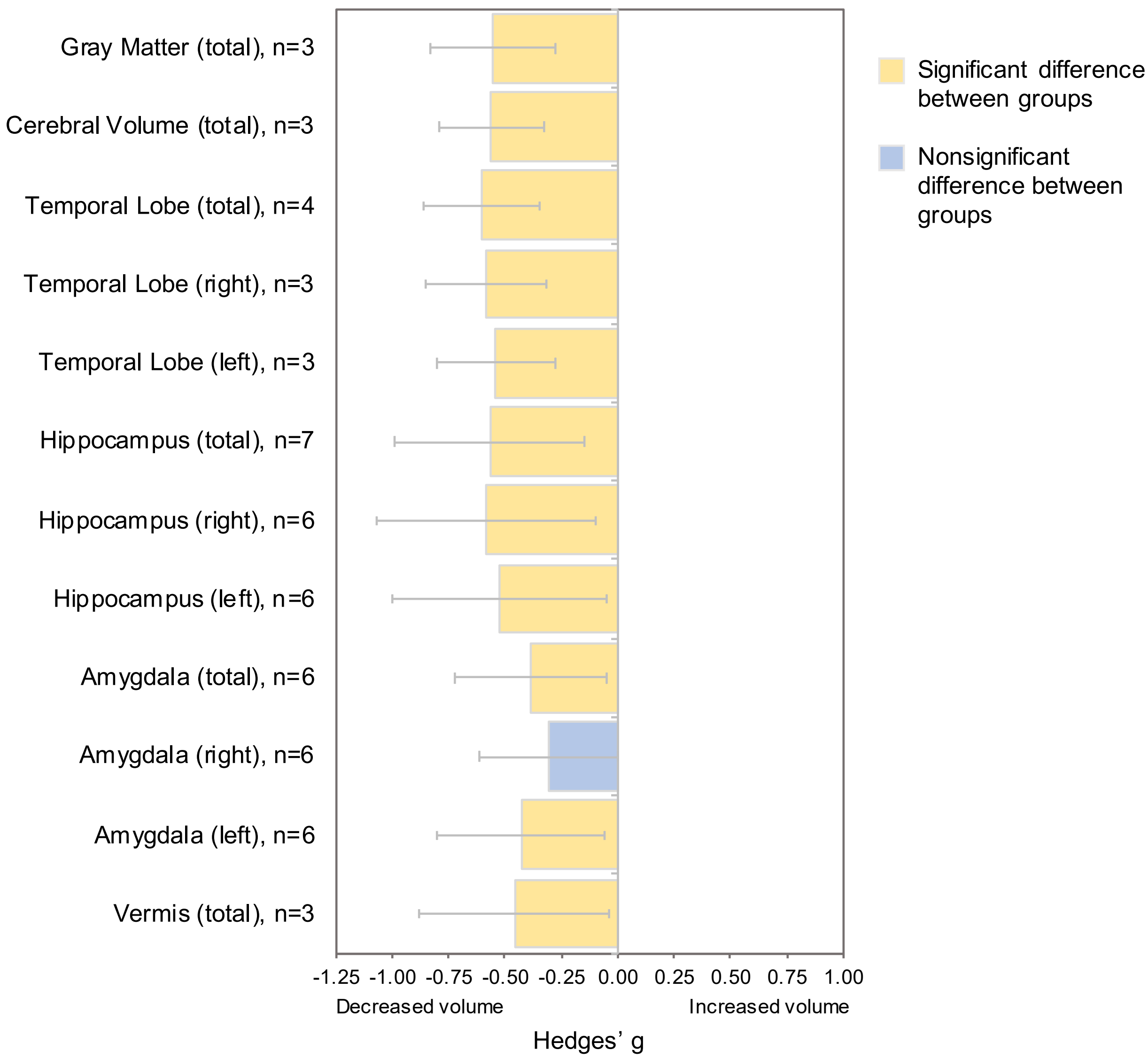

Figure S1. Meta-analysis results of comparison between pediatric participants with PTSD and all participants without PTSD only including studies that use only hand tracing methods. For each of the 12 regions in the meta-analysis, Hedges' g values are reported with 95% confidence intervals. Positive Hedges' g values indicate increased structural volume in pediatric participants diagnosed with PTSD. Negative Hedges' g values indicate smaller structural volumes in participants with pediatric PTSD. The number of studies included in the meta-analysis (n) that report on the relevant region is listed for each region. Error bars represent width of 95% confidence interval.

			Moderator: Age			Moderator: Sex		
Region	I^2%	I^2% (p-value)	R^2(%)	Test of moderator (QM)	Test of moderator (p-value)	R^2(%)	Test of moderator (QM)	Test of moderator (p-value)
Hippocampus (total)	**75.45**	**0.00**	90.08	15.33	**< .0001**	82.94	12.22	**0.0005**
Hippocampus (right)	**78.56**	**0.00**	96.98	17.75	**< .0001**	74.79	9.30	**0.0023**
Hippocampus (left)	**77.93**	**0.00**	84.52	12.55	**0.0004**	100.00	18.96	**< .0001**
Amygdala (total)	**58.81**	**0.03**	100	9.67	**0.002**	65.09	5.03	**0.025**
Amygdala (right)	51.71	0.07	100	9.19	0.002	55.88	3.68	0.055
Amygdala (left)	**65.57**	**0.01**	76.45	6.69	**0.010**	61.01	5.40	**0.020**

Table S4. Meta-regression results for meta-analysis only including studies that use only hand tracing methods. I^2: meta-analysis heterogeneity, R^2: amount of heterogeneity accounted for by moderator.

Comparison Type	Study	Participants with Comparison Condition (N)	Participants without Comparison Condition (N)	Participants with Comparison Condition Average Age (SD)	Participants without Comparison Condition Average Age (SD)	Participants with Comparison Condition Sex (Female/Male)	Participants without Comparison Condition Sex (Female/Male)
Pediatric Depression	Whittle et al., 2014	30	56	16.4 (0.42)	16.4 (0.55)	20/10	21/35
Pediatric Anxiety	Gold et al., 2017	75	76	12.1 (2.98)	12.8 (2.54)	44/31	43/33
Pediatric Exposure to Trauma without PTSD	Morey et al., 2016	32	57	10.0 (2.7)	10.82 (2.5)	17/15	32/25
Adult PTSD	Bromis et al., 2018						
Total Hippocampus		909	991	41.4 (8.23)	41.6 (8.78)	409/500	445/546
Right & Left Hippocampus		799	842	42.0 (7.99)	41.7 (8.78)	366/433	383/459
Total Amygdala		578	652	38.9 (8.71)	39.2 (8.83)	311/267	345/307
Right & Left Hippocampus		499	532	39.08 (8.60)	38.8 (8.92)	295/204	309/223

Table S5. Studies included for comparison analyses to pediatric PTSD. In studies included for pediatric depression, anxiety, and exposure to trauma without PTSD, sample sizes remained consistent across ROIs. For the adult PTSD meta-analytic study, sample size varied across ROIs.

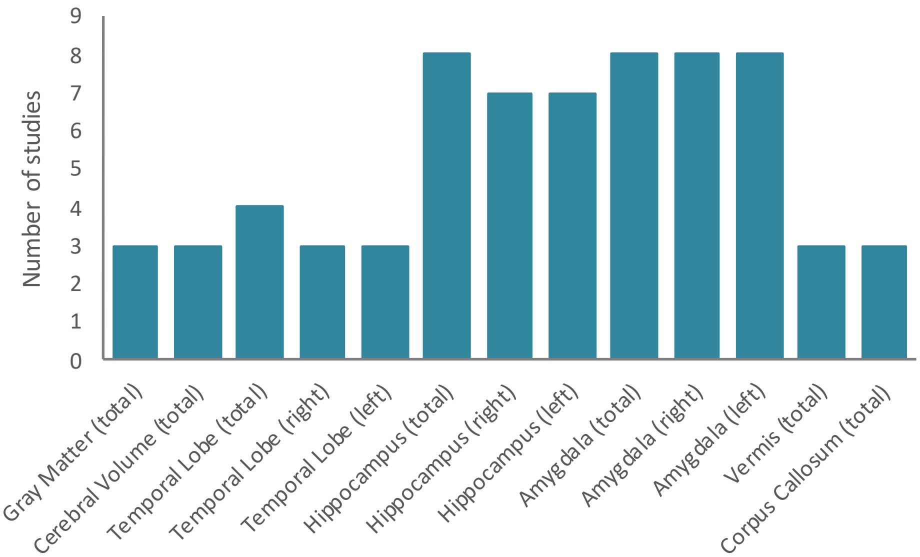

Figure S2. Frequency distribution of number of studies included in the present primary meta-analysis with 15 studies (including studies that use automated and tracing methods) that include a specific ROI.

	Pediatric PTSD Versus No Pediatric PTSD				Adult PTSD Versus No Adult PTSD				Pediatric PTSD Versus Adult PTSD	
Region	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	p	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	p	Z	p
Total Hippocampus	**150**	**238**	**-0.58**	**0.01**	**909**	**991**	**-0.47**	**0.00**	-1.02	0.39
Right Hippocampus	**150**	**238**	**-0.52**	**0.02**	**799**	**842**	**-0.42**	**0.00**	-0.35	0.19
Left Hippocampus	**159**	**238**	**-0.39**	**0.03**	**799**	**842**	**-0.38**	**0.00**	-1.51	0.24
Total Amygdala	**159**	**238**	**-0.30**	**0.02**	**578**	**652**	**-0.26**	**0.04**	0.90	0.25
Right Amygdala	159	238	-0.43	0.05	499	532	-0.24	0.09	0.31	0.59
Left Amygdala	**150**	**238**	**-0.58**	**0.02**	499	532	-0.28	0.05	1.36	0.22

Table S6. Statistical comparison of the present pediatric PTSD meta-analysis including only studies that use hand tracing methods to adult PTSD meta-analysis. For all comparisons summarized in the table, boldface text indicates significant differences between pediatric or adult PTSD and the comparison sample.

	Pediatric PTSD Versus No Pediatric PTSD			Trauma Exposure without PTSD Versus No Trauma Exposure		
Region	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	Participants with Trauma Exposure (N)	Participants without Trauma Exposure (N)	ES (g)
Total Hippocampus	150	238	-0.58	32	57	0.24
Right Hippocampus	150	238	-0.52	32	57	0.29
Left Hippocampus	159	238	-0.39	32	57	0.16
Total Amygdala	159	238	-0.30	32	57	0.42
Right Amygdala	159	238	-0.43	32	57	0.29
Left Amygdala	150	238	-0.58	32	57	0.46

Table S7. Comparison of the present pediatric PTSD meta-analysis including only studies that use hand tracing methods to pediatric exposure to trauma without PTSD.

	Pediatric PTSD Versus No Pediatric PTSD			Pediatric Depression Versus No Pediatric Depression		
Region	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	Participants with Depression (N)	Participants without Depression (N)	ES (g)
Total Hippocampus	150	238	-0.58	30	56	0.20
Right Hippocampus	150	238	-0.52	30	56	0.07
Left Hippocampus	159	238	-0.39	30	56	0.31
Total Amygdala	159	238	-0.30	30	56	0.20
Right Amygdala	159	238	-0.43	30	56	0.24
Left Amygdala	150	238	-0.58	30	56	0.11

Table S8. Comparison of the present pediatric PTSD meta-analysis including only studies that use hand tracing methods to pediatric depression.

Region	Pediatric PTSD Versus No Pediatric PTSD			Pediatric Anxiety Versus No Pediatric Anxiety		
	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	Participants with Anxiety (N)	Participants without Anxiety (N)	ES (g)
Total Hippocampus	150	238	-0.58	75	76	-0.38
Right Hippocampus	150	238	-0.52	75	76	-0.38
Left Hippocampus	159	238	-0.39	75	76	-0.31
Total Amygdala	159	238	-0.30	75	76	-0.17
Right Amygdala	159	238	-0.43	75	76	-0.06
Left Amygdala	150	238	-0.58	75	76	-0.25

Table S9. Comparison of the present pediatric PTSD meta-analysis including only studies that use hand tracing methods to pediatric anxiety.

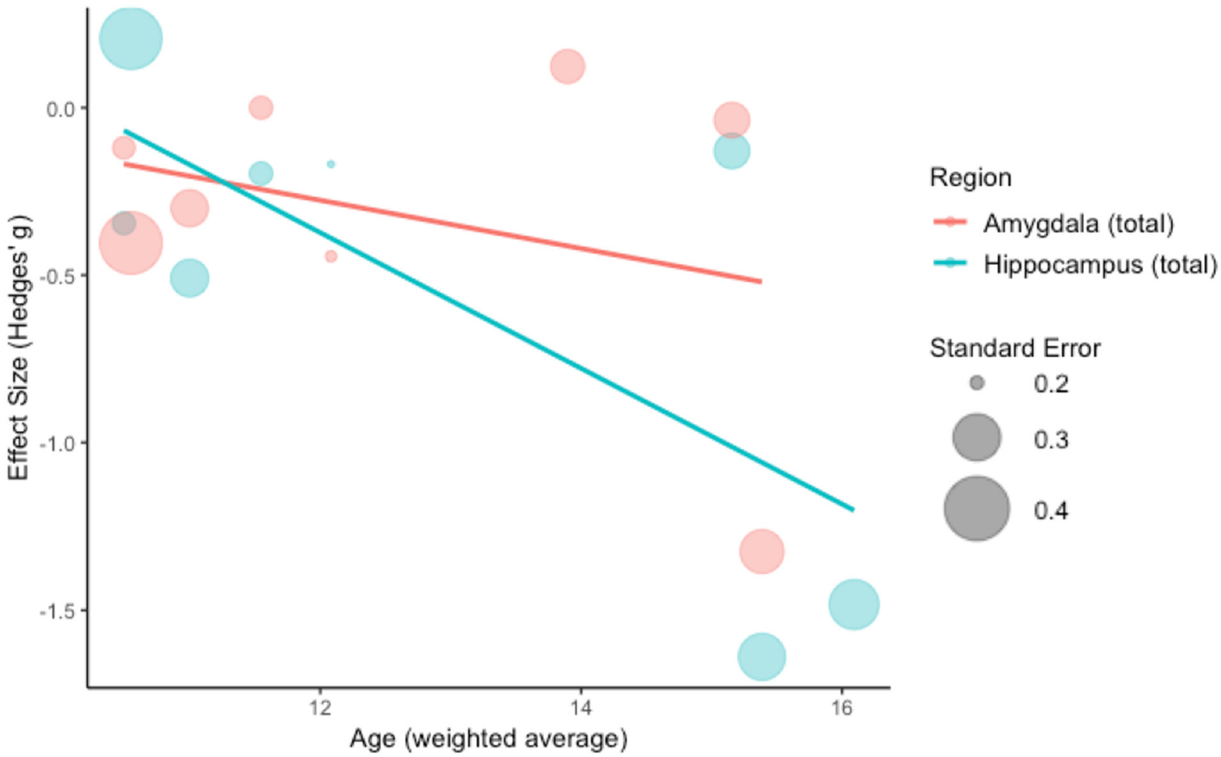

Figure S3. Bubble plot showing association between age and effect size across all studies (automated and tracing approaches) included in the meta-analysis. Older age appears to be associated, in some studies, with larger negative effect sizes for total hippocampal and total amygdala volume. Specifically, among some studies with older participants (ages 15 and older), pediatric PTSD is associated with smaller hippocampal and amygdala volumes (relative to no PTSD) to a greater degree than among studies with younger participants (approximately ages 9-13).

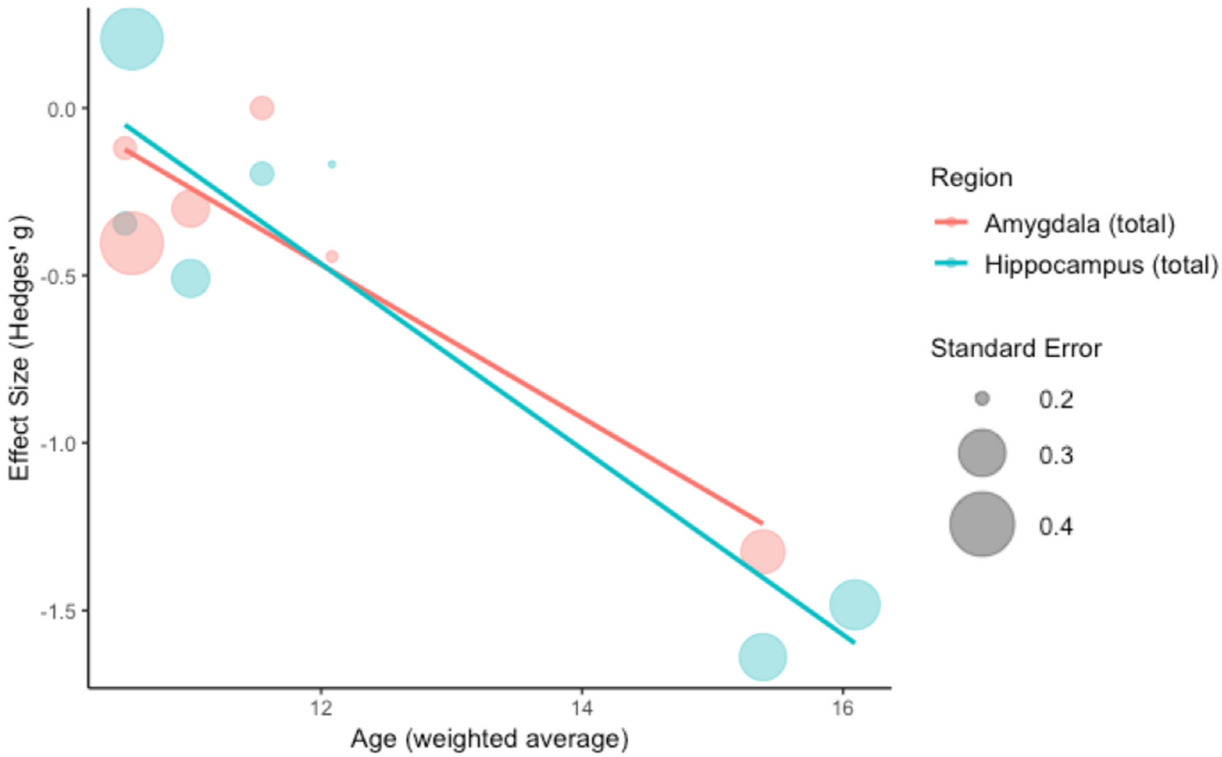

Figure S4. Bubble plot showing association between age and effect size only including studies that used tracing methods. After only studies including tracing methods were included in the database, all studies with younger participants exhibit low to moderate negative effect sizes for hippocampal amygdala volume, in which a negative effect size indicates smaller volume in the pediatric PTSD group relative to no PTSD. Studies with older participants show larger negative effect sizes, such that pediatric PTSD is associated with smaller hippocampal and amygdala volumes relative to no PTSD to a greater degree than in studies with younger participants.

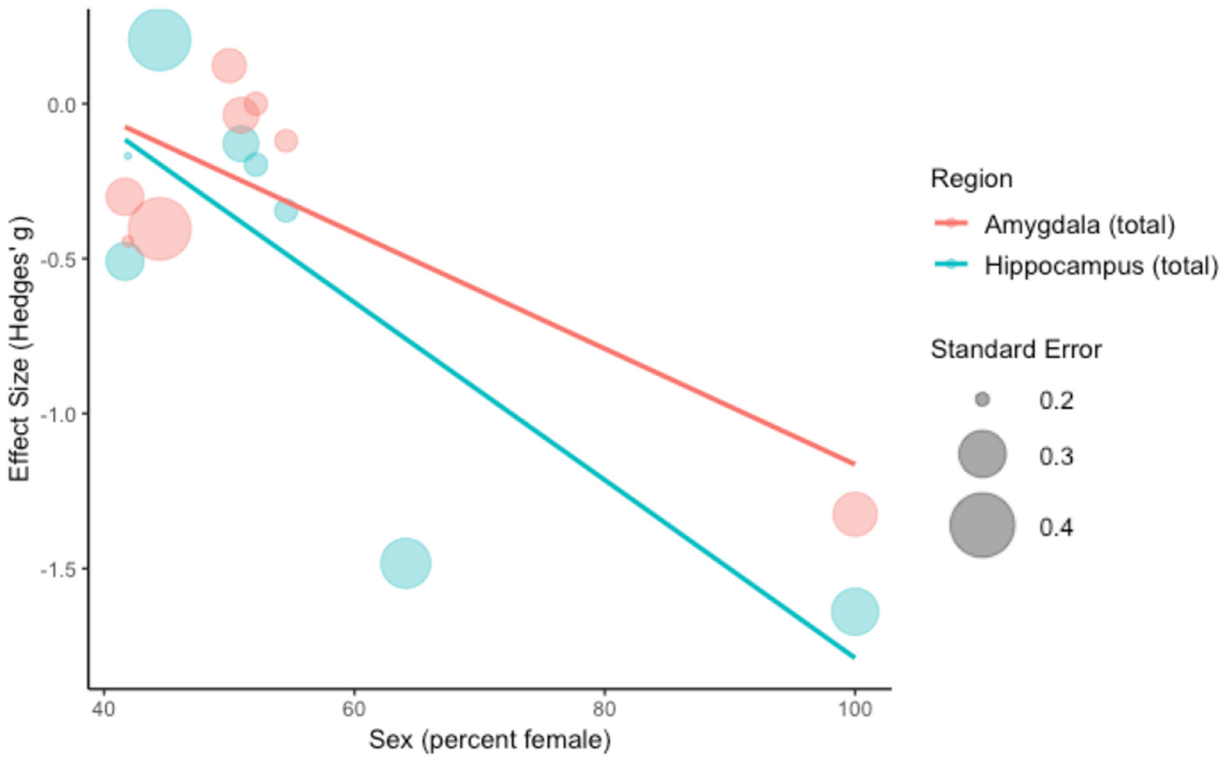

Figure S5. Bubble plot showing association between sex and effect size across all studies (automated and tracing approaches) included in the meta-analysis. Although most studies had an approximately equal number of male and female participants in the study sample, some studies had a sample that was more than 60% female. Among these studies, effect sizes were larger for hippocampal and amygdala volumes relative to studies with an approximately equal distribution of males and females. Thus, sex emerged as a significant moderator of heterogeneity such that a higher percentage of female participants was associated with larger negative effect sizes for total hippocampal and total amygdala volume.

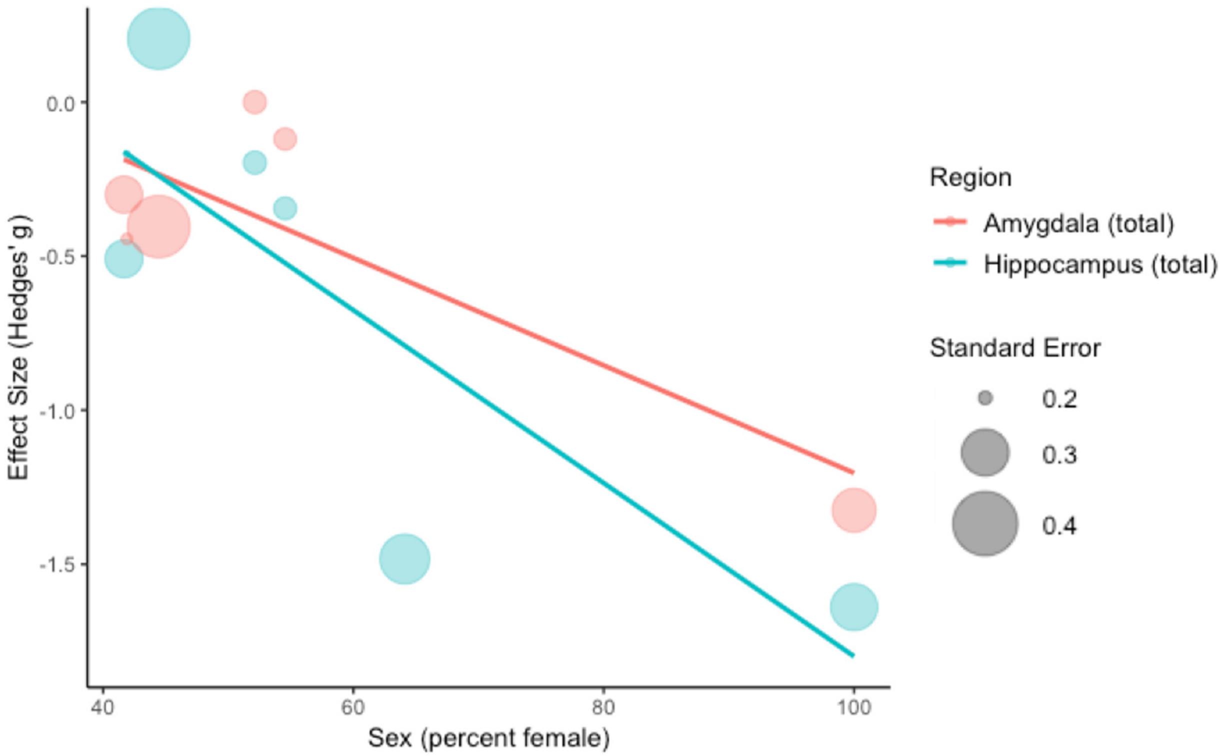

Figure S6. Bubble plot showing association between sex and effect size only including studies that used tracing methods. When only studies including tracing methods were included in the database, it remained that most studies had an approximately equal number of male and female participants in the study sample, and some studies had a sample that was more than 60% female. Among these studies, effect sizes were larger for hippocampal and amygdala volumes relative to studies with an approximately equal distribution of males and females. Thus, sex emerged as a significant moderator of heterogeneity such that a higher percentage of female participants was associated with larger negative effect sizes for total hippocampal and total amygdala volume.

Region	Pediatric PTSD Versus No Pediatric PTSD				Adult PTSD Versus No Adult PTSD				Pediatric PTSD Versus Adult PTSD	
	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	p	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	p	Z	p
Total Hippocampus	**195**	**294**	**-0.51**	**0.007**	**909**	**991**	**-0.47**	**0.00**	-0.34	0.73
Right Hippocampus	**171**	**270**	**-0.51**	**0.016**	**799**	**842**	**-0.42**	**0.00**	-0.76	0.44
Left Hippocampus	**171**	**270**	**-0.46**	**0.030**	**799**	**842**	**-0.38**	**0.00**	-0.63	0.53
Total Amygdala	208	296	-0.28	0.052	**578**	**652**	**-0.26**	**0.04**	-0.15	0.88
Right Amygdala	208	296	-0.23	0.060	499	532	-0.24	0.09	0.07	0.94
Left Amygdala	208	296	-0.29	0.073	**499**	**532**	**-0.28**	**0.05**	-0.07	0.94

Table S10. Statistical comparison of the present pediatric PTSD meta-analysis to adult PTSD meta-analysis. For all comparisons summarized in the table, boldface text indicates significant differences between pediatric or adult PTSD and the comparison sample.

Region	Pediatric PTSD Versus No Pediatric PTSD			Trauma Exposure without PTSD Versus No Trauma Exposure		
	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	Participants with Trauma Exposure (N)	Participants without Trauma Exposure (N)	ES (g)
Total Hippocampus	195	294	-0.51	32	57	0.24
Right Hippocampus	171	270	-0.51	32	57	0.29
Left Hippocampus	171	270	-0.46	32	57	0.16
Total Amygdala	208	296	-0.28	32	57	0.42
Right Amygdala	208	296	-0.23	32	57	0.29
Left Amygdala	208	296	-0.29	32	57	0.46

Table S11. Comparison of the present pediatric PTSD meta-analysis to pediatric exposure to trauma without PTSD.

Region	Pediatric PTSD Versus No Pediatric PTSD			Pediatric Depression Versus No Pediatric Depression		
	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	Participants with Depression (N)	Participants without Depression (N)	ES (g)
Total Hippocampus	195	294	-0.51	30	56	0.20
Right Hippocampus	171	270	-0.51	30	56	0.07
Left Hippocampus	171	270	-0.46	30	56	0.31
Total Amygdala	208	296	-0.28	30	56	0.20
Right Amygdala	208	296	-0.23	30	56	0.24
Left Amygdala	208	296	-0.29	30	56	0.11

Table S12. Comparison of the present pediatric PTSD meta-analysis to pediatric depression.

Region	Pediatric PTSD Versus No Pediatric PTSD			Pediatric Anxiety Versus No Pediatric Anxiety		
	Participants with PTSD (N)	Participants without PTSD (N)	ES (g)	Participants with Anxiety (N)	Participants without Anxiety (N)	ES (g)
Total Hippocampus	195	294	-0.51	75	76	-0.38
Right Hippocampus	171	270	-0.51	75	76	-0.38
Left Hippocampus	171	270	-0.46	75	76	-0.31
Total Amygdala	208	296	-0.28	75	76	-0.17
Right Amygdala	208	296	-0.23	75	76	-0.06
Left Amygdala	208	296	-0.29	75	76	-0.25

Table S13. Comparison of the present pediatric PTSD meta-analysis to pediatric anxiety.

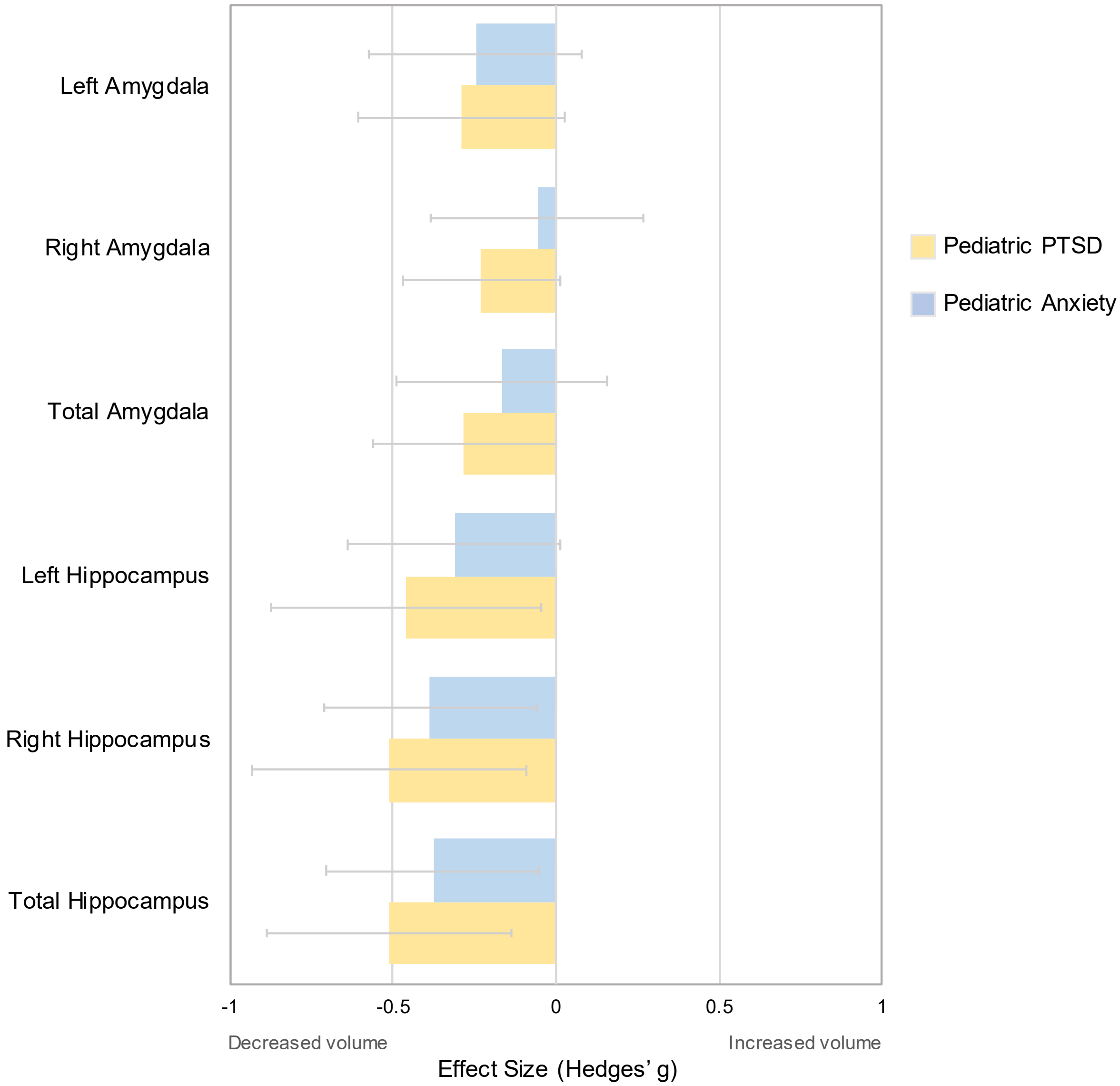

Figure S7. Comparison analysis of hippocampal and amygdala volumes between pediatric PTSD and pediatric anxiety. The comparison study is one in which pediatric anxiety (n=75) was compared to a comparison group without anxiety (n=56) (Gold et al., 2016). Positive Hedges' g values indicate increased structural volume in pediatric participants with the condition indicated in the legend. Negative Hedges' g values indicate smaller structural volumes in participants with the condition indicated in the legend. Error bars represent width of 95% confidence interval.

Supplemental References

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