

Original Article

Cite this article: Bounoua N, Miglin R, Spielberg JM, Johnson CL, Sadeh N (2020). Childhood trauma moderates morphometric associations between orbitofrontal cortex and amygdala: implications for pathological personality traits. *Psychological Medicine* 1–10. <https://doi.org/10.1017/S0033291720004468>

Received: 9 October 2020

Revised: 1 November 2020

Accepted: 5 November 2020

Key words:


Antagonism; childhood adversity; cortical volume; disinhibition; stress exposure; subcortical volume

Author for correspondence:

Nadia Bounoua,

E-mail: nbounoua@udel.edu

Childhood trauma moderates morphometric associations between orbitofrontal cortex and amygdala: implications for pathological personality traits

Nadia Bounoua , Rickie Miglin, Jeffrey M. Spielberg, Curtis L. Johnson and Naomi Sadeh

Department of Psychological and Brain Sciences, University of Delaware, 108 Wolf Hall, Newark, 19716, DE, USA

Abstract

Background. Research has demonstrated that chronic stress exposure early in development can lead to detrimental alterations in the orbitofrontal cortex (OFC)–amygdala circuit. However, the majority of this research uses functional neuroimaging methods, and thus the extent to which childhood trauma corresponds to morphometric alterations in this limbic-cortical network has not yet been investigated. This study had two primary objectives: (i) to test whether anatomical associations between OFC–amygdala differed between adults as a function of exposure to chronic childhood assaultive trauma and (ii) to test how these environment-by-neurobiological effects relate to pathological personality traits.

Methods. Participants were 137 ethnically diverse adults (48.1% female) recruited from the community who completed a clinical diagnostic interview, a self-report measure of pathological personality traits, and anatomical MRI scans.

Results. Findings revealed that childhood trauma moderated bilateral OFC–amygdala volumetric associations. Specifically, adults with childhood trauma exposure showed a *positive* association between medial OFC volume and amygdalar volume, whereas adults with no childhood exposure showed the *negative* OFC–amygdala structural association observed in prior research with healthy samples. Examination of the translational relevance of trauma-related alterations in OFC–amygdala volumetric associations for disordered personality traits revealed that trauma exposure moderated the association of OFC volume with antagonistic and disinhibited phenotypes, traits characteristic of Cluster B personality disorders.

Conclusions. The OFC–amygdala circuit is a potential anatomical pathway through which early traumatic experiences perpetuate emotional dysregulation into adulthood and confer risk for personality pathology. Results provide novel evidence of divergent neuroanatomical pathways to similar personality phenotypes depending on early trauma exposure.

Introduction

Trauma exposure in childhood is one of the most well-established and robust risk factors for the development of a range of psychiatric disorders, including increased risk for depression and suicidality (Carr, Martins, Stingel, Lemgruber, & Juruena, 2013; Pine & Cohen, 2002; Pompili et al., 2014). Given its transdiagnostic relevance, it is likely that early exposure to traumatic events disrupts the typical development of brain regions supporting affective systems, including the orbitofrontal cortex (OFC)–amygdala circuit. OFC is frequently implicated in the top-down processing of emotions (Garcia, Vouimba, Baudry, & Thompson, 2014; Ghashghaei, Hilgetag, & Barbas, 2007; Wright et al., 2008), such as recognizing and perceiving emotional responses (Adolphs, 2002), modulating fear responses (Phan et al., 2005), and reinforcement learning (Groman et al., 2019). Critical to these processes is OFC's reciprocal communication with amygdala, a subcortical structure that supports the acquisition and expression of emotions, including fear expression (Öhman, 2005) and memory consolidation of emotional experiences (McGaugh, 2002). OFC is thought to play a critical regulatory role over amygdala, with the most replicated findings showing inverse correlations between prefrontal and OFC activity during tasks eliciting emotional responses (Ochsner et al., 2004; Stein et al., 2007) and at rest (Kim, Gee, Loucks, Davis, & Whalen, 2011; Roy et al., 2009) in healthy samples.

The OFC and amygdala are both highly susceptible to the effects of early life stress (Shonkoff et al., 2012) and essential to key regulatory processes (Bechara, Damasio, & Damasio, 2000; Phillips, Ladouceur, & Drevets, 2008), which is why we focused on these regions in this study. For example, extant research has identified alterations in the structural integrity of OFC and amygdala following exposure to early, repeated childhood stress, typically

in the form of maltreatment exposure (Hanson et al., 2010; Hart & Rubia, 2012; Lim, Radua, & Rubia, 2014; Lupien, McEwen, Gunnar, & Heim, 1993; Moreno-López et al., 2020; Tottenham & Galván, 2016). Specifically, empirical studies have shown that childhood maltreatment is associated with reduced volume in cortical and subcortical regions, including in the OFC and amygdala (Cassiers et al., 2018; Edmiston & Blackford, 2013; Lim et al., 2019; Morey, Haswell, Hooper, & De Bellis, 2016) and alterations in amygdala–prefrontal circuitry (McLaughlin & Lambert, 2017; Paquola et al., 2019). While mounting evidence suggests that childhood trauma has detrimental effects on the functioning of OFC–amygdala interactions (Hart & Rubia, 2012), the extent to which alterations in OFC–amygdala circuitry related to early traumatic stress can be observed at a purely structural level has been relatively understudied. Based on recent arguments that examining structural covariation between brain regions is necessary to further understanding of brain networks initially established at a functional level (Gong, He, Chen, & Evans, 2012; He, Chen, & Evans, 2007; Zielinski, Gennatas, Zhou, & Seeley, 2010), the primary aim of this study was to address this gap in relation to OFC–amygdala connectivity.

To our knowledge, only two studies have investigated structural associations between amygdala and cortex. In a healthy youth sample, Albaugh et al. (2013) found that amygdala volume was inversely related to cortical thickness in several regions of PFC, including bilateral OFC. Blackmon et al. (2011) reported a similar inverse association between amygdala volume and thickness in the left lateral OFC (lOFC) in a sample of healthy adults. These studies provide a starting point for understanding morphometric associations between amygdala and OFC in healthy adult samples by providing preliminary evidence of inverse structural associations that mirror functional connectivity findings. Given research suggesting that early trauma exposure detrimentally impacts functional OFC–amygdala circuitry, it is likely that the structural associations between these regions may also be impacted by chronic childhood stress exposure. However, to our knowledge, this question has not yet been investigated.

Implications for the development of pathological personality

A large body of literature has implicated both trauma exposure early in life (e.g. Ball & Links, 2009; Goodman & Yehuda, 2002) and reductions in OFC cortical volume in the development of personality disorders (PDs), particularly those marked by emotional and behavioral dysregulation (e.g. borderline, antisocial PDs) (Chanen et al., 2018; Raine, 2018; Tebartz van Elst et al., 2003; Yang & Raine, 2009). Further, results from a prospective twin study showed that personality pathology is best understood in the context of both environmental (i.e. childhood maltreatment) and biological factors (Berenz et al., 2013). Research on the neurobiology of personality has consistently implicated alterations in OFC–amygdala circuitry that account for variation in trait-level personality dimensions central to PDs, including disinhibition, antagonism, and negative affectivity (Ameis et al., 2014; Banks, Eddy, Angstadt, Nathan, & Phan, 2007; Blair, Tinkelman, Moita, & LeDoux, 2003; Coccaro, Lee, McCloskey, Csernansky, & Wang, 2015; Saxbe et al., 2018; Tebartz van Elst et al., 2003). For example, Coccaro et al. (2015) found that individuals with elevated impulsivity and aggression exhibited exaggerated amygdala reactivity and diminished OFC activation during a social threat task. Similarly, disruption in neural networks involving the amygdala and OFC has been implicated in emotion dysregulation

among individuals with BPD (Soloff, Abraham, Ramaseshan, Burgess, & Diwadkar, 2017). Taken together, it appears that the OFC–amygdala relationship is critical to understanding links between trauma exposure and trait levels of emotional and behavioral dysregulation. However, the majority of this research has focused on either structural alterations in specific neural regions (e.g. OFC and/or amygdala individually) or in the functioning of OFC–amygdala circuitry. Research to date has yet to examine the clinical implications of early trauma exposure for OFC–amygdala morphometric associations and the manifestation of pathological personality traits in adulthood.

Current study

A gap in this line of work is knowledge of how structural covariation between the amygdala and OFC may be affected by developmental experiences that are known to impact emotion regulation, and in turn, confer risk for psychopathology. The primary objective of the current study was to investigate the extent to which morphometric associations between the amygdala and regions of the OFC vary as a function of childhood trauma exposure. We also explored the clinical relevance of these associations for pathological personality traits by examining the interactive effects of trauma exposure and OFC volume in regions found to covary with amygdala. We focused on assaultive trauma experiences, because these forms of childhood trauma have been robustly linked to chronic activation of the HPA-axis (Cross, Fani, Powers, & Bradley, 2017; Tarullo & Gunnar, 2006), which is posited to have long-term deleterious effects on the developing cortex (Gee & Casey, 2015; Tottenham & Galván, 2016). Consistent with past work in samples of healthy adults without trauma exposure (Albaugh et al., 2013; Blackmon et al., 2011), we hypothesized that there would be an inverse association between OFC and amygdala volume in those without a trauma history in our sample. Conversely, we hypothesized that this relationship would be absent or even positive in those with a trauma history.

Methods and materials

Participants

Participants were 137 ethnically diverse adults recruited from the community using flyers and online postings. Inclusion criteria: between ages 18 and 55, fluency in English. Exclusion criteria were current psychosis or a current diagnosis of a psychotic disorder, estimated IQ in the Intellectual Disability range, serious medical/neurological condition, history of head injuries with lasting effects, MRI contraindications, and imminent suicide risk. No other psychiatric conditions were considered exclusionary conditions. All participants with complete interview, self-report, and MRI data were included in the analysis. Two participants who reported more than one previous head injury were removed from analysis to reduce the potential impact of these events.

The final sample consisted of 135 participants [$M(S.D.)_{age} = 31.81(9.18)$; 48.1% men]. Sample characteristics are presented in Table 1. Approximately half of the sample self-identified as Caucasian/White (53.0%), followed by Black (35.1%), Asian (7.5%), or Biracial/Other (4.3%). Past year income for the sample ranged from \$0 to \$300 000 [$M(S.D.) = \$50\,357.028$ (\$46 424.92)]. The majority of participants came from communities with high violent crime rates (www.neighborhoodscout.com/de/wilmington/crime on 06/07/2020), suggesting the sample is

Table 1. Sample characteristics and zero-order correlations ($N = 135$) among study variables

	Mean	s.d.	1	2	3	4	5	6	7	8
(1) Age (years)	31.81	9.18	—							
(2) Sex	0.48	0.50	0.04	—						
(3) Race	0.46	0.50	-0.13	0.05	—					
(4) Income (\$)	50 357.28	46 424.92	-0.09	-0.05	-0.02	—				
(5) Childhood assaultive trauma exposure	0.37	0.48	0.13	-0.13	0.10	-0.17	—			
(6) Antagonism	2.81	2.59	-0.02	0.06	-0.01	-0.15	0.12	—		
(7) Disinhibition	3.73	3.68	-0.01	-0.06	-0.10	-0.24*	0.21*	0.57*	—	
(8) Negative affectivity	5.31	3.92	-0.02	-0.23*	-0.10	-0.02	0.12	0.40*	0.47*	—

Note. Sex was coded as 0-female; 1-male; Race was dummy-coded as 0-White, 1-Non-White; Trauma Exposure was coded as 0-absent, 1-present. * $p < 0.05$.

at relatively higher risk for exposure to assaultive trauma than other community samples.

Procedures

Written and oral consent was obtained from all individuals before participation. Participants completed a battery of assessments, including a structured clinical interview and a neuroimaging protocol across two study visits. The University Institutional Review Board approved all protocols and procedures (Protocol #'s: 1073423-17, 1361164-1).

Measures

Childhood assaultive trauma exposure

The *Detailed Trauma Screen from the SCID-5-RV Stressor Related Disorders* module (First, 2014) was used to assess the history of exposure to traumatic events. Participants completed this measure via a clinical interview conducted by, or under the supervision of a licensed clinical psychologist ($n = 72$), or via a self-report survey ($n = 63$). Assessment method was not uniquely associated with any study variables of interest (p 's > 0.05); thus, the samples were combined in all analyses.

Consistent with previous research quantifying childhood trauma exposure (e.g. Bounoua, Miglin, Spielberg, & Sadeh, 2020), we compared adults with chronic exposure to childhood assaultive trauma, defined as experiencing multiple assaultive traumas prior to the age 13, to those individuals who either did not experience any assaultive trauma, only reported a single exposure in childhood, or reported assaultive trauma that only occurred later in life. Assaultive trauma was operationalized as direct exposure to threatened or actual physical violence (e.g. assault, domestic violence, or physical or sexual abuse). Non-assaultive events included exposure to life-threatening danger that did not involve threatened or actual physical violence (e.g. natural disasters) (Cisler et al., 2012; Sadeh, Miller, Wolf, & Harkness, 2015).

The sample reported a range of lifetime trauma exposure (Min/Max = 0/6 events), with a little over a third of the sample (37.0%, $n = 50$) meeting criteria for inclusion in the repeated childhood assaultive trauma group. Among individuals with repeated childhood assault exposure, the most common forms

were physical abuse (82.0%), sexual abuse (20.0%), and witnessing violence perpetrated against others (14.0%).

Pathological personality traits

Three dimensions of pathological personality that have been associated with OFC-amygdala circuitry in prior work were assessed using the *Personality Inventory for DSM-5-Brief Form (PID-5-BF)*; Krueger, Derringer, Markon, Watson, & Skodol, 2013). Participants rated the extent to which each item best described them from 0 (Very False/Often False) to 3 (Very True/Often True). An Antagonism score was created by summing five items measuring the degree to which individuals are self-focused and disregard the needs of others (e.g. 'I use people to get what I want.') [M/s.d. = 2.81/2.59]. A Disinhibition score was created by summing five items that measure the tendency to engage in risky and impulsive behaviors (e.g. 'I feel like I act totally on impulse.') [M/s.d. = 3.74/3.68]. A Negative Affectivity score was created by summing five items measuring the tendency to experience negative emotions (e.g. 'I get emotional easily, often for very little reason.') [M/s.d. = 5.31/3.92]. Average scores on these disordered personality traits in the current sample fell between means reported for clinical and non-clinical samples in previous work (Bach, Sellbom, & Simonsen, 2018). Previous work has demonstrated that the *PID-5-BF* shows excellent reliability and construct validity across a range of samples (Anderson, Sellbom, & Salekin, 2018).

MRI acquisition

Data were collected using a Siemens 3 T Magnetom Prisma scanner with a 64-channel head coil. A T1-weighted multi-echo MPRAGE anatomical scan (resolution = 1 mm³, TR = 2530 ms, TEs = 1.69, 3.55, 5.41, 7.27 ms) was collected, which has the advantage of less distortion and higher contrast than standard MPRAGE sequences, resulting in more reliable cortical models (van der Kouwe, Benner, Salat, & Fischl, 2008). A T2-weighted variable flip-angle turbo spin-echo scan (resolution = 1 mm³, TR = 3200 ms, TE = 564 ms) was collected, which is used in FreeSurfer to better differentiate the gray-matter-dura boundary.

Amygdala volume

We used FreeSurfer's (v6) probabilistic atlas tool to segment amygdala (Saygin et al., 2017). The tool is based on a generative

Table 2. Childhood trauma exposure moderates the volumetric associations between amygdala and clusters within the orbitofrontal cortex

Cluster No.	Cluster	Peak <i>F</i> value	Peak MNI (<i>x</i> , <i>y</i> , <i>z</i>)	No. of vertices	Cluster size (mm ³)
A	Left medial OFC/lateral OFC	3.44	−11.4, 15.7, −14.4	507	220.47
B	Right medial OFC	2.56	9.8, 39.6, −10.1	1053	532.18

OFC, orbitofrontal cortex.

model, where the registered atlas is combined with a subject-specific likelihood model to produce a segmentation specific to that individual's brain.

OFC cortical volume

The cortical volume of each OFC vertex was estimated using FreeSurfer's (v6) standard morphometric pipeline (Salat et al., 2004). Data were spatially smoothed using a Gaussian kernel of 15 mm full-width at half-maximum.

Data analytic plan

Age, biological sex, body mass index (BMI), and estimated intracranial volume (eTIV) were entered as covariates of no interest in all analyses, given associations between these variables, trauma exposure, and neural morphology in previous research (e.g. Chen, Sachdev, Wen, & Anstey, 2007; Taki & Kawashima, 2012). All analyses were conducted within each hemisphere separately, given evidence of lateralization of amygdala function (Baas, Aleman, & Kahn, 2004).

FreeSurfer's QDEC application was used to examine associations between childhood trauma, amygdala volume, and OFC cortical volume using general linear models. We created an OFC mask by merging the lateral and medial orbitofrontal parcellations of the Desikan-Killiany Atlas. Main effects between amygdala and OFC cortical volume were examined. Next, OFC cortical volume was regressed on the interaction of childhood trauma and amygdala volume, with the main effects of childhood trauma and amygdala volume included in the model as well as the covariates (age, sex, BMI, and eTIV). To correct for multiple comparisons within OFC, we applied a standard correction procedure using the FreeSurfer analysis software. Volumetric results were corrected for the number tests conducted using pre-cached Gaussian Monte Carlo simulation (10 000 iterations, cluster-wise threshold: $p < 0.05$, sign: absolute) that was created based on the size of the ROI examined (Hagler, Saygin, & Sereno, 2006). Bonferroni correction was also applied to take into account the number of comparisons conducted across both hemispheres.

Follow-up linear regression analyses were conducted to test associations between OFC cortical volume in the identified clusters and disordered personality traits. Finally, to examine the clinical relevance of trauma-related differences in OFC–amygdala volumetric associations, we conducted moderation analyses to test whether cortical volume in OFC regions linked to amygdala volume was also related to pathological personality traits. Specifically, we modeled the interactive effect of childhood trauma and OFC cortical volume (in the regions associated with amygdala volume in the QDEC analysis) on disordered personality traits. Moderation analyses were conducted using PROCESS Macro v3.3 (Hayes, 2018) in SPSS v26 (IBM Corp, 2013). One participant had missing data on the *PID-5-BF* and was excluded from this analysis.

Results

Impact of childhood trauma on OFC–amygdala volumetric associations

We first examined whether the inverse association between amygdala volume and OFC structure reported in previous work (e.g. Albaugh et al., 2013) was present across our sample. Results revealed that no main effects of amygdala volume on OFC volume survived following correction for multiple comparisons.

Next, we examined whether associations between amygdala and OFC cortical volume differed between adults with and without assaultive trauma in childhood. Significant interaction effects emerged for both hemispheres (see Table 2 and Fig. 1), indicating that the relationship of amygdala with OFC cortical volume varied as a function of childhood trauma exposure.

In the right hemisphere, childhood trauma moderated the association between amygdala and cortical volume in a cluster that peaked in medial OFC (mOFC). Consistent with prior work, amygdala volume showed a trending inverse relationship with mOFC volume ($t = -1.41$; 95% CI -0.46 to 0.08) in individuals without a history of assaultive childhood trauma. Conversely, a significant positive association between amygdala and cortical volume in this cluster was observed in adults with chronic assaultive trauma exposure in childhood ($t = 1.99$; 95% CI 0.002 – 0.62).

A similar pattern of findings was evident in the left hemisphere. Childhood trauma moderated the association between amygdala and cortical volume in a cluster that peaked in mOFC and included IOFC. Follow-up analyses revealed a significant negative association between left amygdala and OFC cortical volume in the non-trauma exposed group ($t = -2.93$; 95% CI -0.31 to -0.06). Among adults with childhood assaultive trauma exposure, this relationship between amygdala and OFC cortical volume showed a trend in the positive direction ($t = 0.65$; 95% CI -0.10 to 0.19).

Exploratory examination of sex differences

Given extant research suggesting that biological sex moderates the effect of trauma exposure on neurobiological systems (e.g. van voorhees & Scarpa, 2004), we ran exploratory three-way interaction analyses to test whether sex moderated the observed associations. No significant results emerged [i.e. sex did not moderate the interactive effect of childhood trauma and amygdala volume on cortical volume in the left ($t = 1.47$, 95% CI -0.09 to 0.63) or right ($t = -0.29$, 95% CI -0.89 to 0.67) OFC clusters]. We also tested for, and did not find, any new cortical clusters where sex moderated the childhood trauma \times amygdala association when we ran whole cortex analyses in QDEC.

Links with pathological personality

We investigated the translational relevance of trauma-related alterations in OFC–amygdala volumetric associations for

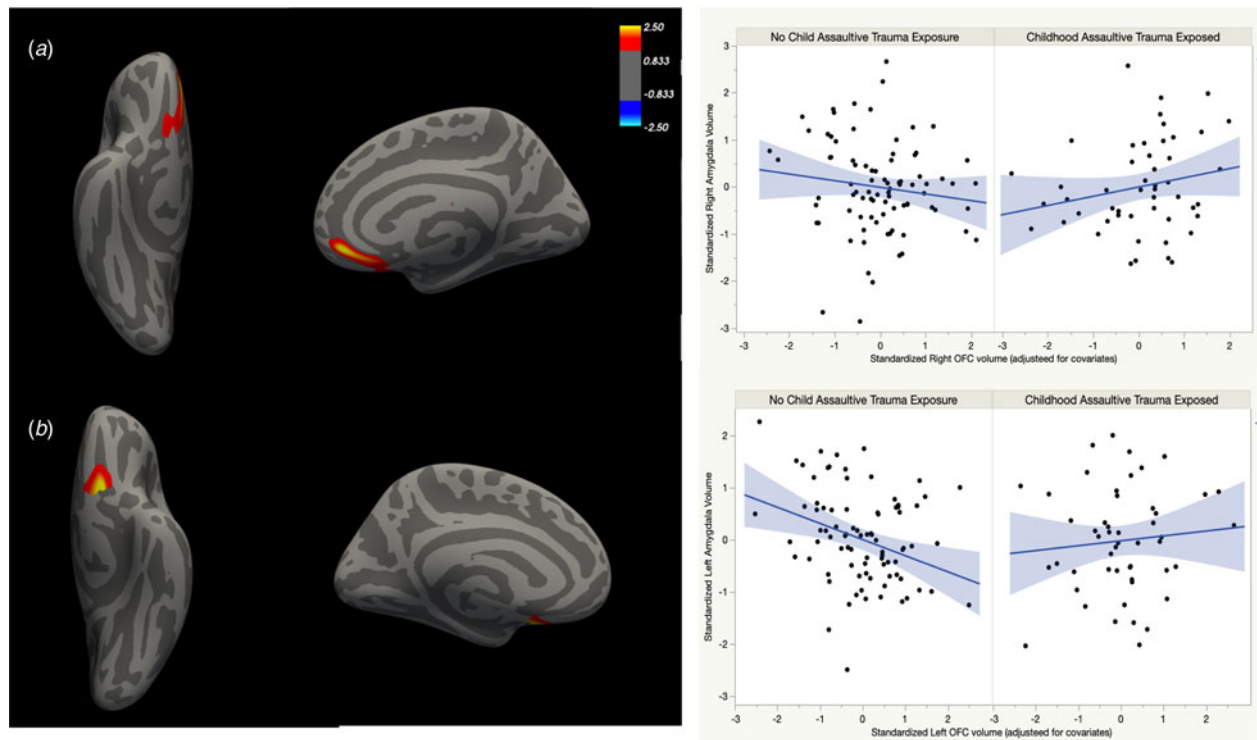


Fig. 1. Chronic childhood trauma exposure moderates the volumetric association between amygdala and regions of the OFC, after controlling for age, sex, BMI, and eTIV. (a) Right medial OFC. (b) Left medial and lateral OFC.

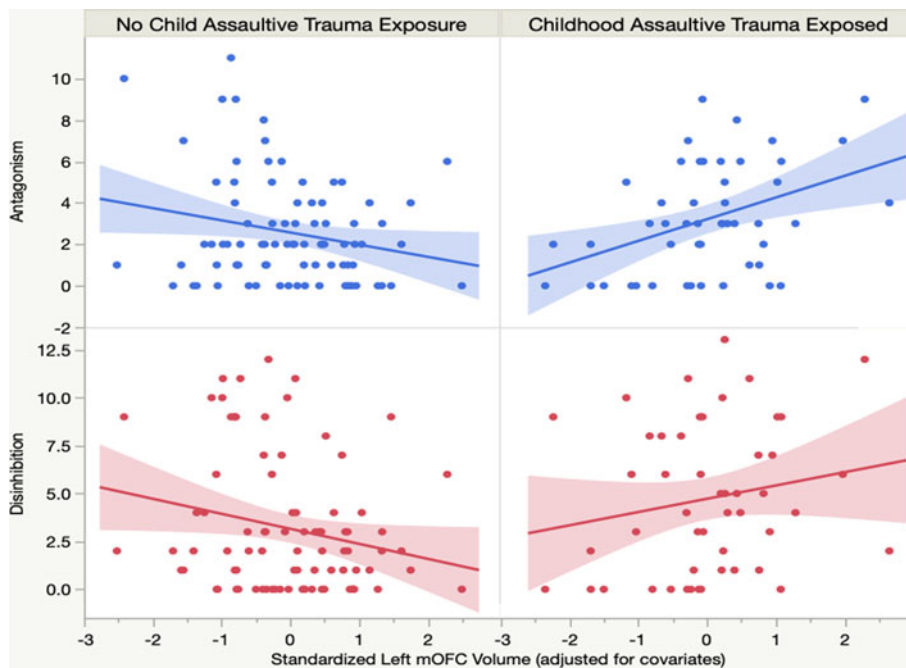


Fig. 2. Childhood trauma exposure moderates associations between left OFC volume and disordered personality traits.

understanding disordered personality traits. More specifically, we tested whether the OFC clusters identified above explained variance in disordered personality traits as a function of childhood trauma exposure. Interaction findings are depicted in Fig. 2.

Antagonism

No main effects emerged for the left or right OFC clusters and antagonistic personality traits. However, childhood trauma

exposure moderated the association between the left OFC cluster and antagonism ($\Delta R^2 = 0.07$, $p = 0.003$). In the trauma-exposed group, left OFC cortical volume was significantly and *positively* associated with trait antagonism ($t = 2.03$, 95% CI 0.0002 to 0.01), indicating that callous, manipulative, and grandiose traits increased as OFC cortical volume increased in this group. In contrast, in the non-trauma exposed group, left OFC cortical volume showed a *negative* trend with antagonistic personality traits

($t = -1.25$; 95% CI -0.01 to 0.001). No significant interaction emerged in the right hemisphere.

Disinhibition

No main effects emerged between cortical volume in the left or right amygdala-related OFC clusters and trait disinhibition. However, a significant interaction emerged between childhood trauma and OFC cortical volume for disinhibition ($\Delta R^2 = 0.06$, $p = 0.004$). Among individuals *with* childhood trauma, disinhibition showed a trending positive association with left OFC cortical volume ($t = 1.21$; 95% CI -0.003 to 0.01), indicating that more cortical volume in left OFC was associated with a greater tendency to act impulsively. In the non-trauma exposed group, left OFC cortical volume was significantly and inversely associated with disinhibition ($t = -2.22$; 95% CI -0.02 to -0.001), such that impulsivity increased as OFC cortical volume decreased in this group. No significant interaction emerged in the right hemisphere.

Negative affectivity

No significant main or moderation effects emerged for the left or right amygdala-related OFC clusters and negative affectivity.

Specificity of childhood assaultive trauma exposure

We conducted supplementary analyses to ensure the interactive effect of childhood trauma and amygdala volume on OFC volume could not be accounted for by assaultive trauma exposure in adulthood. These analyses revealed that childhood trauma remained a significant moderator of the association between amygdala and OFC volume when adult trauma exposure was entered into the model for both the left ($p = 0.002$) and right ($p = 0.002$) hemispheres. Similar analyses were conducted to test whether the moderating effect of childhood trauma on the association between left OFC volume and personality traits persisted after accounting for adult assaultive trauma exposure. Results indicated that childhood assaultive trauma remained a significant moderator of the effect of left OFC volume on antagonism ($\Delta R^2 = 0.07$, $p = 0.003$) and disinhibition ($\Delta R^2 = 0.06$, $p = 0.004$).

Discussion

Childhood trauma has been consistently implicated in a range of clinical disorders, particularly through its effect on underlying neurobiological processes (Heim & Nemeroff, 2001; Tottenham & Galván, 2016). The OFC–amygdala circuit is heavily involved in emotion regulatory processes (Bechara et al., 2000; Phillips et al., 2008) and is particularly vulnerable to early life stress (Tottenham & Galván, 2016). The present study revealed that trauma exposure moderates the anatomical associations between amygdala and OFC volume (see Fig. 1). Notably, volume in the identified clusters was also related to pathological personality traits in adulthood, such that disinhibition and antagonism exhibited different relationships with OFC volume in trauma-exposed *v.* non-exposed adults. Results provide new insights into the long-term neuroanatomical correlates of childhood trauma exposure and advance our understanding of the etiopathogenesis of pathological personality.

Importantly, supplementary analyses indicated that our findings appear to be relatively specific to childhood assaultive trauma. We found the effect of childhood trauma exposure on OFC–amygdala volumetric associations remained significant

after accounting for assaultive trauma first experienced after the age of 18. This finding is consistent with existing work that underscores the vulnerability of amygdala–prefrontal circuitry to chronic stress early in development (Tottenham & Galván, 2016). Similarly, the moderating effect of childhood trauma on the association between left OFC volume and trait levels of antagonism and disinhibition remained significant after accounting for adult-only trauma exposure. Previous work has demonstrated that early trauma may lead to pathological personality traits via changes on neurobiological systems that support emotional and behavioral regulatory processes, including the amygdala and OFC (e.g. Raine, 2008). Taken together, these findings point to the impact of chronic childhood trauma exposure, in particular, on OFC–amygdala morphometric associations and associated links with inhibition and antagonism.

Impact of childhood trauma on OFC–amygdala morphology

We found that trauma exposure impacted the volumetric association between amygdala and bilateral mOFC, extending into IOFC/ACC in the right hemisphere. Specifically, amygdala and OFC volumes were *positively* correlated in adults with a history of childhood assaultive trauma, whereas this relationship was reversed in non-exposed individuals (Fig. 1). The inverse association in those *without* trauma is consistent with previous anatomical studies (Albaugh et al., 2013; Blackmon et al., 2011), and parallels the inverse frontolimbic connectivity patterns observed at rest among healthy adults (Roy et al., 2009). Thus, previous findings appear to reflect structural relationships only in those without childhood trauma.

To our knowledge, our findings provide the first evidence of the role of childhood trauma exposure on morphometric relations between amygdala and OFC. In particular, the positive volumetric association between OFC and amygdala among individuals with childhood trauma suggests a mechanism through which chronic stress may impact neurobiological development. Given that the OFC regions that we identified have previously been linked to impulsivity/decision making (Antonucci et al., 2006; Wang et al., 2016; Wilbertz et al., 2012) and reward anticipation (Hahn et al., 2009), a positive OFC–amygdala association may reflect the weakened or disturbed top-down regulation circuit that is well-documented in the trauma literature (van der Werff et al., 2013). This association may also reflect a mechanism by which repeated HPA-axis hyperactivation following chronic stress leads to amygdala hyperexcitability and concurrent structural atrophy in amygdala and OFC (Albaugh et al., 2013; Dedovic, Duchesne, Andrews, Engert, & Pruessner, 2009). Thus, the findings from this study underscore childhood trauma exposure as an important environmental factor that may impact critical frontolimbic circuitry.

Implications for etiological models of personality pathology

Present findings also have important implications for understanding heterogeneity in the etiology of PDs. In particular, we found that childhood trauma exposure modulated the relationship between volume in amygdala-linked OFC regions and pathological disinhibition and antagonism. As seen in Fig. 2, among non-exposed individuals, OFC volume was *inversely* associated with pathological personality, such that less OFC volume was associated with more trait impulsivity and antagonistic personality traits, a pattern that is consistent with much of the existing

research (Antonucci et al., 2006; Blair, 2004; Coccaro et al., 2016; Johnson, Elliott, & Carver, 2020; Yang & Raine, 2007). In contrast, among trauma-exposed individuals, OFC volume was *positively* associated with impulsive and antagonistic personality traits. Interestingly, in a study of healthy adults, Cho et al. (2013) also found that mOFC volume was positively correlated with impulsivity, and authors speculated that this may be indicative of more engagement in OFC systems among impulsive individuals. Based on the findings of this study, it may be the case that trauma exposure is a critical moderating factor in the complex association between OFC morphometry and impulsivity in adulthood.

Furthermore, the divergent associations between OFC volume and impulsive/antagonistic personality traits in the exposed and non-exposed groups are intriguing in that they follow the pattern of findings for amygdalar volume. That is, among individuals with a history of assaultive childhood trauma, greater OFC volume was linked to both greater amygdalar volume and higher levels of pathological personality traits, whereas among individuals without this history, less OFC volume was associated with both greater amygdala volume and higher levels of pathological personality traits. Given the cross-sectional nature of the data, it is impossible to infer directionality in the relations among these variables. However, future research examining the joint influence of trauma exposure on the OFC–amygdala circuit and clinical phenotypes over time could clarify these interactive effects over the lifespan.

Although personality traits have a strong genetic basis and tend to remain stable over time (DeYoung, 2010; DeYoung et al., 2010), few studies have examined the neuroanatomical correlates of personality pathology. As research has already demonstrated personality pathology-related differences in functional coupling between amygdala and PFC (Kerr et al., 2015), examination of structural associations between amygdala and OFC provides sorely needed insights into the neural substrates of pathological personality. Indeed, prominent theories of personality development highlight the dynamic interplay between biology and environmental factors (Heim & Nemeroff, 2001; Linehan, 1993; Raine, 2008). Given the overwhelming evidence that many PDs are characterized by exposure to childhood adversity (DeLisi, Drury, & Elbert, 2019; Porter et al., 2020; Raine, 2008), the present findings shed light on potential divergent etiological pathways to PD development.

Strengths and limitations

The study had several strengths, including a vertex-wise analytic approach (*v.* treating OFC as a single entity), which is consistent with recommendations to examine amygdala connections with specific OFC locations (Ray & Zald, 2012), and recruitment of an ethnically diverse sample of adults with elevated rates of childhood trauma exposure. Nonetheless, results should be considered in light of some study limitations. First, in this study, we took a theory-driven approach and, consequently, focused specifically on the relations between OFC and amygdala. To comprehensively understand how childhood trauma impacts connections between subcortical regions and prefrontal regulatory processes, additional research is needed. For example, future examinations of whether childhood trauma exposure moderates structural and functional associations between amygdala (and other subcortical regions) with the whole cortex will be necessary to extend the current findings. Second, we used a conservative approach in our multiple

comparison correction (i.e. we did not look at associations with the volume of the entire OFC), which may explain why we did not find significant associations between OFC cortical volume and trait levels of negative affectivity previously reported in the literature (Jackson, Balota, & Head, 2011; Kalin, Shelton, & Davidson, 2007; Mincic, 2015; Wright et al., 2006). Given research suggesting that biological sex moderates the effect of trauma exposure and neurobiological systems (e.g. van voorhees and Scarpa, 2004), future research should further explore potential sex differences in the impact of childhood trauma exposure on OFC–amygdala morphometry.

Conclusions

Taken together, these findings provide novel insights into the impacts of childhood trauma on OFC–amygdala morphometric relations, extending previous research primarily focused on functional alterations. Specifically, results indicate that the widely-cited impact of early life stress exposure on OFC–amygdala circuitry can be observed at a purely structural level. These findings may provide important insight in the examination of structurally-based networks of neural regions involved in key transdiagnostic regulatory processes by underscoring the importance of considering early environmental factors that may fundamentally alter morphometric associations apparent in adulthood. Further, present findings provide novel empirical evidence for an environment \times neurobiology effect on pathological personality traits. While previous work has focused on direct associations between OFC volume and pathological personality presentations, these findings point to divergent neuroanatomical associations with disordered personality that depend on childhood trauma exposure. This knowledge has the potential to inform etiological models of personality development that may eventually have implications for the treatment of pathological personality traits.

Acknowledgements. This research was supported in part by the National Institutes of General Medical Sciences [NS, 2P20GM103653-06-6527] and Mental Health [NB, 1F31MH120936-01A1], [NS, 1R01MH116228-01A1, L30MH117623], [JMS, L30MH117662].

Conflict of interest. None.

References

- Adolphs, R. (2002). Neural systems for recognizing emotion. *Current Opinion in Neurobiology*, 12(2), 169–177. doi:10.1016/s0959-4388(02)00301-x.
- Albaugh, M. D., Ducharme, S., Collins, D. L., Botteron, K. N., Althoff, R. R., Evans, A. C., ... Hudziak, J. J., & Brain Development Cooperative Group (2013). Evidence for a cerebral cortical thickness network anti-correlated with amygdalar volume in healthy youths: Implications for the neural substrates of emotion regulation. *NeuroImage*, 71, 42–49. doi:10.1016/j.neuroimage.2012.12.071.
- Ameis, S. H., Ducharme, S., Albaugh, M. D., Hudziak, J. J., Botteron, K. N., Lepage, C., ... Karama, S. (2014). Cortical thickness, cortico-amygdalar networks, and externalizing behaviors in healthy children. *Biological Psychiatry*, 75(1), 65–72. doi:10.1016/j.biopsych.2013.06.008.
- Anderson, J. L., Sellbom, M., & Salekin, R. T. (2018). Utility of the personality inventory for DSM-5-brief form (PID-5-BF) in the measurement of maladaptive personality and psychopathology. *Assessment*, 25(5), 596–607. doi:10.1177/1073191116676889.
- Antonucci, A. S., Gansler, D. A., Tan, S., Bhadelia, R., Patz, S., & Fulwiler, C. (2006). Orbitofrontal correlates of aggression and impulsivity in psychiatric patients. *Psychiatry Research: Neuroimaging*, 147(2–3), 213–220. doi:10.1016/j.psychres.2005.05.016.

- Baas, D., Aleman, A., & Kahn, R. S. (2004). Lateralization of amygdala activation: A systematic review of functional neuroimaging studies. *Brain Research. Brain Research Reviews*, 45(2), 96–103. doi:10.1016/j.brainresrev.2004.02.004.
- Bach, B., Sellbom, M., & Simonsen, E. (2018). Personality inventory for DSM-5 (PID-5) in clinical versus nonclinical individuals: Generalizability of psychometric features. *Assessment*, 25(7), 815–825. doi:10.1177/1073191117709070
- Ball, J. S., & Links, P. S. (2009). Borderline personality disorder and childhood trauma: Evidence for a causal relationship. *Current Psychiatry Reports*, 11(1), 63–68. doi:10.1007/s11920-009-0010-4.
- Banks, S. J., Eddy, K. T., Angstadt, M., Nathan, P. J., & Phan, K. L. (2007). Amygdala-frontal connectivity during emotion regulation. *Social Cognitive and Affective Neuroscience*, 2(4), 303–312. doi:10.1093/scan/nsm029.
- Bechara, A., Damasio, H., & Damasio, A. R. (2000). Emotion, decision making and the orbitofrontal cortex. *Cerebral Cortex (New York, N.Y.: 1991)*, 10(3), 295–307. doi: 10.1093/cercor/10.3.295.
- Berenz, E. C., Amstadter, A. B., Aggen, S. H., Knudsen, G. P., Reichborn-Kjennerud, T., Gardner, C. O., & Kendler, K. S. (2013). Childhood trauma and personality disorder criterion counts: A co-twin control analysis. *Journal of Abnormal Psychology*, 122(4), 1070–1076. doi: 10.1037/a0034238.
- Blackmon, K., Barr, W. B., Carlson, C., Devinsky, O., DuBois, J., Pogash, D., ... Thesen, T. (2011). Structural evidence for involvement of a left amygdala-orbitofrontal network in subclinical anxiety. *Psychiatry Research: Neuroimaging*, 194(3), 296–303. doi:10.1016/j.psychres.2011.05.007.
- Blair, R. J. R. (2004). The roles of orbital frontal cortex in the modulation of antisocial behavior. *Brain and Cognition*, 55(1), 198–208. doi:10.1016/S0278-2626(03)00276-8.
- Blair, H. T., Tinkelman, A., Moita, M. A. P., & LeDoux, J. E. (2003). Associative plasticity in neurons of the lateral amygdala during auditory fear conditioning. *Annals of the New York Academy of Sciences*, 985, 485–487. doi:10.1111/j.1749-6632.2003.tb07106.x.
- Bounoua, N., Miglin, R., Spielberg, J. M., & Sadeh, N. (2020). Childhood assaultive trauma and physical aggression: Links with cortical thickness in prefrontal and occipital cortices. *NeuroImage: Clinical*, 27, 102321. doi:10.1016/j.nicl.2020.102321.
- Carr, C. P., Martins, C. M. S., Stingel, A. M., Lemgruber, V. B., & Jurueña, M. F. (2013). The role of early life stress in adult psychiatric disorders: A systematic review according to childhood trauma subtypes. *The Journal of Nervous and Mental Disease*, 201(12), 1007–1020. doi:10.1097/NMD.0000000000000049.
- Cassiers, L. L. M., Sabbe, B. G. C., Schmaal, L., Veltman, D. J., Penninx, B. W. J. H., & Van Den Eede, F. (2018). Structural and functional brain abnormalities associated with exposure to different childhood trauma subtypes: A systematic review of neuroimaging findings. *Frontiers in Psychiatry*, 9, 329. doi:10.3389/fpsy.2018.00329.
- Chanen, A. M., Velakoulis, D., Carison, K., Gaunson, K., Wood, S. J., Yuen, H. P., ... Pantelis, C. (2008). Orbitofrontal, amygdala and hippocampal volumes in teenagers with first-presentation borderline personality disorder. *Psychiatry Research: Neuroimaging*, 163(2), 116–125. doi:10.1016/j.psychres.2007.08.007.
- Chen, X., Sachdev, P. S., Wen, W., & Anstey, K. J. (2007). Sex differences in regional gray matter in healthy individuals aged 44–48 years: A voxel-based morphometric study. *NeuroImage*, 36(3), 691–699. doi:10.1016/j.neuroimage.2007.03.063.
- Cho, S. S., Pellecchia, G., Aminian, K., Ray, N., Segura, B., Obeso, I., & Strafella, A. P. (2013). Morphometric correlation of impulsivity in medial prefrontal cortex. *Brain Topography*, 26(3), 479–487. doi:10.1007/s10548-012-0270-x.
- Cisler, J. M., Begle, A. M., Amstadter, A. B., Resnick, H. S., Danielson, C. K., Saunders, B. E., & Kilpatrick, D. G. (2012). Exposure to interpersonal violence and risk for PTSD, depression, delinquency, and binge drinking among adolescents: Data from the NSA-R. *Journal of Traumatic Stress*, 25(1), 33–40. doi:10.1002/jts.21672.
- Coccaro, E. F., Keedy, S. K., Gorka, S. M., King, A. C., Fanning, J. R., Lee, R. J., & Phan, K. L. (2016). Differential fMRI BOLD responses in amygdala in intermittent explosive disorder as a function of past alcohol use disorder. *Psychiatry Research: Neuroimaging*, 257, 5–10. doi:10.1016/j.psychres.2016.09.001.
- Coccaro, E. F., Lee, R., McCloskey, M., Csernansky, J. G., & Wang, L. (2015). Morphometric analysis of amygdala and hippocampus shape in impulsively aggressive and healthy control subjects. *Journal of Psychiatric Research*, 69, 80–86. doi:10.1016/j.jpsychires.2015.07.009.
- Cross, D., Fani, N., Powers, A., & Bradley, B. (2017). Neurobiological development in the context of childhood trauma. *Clinical Psychology: Science and Practice*, 24(2), 111–124.
- Dedovic, K., Duchesne, A., Andrews, J., Engert, V., & Pruessner, J. C. (2009). The brain and the stress axis: The neural correlates of cortisol regulation in response to stress. *NeuroImage*, 47(3), 864–871. doi:10.1016/j.neuroimage.2009.05.074.
- DeLisi, M., Drury, A. J., & Elbert, M. J. (2019). The etiology of antisocial personality disorder: The differential roles of adverse childhood experiences and childhood psychopathology. *Comprehensive Psychiatry*, 92, 1–6. doi:10.1016/j.comppsy.2019.04.001.
- DeYoung, C. G. (2010). Personality neuroscience and the biology of traits. *Social and Personality Psychology Compass*, 4(12), 1165–1180.
- DeYoung, C. G., Hirsh, J. B., Shane, M. S., Papademetris, X., Rajeevan, N., & Gray, J. R. (2010). Testing predictions from personality neuroscience. Brain structure and the big five. *Psychological Science*, 21(6), 820–828. doi:10.1177/0956797610370159.
- Edmiston, E. K., & Blackford, J. U. (2013). Childhood maltreatment and response to novel face stimuli presented during functional magnetic resonance imaging in adults. *Psychiatry Research: Neuroimaging*, 212(1), 36–42. doi:10.1016/j.psychres.2012.11.009.
- First, M. B. (2014). Structured clinical interview for the DSM (SCID). *The Encyclopedia of Clinical Psychology*, 1–6.
- Garcia, R., Vouimba, R.-M., Baudry, M., & Thompson, R. F. (1999). The amygdala modulates prefrontal cortex activity relative to conditioned fear. *Nature*, 402(6759), 294–296.
- Gee, D. G., & Casey, B. J. (2015). The impact of developmental timing for stress and recovery. *Neurobiology of Stress*, 1, 184–194. doi:10.1016/j.ynstr.2015.02.001.
- Ghashghaei, H. T., Hilgetag, C. C., & Barbas, H. (2007). Sequence of information processing for emotions based on the anatomic dialogue between prefrontal cortex and amygdala. *NeuroImage*, 34(3), 905–923. doi:10.1016/j.neuroimage.2006.09.046.
- Gong, G., He, Y., Chen, Z. J., & Evans, A. C. (2012). Convergence and divergence of thickness correlations with diffusion connections across the human cerebral cortex. *NeuroImage*, 59(2), 1239–1248. doi:10.1016/j.neuroimage.2011.08.017.
- Goodman, M., & Yehuda, R. (2002). The relationship between psychological trauma and borderline personality disorder. *Psychiatric Annals*, 32(6), 337–345.
- Groman, S. M., Keistler, C., Keip, A. J., Hammarlund, E., DiLeone, R. J., Pittenger, C., ... Taylor, J. R. (2019). Orbitofrontal circuits control multiple reinforcement-learning processes. *Neuron*, 103(4), 734–746.
- Hagler, Jr D. J., Saygin, A. P., & Sereno, M. I. (2006). Smoothing and cluster thresholding for cortical surface-based group analysis of fMRI data. *NeuroImage*, 33(4), 1093–1103.
- Hahn, T., Dresler, T., Ehlis, A.-C., Plichta, M. M., Heinz, S., Polak, T., ... Fallgatter, A. J. (2009). Neural response to reward anticipation is modulated by Gray's impulsivity. *NeuroImage*, 46(4), 1148–1153.
- Hanson, J. L., Chung, M. K., Avants, B. B., Shirtcliff, E. A., Gee, J. C., Davidson, R. J., & Pollak, S. D. (2010). Early stress is associated with alterations in the orbitofrontal cortex: A tensor-based morphometry investigation of brain structure and behavioral risk. *Journal of Neuroscience*, 30(22), 7466–7472.
- Hart, H., & Rubia, K. (2012). Neuroimaging of child abuse: A critical review. *Frontiers in Human Neuroscience*, 6, 52.
- Hayes, A. F. (2018). *Introduction to mediation, moderation, and conditional process analysis second edition: A regression-based approach*. New York, NY: Ebook The Guilford Press. Google Scholar.
- He, Y., Chen, Z. J., & Evans, A. C. (2007). Small-world anatomical networks in the human brain revealed by cortical thickness from MRI. *Cerebral Cortex*, 17(10), 2407–2419. doi:10.1093/cercor/bhl149.

- Heim, C., & Nemeroff, C. B. (2001). The role of childhood trauma in the neurobiology of mood and anxiety disorders: Preclinical and clinical studies. *Biological Psychiatry*, 49(12), 1023–1039. doi:10.1016/S0006-3223(01)01157-X.
- IBM SPSS (n.d.). Corp (2013). *IBM SPSS statistics for windows, version 22.0*. Armonk, NY: IBM Corp.
- Jackson, J., Balota, D. A., & Head, D. (2011). Exploring the relationship between personality and regional brain volume in healthy aging. *Neurobiology of Aging*, 32(12), 2162–2171. doi:10.1016/j.neurobiolaging.2009.12.009.
- Johnson, S. L., Elliott, M. V., & Carver, C. S. (2020). Impulsive responses to positive and negative emotions: Parallel neurocognitive correlates and their implications. *Biological Psychiatry*, 87(4), 338–349. doi:10.1016/j.biopsych.2019.08.018.
- Kalin, N. H., Shelton, S. E., & Davidson, R. J. (2007). Role of the primate orbitofrontal cortex in mediating anxious temperament. *Biological Psychiatry*, 62(10), 1134–1139. doi:10.1016/j.biopsych.2007.04.004.
- Kerr, K. L., Avery, J. A., Barcalow, J. C., Moseman, S. E., Bodurka, J., Bellgowan, P. S. F., & Simmons, W. K. (2015). Trait impulsivity is related to ventral ACC and amygdala activity during primary reward anticipation. *Social Cognitive and Affective Neuroscience*, 10(1), 36–42. doi: 10.1093/scan/nsu023.
- Kim, M. J., Gee, D. G., Loucks, R. A., Davis, F. C., & Whalen, P. J. (2011). Anxiety dissociates dorsal and ventral medial prefrontal cortex functional connectivity with the amygdala at rest. *Cerebral Cortex*, 21(7), 1667–1673. doi:10.1093/cercor/bhq237.
- Krueger, R. F., Derringer, J., Markon, K. E., Watson, D., & Skodol, A. E. (2013). *The personality inventory for DSM-5 – brief form (PID-5-BF) – adult*. Washington, DC: American Psychiatric Association.
- Lim, L., Hart, H., Howells, H., Mehta, M. A., Simmons, A., Mirza, K., & Rubia, K. (2019). Altered white matter connectivity in young people exposed to childhood abuse: A tract-based spatial statistics (TBSS) and tractography study. *Journal of Psychiatry & Neuroscience: JPN*, 44(4), E11–E20. doi: 10.1503/jpn.170241.
- Lim, L., Radua, J., & Rubia, K. (2014). Gray matter abnormalities in childhood maltreatment: A voxel-wise meta-analysis. *American Journal of Psychiatry*, 171(8), 854–863. doi: 10.1176/appi.ajp.2014.13101427.
- Linehan, M. M. (1993). *Skills training manual for treating borderline personality disorder* (pp. xii). New York City, NY: Guilford Press.
- Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, 10(6), 434–445. doi: 10.1038/nrn2639.
- McGaugh, J. L. (2002). Memory consolidation and the amygdala: A systems perspective. *Trends in Neurosciences*, 25(9), 456–461. doi:10.1016/S0166-2236(02)02211-7.
- McLaughlin, K. A., & Lambert, H. K. (2017). Child trauma exposure and psychopathology: Mechanisms of risk and resilience. *Current Opinion in Psychology*, 14, 29–34. doi: 10.1016/j.copsyc.2016.10.004.
- Mincic, A. M. (2015). Neuroanatomical correlates of negative emotionality-related traits: A systematic review and meta-analysis. *Neuropsychologia*, 77, 97–118. doi: 10.1016/j.neuropsychologia.2015.08.007.
- Moreno-López, L., Ioannidis, K., Askelund, A. D., Smith, A. J., Schueler, K., & van Harmelen, A.-L. (2020). The resilient emotional brain: A scoping review of the medial prefrontal cortex and limbic structure and function in resilient adults with a history of childhood maltreatment. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 5(4), 392–402. doi:10.1016/j.bpsc.2019.12.008.
- Morey, R. A., Haswell, C. C., Hooper, S. R., & De Bellis, M. D. (2016). Amygdala, hippocampus, and ventral medial prefrontal cortex volumes differ in maltreated youth with and without chronic posttraumatic stress disorder. *Neuropsychopharmacology*, 41(3), 791–801. doi:10.1038/npp.2015.205.
- Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D., & Gross, J. J. (2004). For better or for worse: Neural systems supporting the cognitive down-and up-regulation of negative emotion. *NeuroImage*, 23(2), 483–499.
- Öhman, A. (2005). The role of the amygdala in human fear: Automatic detection of threat. *Psychoneuroendocrinology*, 30(10), 953–958. doi:10.1016/j.psyneuen.2005.03.019.
- Paquola, C., Wael, R. V. D., Wagstyl, K., Bethlehem, R. A. I., Hong, S.-J., Seidlitz, J., ... Bernhardt, B. C. (2019). Microstructural and functional gradients are increasingly dissociated in transmodal cortices. *PLoS Biology*, 17(5), e3000284. doi:10.1371/journal.pbio.3000284.
- Phan, K. L., Fitzgerald, D. A., Nathan, P. J., Moore, G. J., Uhde, T. W., & Tancer, M. E. (2005). Neural substrates for voluntary suppression of negative affect: A functional magnetic resonance imaging study. *Biological Psychiatry*, 57(3), 210–219. doi:10.1016/j.biopsych.2004.10.030.
- Phillips, M. L., Ladouceur, C. D., & Drevets, W. C. (2008). A neural model of voluntary and automatic emotion regulation: Implications for understanding the pathophysiology and neurodevelopment of bipolar disorder. *Molecular Psychiatry*, 13(9), 829, 833–857. doi:10.1038/mp.2008.65.
- Pine, D. S., & Cohen, J. A. (2002). Trauma in children and adolescents: Risk and treatment of psychiatric sequelae. *Biological Psychiatry*, 51(7), 519–531. doi:10.1016/S0006-3223(01)01352-X.
- Pompili, M., Innamorati, M., Lamis, D. A., Erbuto, D., Venturini, P., Ricci, F., ... Girardi, P. (2014). The associations among childhood maltreatment, 'male depression' and suicide risk in psychiatric patients. *Psychiatry Research*, 220(1), 571–578. doi: 10.1016/j.psychres.2014.07.056.
- Porter, C., Palmier-Claus, J., Branitsky, A., Mansell, W., Warwick, H., & Varese, F. (2020). Childhood adversity and borderline personality disorder: A meta-analysis. *Acta Psychiatrica Scandinavica*, 141(1), 6–20. doi:10.1111/acps.13118.
- Raine, A. (2008). From genes to brain to antisocial behavior. *Current Directions in Psychological Science*, 17(5), 323–328. doi:10.1111/j.1467-8721.2008.00599.x.
- Raine, A. (2018). Antisocial personality as a neurodevelopmental disorder. *Annual Review of Clinical Psychology*, 14(1), 259–289. doi:10.1146/annurev-clinpsy-050817-084819.
- Ray, R. D., & Zald, D. H. (2012). Anatomical insights into the interaction of emotion and cognition in the prefrontal cortex. *Neuroscience & Biobehavioral Reviews*, 36(1), 479–501. doi:10.1016/j.neubiorev.2011.08.005.
- Roy, A. K., Shehzad, Z., Margulies, D. S., Kelly, A. M. C., Uddin, L. Q., Gotimer, K., ... Milham, M. P. (2009). Functional connectivity of the human amygdala using resting state fMRI. *NeuroImage*, 45(2), 614–626. doi:10.1016/j.neuroimage.2008.11.030.
- Sadeh, N., Miller, M. W., Wolf, E. J., & Harkness, K. L. (2015). Negative emotionality and constraint influence PTSD symptom course via exposure to new major adverse life events. *Journal of Anxiety Disorders*, 31, 20–27. doi:10.1016/j.janxdis.2015.01.003.
- Salat, D. H., Buckner, R. L., Snyder, A. Z., Greve, D. N., Desikan, R. S. R., Busa, E., ... Fischl, B. (2004). Thinning of the cerebral cortex in aging. *Cerebral Cortex*, 14(7), 721–730. doi:10.1093/cercor/bhh032.
- Saxbe, D., Lyden, H., Gimbel, S. I., Sachs, M., Piero, L. B. D., Margolin, G., & Kaplan, J. T. (2018). Longitudinal associations between family aggression, externalizing behavior, and the structure and function of the amygdala. *Journal of Research on Adolescence*, 28(1), 134–149. doi:10.1111/jora.12349.
- Saygin, Z. M., Kliemann, D., Iglesias, J. E., van der Kouwe, A. J. W., Boyd, E., Reuter, M., ... Augustinack, J. C. (2017). High-resolution magnetic resonance imaging reveals nuclei of the human amygdala: Manual segmentation to automatic atlas. *NeuroImage*, 155, 370–382. doi:10.1016/j.neuroimage.2017.04.046.
- Shonkoff, J. P., Garner, A. S., The Committee on Psychosocial Aspects of Child and Family Health; Committee on Early Childhood, Adoption, and Dependent Care; Section on Developmental and Behavioral Pediatrics, Siegel, B. S., Dobbins, M. I., Earls, M. F., Garner, A. S., ... Wood, D. L. (2012). The lifelong effects of early childhood adversity and toxic stress. *Pediatrics*, 129(1), e232–e246. doi:10.1542/peds.2011-2663.
- Soloff, P. H., Abraham, K., Ramaseshan, K., Burgess, A., & Diwadkar, V. A. (2017). Hyper-modulation of brain networks by the amygdala among women with borderline personality disorder: Network signatures of affective interference during cognitive processing. *Journal of Psychiatric Research*, 88, 56–63. doi:10.1016/j.jpsychires.2016.12.016.
- Stein, J. L., Wiedholz, L. M., Bassett, D. S., Weinberger, D. R., Zink, C. F., Mattay, V. S., & Meyer-Lindenberg, A. (2007). A validated network of effective amygdala connectivity. *NeuroImage*, 36(3), 736–745. doi:10.1016/j.neuroimage.2007.03.022.
- Taki, Y., & Kawashima, R. (2012). Brain development in childhood. *The Open Neuroimaging Journal*, 6, 103–110. doi:10.2174/1874440001206010103.
- Tarullo, A. R., & Gunnar, M. R. (2006). Child maltreatment and the developing HPA axis. *Hormones and Behavior*, 50(4), 632–639. doi:10.1016/j.yhbeh.2006.06.010.

- Tebartz van Elst, L., Hesslinger, B., Thiel, T., Geiger, E., Haegele, K., Lemieux, L., ... Ebert, D. (2003). Frontolimbic brain abnormalities in patients with borderline personality disorder: A volumetric magnetic resonance imaging study. *Biological Psychiatry*, *54*(2), 163–171. doi:10.1016/S0006-3223(02)01743-2.
- Tottenham, N., & Galván, A. (2016). Stress and the adolescent brain: Amygdala-prefrontal cortex circuitry and ventral striatum as developmental targets. *Neuroscience & Biobehavioral Reviews*, *70*, 217–227. doi:10.1016/j.neubiorev.2016.07.030.
- van der Kouwe, A. J. W., Benner, T., Salat, D. H., & Fischl, B. (2008). Brain morphometry with multiecho MPRAGE. *NeuroImage*, *40*(2), 559–569. doi:10.1016/j.neuroimage.2007.12.025.
- van der Werff, S. J. A., Pannekoek, J. N., Veer, I. M., van Tol, M.-J., Aleman, A., Veltman, D. J., ... van der Wee, N. J. A. (2013). Resting-state functional connectivity in adults with childhood emotional maltreatment. *Psychological Medicine*, *43*(9), 1825–1836. doi:10.1017/S0033291712002942.
- van voorhees, E., & Scarpa, A. (2004). The effects of child maltreatment on the hypothalamic-pituitary-adrenal axis. *Trauma, Violence, & Abuse*, *5*(4), 333–352. doi:10.1177/1524838004269486.
- Wang, Q., Chen, C., Cai, Y., Li, S., Zhao, X., Zheng, L., ... Xue, G. (2016). Dissociated neural substrates underlying impulsive choice and impulsive action. *NeuroImage*, *134*, 540–549. doi:10.1016/j.neuroimage.2016.04.010.
- Wilbertz, G., Tebartz van Elst, L., Delgado, M. R., Maier, S., Feige, B., Philipsen, A., & Blechert, J. (2012). Orbitofrontal reward sensitivity and impulsivity in adult attention deficit hyperactivity disorder. *NeuroImage*, *60*(1), 353–361. doi:10.1016/j.neuroimage.2011.12.011.
- Wright, P., Albarracin, D., Brown, R. D., Li, H., He, G., & Liu, Y. (2008). Dissociated responses in the amygdala and orbitofrontal cortex to bottom-up and top-down components of emotional evaluation. *NeuroImage*, *39*(2), 894–902. doi:10.1016/j.neuroimage.2007.09.014.
- Wright, C. I., Williams, D., Feczko, E., Barrett, L. F., Dickerson, B. C., Schwartz, C. E., & Wedig, M. M. (2006). Neuroanatomical correlates of extraversion and neuroticism. *Cerebral Cortex*, *16*(12), 1809–1819. doi:10.1093/cercor/bhj118.
- Yang, Y., & Raine, A. (2007). Functional and structural brain imaging research on psychopathy. *International Handbook of Psychopathic Disorders and the Law*, *1*, 69–81. <https://doi.org/10.1002/9780470516157.ch4>.
- Yang, Y., & Raine, A. (2009). Prefrontal structural and functional brain imaging findings in antisocial, violent, and psychopathic individuals: A meta-analysis. *Psychiatry Research: Neuroimaging*, *174*(2), 81–88. doi:10.1016/j.psychres.2009.03.012.
- Zielinski, B. A., Gennatas, E. D., Zhou, J., & Seeley, W. W. (2010). Network-level structural covariance in the developing brain. *Proceedings of the National Academy of Sciences of the USA*, *107*(42), 18191–18196. doi:10.1073/pnas.1003109107.