Increased activation of the fear neurocircuitry in children exposed to violence

Sanne van Rooij, Emory University
Ryan Smith, Emory University
Anais F Stenson, Wayne State University
Timothy D Ely, Emory University
Xinyi Yang, Colorado School of Public Health
Nim Tottenham, Columbia University
Jennifer Stevens, Emory University
Tanja Jovanovic, Emory University

Journal Title: DEPRESSION AND ANXIETY
Volume: Volume 37, Number 4
Publisher: WILEY | 2020-01-17, Pages 303-312
Type of Work: Article | Post-print: After Peer Review
Publisher DOI: 10.1002/da.22994
Permanent URL: https://pid.emory.edu/ark:/25593/vv0fc

Final published version: http://dx.doi.org/10.1002/da.22994

Accessed September 2, 2023 9:18 AM EDT
Increased Activation of the Fear Neurocircuitry in Children Exposed to Violence

Sanne J.H. van Rooij, PhD¹, Ryan D. Smith, MD², Anaïs F. Stenson, PhD³, Timothy D. Ely, BA¹, Xinyi Yang, MS⁴, Nim Tottenham, PhD⁵, Jennifer S. Stevens, PhD¹, Tanja Jovanovic, PhD³

¹Emory University School of Medicine, Department of Psychiatry and Behavioral Sciences
²Emory University School of Medicine, Department of Family and Preventive Medicine
³Wayne State University, Department of Psychiatry and Neuroscience
⁴Colorado School of Public Health, Department of Biostatistics and Informatics
⁵Columbia University, Department of Psychology

Abstract

Most studies investigating the effect of childhood trauma on the brain are retrospective and mainly focus on maltreatment, whereas different types of trauma exposure such as growing up in a violent neighborhood, as well as developmental stage, could have differential effects on brain structure and function. The current magnetic resonance imaging (MRI) study assessed the effect of trauma exposure broadly and violence exposure more specifically, as well as developmental stage on the fear neurocircuitry in 8–14-year-old children and adolescents (N=69). We observed reduced hippocampal and increased amygdala volume with increasing levels of trauma exposure. Second, higher levels of violence exposure were associated with increased activation in the amygdala, hippocampus and vmPFC during emotional response inhibition. This association was specifically observed in children younger than 10 years. Finally, increased functional connectivity between the amygdala and brainstem was associated with higher levels of violence exposure. Based on the current findings, it could be hypothesized that trauma exposure during childhood results in structural changes that are associated with later risk for psychiatric disorders. At the same time, it could be postulated that growing up in an unsafe environment leads the brain to functionally adapt to this situation in a way that promotes survival, where the long-term costs or consequences of these adaptations are largely unknown and an area for future investigations.

Keywords

childhood trauma; response inhibition; amygdala; hippocampus; ventromedial prefrontal cortex (vmPFC); functional magnetic resonance imaging (fMRI); brain structure

Corresponding author: Sanne J.H. van Rooij, PhD, Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, 69 Jesse Hill Jr Dr SE, Atlanta, GA 30303.

Conflict of interest Authors report no conflict of interest.

Data sharing Part of the data is shared through RDoCdb (NIH data archive). The other data that support the findings of this study are available from the corresponding author upon reasonable request.
Introduction

Childhood adversity has been shown to increase risk for psychiatric disorders across the lifespan, including posttraumatic stress disorder (PTSD; Dunn, 2016; McLaughlin, 2010; McLaughlin, 2012; Norman, 2012; Widom, 2007) and depression (Dunn, 2016). One of the primary mechanisms by which childhood trauma is theorized to contribute to PTSD and similar pathologies is through alterations to the fear neural circuitry (Jovanovic & Ressler, 2010); however, the influence of trauma exposure on this circuitry during development is not fully understood.

The primary brain regions involved in the fear inhibition circuit are the amygdala, hippocampus, and ventromedial prefrontal cortex (vmPFC). The amygdala serves as an essential locus for fear acquisition, memory, and expression (Kim & Jung, 2006). Increased amygdala activation has been demonstrated in adults reporting childhood maltreatment (Dannlowski, 2013; Dannlowski, 2012; Grant, 2011; van Harmelen, 2013) as well as in maltreated or neglected children (Maheu, 2010; McCrory, 2013; Suzuki, 2014; Tottenham, 2011). Most structural MRI studies in children or adolescents with Adverse Childhood Events (ACEs) reported decreased amygdala volumes (Edmiston, 2011; Hanson, 2015; Luby, 2019; McLaughlin, 2016), though larger volumes were observed in previously institutionalized children (Mehta, 2009; Tottenham, 2010). The hippocampus functions to contextualize memory and learning, and is thought to contribute to inhibition based on contextual information (Milad, 2007). Increased hippocampal activation to threatening faces has been observed in maltreated children (Maheu, 2010). Reduced hippocampal volume has repeatedly been demonstrated in adults reporting childhood trauma (e.g. (Bremner, 2003; Stein, 1997; Teicher, 2012; Vythilingam, 2002) and in a small number of studies that investigated children or adolescents with ACEs (Hanson, 2015; Luby, 2019; McLaughlin, 2016; Paquola, 2017; Rao, 2010). Via a close interconnection with the amygdala, the vmPFC modulates and inhibits amygdala-expressed fear responses (Milad & Quirk, 2012; Phelps, 2004; Stevens, 2013). Where retrospective studies showed decreased vmPFC activation in adults with childhood adversity (Stevens, 2016; van Harmelen, 2014), studies in adolescents with early-life stress showed increased vmPFC activation on response inhibition tasks (Carrion, 2008; Mueller, 2010). Decreased resting state amygdala-vmPFC and hippocampus-vmPFC connectivity was observed in maltreated adolescents compared to controls (Herringa, 2013). Taken together, there is substantial evidence that childhood trauma impacts the fear neurocircuitry.

Inhibition also takes place on a cognitive level via response inhibition, where a learned response must be suppressed. A Go/NoGo task is frequently used to measure response inhibition, and trauma exposure and PTSD have been associated with impaired brain responses on this task (Falconer, 2008; Jovanovic, 2013; Stevens, 2016; van Rooij, 2016; van Rooij, 2018). Interestingly, impairments were found in fear inhibition regions such as the vmPFC (Jovanovic, 2013; Stevens, 2016) and hippocampus (van Rooij, 2016; van Rooij, 2018), and several prior studies used (emotional) response inhibition tasks to show alterations in the fear neurocircuitry in maltreated children (Carrion, 2008; Mueller, 2010; Tottenham, 2011).
The majority of prior studies have focused on childhood maltreatment or neglect, whereas much less is known about the effects of exposure to other types of trauma, such as violence exposure. The Grady Trauma Project is an ongoing study of PTSD risk factors in a low-income population in Atlanta, GA. Most participants live in unsafe neighborhoods in inner-city Atlanta and report high levels of trauma exposure, and PTSD and depression symptoms (Gillespie, 2009). While trauma research has focused extensively on the effects of continuous exposure to stress and trauma in an unsafe environment as part of military deployment, little is known about the neurobiological consequences of growing up in a dangerous environment and being exposed to violence on a regular basis as a normal part of life. The current study focused on the children of our adult participants to assess the effect of trauma and violence exposure during development on the fear neurocircuitry.

In line with retrospective structural MRI studies, we hypothesized that more trauma exposure would be negatively associated with hippocampal and amygdala volume. Following MRI studies suggesting associations specifically between left hippocampal volumes and PTSD symptoms (Nelson 2017) or major or bipolar depression (MacMaster 2014), we analyzed structural findings per hemisphere. Second, we expected to see a positive correlation between both trauma exposure broadly, and violence exposure more specifically, with amygdala, hippocampal and vmPFC activation during a Go/NoGo task that measured response inhibition in an emotional context. Analyses were performed for bilateral structures as there were no specific hypotheses regarding functional laterality. Finally, functional connectivity analyses were conducted to investigate if trauma or violence exposure was associated with increases in functional connectivity within the fear neurocircuitry, presented in the Supplementary Materials.

In addition to a paucity of investigation of different types of trauma, few studies have assessed the effect of developmental stage. Using retrospective recall, age 9 was identified as the age when the impact of the trauma on the fear neurocircuitry was largest, for example Teicher et al demonstrated differential effects of age and type of trauma on hippocampal and amygdala volumes (Teicher 2016; 2018). Furthermore, Gee and colleagues (2013) have found evidence of a developmental shift in neural (stimulus-elicited) connectivity around age 10, such that positive functional connectivity between the amygdala and PFC shifts to a negative connectivity pattern (Gee, 2013). Studies on sensitive periods in brain development and physiology revealed this age as a critical window in which environmental influences, such as trauma exposure, can induce long-lasting neurobiological effects (Glenn, 2012; Jovanovic, 2014). In addition to including age as a continuous covariate in the correlation analyses, we stratified by age group to assess the differential patterns of violence exposure within each age category. We therefore performed secondary analyses to assess the effect of this critical period by splitting the children in younger than 10 and 10 and older, and hypothesized that trauma exposure differentially effects the fear neurocircuitry in the two age groups.
Materials and Methods

Participants

African American children and adolescents age 8–14 years (N=69, 36 female) were recruited through the Grady Trauma Project (Gillespie, 2009). Exclusion criteria for children were a history of bipolar disorder or schizophrenia, active psychotic symptoms, or 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, or hearing or vision impairment unable to be corrected by glasses.

Testing took place at Grady Memorial Hospital and the scan at Facility for Education and Research in Neuroscience at Emory University. The protocol was approved by the Institutional Review Boards of Emory University and Research Oversight Committee at Grady Memorial Hospital. Written consent was obtained from a legal guardian of the child participant and oral (younger than 11) or written (ages 11 and older) consent was obtained from child participants.

Trauma and Violence Assessment

Interviews were conducted with each child to assess for trauma exposure broadly, violence exposure more specifically, as well as PTSD, anxiety and depression symptoms. Child-reported trauma exposure was assessed with the Traumatic Events Screening Inventory (TESI) for children (Ribbe, 1996). This 19-item questionnaire assessed a variety of potential traumatic events, such as disasters, accidents, injuries, violence and abuse, and was answered with Yes or No to each item. The total score was used in the analyses as a measure for trauma exposure broadly. Exposure to violence specifically was measured using the Violence Exposure Scale for Children-Revised (VEX-R)(Fox & Leavitt, 1995), which specifically assesses exposure to violent events. The 25-item questionnaire has a male and female version of drawings that accompany questions and a frequency rating scale to inquire about exposure to violence in the home, school, and community. This assessment has been previously used with children from the Grady Trauma Project demonstrating high rates of violence exposure (Cross, 2018). Current PTSD symptoms were assessed using the child-report UCLA PTSD Reaction Index (UCLA-RI) (Steinberg, 2004). The Behavioral Assessment System for Children (BASC) was used to assess anxiety and depression symptoms (Reynolds 2011). The BASC score is a gender- and age-corrected t-value with 50 indicating the mean.

Emotional Go/NoGo fMRI Task

The emotional Go/NoGo (eGNG) task has been previously used by Tottenham (2011) in a study with children with early life stress. Participants were instructed to press a button for fearful faces (Go trial) and withhold responses for neutral faces (NoGo trial), or vice versa, and the order of runs was counterbalanced among participants. Each stimulus was followed by a varied inter-trial interval ranging from 2500 to 15000ms. There were two runs with 36 Go trials and 12 NoGo trials in each run.
Overall reaction time, % correct Go’s, % correct NoGo’s and accuracy [correct Go’s–incorrect NoGo’s)/total number of trials] were calculated for behavioral analyses. The contrast for correct NoGo trials larger than Go trials was used for the fMRI analyses. Only accurate trials were included in the imaging analyses to ensure proper engagement of participants with the task.

**MRI Procedures and Analyses**

Participants completed a mock scan protocol at a visit prior to their actual scan during which they were acclimated to the scanner. Participants completed practice sessions of the study tasks both inside and outside of the mock scanner to ensure that they understood how to complete the task.

Functional and structural MRI scans were acquired on a 3.0-T Siemens Trio (whole-body) MR scanner using a 32-channel head coil. A T1-weighted image (176 slices, TR= 2250ms TE= 4.18ms and voxel size 1×1×1mm) was used for within-subject registration and to measure left and right hippocampal and amygdala 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 volumes, and intracranial volumes were extracted and exported to SPSS 26.0.

Two runs of 131 echo planar imaging (EPI) blood oxygen level dependent (BOLD) images (total of 262) were acquired during which the participants performed the emotional Go/NoGo task. Volumes contained 44 slices of 2.5mm thickness acquired in a descending sequential slice order parallel to the anterior-posterior commissure line, with a 0.5mm slice gap. GRAPPA parallel imaging with an acceleration factor of 2 was used to facilitate speed of acquisition. The following parameters were used: repetition time (TR)=2330ms, echo time (TE)=30ms, flip angle= 90 degrees, and voxel size 3×3×3mm.

Functional images were analyzed (file conversion, image preprocessing and statistical analyses) using Statistical Parametric Mapping, version 8 (SPM8, http://www.fil.ion.ucl.ac.uk/spm/). ArtRepair was used to detect and repair bad slices. Functional images were slice-time corrected and realigned to the first image in the session to correct for motion. Next, ArtRepair was used to detect and repair bad volumes and to test if participants exceeded the motion threshold set for exclusion (>2mm/TR). The average maximum (framewise) motion was 1.06mm/TR. Bad volumes were interpolated, a maximum of 10% per participant with an average of 3.9% for included participants. The structural T1 volume was co-registered to the mean of the realigned functional images and spatially normalized to standardized Montreal Neurological Institute (MNI) space. The normalization parameters were then applied to the functional volumes and the images smoothed with a 6mm full-width at half maximum Gaussian kernel.

Subject-level statistical maps were created for the correct NoGo>Go contrast. Data were extracted for a priori regions of interest (ROIs) and as there were no specific hypotheses for unilateral analyses, bilateral ROIs were extracted in accordance with prior studies (Stevens, 2014; van Rooij, 2018): bilateral amygdala based on the Anatomical Automatic Labeling
Group Analyses

For both trauma exposure broadly (TESI) and violence exposure specifically (VEX-R frequency) we performed correlation analyses with behavioral data, structural measures of the hippocampus and amygdala, and functional measures of bilateral hippocampal, amygdala and vmPFC activation. Second, partial correlations correcting for age, sex, and intracranial volume (ICV) for structural measures were performed.

Exploratory regression analyses were performed for significant correlations to assess the effect of age group (<10 and >=10) by creating interaction terms for trauma or violence exposure * age group and adding them to the model along with main effects.

Whole brain analyses and functional connectivity analyses were performed, and methods, results and discussion of the findings are presented in the Supplementary Materials. Additional correlation analyses with PTSD symptoms and regression analyses assessing the differential effect of sex are also presented in the Supplementary Materials.

Results

Participants

Sixty-nine African American children and adolescents (8 to 14 years) were scanned (Table 1) and data from these participants was included in the structural analyses, functional analyses or both, resulting in different analytical datasets. Structural data of 6 participants was unusable for analyses due to motion, resulting in N=63 for the structural analyses. Functional eGNG data was collected on 66 participants, however, 15 participants exceeded the motion threshold of 2mm/TR, 2 participants fell asleep during the scan, and 2 participants did not (correctly) press any buttons, resulting in a sample of N=47. Behavioral response inhibition data was available for 62 participants. No significant differences were observed in demographics for participants included in the structural and functional analyses. Age (in months) and sex were included as covariates in secondary analyses.

Behavioral findings

The group means for accuracy, % correct Go’s, % correct NoGo’s, and overall Go reaction time are presented in Table 2. The means for the N=62 participants did not significantly differ from means of the N=47 included in the functional MRI analyses.

There were no significant correlations between trauma exposure and the behavioral measures. There was a significant negative correlation of violence exposure with reaction time ($r=-0.34, p=0.008$), however, after correcting for age and sex, this effect was no longer significant ($r=-0.14, p=0.263$). Follow-up analyses showed a positive correlation between age and violence exposure ($r=0.32, p=0.008$), and a negative correlation between age and reaction time ($r=-0.51, p<0.001$).
Trauma exposure

More trauma exposure correlated with smaller left and right hippocampal volume (Table 3a, Figure 1). After correcting for ICV, age and sex, the negative correlation with the left hippocampus remained significant, and a positive correlation with the left amygdala was observed. Only the correlations with the left hippocampus survived correction for multiple comparisons. There was no effect of trauma exposure on the functional measures.

Violence exposure

More violence exposure correlated with more activation in the bilateral hippocampus and amygdala, and marginally with the vmPFC (Table 3b, Figure 2). After correcting for age and sex, all 3 correlations were significant. Only the correlation with bilateral hippocampal activation survived correction for multiple comparisons. No correlations were observed between violence exposure and structural measures.

Exploratory regression analyses were performed to assess the effect of age group (<10, N=15 vs. ≥10, N=32) on the relation between violence exposure and functional outcomes, because significant correlations were observed in the initial analyses. A significant interaction between age group and violence exposure was observed for hippocampal activation (F(3,46)=4.63, p=0.007; interaction, t=−2.08, p=0.043) and amygdala activation (F(3,46)=3.59, p=0.021; interaction, t=−2.42, p=0.020), such that significant correlations were only observed in younger children (hippocampus, r=0.59, p=0.037; amygdala, r=0.75, p=0.003).

Discussion

The current study in 69 children and adolescents showed that more trauma exposure in general (including multiple types of trauma) was associated with structural changes in the hippocampus and amygdala, whereas more violence exposure specifically correlated with more functional changes in the amygdala, hippocampus and vmPFC, particularly in children younger than 10 years of age. Furthermore, more violence exposure was related to stronger functional connectivity between the left amygdala and the brainstem (in Supplementary Materials).

As hypothesized, more trauma exposure was associated with smaller (left) hippocampal volume. This effect has been demonstrated repeatedly in prior adult retrospective studies and a few pediatric studies, but here we build on prior work by showing this effect can already be observed during development in a non-clinical sample of children and adolescents. This is important given that reduced hippocampal volume, in turn, has been shown to be a risk factor for the development of PTSD (Gilbertson, 2002) and depression (Rao, 2010). We also showed that only trauma exposure more broadly, but not violence exposure specifically, was related to reduced hippocampal volume. Amygdala volume was found to be positively correlated with trauma exposure, which parallels studies in previously institutionalized children (Mehta, 2009; Tottenham, 2010), but contradicts studies on maltreatment showing reduced amygdala volume (Edmiston, 2011; Hanson, 2015; Luby, 2019; McLaughlin, 2016).
However, as our amygdala finding did not survive correction for multiple comparisons, replication is warranted before further interpretation.

Further, increased levels of violence exposure were associated with more activation in the amygdala, hippocampus and vmPFC during emotional response inhibition. These findings parallel studies in maltreated or neglected children who demonstrated more amygdala activation compared to controls (Maheu, 2010; McCrory, 2013; Tottenham, 2011), and increased hippocampal activation (Maheu, 2010) to emotional faces. Our findings also correspond with increased mPFC activation observed on a Go/NoGo task in children with trauma exposure and PTSS (Carrion, 2008) and adolescents with early life stress (Mueller, 2010). However, these previous studies only demonstrated group differences and did not show a continuous association between trauma exposure and brain function as we have demonstrated. Only Suzuki et al (2015) showed a dose-response relation between number of cumulative stressful and/or traumatic life events and amygdala, sgACC and hippocampal activation in response to emotional faces. Furthermore, in a retrospective study in adults, more childhood trauma was found to positively correlate with hippocampal activation during a Go/NoGo task, but only in individuals with the COMT Val/Val genotype (van Rooij, 2016), suggesting the need for further assessment of genetic influences.

A possible explanation for the positive correlation between violence exposure and amygdala, hippocampus and vmPFC activation is that children with high levels of violence exposure show an appropriate, increased attention-directing response. Following prior work by Tottenham (2011), it could be suggested that increased amygdala activation is a manifestation of increased vigilance to emotional stimuli, provoked by exposure to violence in our population. Based on prior studies on the role of the hippocampus and vmPFC in fear regulation, it can be hypothesized that increased hippocampal recruitment could help children contextualize experiences, and augmented prefrontal control could regulate fear accordingly. Therefore, increased fear neurocircuitry activation with higher levels of exposure to violence may reflect an adaptive brain response to growing up in a dangerous, violent environment, especially since this association in our non-clinical population is only observed for violence exposure specifically, and not trauma exposure in general.

Levels of psychopathology in our population were relatively low considering the high levels of trauma exposure. Moreover, there was no relation between PTSD symptoms and brain structure or function (in Supplementary Materials). Importantly, while heightened neural activation may be an adaptive mechanism during childhood in an adverse environment, the long-term potentially excitotoxic effects of this over-engagement of the fear neurocircuitry and its risk for later psychopathology are not clear. It is possible that chronic, adaptive vmPFC and hippocampal overactivation in childhood lead to maladaptive vmPFC and hippocampal underactivation in adulthood, patterns observed in adults with PTSD (Jovanovic, 2013; van Rooij, 2016). This pattern was suggested by Tarullo and Gunnar (2006) as the explanation for why maltreated children over-secrete cortisol while adults with childhood maltreatment under-secrete cortisol. Yet, as our study population is not a clinical population, many of the participants may become resilient adults and these brain alterations may promote this as suggested in (van Rooij, 2016). Therefore, based on this study we
cannot conclude whether the observed correlation between violence exposure and brain activation is a marker of future resilience or psychiatric risk.

As hypothesized, we observed an effect of developmental stage on our functional outcomes. Variability in the amygdala, hippocampus and vmPFC activation was tightly linked with violence exposure specifically in younger children. This could be explained by a variety of maturation processes, such as critical periods for brain development (Knudsen, 2004), prefrontal maturation during adolescence (Caballero, 2016), changes in amygdala-vmPFC functional and structural connectivity (Gee, 2013; Jalbrzikowski, 2017), improvements in safety signal processing in older children (Jovanevic, 2014), and changes in social functioning, though these hypotheses require further exploration. Notably, the sample size of the younger children was relatively small (N=15) and replication in a larger sample is warranted. However, this is a very difficult sample to collect and therefore largely understudied, and much needed data to be added to the literature.

Other limitations of this study included that it is a cross-sectional study, and therefore no directional conclusions can be drawn from this data, and it is unclear if the associations we observed between brain function and violence exposure indicate a long-term protective or harmful effect. Second, the participants have a somewhat wide age range (8–14) across pre- and post-pubertal developmental stages. Though we assessed the effects of age by stratifying participants by age group (<10 and >=10) and included age in months as a covariate in our secondary analyses, it would be informative to more carefully control for age and pubertal stage in future studies. Third, the findings in our high-risk African-American population from inner-city Atlanta may not generalize to other populations. Finally, many children who grow up in an unsafe environment live below the poverty line. Research has shown pervasive effects of poverty on brain structure (Hair, 2015), including the hippocampus and amygdala (Luby, 2013). In this study we did not separately assess the effects of poverty, because the majority of our participants were from low income families with little variation to include in the analyses. On the other hand, this population therefore better allowed us to examine the effects of trauma and violence exposure than in studies with a wide income range where poverty effects can confound the effects of trauma/violence.

**Conclusion**

In this neuroimaging study in an at-risk pediatric population ages 8–14, we observed (1) an association between structural brain alterations and childhood trauma more generally, and (2) functional changes which correlated with violence exposure specifically. Based on the current findings, it could be hypothesized that general trauma exposure during childhood results in structural changes in the hippocampus (and amygdala) that are associated with later risk for psychiatric disorders. At the same time, it can be postulated that growing up in an unsafe environment with high levels of violence exposure leads the brain to functionally adapt to this situation in a way that promotes survival, where the long-term costs or consequences of these adaptations are largely unknown and an area for future investigations. Given the importance of the fear neurocircuitry for psychiatric disorders, increased understanding of the effects of trauma exposure on the developing brain is essential for early detection of individuals at risk for developing psychiatric disorders.
Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We like to thank Bekh Bradley, Rebecca Hinrichs, Angelo Brown, Alexander Vance, Ye Ji Kim, Vasiliki Michopoulos, Abigail Powers, and the staff and volunteers of the Grady Trauma Project.

Funding

This project was funded by the National Institute of Mental Health (MH111682 and MH100122 to TJ, and 2R01MH091864 to NT) and the Brain and Behavior Research Foundation (NARSAD; to TJ).

References


*Depress Anxiety.* Author manuscript; available in PMC 2021 April 01.
Figure 1. Correlation analyses of trauma exposure with brain structure

*Figure 1* displays the correlation between trauma exposure measured as number of traumas with the TESI, and hippocampal and amygdala volume (N=63). The figures display the uncorrected correlation analyses, the results from the corrected analyses (correcting for intracranial volume (ICV), age and sex) can be found in Table 3. Note that the association between trauma exposure and the left amygdala was only significant after correcting for ICV, age and sex.
Figure 2. Correlation analyses of violence exposure with brain function

**Figure 2** displays the correlation between violence exposure measured as frequency of exposure to violence with the VEX-R, and hippocampal, amygdala, and vmPFC activation as measured during response inhibition (NoGo>Go trials). The figures display the uncorrected correlation analyses, the corrected analyses (correcting for age and sex) can be found in Table 3.
Table 1.

Demographics and clinical data

<table>
<thead>
<tr>
<th></th>
<th>N=69</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in months)</td>
<td>130.0</td>
<td>19.4</td>
<td>99-177</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (% females)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>52.2%</td>
</tr>
<tr>
<td>Household income (% &lt; 2019 federal poverty level)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>76.9%</td>
</tr>
<tr>
<td>Global Trauma exposure (TESI)</td>
<td>5.5</td>
<td>3.4</td>
<td>0-18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Violence exposure (VEX-R)</td>
<td>14.1</td>
<td>8.3</td>
<td>1-44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSD symptoms</td>
<td>14.7</td>
<td>11.5</td>
<td>0-41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meet for PTSD (DSM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15.9%</td>
</tr>
<tr>
<td>Anxiety symptoms T-score (BASC)</td>
<td>48.4</td>
<td>12.0</td>
<td>29-77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1SD above mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14.5%</td>
</tr>
<tr>
<td>Depression symptoms T-score (BASC)</td>
<td>50.5</td>
<td>10.15</td>
<td>37-80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1SD above mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>16.1%</td>
</tr>
</tbody>
</table>
Table 2.

Behavioral data

<table>
<thead>
<tr>
<th></th>
<th>N=62 (behavioral data available)</th>
<th>N=47 (included in fMRI analyses)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>77.3</td>
<td>15.8</td>
</tr>
<tr>
<td>Correct Go’s (%)</td>
<td>85.4</td>
<td>16.2</td>
</tr>
<tr>
<td>Correct NoGo’s (%)</td>
<td>75.7</td>
<td>19.2</td>
</tr>
<tr>
<td>Go reaction time (ms)</td>
<td>830.4</td>
<td>204.6</td>
</tr>
</tbody>
</table>
Table 3.
Correlation analyses for trauma and violence exposure with structural and functional MRI measures

<table>
<thead>
<tr>
<th></th>
<th>Brain volumes</th>
<th>Inhibition-related activation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>L HPC</td>
<td>R HPC</td>
</tr>
<tr>
<td>a. Trauma exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>−0.33</td>
<td>−0.26</td>
</tr>
<tr>
<td>p</td>
<td>0.008</td>
<td>0.042</td>
</tr>
<tr>
<td>corrected for age, sex (and ICV for volumes)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>−0.35</td>
<td>−0.20</td>
</tr>
<tr>
<td>p</td>
<td>0.006</td>
<td>0.125</td>
</tr>
<tr>
<td>b. Violence exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>0.04</td>
<td>−0.01</td>
</tr>
<tr>
<td>p</td>
<td>0.732</td>
<td>0.965</td>
</tr>
<tr>
<td>corrected for age, sex (and ICV for volumes)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>−0.01</td>
<td>−0.05</td>
</tr>
<tr>
<td>p</td>
<td>0.934</td>
<td>0.731</td>
</tr>
</tbody>
</table>

ICV, intracranial volume