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Machine Learning Analysis of the Relationships Between Gray Matter Volume and Childhood Trauma in a Transdiagnostic Community-Based Sample

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ABSTRACT

BACKGROUND: Childhood trauma is a significant risk factor for adult psychopathology. Previous investigations have implicated childhood trauma–related structural changes in anterior cingulate, dorsolateral prefrontal and orbitofrontal cortex, and hippocampus. Using a large transdiagnostic community sample, the goal of this investigation was to differentially associate regional gray matter (GM) volume with childhood trauma severity specifically, distinct from adult psychopathology.

METHODS: A total of 577 non–treatment-seeking adults (n = 207 men) completed diagnostic, childhood trauma, and structural magnetic resonance imaging assessments with regional GM volume estimated using FreeSurfer. Elastic net analysis was conducted in a nested cross-validation framework, with GM volumes, adult psychopathology, age, education, sex, and magnetic resonance imaging coil type as potential predictors for childhood trauma severity.

RESULTS: Elastic net identified age, education, sex, medical condition, adult psychopathology, and 13 GM regions as predictors of childhood trauma severity. GM regions identified included right caudate; left pallidum; bilateral insula and cingulate sulcus; left superior, inferior, and orbital frontal regions; and regions within temporal and parietal lobes and cerebellum.

CONCLUSIONS: Results from this large, transdiagnostic sample implicate GM volume in regions central to current neurobiological theories of trauma (e.g., prefrontal cortex) as well as additional regions involved in reward, interoceptive, attentional, and sensory processing (e.g., striatal, insula, and parietal/occipital cortices). Future longitudinal studies examining the functional impact of structural changes in this broader network of regions are needed to clarify the role each may play in longer-term outcomes following trauma.

Keywords: Adult psychopathology, Childhood, Elastic net, Gray matter volume, MRI, Trauma exposure

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Approximately 77% of adults receiving mental health treatment in the United States endorse having experienced at least one form of childhood trauma (1). Childhood trauma can include emotional abuse and neglect, physical abuse and neglect, and sexual abuse. Greater severity of childhood trauma has been associated with increased rates of chronic mental health diagnoses, including mood, anxiety, trauma, psychotic, and substance use disorders (2–12). The occurrence of childhood trauma is associated not only with the presence of adult psychopathology but also with greater severity of adult psychopathology (8) and worse treatment outcomes following diagnosis (13). Given that childhood trauma is strongly associated with both the likelihood of adult mental health diagnoses and the severity of those diagnoses, childhood trauma indirectly results in an enormous cost to society in terms of monetary cost of medical and mental health care, loss of productivity, and emotional and support costs paid by families or communities (14).

Whereas a strong link between childhood trauma and increased rates of adult psychopathology has been demonstrated, the existence and nature of a neurobiological signature of childhood trauma beyond the impact on adult psychopathology is less clear. Biological models of childhood trauma suggest that alterations in neurobiology occur on multiple levels. These alterations include changes in hormonal regulation and neurotransmission and subsequent changes in regional brain development (15). With respect to hormone regulation, the principal focus has been on the impact of childhood trauma on the hypothalamic-pituitary-adrenal axis, which is implicated in regulation of neuroendocrine stress responses (16). Childhood trauma is thought to sensitize or increase the hormonal response of the hypothalamic-pituitary-

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adrenal axis, particularly via increased release of corticotropin-releasing factor, which can initiate changes in the neuroendocrine system (17). Previous research has identified changes in the neuroendocrine system following exposure to childhood trauma, including increased central corticotropin-releasing factor levels, immune activation, sensitization of neuroendocrine stress responses, and glucocorticoid resistance (17,18). Similar changes have also been identified in individuals with depression, suggesting that changes in neuroendocrine regulation may make an individual more susceptible to developing depression (17). Increased levels of dopamine and decreased levels of serotonin have been associated with childhood trauma (19), providing additional evidence for a neurobiological link between childhood trauma and adult psychopathology. Notably, changes within the neuroendocrine system are also linked with poorer physical health outcomes (20), which suggests that individuals who experience childhood trauma are also at an increased risk for poorer physical health. However, these models have yet to identify unique correlates of childhood trauma in adult populations beyond the influence of adult psychopathology.

Changes in regional brain volume represent another layer of biological alterations that may link childhood trauma and adult psychopathology. Both childhood trauma and adult psychopathology have been related to alterations in gray matter (GM) volume. For instance, it has been suggested that exposure to childhood trauma may negatively impact whole-brain and regional GM volume and increase susceptibility to adult psychopathology (21,22). Structural magnetic resonance imaging (MRI) research indicates that both childhood trauma and adult psychopathology relate to changes in brain morphology, including in the prefrontal cortex, amygdala, hippocampus, cerebellum, orbitofrontal cortex, insula, anterior cingulate, and caudate (23–27). A recent review has suggested that the most reliable morphological changes occur within the anterior cingulate, dorsolateral prefrontal and orbitofrontal cortex, and hippocampus (23,28). Childhood trauma has been consistently linked with decreased volume within these regions, which are heavily involved in emotional processing (29). However, there is some indication that age and additional exposure to traumatic events since childhood may impact the directionality or robustness of these findings. For example, childhood trauma has been linked with increased GM volume of the amygdala for children and adolescents—which may be a result of dendritic branching directly following stress exposure (23).

Limited sample sizes of previous studies have made it difficult to identify neurobiological differences that may be uniquely related to childhood trauma, rather than being primarily driven by current mental health diagnoses (21). Perhaps as a result, previous research has predominately focused on interpretations of morphological changes as maladaptive responses associated with mental health diagnoses, which may also limit our understanding of how morphological changes may relate to childhood trauma specifically, rather than the often-comorbid psychopathology. Furthermore, previous research has heavily relied on theory-driven approaches to identify which regions of interest (ROIs) to examine and thus may limit identification of ROIs associated with childhood trauma severity. The focus on a priori defined ROIs and the emphasis on maladaptive responses to trauma highlight the need for research examining brain regions that may be involved in both adaptive and maladaptive responses to childhood trauma.

Data-driven or machine learning approaches allow for a more thorough identification of regions that may relate to childhood trauma severity across the entire brain. The current study used MRI data from a large transdiagnostic sample to delineate relationships between regional GM volume (in regions across the entire brain) and childhood trauma that may be distinct from the impact of psychopathology, using a data-driven (elastic net) approach. The use of such an approach allows for the opportunity to either confirm previous hypotheses-driven analyses or identify novel brain regions that may be implicated in childhood trauma. Whereas our approach is hypothesis generating, we anticipated that we may identify relationships between childhood trauma and decreased GM volume in regions previously implicated in emotional processing and trauma, including the amygdala, hippocampus, insular cortex, dorsal lateral prefrontal cortex, and anterior cingulate. Furthermore, we anticipated that these regions would relate to childhood trauma independent of the effects of adult psychopathology.

METHODS AND MATERIALS

Participants

Participants were identified for the current analyses from nine previous or ongoing studies at the Laureate Institute for Brain Research between November 2010 and September 2015 (30). Participants included both men (n = 207) and women (n = 370) between 18 and 59 years of age (mean [SD] age 32.25 [10.58] years). Participants included healthy comparison subjects (n = 276) and individuals who met criteria for at least one psychological disorder (n = 301) as determined by either the Mini-International Neuropsychiatric Interview (31) or the Structured Clinical Interview for DSM-IV Axis I Disorders (32) (see Psychological Assessment below). All participants completed a telephone screen and initial assessment to determine eligibility for imaging studies before enrollment in a specific study protocol. Thus, whereas there were study-specific inclusion and exclusion criteria, there were also common criteria across all studies. Participants were excluded at the screening visits if they endorsed any medical conditions affecting the hemodynamic response, moderate to severe head injury or neurological disorder, or metal implants or devices contraindicated for functional MRI. Participants were included in the present analysis if they completed a Childhood Trauma Questionnaire (CTQ), an assessment of current psychopathology, and a structural neuroimaging assessment. A total of 605 individuals met inclusion criteria for the present analysis. However, 23 scans failed quality assurance (i.e., poor segmentation of GM that was not improved with manual editing) and were excluded, leaving data for 577 participants available for analysis; Table 1 summarizes demographic information.

Psychological Assessment

Diagnostic assessment was based on the DSM-IV-TR (33). Adult psychopathology was assessed using a clinically

administered interview by a trained evaluator. Depending on the study protocol, participants completed either the Structured Clinical Interview for DSM-IV Axis I Disorders (32) or the Mini-International Neuropsychiatric Interview (31). Individuals meeting criteria for at least one current or past psychiatric diagnosis were included in the adult psychopathology group. Psychiatric diagnoses included mood and anxiety disorders (including trauma-related disorders), substance use disorders, bipolar disorder, and eating disorders (Table 1). Participants who did not meet diagnostic criteria for a current or past psychiatric disorder were considered to be psychiatrically healthy and were classified as healthy comparison subjects.

Childhood trauma was assessed using the CTQ (34). The CTQ is a 28-item self-reported assessment of traumatic events an individual may or may not have experienced in his or her lifetime and the frequency of those events. The measure yields a total score indicating overall severity of childhood trauma and five subscales assessing emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse. Total CTQ scores range from 25, indicating no endorsement of childhood trauma, to 125, indicating severe levels of childhood trauma.

Anatomical Assessment

All participants completed an MRI scan as part of each respective study protocol. Scanning was conducted on a GE Discovery MR750 (GE Healthcare, Waukesha, WI) 3.0T MRI scanner. A T1-weighted anatomical scan was acquired using a three-dimensional magnetization prepared rapid gradient echo sequence, with 175 participants scanned using a 32-channel coil (repetition time = 6 ms, echo time = 2 ms, 1-mm slice, matrix = 256 × 256, field of view = 192, flip angle = 8°) and 402 participants scanned using an eight-channel coil (repetition time = 6 ms, echo time = 2 ms, 1-mm slice, matrix = 240 × 240, field of view = 216, flip angle = 8°). Images were preprocessed using FreeSurfer (recon-all command) version 5.3.0 image analysis suite (http://surfer.nmr.mgh.harvard.edu/). We employed the FreeSurfer automated preprocess pipeline (recon-all) to extract estimates of GM volume. Quality assurance and manual editing were conducted by two trained raters (DW and JP). Bilateral and whole-brain estimates of GM volume (cortical and subcortical regions) were extracted from individual anatomical images. A ratio adjusting for whole-brain volume (ROI/whole-brain volume) was calculated for each ROI before analysis. ROIs were identified based on FreeSurfer anatomical labeling using the Destrieux 2009 atlas for cortical regions, including segmentation of 148 cortical ROIs (35), and the FreeSurfer probabilistic atlas for subcortical regions, which segments 40 subcortical ROIs (36).

Statistical Analyses

Our goal was to build a predictive model of childhood trauma total score. Potential predictors included regional GM volume, adulthood psychopathology, and six covariates: age, sex, education, self-reported medical comorbidities, number of medications (see Table 1 for medical comorbidities and medication information), and coil used during MRI (eight-channel vs. 32-channel). Across all 577 participants, 10 participants were missing one itemized response for CTQ data, and 11 participants were missing educational data. Missing values were imputed using the k = 10 nearest neighbors.

To reduce the risk of overfitting and ensure reproducibility, we built prediction models in nested cross-validation (37). In the outer loop, the whole dataset was split into k parts (k = 5), where each part served as a testing set and the remaining (k − 1) parts served as a training set; in the inner loop, each training set was used to train a model (i.e., to optimize tuning parameters) using standard k-fold cross-validation. The trained models were then applied to make predictions on the unseen testing sets in the outer loop and to assess their performance. Here, we chose k = 5 in both loops and repeated the whole process five times, which resulted in 5 × 5 = 25 final models

Table 1. Sample Demographics (*N* = 577)

	Mean (SD)	Endorsed, *n* (%)	Missing, *n*
Age, Years	32 (11)	—	0
Education, Years	14 (2)	—	12
Sex, Male	—	207 (35.9)	0
Number of Medical Conditions	6 (5)	—	4
MRI Coil, 8-Channel	—	175 (30.3)	0
Childhood Trauma Questionnaire Total Score	47 (14)	—	9
Sexual abuse subscale	9 (3)	—	2
Physical neglect subscale	9 (2)	—	3
Physical abuse subscale	10 (3)	—	0
Emotional neglect subscale	9 (5)	—	1
Emotional abuse subscale	9 (4)	—	2
Adult Psychopathology Present	—	301 (52.2)	0
Mood/Anxiety/Trauma Disorders	—	264 (61.1)	0
ED	—	1 (<1)	0
Bipolar disorder	—	14 (2.4)	0
SUD	—	5 (<1)	0
Mood/anxiety/trauma + SUD	—	8 (1.4)	0
Mood/anxiety/trauma + ED	—	9 (1.6)	0
Medications			5
Psychotropics	0.36 (0.88)	205 (35.8)	6
Muscle joint pain	0.11 (0.41)	74 (13.0)	6
Allergy or COPD	0.13 (0.17)	5 (0.9)	6
Metabolic	0.01 (0.31)	63 (11.0)	6
Gastrointestinal	0.06 (0.29)	36 (6.3)	6
Cardiovascular	0.06 (0.26)	37 (6.5)	6
Birth control	0.11 (0.43)	84 (14.7)	6
Miscellaneous	0.15 (0.39)	60 (10.5)	6
Total number	0.99 (1.44)	564 (98.8)	
Medical Conditions			4
Constitutional	0.69 (0.46)	397 (69.3)	4
Ear, nose, and throat	0.53 (0.50)	304 (53.1)	4
Cardiovascular	0.18 (0.39)	105 (18.3)	4
Respiratory	0.13 (0.34)	74 (12.9)	4
Gastrointestinal	0.25 (0.43)	142 (24.8)	4
Musculoskeletal	0.24 (0.43)	138 (24.1)	4
Neurological	0.55 (0.50)	315 (55.0)	4

COPD, chronic obstructive pulmonary disease; ED, eating disorder; MRI, magnetic resonance imaging; SUD, substance use disorder.

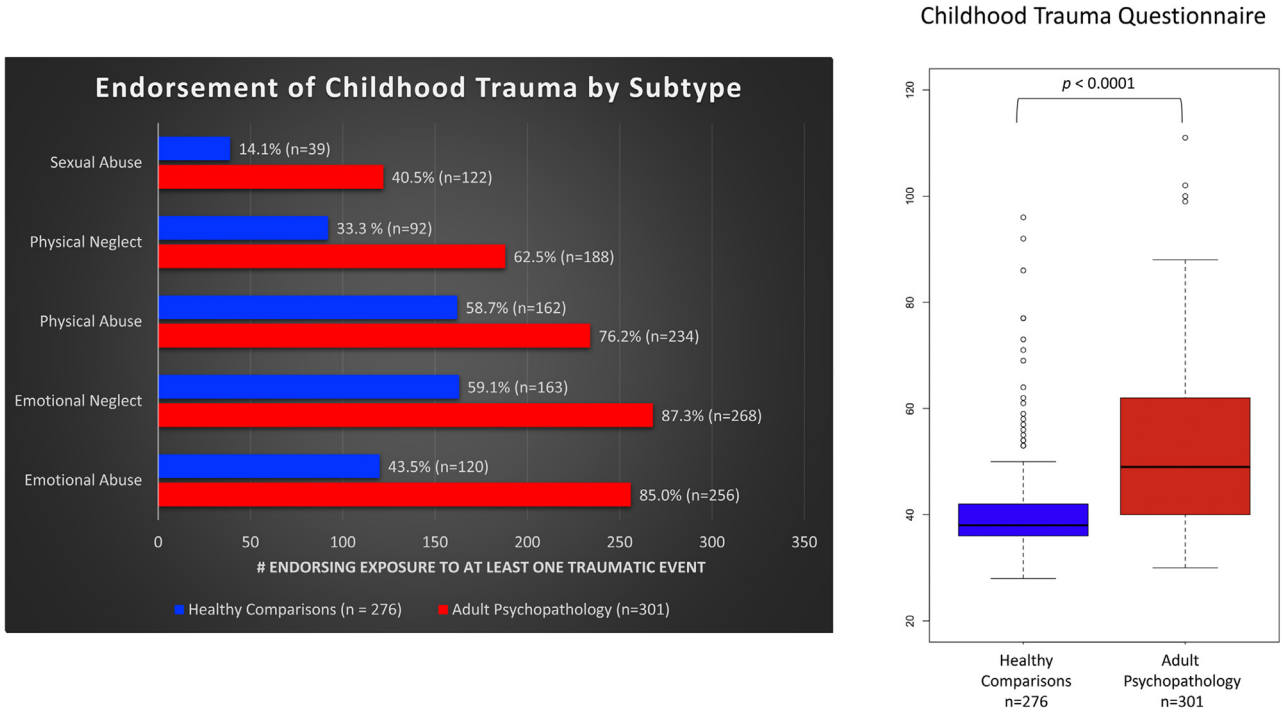

Figure 1. Endorsement of total childhood trauma severity, as assessed by the Childhood Trauma Questionnaire (score range, 25–125), and endorsement by subtype for healthy control subjects and subjects with adult psychopathology. Overall, participants with adult psychopathology (n = 301) displayed significantly higher levels of childhood trauma severity as well as significantly higher rates of childhood trauma subtypes, including sexual abuse, physical abuse and neglect, and emotional abuse and neglect, compared with participants in the healthy comparison group (n = 276; all $p > .001$). Percentages shown reflect the percent of individuals within each group that endorsed a particular type of trauma.

and allowed for assessing the variability of model performance and variable selection. The details of repeated nested cross-validation have been previously published (37,38).

Because we were interested in identifying brain regions predictive of childhood trauma, we chose elastic net regularization as the model-building algorithm owing to its embedded nature for feature selection and ability to select correlated important predictors (39). Elastic net is a linear model-based methodology and shrinks regression coefficients toward zero and automatically selects predictors with nonzero coefficients. Elastic net contains two tuning parameters, α and λ: the former controls the behavior of elastic net to be more similar to ridge regression ($\alpha = 0$) or LASSO ($\alpha = 1$), whereas the latter controls the amount of penalty. We chose to evaluate 10 (α values) $\times$ 10 (λ values) = 100 parameter combinations for each training set in the inner loop (see Supplement 2 for values of tuning parameters actually evaluated) using root mean square error (RMSE) as the evaluation metric; the optimal tuning parameters were chosen by the 1 SE rule, i.e., the optimal parameters were those whose RMSE fell within 1 SE from the minimal RMSE of all parameters [e.g., see Figure 3.7 in (40)]. As mentioned above, the 25 models would provide 25 sets of regression coefficients, and we computed mean and SE of these coefficients. A predictor was selected if its coefficient mean $\pm$ SE excluded zero. We examined the significance of the prediction accuracy and errors via permutation testing (see Supplement 1 for model comparison). Specifically, we first randomly shuffled the log-transformed childhood trauma total scores but kept the rows of the predictor matrix unchanged and then repeated the nested cross-validation procedure described above 200 times. p Values were then computed as the proportion of R^2 (mean absolute error and RMSE) values from the original data that were larger (or smaller) than values from the permutation repetitions. Considering that elastic net is a linear model–based method, we also explored two popular machine learning algorithms without linearity assumptions: random forest and support vector regression using radial kernel. Permutation testing as described above was also applied to random forest and support vector regression models. Results comparing the three machine learning algorithms are included in Supplement 1. Childhood trauma total scores were skewed and therefore log-transformed as the response variable.

All analyses were conducted using R Statistical Software Package version 3.5.1 (41), using the DMwR package for kNN imputation version 0.4.1 (42), the caret package version 6.0-80 for general cross-validation framework (43), the glmnet package version 2.0-16 (44) for elastic net, the ranger package version 0.10.1 (45) for random forest, and the kernlab package version 0.9-27 (46) for support vector regression (see Supplement 3 for R markdown).

RESULTS

All 577 participants indicated some form of childhood trauma, meaning each participant endorsed at least one item on the CTQ (Figure 1, Table 1). Endorsement and average rates of

childhood trauma (mean [SD] CTQ score 46.2 [13.7]) and type of childhood trauma in the present sample are similar to data reported in previous studies of treatment-seeking adults (1). The most common form of abuse was emotional neglect (74.7%). Healthy comparison subjects endorsed significantly less childhood trauma overall ($t_{575} = -11.32$, $p < .0001$) as well as significantly fewer experiences of the various trauma subtypes compared with subjects with adult psychopathology (all $p < .001$) (Figure 1).

Assessment of potential covariates revealed increased age ($r = .15$, $p < .001$), medical comorbidities ($r = .29$, $p < .001$), lower education ($r = -.20$, $p < .001$), and female sex ($t_{558.92} = 4.18$, $p < .001$) were associated with increased childhood trauma severity. Although MRI coil did not relate to childhood trauma severity, it was included in the model as a potential predictor of childhood severity given the potential impact of coil type on regional GM volume.

Elastic net performed slightly better than the other two algorithms (Figure S1 in Supplement 1), and thus we focused its results. The performance metrics were mean absolute error, .179 ± .003 (training) and .179 ± .009 (testing); RMSE, .229 ± .004 (training) and .228 ± .013 (testing); R^2, .213 ± .021 (training) and .227 ± .068 (testing). Permutation testing revealed that each metric (RMSE, mean absolute error, and R^2) for the elastic net model was statistically significant ($p < .005$) (Figure S2 in Supplement 1). The elastic net revealed 18 variables uniquely related to childhood trauma severity (Table 2): age; sex; education; number of medical conditions; adult psychopathology; and 13 GM regions (Figure 2), including 1) increased GM volume within the right anterior transverse temporal gyrus, right inferior aspect of the insula, right suborbital sulcus, left medial cingulate sulcus, and left palladium, and 2) lower GM volume within the right medial cingulate, right parieto-occipital sulcus, right cerebellum, right caudate, left anterior aspect of the insula, left superior and inferior frontal gyri, and left orbital gyrus.

Table 2. Predictors of Childhood Trauma Severity

	Regularized Regression Coefficient
Regions of Interest in Left Hemisphere	
Pallidum	.008
Opercular part of inferior frontal gyrus	.003
Orbital gyri	−.004
Anterior aspect of circular sulcus of the insula	−.008
Superior frontal gyrus	−.004
Marginal branch of cingulate sulcus	.003
Regions of Interest in Right Hemisphere	
Anterior transverse temporal gyrus	.004
Marginal branch of cingulate sulcus	−.007
Inferior aspect of circular sulcus of the insula	.008
Parieto-occipital sulcus	−.005
Caudate	−.007
Cerebellum	−.003
Suborbital sulcus	.003
Demographic and Clinical Variables	
Adult psychopathology	.067
Education	−.022
Medical conditions	.024
Sex	−.007
Age	.008

DISCUSSION

This study examined the unique impact of childhood trauma severity on brain morphology in a large transdiagnostic community sample of men and women (35.9% men). We specifically sought to identify a neurobiological signature, as defined by regional GM volume, of childhood trauma severity, above and beyond the influence of adult psychopathology. Using elastic net, we identified 13 brain regions that related to childhood trauma severity, including right caudate, bilateral insular cortex, prefrontal (orbital, superior frontal), and additional GM regions within temporal and parietal cortices and cerebellum.

Structural neuroimaging research on childhood trauma has focused primarily on the hippocampus, amygdala, and prefrontal regions, given the centrality of these regions to traditional theories of emotional processing in mental health. By restricting the focus of investigation to regions implicated in a narrow range of dysfunctional processes in mental health samples, we limit the ability to understand how childhood trauma impacts the brain more generally. To overcome this limitation, the present study used a data-driven machine learning approach, elastic net, in a large adult sample with and without psychiatric disorders to explore relationships between regional GM volume and childhood trauma severity. We identified 13 neurobiological predictors of childhood trauma severity above and beyond the impact of demographic variables such as age and sex as well as the presence of adult psychopathology. Consistent with previous findings (23–28), our findings highlight that childhood trauma severity is associated with morphological changes in a network of regions involved in emotional and interoceptive processing and regulation, including smaller regional GM volume within the left superior frontal cortex and right medial cingulate cortex and higher regional GM volume within the left medial cingulate cortex. Additionally, higher GM volume within the right inferior insular cortex and lower GM volume within the left anterior insula related to childhood trauma severity. Whereas functional neuroimaging studies suggest a central role for the insula in the pathology of posttraumatic stress disorder (PTSD) and other anxiety-related disorders particularly related to interoceptive processing (47,48), the present results provide structural evidence to corroborate the involvement of insula abnormalities as a transdiagnostic sequela of trauma. The subregions of the insula identified in the current study have been consistently related to interoceptive processing (49), suggesting that investigations to determine whether interoceptive dysfunction in the insula is a consequence of traumatic exposure may be warranted.

In addition to replicating theory-driven research findings, our approach also identified relationships between childhood trauma severity and regions that have not been a focus of previous theory-driven investigations. We identified smaller

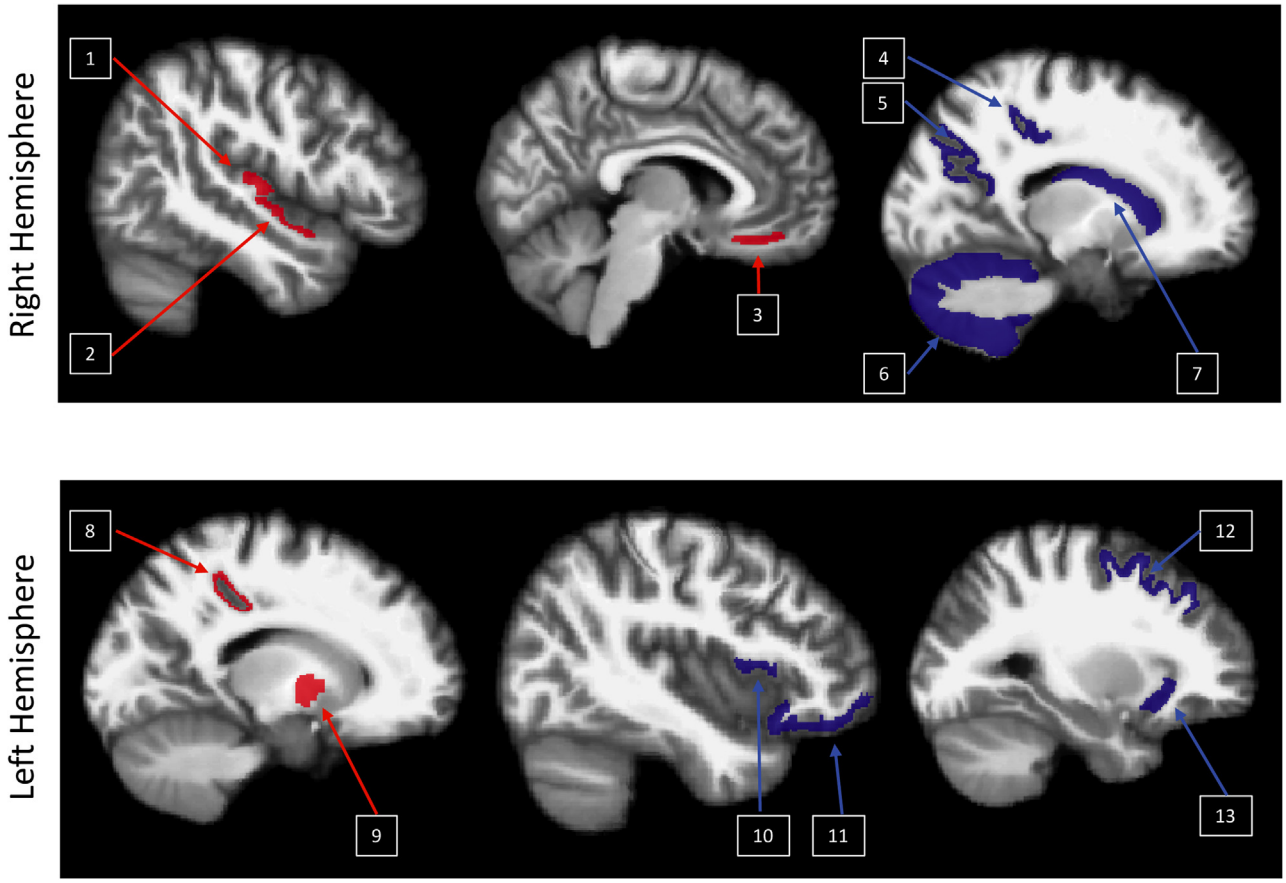

Figure 2. Regions in which gray matter volume significantly predicts childhood trauma severity, as determined by elastic net analysis. Regions displayed in red are regions in which higher gray matter volume relates to increased childhood trauma severity, and regions in blue represent regions in which lower gray matter volume relates to increased childhood trauma severity. Within the right hemisphere, the following regions were identified as predictors of childhood trauma severity: anterior transverse temporal gyrus (1); inferior aspect of the circular sulcus of the insula (2); suborbital sulcus (3); medial cingulate sulcus (4); parieto-occipital sulcus (5); cerebellum (6); caudate (7). Regions identified within the left hemisphere include the following: medial cingulate sulcus (8); pallidum (9); opercular part of the inferior frontal gyrus (10); orbital gyrus (11); superior frontal gyrus (12); left anterior aspect of the circular sulcus of the insula (13).

GM volume of the left ventromedial prefrontal cortex, specifically the left orbital cortex, right suborbital sulcus, and right caudate, as well as increased GM volume in the left pallidum, all of which have been implicated in processing of reward, value, or subsequent decision making. The pallidum and caudate have been associated with reward processing, which may motivate decision-making processes and behavior (50,51). Interestingly, the relationship between childhood trauma and negative psychosocial outcomes has been mitigated by increased reactivity to positive social stimuli within the pallidum, suggesting that increased reactivity to rewarding stimuli in this region may represent a resilience or protective factor for childhood trauma (52,53). Furthermore, adults with PTSD exhibit reduced GM volume within the caudate and smaller activations to monetary gains versus losses (51). Our results indicate that increased volume within the left pallidum and smaller volume within the right caudate significantly predict report of childhood trauma severity. Therefore, alterations in GM volume may be related to dysfunction in these regions implicated in reward processing. Relatedly, the ventromedial prefrontal cortex is associated with evaluation and decision making (54). Reduced volume within this region has been previously reported in maltreated youths with PTSD (55) as well as with increased severity of combat experiences and higher unit support (56), suggesting that this alteration in GM volume may not simply be a pathological result but perhaps may relate to resilience. The present results indicate that childhood trauma relates to smaller GM volume in the left orbital gyrus in adults with and without adult psychopathology, suggesting that smaller GM volume in this region may be a by-product of childhood trauma exposure as opposed to a specific psychiatric disorder.

Elastic net also identified decreased GM volume in the right cerebellum as a predictor of increased childhood trauma severity. The cerebellum has been associated with many functions but is thought to play a critical role in emotional and cognitive development, and reduced GM volume in these regions has been previously linked to PTSD in children and adolescents (57). As FreeSurfer does not currently segment subregions of the cerebellum, future studies examining specificity of cerebellar findings will help clarify the functional implications of this result. Lastly, the present results highlight a

role for the right anterior transverse temporal (Heschl's) gyrus, a temporal region associated with auditory processing (58), in predicting childhood trauma severity. PTSD has been associated with lower activation of this region during target detection (novel vs. standard auditory stimuli) (59) and reduced resting-state connectivity with insular and other temporal lobe regions (60). However, the present findings suggest that smaller GM volume within the right anterior transverse temporal gyrus may relate to childhood trauma severity. In sum, current findings implicate a broader network of parietal, temporal, occipital, and cerebellar regions that have not yet been considered central to neurobiological theories of trauma. Future longitudinal research examining the functional impact of structural changes in this broader network of regions is needed to clarify the protective or pathological role each may play in longer-term outcomes following trauma.

Another notable observation was that the childhood trauma prevalence rate was much higher in the current study, with all participants reporting some form of childhood trauma, than reported in previous studies with non–treatment seeking, community samples (15%–40%) (3,61,62). The heightened prevalence rates and types of childhood trauma in the present sample were more similar to adults receiving mental health treatment (1); this is likely due to the specific inclusion of individuals with psychiatric diagnosis. Additionally, endorsement of childhood trauma in the present sample may be reflective of the elevated rates of childhood trauma in the state of Oklahoma, where the percentage of children who experience an adverse life event each year is approximately 10% higher than the national average (63). Similar to previous studies (2–11), our results provide additional support for a link between greater levels of childhood trauma severity and presence of adult psychopathology despite demographic variables such as increased age, lower educational attainment, female sex, and increased number of medical comorbidities. Taken together, these results underscore the importance of assessment and impact of childhood trauma in non–mental health contexts, such as primary care settings.

Limitations

While the present results provide initial evidence for a role of the anterior and posterior segments of the circular sulcus of the insula in relation to childhood trauma severity, the study was limited by retrospective report of childhood trauma, which may influence recall and reporting, and a cross-sectional design, which limits the ability to assess temporal relationships. Other statistical approaches with larger or longitudinal samples may be used to clarify temporal relationships. Additionally, we did not assess age at which the childhood trauma occurred. Given the differential rate of development in brain regions (64), it will be important for future research to examine if age at which trauma occurred impacts regional GM volume. Furthermore, we were unable to tease apart unique contributions of various subtypes of childhood trauma (e.g., physical and emotional abuse vs. neglect) owing to high correlations among these subtypes in the present sample. Selection of assessment measures was not consistent across samples included in the present analysis, making it difficult to examine moderating variables, such as intelligence and socioeconomic status. Last, this study leveraged a large cross-study sample to support a data-driven approach to analysis, which is important for complementing the more numerous studies using smaller samples and theory-driven approaches. However, these results would benefit from external replication in an independent sample.

Conclusions

The present study used a data-driven, machine learning approach in a large community-based adult sample to explore relationships between regional GM volume and severity of childhood trauma exposure. Results suggest that severity of childhood trauma is linked with alterations of GM volume in numerous regions implicated in emotional processing as well as additional regions involved in reward, interoceptive, attentional, and sensory processing (e.g., striatal, insula, and parietal and occipital cortices). Use of longitudinal research designs and tasks that causally probe each process will further clarify the functional and clinical significance of these findings.

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