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Regular Article

Unraveling the link between childhood maltreatment and depression: Insights from the role of ventral striatum and middle cingulate cortex in hedonic experience and emotion regulation

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Abstract

Childhood maltreatment is an established risk factor for psychopathology. However, it remains unclear how childhood traumatic events relate to mental health problems and how the brain is involved. This study examined the serial mediation effect of brain morphological alterations and emotion-/reward-related functions on linking the relationship from maltreatment to depression. We recruited 156 healthy adolescents and young adults and an additional sample of 31 adolescents with major depressive disorder for assessment of childhood maltreatment, depressive symptoms, cognitive reappraisal and anticipatory/consummatory pleasure. Structural MRI data were acquired to identify maltreatment-related cortical and subcortical morphological differences. The mediation models suggested that emotional maltreatment of abuse and neglect, was respectively associated with increased gray matter volume in the ventral striatum and greater thickness in the middle cingulate cortex. These structural alterations were further related to reduced anticipatory pleasure and disrupted cognitive reappraisal, which contributed to more severe depressive symptoms among healthy individuals. The above mediating effects were not replicated in our clinical group partly due to the small sample size. Preventative interventions can target emotional and reward systems to foster resilience and reduce the likelihood of future psychiatric disorders among individuals with a history of maltreatment.

Keywords: childhood maltreatment; depression; brain structures; cognitive appraisal; anticipatory pleasure

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Introduction

Childhood maltreatment, including physical, sexual and emotional abuse and neglect, has deleterious effects on physical and psychological functioning across the life span (Green et al., 2010). Such early adversities may represent the most potent predictor for a wide range of psychiatric disorders such as depression (Kuzminskaite et al., 2021). Moreover, depressive disorders in individuals who have experienced childhood maltreatment are more likely to be persistent and recurrent, with more severe symptoms and an increased risk of comorbidity and treatment-resistance (Hovens et al., 2012; Nanni et al., 2012). Even in general populations with the absence of any psychiatric disorder, childhood maltreatment is associated with alterations in social perception (Salokangas et al., 2018) and brain structural and functional differences across emotional and cognitive domains (Dannlowski et al., 2013; Duncan et al., 2015; Weissman et al., 2020), which are similar to the neurocognitive abnormalities documented in clinical patients with depression and other mental disorders.

Therefore, the mechanisms underlying the association between childhood maltreatment and psychopathology, and how brain differences relate to that, are an important topic to investigate. One potential theory of latent vulnerability proposes that a set of neurocognitive systems are altered following maltreatment, which in turn may embed latent vulnerability to future mental health problems (McCrory & Viding, 2015). Among the varied set of candidate neurocognitive systems, reward processing and emotion regulation have received much research attention because of their established close relationship with both childhood traumatic events and internalizing problems (Jaffee, 2017; McCrory et al., 2017; Teicher & Samson, 2016). On one hand, the development of reward processing and emotion regulation is thought to be driven by an interplay between the maturation of neuroendocrine systems

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and social learning opportunities, both of which are particularly sensitive to childhood stressful events (Miu et al., 2022; Novick et al., 2018). On the other hand, both disrupted reward processing and impaired emotion regulation are transdiagnostic features of psychopathology (e.g., depression, anxiety, substance use disorders) (Aldao et al., 2010; Zald & Treadway, 2017), making them a candidate mechanism to explore individual differences in the psychological consequences of childhood adversity.

Differences in reward behavior, for example, have been consistently found in individuals who have histories of maltreatment (Novick et al., 2018). They have difficulties in reinforcement learning and demonstrate reduced approach motivation. In the monetary incentive delay task, both maltreated children and adults show blunted BOLD response to anticipated rewards in the ventral striatum (Teicher & Samson, 2016). The alterations in reward-related neural systems may further represent a marker of vulnerability for future emergence of clinical depression (Stringaris et al., 2015). In addition to the robust findings of altered striatal function (see reviews, McCrory et al., 2017; Novick et al., 2018; Teicher & Samson, 2016), a few studies have also reported associations between maltreatment and structural alterations of striatal regions, although the results are inconsistent (Teicher & Samson, 2016). One possible reason is that different types of maltreatment (e.g., abuse, early deprivation, bullying, domestic violence) and different onset time of childhood stressful events might result in different alterations in brain morphology (Baker et al., 2013; Teicher & Samson, 2016).

As for emotion regulation, childhood maltreatment is associated with more habitual use of maladaptive strategies such as rumination and suppression, as well as less frequent and effective use of adaptive strategies particularly cognitive reappraisal in childhood (Lavi et al., 2019) and adulthood (Miu et al., 2022). These emotion regulation difficulties serve as mediators in the relation between childhood adversity and psychopathology (Miu et al., 2022). Moreover, longitudinal studies with maltreated children (aged 6–12 years) suggest that impaired emotion regulation is not only correlated with depression, but also predictive of development of future psychiatric conditions (Kim & Cicchetti, 2010). Regarding the corresponding neural substrates, neuroimaging studies have found atypical brain activity in regulatory regions such as the anterior cingulate cortex, and altered connectivity in frontal-limbic circuits (e.g., amygdala–medial prefrontal cortex connectivity) associated with emotion dysregulation in children and adolescents with exposure to maltreatment (McCrory et al., 2017). Childhood maltreatment is also associated with morphological abnormalities in prefrontal regions, including reduced gray matter volume or thickness in anterior cingulate cortex, ventromedial and dorsolateral prefrontal regions (Teicher & Samson, 2016). These differences in brain regions relevant for emotion regulation have been found to be a pronounced feature of patients with major depressive disorders (Schmaal et al., 2017), and can be predictive of future depression onset and relapse (Opel et al., 2019).

Although accumulating evidence has supported the key role of reward processing and emotion regulation in linking the path from childhood maltreatment to later psychopathology, most of these studies have solely relied on behavioral measures, such as self-report questionnaires or psychological tests, to examine the mediating effects (Miu et al., 2022). Alternatively, a limited number of studies have explored the impact of maltreatment on brain morphology or function, observing alterations in specific regions associated with reward responses and emotion regulation, including the prefrontal areas, striatum, amygdala, hippocampus, and insula (He et al., 2022; Luo et al., 2022; Opel et al., 2019; Popovic et al., 2020; Wan et al., 2022). By considering the established role of these brain regions, researchers have indirectly inferred the detrimental influence of maltreatment on reward- and emotion-related processes (e.g., Wan et al., 2022). However, very few studies have directly explored the serial mediation effect of brain structure and behavioral assessments. In other words, it remains unclear how childhood maltreatment disturbs brain structural development, which in turn undermines an individual's cognitive, emotional and social processes, and ultimately increases psychiatric vulnerability.

Another notable limitation of previous studies is the tendency to approach different forms of childhood adversities as a homogeneous construct, without adequately exploring the distinct contributions of specific subtypes of maltreatment. However, current theories suggest that distinct forms of maltreatment may have differential impact on neural development (Cassiers et al., 2018). For instance, abuse is more strongly associated with altered emotional processing such as fear learning and threat identification, but neglect/deprivation may be more closely linked to deficits in processing complex social and cognitive inputs (Sheridan & McLaughlin, 2014). Moreover, meta-analytical results indicate that psychological forms of maltreatment (i.e., emotional abuse and neglect) are more strongly associated with depression outcomes compared with other types of child trauma like sexual and physical abuse (Infurna et al., 2016; Mandelli et al., 2015). Based on Bowlby's (1982) attachment theory, caregivers are fundamental for the development of the child´s internal working models of the world. Early emotional abuse or neglect may therefore be particularly maladaptive because harmful behaviors (e.g., criticism and insults) are perpetrated directly by primary attachment figures, which can easily activate a negative model of the self and others. The resultant low self-esteem and feelings of distrust and powerlessness would foster internalizing problems later in life (Shapero et al., 2014). All the above findings emphasize the significance of examining specific types of maltreatment when exploring their associations with depression.

In this study, the roles of different types of maltreatment were separately examined, with the aim to better elucidate their relationship with depressive symptoms in healthy adolescents and young adults ($n = 156$). Furthermore, unlike most of previous studies only investigating mediation effects at a single behavioral or neural level, we examined the serial mediating role of brain structure and emotion-/reward-related processes (i.e., emotion regulation of reappraisal, hedonic capacity of anticipatory and consummatory pleasure). To further explore whether maltreatment-related alterations were present regardless of depression diagnosis, we also recruited a small sample of patients with major depressive disorders (MDD) ($n = 31$). We hypothesized that (1) increased levels of maltreatment, especially emotional abuse and neglect, would be associated with more severe depressive symptoms; (2) childhood maltreatment would also be associated with brain structural alterations (especially in the prefrontal and striatal regions), reduced hedonic experiences and disrupted emotion regulation; (3) maltreatment-related brain structural differences would further be related to altered reward and emotion functions; (4) these neural and behavioral differences would serially mediate the association between maltreatment and depression. Finally, we hypothesized that the above associations and mediating effects in healthy youth would be replicated in clinical populations with depression.

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Methods

Participants

The data were collected from two research projects investigating internalizing problems in adolescents (Project 1) and young adults (Project 2). In Project 1, 40 healthy adolescents (12–23 years; Mean age = 16.1 years, SD = 2.88; 16 males) and 31 adolescents with MDD (13–24 years, Mean age = 15.52 years, SD = 2.42; 8 males) completed the self-report questionnaires and had T1 images with good quality. The clinical adolescents met the diagnostic criteria for MDD using a Structured Clinical Interview according to the Diagnostic Statistical Manual of Mental Disorder, Fifth Edition (DSM-5), and had no comorbid psychiatric disorders. In Project 2, 116 healthy college students (18–26 years, Mean age = 20.63 years, SD = 2.47; 31 males) were included in the final analysis. To maximize the detect power, we combined the healthy youth in Project 1 and 2 to represent the non-clinical population ($n = 156$). Both of these projects utilized the same MRI scanner, and both projects assessed the self-report childhood maltreatment, depressive symptoms, emotion regulation and hedonic capacity. Note that they used different scales to measure emotion regulation (see the Measures section).

For all the participants, exclusion criteria were any neurological abnormalities, a history of epilepsy or head trauma, and a history of substance use disorders. The healthy participants also reported no personal or family history of any psychiatric disorders. All adult participants and parents of adolescent participants gave written informed consent before the start of the study. All adolescents also gave their assent to participate in this study. This research was approved by the Human Subjects Protection Committee of the University (approval number: HR-0133-2018; HR-472-2019).

Measures

Childhood trauma questionnaire (CTQ)

The CTQ is a 28-item self-report questionnaire that retrospectively assesses childhood experiences of abuse or neglect in clinical and non-clinical samples (Bernstein & Fink, 1998). It inquires about five types of childhood adversities: emotional abuse, emotional neglect, physical abuse, physical neglect and sexual abuse. Every subtype of maltreatment has 5 items rated on a 5-point Likert scale (range 5–25). Higher scores indicate more severe and chronic exposures to childhood trauma. Individuals who scored higher than the moderate-severe threshold of any CTQ subscale were treated as existence of childhood maltreatment. The cutoff scores of each subscale were (1) emotional abuse $\geq$ 13, (2) emotional neglect $\geq$ 15, (3) sexual abuse $\geq$ 8, (4) physical abuse $\geq$ 10, and (5) physical neglect $\geq$ 10 (Bernstein & Fink, 1998). The Chinese version of the CTQ was used in this study, which showed good reliability and validity (Zhao et al., 2005). The CTQ had a Cronbach's α of 0.91 across groups in this study.

Depressive symptoms

The Beck Depression Inventory (BDI) (Beck, 1961; Chinese version: Zheng & Lin, 1991) was used to evaluate the level of depressive symptoms. This scale consists of 21 items investigating a wide range of emotional, cognitive, somatic, and interpersonal symptoms of depression. Each item is scored on a 4-point Likert scale (0–3), and a higher total score indicates higher levels of depressive symptoms. The BDI scores < 10 indicate no or minimal depression; scores from 10 through 16 indicate mild-to-moderate depression; scores from 17 through 29 indicate moderate-to-severe depression; and scores from 30 through 63 indicate severe depression (Beck & Steer, 1993). In the current sample, the BDI showed good internal consistency (Cronbach's α = 0.95). In Project 1, the 17-item Hamilton Rating Scale for Depression (HAMD-17) (Hamilton, 1967) were additionally administered to assess the severity of illness among clinical adolescents.

Hedonic capacity

The Temporal Experience of Pleasure Scale (TEPS) was used to capture two distinct hedonic constructs of anticipatory pleasure (a feeling of wanting) and consummatory pleasure (a feeling of liking) (Gard et al., 2006). The Chinese version of the TEPS is a 19-item, 6-point-Likert-format measure, with 9 items for anticipatory pleasure (e.g., "When I hear about a new movie starring my favorite actor, I can't wait to see it"), and 10 for consummatory pleasure ("The smell of freshly cut grass is enjoyable to me") (Chan et al., 2012). Higher scores indicate higher hedonic capacity. The subscales of anticipatory and consummatory pleasure had a Cronbach's α of 0.77 and 0.82, respectively, in this study.

Emotion regulation of reappraisal

In Project 1, the 36-item Cognitive Emotion Regulation Questionnaire (CERQ, Garnefski & Kraaij, 2007; Chinese version: Zhu et al., 2008) was used to assess the self-regulatory and cognitive components of emotion regulation. The CERQ distinguishes between 9 different strategies (e.g., rumination, reappraisal). Each cognitive emotion regulation strategy has 4 items measured on a 5-point Likert scale ranging from 1 to 5. In Project 2, the 10-item Emotion Regulation Questionnaire (ERQ, Gross & John, 2003) was used to measure two emotion regulation strategies; the constant tendency to regulate emotions by cognitive reappraisal (6 items) or expressive suppression (4 items). Respondents' answers are scored on a 7-point Likert-type scale ranging from 1 (strongly disagree) to 7 (strongly agree). As we combined the healthy participants in the two projects, we particularly focused on the cognitive reappraisal strategy shared by the two scales. To make the scores comparable across two projects, participants' original scores for reappraisal were divided by the maximum subscale score (ERQ: 7*6 items = 42; CERQ: 5*4 items = 20) to obtain the proportional score of cognitive reappraisal. A higher proportional score indicates a higher tendency to regulate emotion by positive reappraisal. The reappraisal subscale of the ERQ and CERQ had a Cronbach's α = 0.85 and 0.88 in this study.

MRI acquisition, preprocessing and structural MRI analyses

Imaging data were acquired with a 3-Tesla Siemens Prisma scanner. For each participant, T1-weighted high-resolution anatomical images were obtained using a 3-dimensional rapid acquisition gradient echo sequence (echo time = 2.32 ms, inversion time = 1100 ms, repetition time = 2.3 ms, flip angle = 8°, field of view = 256 × 256 mm^2, matrix size = 256 × 256, slice number = 192, thickness/gap = 0.9/0 mm). Foam padding and earplugs were used to minimize head movement and scanner noise. Participants were instructed to stay awake with their eyes closed.

Imaging preprocessing was done in the Computational Anatomy Toolbox (CAT) (http://dbm.neuro.uni-jena.de/cat12/) within SPM12 for voxel-based morphometry (VBM) and surface-based (estimations of cortical thickness) analyses. VBM processing included segmentation, spatial normalization and smoothing. Each participant's T1 image was spatially normalized and segmented into gray matter and white matter and cerebrospinal

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fluid. Modulated normalized gray matter volumes (GMV) were smoothed using a 4 mm Full Width Half Maximum (FWHM) kernel. Cortical thickness was analyzed following the workflow specified by Dahnke et al. (2013) as implemented in CAT12. Specifically, this workflow comprises tissue segmentation to estimate the white matter distance, which in turn is used to project the local maxima to other gray matter voxels. Resampled surface data for cortical thickness were smoothed using a 12-mm FWHM Gaussian kernel.

As for data quality check, each participant's normalized GMV or cortical surface image was first checked visually for artifacts (e.g., motion). In addition, mean correlations of individual GMV or surface data were employed to assess data homogeneity after preprocessing, ensuring the absence of noticeably different data quality (i.e., difference of 3 standard deviations). Quality Check in the CAT allows the evaluation of essential image parameters such as noise, inhomogeneities, and image resolution (details can be found at https://neuro-jena.github.io/cat/). All these quality measures would be summarized to a single aggregate rating. T1 images with a quality rating lower than C- (or 70 points) would be excluded. Using these standards, 3 healthy young adults, 3 healthy adolescents and 1 MDD adolescent were excluded, resulting in the abovementioned final sample sizes ($n = 156$ healthy participants, $n = 31$ MDD participants). All the included participants had a CAT12 quality categorization of C and above.

Statistical analysis

Log transformations were applied to reduce the skewness of the childhood trauma variables that were not normally distributed. Among healthy participants, Pearson correlation estimates were calculated between variables of childhood maltreatment, depressive symptoms, cognitive reappraisal and anticipatory/consummatory pleasure. Group comparisons (Project 1: healthy ($n = 40$) vs MDD adolescents ($n = 31$)) of these behavioral variables were performed using independent two-sample t tests. The Bonferroni correction was used to adjust the p values when making group comparisons.

To explore maltreatment-related GMV and cortical thickness differences in our healthy sample, whole brain multiple regression analyses were conducted separately for each subtype of childhood maltreatment. Age, age-squared (age ^ 2) and sex were included as nuisance covariates. We corrected for total intracranial volume (TIV) by using global scaling to account for different brain sizes in VBM analysis. We did not choose ANCOVA to control for TIV as it was correlated with the parameter of interest. To control for false-positive results, significant gray matter clusters were chosen as Regions of Interest (ROIs), using an uncorrected voxel-level threshold of $p < 0.001$ (GMV) or $p < 0.005$ (cortical thickness) and a cluster-level family-wise error (FWE) corrected threshold of $p < 0.005 = 0.05/10$ times of tests (5 subscales of the CTQ * 2 kinds of structural indictors). Then, the Pearson correlations between the maltreatment-related brain structure and other self-report scale scores (i.e., BDI, two subscales of the TEPS, reappraisal) were calculated. Correlations were regarded as significant when Bonferroni (4 times of tests performed) corrected $p < .05$ (uncorrected $p < .0125$). We further performed mediation analysis using the PROCESS tool (Model 6) (Hayes & Rockwood, 2017) to test whether there existed serial mediating effect of brain structural differences and reappraisal/hedonic capacity linking from maltreatment to depressive symptoms. Finally, as exploratory analysis, we compared the maltreatment-related brain structures between healthy adolescents and MDD adolescents, and calculated the correlations between those brain structures and self-report measures within the MDD group. Mediation analysis in the MDD group would only be conducted when significant correlations were found between variables.

Results

Demographic characteristics of healthy youth are summarized in Table 1. Using the cutoff scores of the CTQ, 34.62% ($n = 54$) of non-clinical participants reported having experienced at least one type of childhood maltreatment (n = 12 abuse only, 30 neglect only, 12 both abuse and neglect), while more than half of (56.67%, $n = 17$) the MDD patients reported having a maltreatment history (5 abuse only, 2 neglect only and 10 both abuse and neglect). The majority of our non-clinical sample (75%) had no or minimal depression (BDI < 10); 17.3% ($n = 27$) showed mild-to-moderate depression, and the remaining 7.7% reported moderate-to-severe ($n = 10$) or severe (n = 2) depression. In the clinical MDD sample ($n = 31$), depressive symptoms were present for most participants (93.55% BDI > 10), with much greater severity (12.90% mild to moderate, 38.71% moderate to severe, 41.94% severe).

When comparing healthy adolescents with MDD adolescents (Project 1; see Table 2), the two groups did not show significant differences in age, sex ratio, or years of education. The MDD group had increased levels of depressive symptoms as indicated by higher scores of the BDI and HAMD, reported more severe maltreatment exposure (especially the subtypes of emotional abuse and neglect), used cognitive reappraisal to regulate emotion less frequently, and enjoyed less anticipatory and consummatory pleasure.

Associations between maltreatment, hedonic capacity, cognitive reappraisal and depression

Pearson correlations between variables in the healthy youth sample ($n = 156$) are shown in Table 3. Different types of childhood maltreatment (except for sexual abuse) were positively correlated with the BDI scores, and the strongest correlations with depressive symptoms were found for emotional abuse and neglect. Emotional abuse, physical abuse and emotional neglect were negatively correlated with cognitive reappraisal. Emotional and physical abuse were also significantly correlated with less anticipatory pleasure. Consummatory pleasure, compared with anticipatory pleasure, showed weaker and nonsignificant associations with childhood maltreatment. Finally, depressive symptoms (i.e., BDI scores) were correlated with lower levels of reappraisal and reduced anticipatory and consummatory pleasure.

In the MDD group, we did not find significant correlations between the above key variables, although the directions of correlations were similar to those in the healthy group (Supplementary Table 1).

Brain structural alterations associated with maltreatment

We observed a significant association between GMV of the left ventral striatum (VS) (564 voxels, voxel size = 1.5*1.5*1.5 mm^3, cluster-level FWE $p < .001$; MNI peak (−26, −2, −9)) and emotional abuse, with higher levels of emotional abuse correlated with enlarged GMV after TIV correction with global scaling and controlling for age, age-squared and sex (Fig. 1a). The GMV in the emotional abuse-related region of left VS was also positively correlated with depressive symptoms ($r = 0.259$, Bonferroni corrected $p = .004$), and negatively correlated with reappraisal

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Table 1. Demographic characteristics of the healthy adolescents and young adults

	Healthy youth combined ($n = 156$)	Healthy adolescents (Project 1: $n = 40$)	Healthy adults (Project 2: $n = 116$)
	Mean (SD)	Mean (SD)	Mean (SD)
Age (year)	19.39 (3.24)	16.10 (2.88)	20.63 (2.47)
Sex (male: female)	47:109	16:24	31:85
Years of education	13.52 (2.98)	10.25 (2.84)	14.66 (2.05)
CTQ	37.06 (10.62)	34.20 (9.96)	38.05 (10.71)
EA	7.30 (3.18)	7.45 (2.85)	7.25 (3.30)
PA	5.86 (1.90)	6.45 (2.78)	5.66 (1.45)
SA	5.65 (1.61)	5.35 (0.89)	5.75 (1.78)
EN	10.61 (4.41)	8.85 (3.77)	11.22 (4.46)
PN	7.65 (2.75)	6.10 (2.17)	8.18 (2.73)
TEPS	90.66 (12.74)	87.10 (12.63)	92.23 (12.67)
TEPS-ant	38.92 (6.40)	36.50 (6.15)	39.74 (6.36)
TEPS-con	47.31 (7.29)	46.53 (7.68)	47.91 (7.13)
Reappraisal[a]	0.71 (0.16)	0.67 (0.22)	0.73 (0.13)
BDI	6.13 (7.15)	5.38 (6.75)	6.53 (7.32)

[a]The reappraisal score was the proportional score, and participants' original scores for reappraisal were divided by the maximum subscale score. CTQ = Childhood Trauma Questionnaire; EA = emotional abuse; PA = physical abuse; SA = sexual abuse; EN = emotional neglect; PN = physical neglect; TEPS = Temporal Experience of Pleasure Scale; TEPS-ant = the anticipatory pleasure subscale of the TEPS; TEPS-con = the consummatory pleasure subscale of the TEPS; BDI = Beck Depression Inventory.

Table 2. Group comparisons between MDD and healthy adolescents in project 1

	Healthy adolescents ($n = 40$)	MDD adolescents ($n = 31$)		
	Mean (SD)	Mean (SD)	χ^2/t	Cohen's d
Age (year)	16.10 (2.88)	15.52 (2.42)	0.93	0.22
Sex (male: female)	16:24	8:23	1.57	
Years of education	10.25 (2.84)	9.56 (2.65)	1.04	0.25
CTQ	34.20 (9.96)	44.94 (14.18)	**−3.58****	**−0.88**
EA	7.45 (2.85)	12.10 (4.76)	**−4.81*****	**−1.19**
PA	6.45 (2.78)	7.90 (4.11)	−1.77	−0.41
SA	5.35 (0.89)	5.32 (1.01)	0.12	0.03
EN	8.85 (3.77)	11.71 (4.31)	**−2.98****	**−0.71**
PN	6.10 (2.17)	7.90 (3.21)	**−2.69****	**−0.66**
TEPS	87.10 (12.63)	70.55 (11.08)	**5.77*****	**1.39**
TEPS-ant	36.50 (6.15)	28.58 (6.51)	**5.25*****	**1.25**
TEPS-con	46.53 (7.68)	38.61 (5.41)	**4.87*****	**1.19**
Reappraisal[a]	0.67 (0.22)	0.49 (0.16)	**3.95*****	**0.94**
BDI	5.38 (6.75)	28.55 (11.59)	**−9.91*****	**−2.44**
HAMD-17	2.29 (3.05)	20.80 (8.81)	**−10.45*****	**−2.81**

**uncorrected $p < .01$; ***uncorrected $p < .001$; These significant results except for the group difference in physical neglect (PN) remained significant (corrected $p < .05$) after Bonferroni correction (12 times of comparisons). [a] The reappraisal score was the proportional score, and participants' original scores for reappraisal were divided by the maximum subscale score. CTQ = Childhood Trauma Questionnaire; EA = emotional abuse; PA = physical abuse; SA = sexual abuse; EN = emotional neglect; PN = physical neglect; TEPS = Temporal Experience of Pleasure Scale; TEPS-ant = the anticipatory pleasure subscale of the TEPS; TEPS − con = the consummatory pleasure subscale of the TEPS; BDI = Beck Depression Inventory; HAMD-17 = Hamilton Depression Scale-17.

($r = -0.207$, corrected $p = .04$) and anticipatory pleasure ($r = -0.213$, corrected $p = .032$).

In addition, emotional neglect was associated with increased GMV of the right caudate (825 voxels, cluster-level FWE $p < .001$; MNI peak (20, 6, 15)) and increased GMV of the left VS (537 voxels, cluster-level FWE $p < .001$; MNI peak (−6, 5, −5)) (Fig. 1b). Greater GMV in the emotional neglect-related region of the left VS was associated with more severe depressive symptoms ($r = 0.268$,

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Table 3. Pearson correlations in the healthy youth sample (n = 156)

	EA	PA	SA	EN	PN	BDI	Reappraisal	TEPS-ant	TEPS-con
EA[a]	1	**0.559****	**0.277****	**0.554****	**0.496****	**0.362****	**−0.343****	**−0.203***	−0.005
PA[a]		1	0.126	**0.316****	**0.285****	**0.256****	**−0.255****	**−0.220****	−0.043
SA[a]			1	**0.181***	**0.193***	0.085	0.076	0.086	**0.196***
EN[a]				1	**0.636****	**0.349****	**−0.248****	−0.142	**−0.165***
PN[a]					1	**0.234***	−0.070	−0.107	−0.050
BDI						1	**−0.380****	**−0.338****	**−0.262****
Reappraisal							1	**0.377****	**0.388****
TEPS-ant								1	**0.623****
TEPS-con									1

*$p < .05$; **$p < .01$; [a]Log transformations were applied to reduce the skewness of the childhood trauma variables that were not normally distributed before calculating Pearson correlation estimates. EA = emotional abuse; PA = physical abuse; SA = sexual abuse; EN = emotional neglect; PN = physical neglect; BDI = Beck Depression Inventory; TEPS-ant = the anticipatory pleasure subscale of the Temporal Experience of Pleasure Scale (TEPS); TEPS-con = the consummatory pleasure subscale of the TEPS.

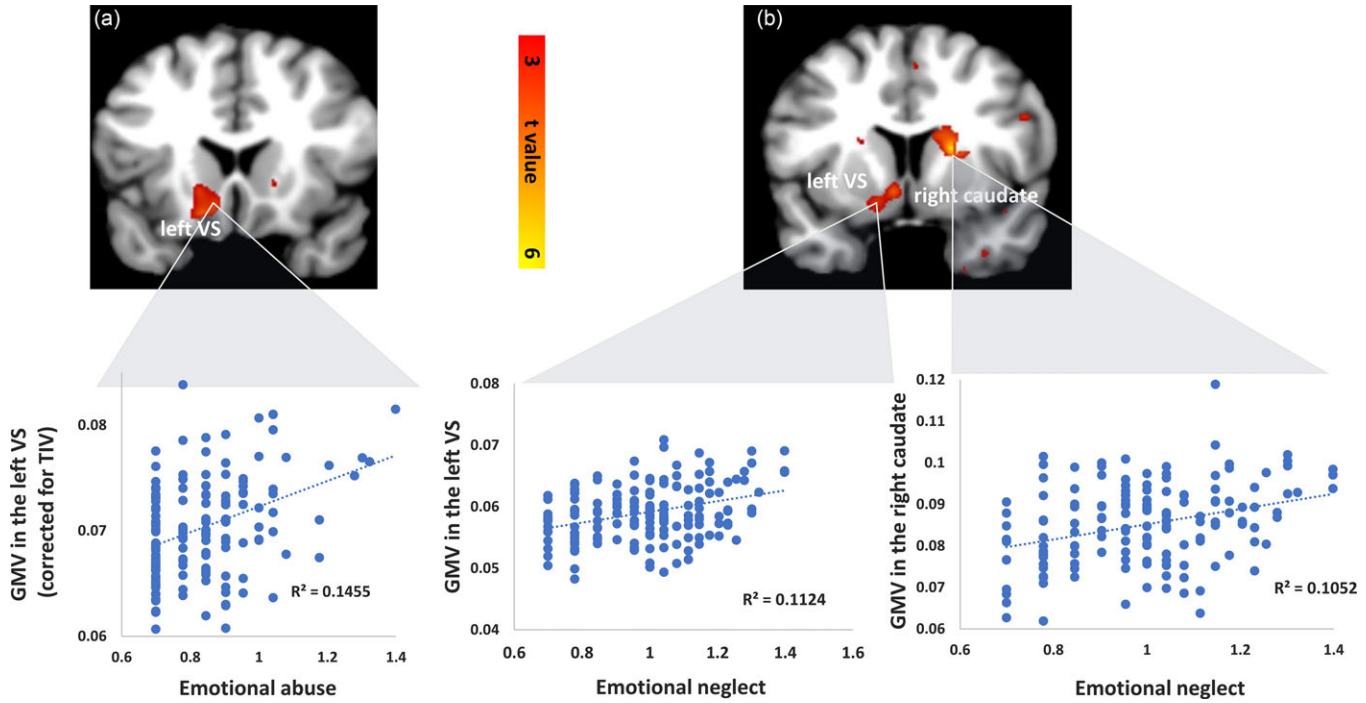

Figure 1. Associations between emotional maltreatment and gray matter volumes (GMV). The mean GMVs (mm^3) in the left ventral striatum (VS) and the right caudate were corrected for total intracranial volume (TIV). The scores of emotional abuse and neglect were log transformed to reduce the skewness.

corrected $p = .004$) and less frequent use of reappraisal ($r = -0.209$, corrected $p = .036$).

As for cortical thickness, more severe emotional neglect was found to be associated with increased thickness in the left middle cingulate cortex (MCC) (225 vertices, cluster FWE $p = .006$; MNI peak (−11, −12, 41)) (Fig. 2), and the mean cortical thickness of this ROI was also negatively correlated with cognitive reappraisal ($r = -0.201$, corrected $p = .048$). Note that the clusters of the left MCC could not survive multiple comparison corrections (cluster-level FWE $p = .006 > .005$), thus this result should be regarded as preliminary. No other significant association between maltreatment and GMV or cortical thickness was found using the applied thresholds.

Serial mediation analyses

For the GMV in the left VS which was related to emotional abuse, we examined whether this brain structural difference and reappraisal/hedonic capacity could serially mediate the association between emotional abuse and depressive symptoms. Similarly, for the GMV in the right caudate, the GMV in the left VS, and the thickness in the left MCC which were significantly correlated with emotional neglect, we tested whether there existed serial mediating effects of these brain structures and reappraisal/hedonic capacity linking from emotional neglect to depressive symptoms. Note that we did not examine possible mediating models between the other three childhood trauma subtypes and depression, as no significant

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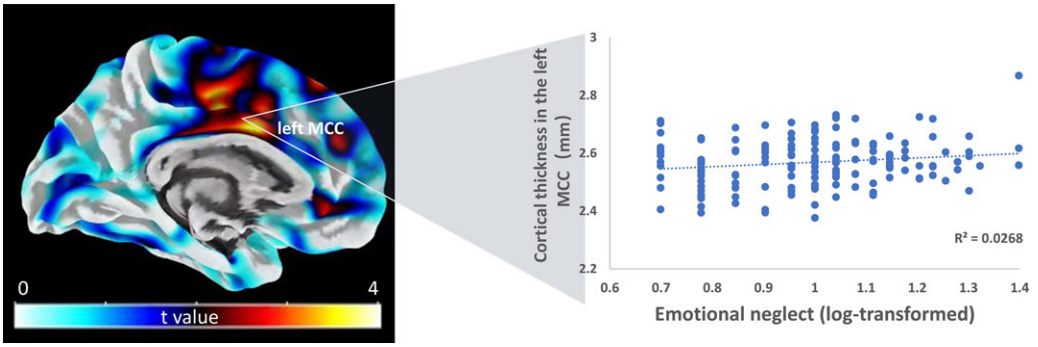

Figure 2. Association between emotional neglect and cortical thickness in the left middle cingulate cortex (MCC).

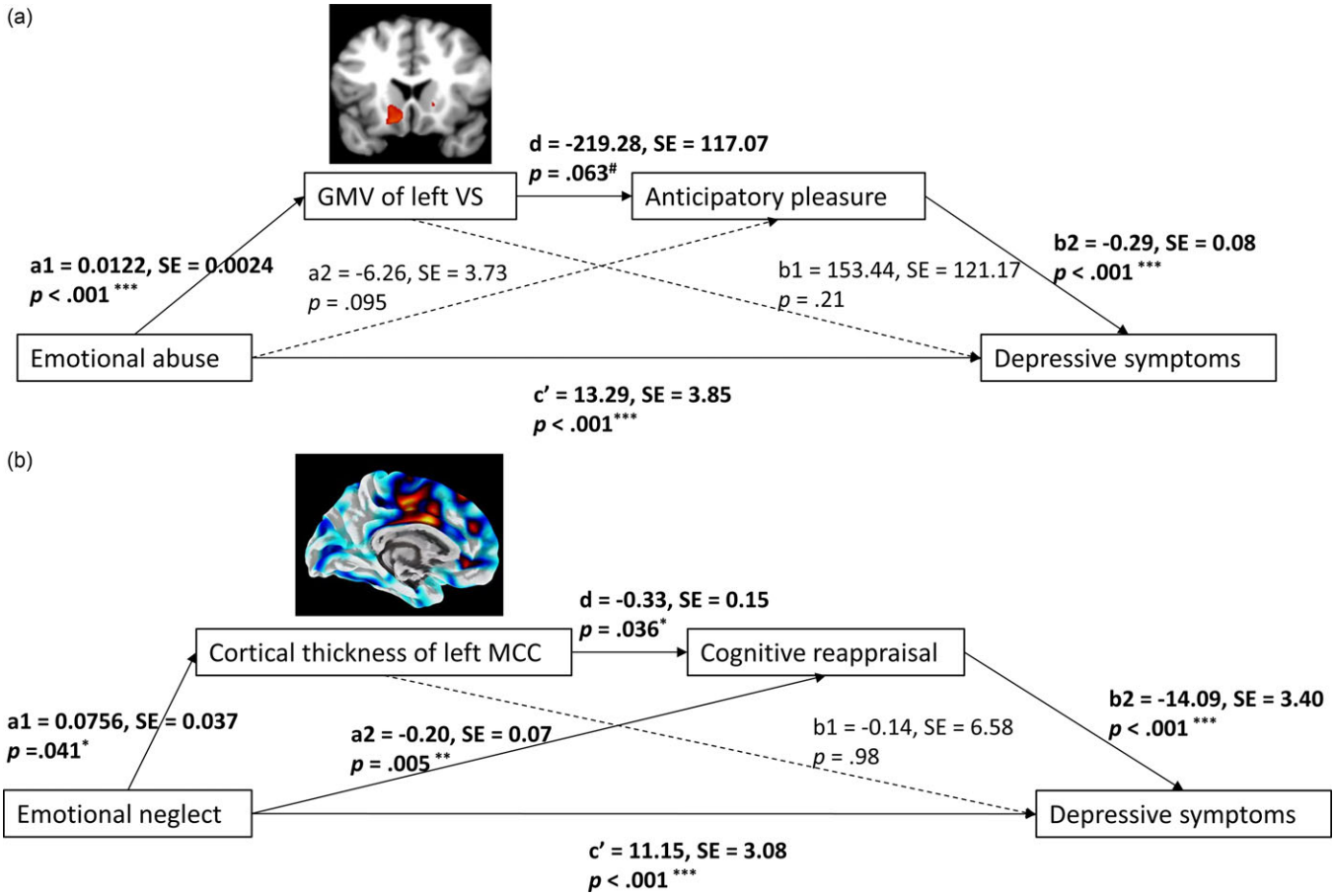

Figure 3. Serial mediation models. #.05 < p < .1; *p < .05; **p < .01; ***p < .001; VS = ventral striatum; MCC = middle cingulate cortex. unstandardized coefficients and standard errors for each path of the mediation model were shown in the figure.

brain structure was found to be correlated with them. Our analysis revealed two significant serial mediating pathways (Fig. 3). Specifically, we observed a positive correlation between emotional abuse and increased GMV in the left VS. Furthermore, this increased GMV in the left VS was associated with reduced anticipatory pleasure, which ultimately predicted more severe depressive symptoms (Fig. 3a). The model yielded a significant positive serial mediation effect (coefficient = 0.78, SE = 0.57, 95% bootstrapped CI (0.08, 2.55);4.37% of the total effect). The indirect effect through single mediators of either GMV in the left VS (coefficient = 1.86, SE = 1.63, 95% bootstrapped CI (−0.81, 5.69)) or anticipatory pleasure (coefficient = 1.82, SE = 1.22, 95% bootstrapped CI (−0.03, 4.96)) was not significant. The direct effect of emotional abuse on depression was still significant (coefficient = 13.29, SE = 3.85, 95% CI (5.68, 20.90)) after accounting for all the indirect effects (25.15% of the total effects), indicating a partial mediating model.

Emotional neglect was associated with increased cortical thickness in the left MCC, and this morphological difference was further correlated with disrupted cognitive reappraisal which in turn led to higher levels of depressive symptoms (Fig. 3b). The model yielded a significant serial mediation effect (coefficient = 0.35, SE = 0.29, 95% bootstrapped CI (0.03, 1.32);2.43% of the total effect). The indirect effect of emotional neglect on depression through reappraisal (coefficient = 2.84, SE = 1.74, 95% bootstrapped CI (0.59, 8.07)) and the direct effect (coefficient = 11.15, SE = 3.08, 95% CI (5.08, 17.23)) were also significant. However, the single mediator path through cortical thickness in the left MCC

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(coefficient = −0.01, SE = 0.49, 95% bootstrapped CI (−0.96, 1.09) was not significant.

We did not find any significant mediating effect of the GMV in the right caudate or the GMV in the left VS on linking emotional neglect to depression.

Maltreatment-related brain structural differences in the MDD group

The GMV in the two clusters of the left VS related to emotional abuse ($t(69) = 1.52$, $p = .13$, Cohen's $d = 0.36$) and emotional neglect ($t(69) = 1.62$, $p = .11$, Cohen's $d = 0.39$), and the GMV in the right caudate related to emotional neglect ($t(69) = 0.65$, $p = .52$, Cohen's $d = 0.15$) were larger in the MDD group compared with healthy adolescents, but the group differences did not reach statistical significance. As for the cortical thickness of the left MCC, we extracted the mean thickness in the left middle-anterior and middle-posterior parts of the cingulate cortex based on the Destrieux atlas (Destrieux et al., 2010) and conducted group comparisons between MDD adolescents and healthy adolescents. Neither MCC part showed significant group differences (anterior MCC: $t(69) = 0.45$, $p = .66$, Cohen's $d = 0.11$; posterior MCC: $t(69) = -0.43$, $p = .67$, Cohen's d = −0.11). Pearson correlations within the MDD group showed that emotional abuse-related GMV in the left VS was positively associated with more severe emotional abuse ($r = 0.409$, $p = .022$, $n = 31$) and decreased consummatory pleasure ($r = -0.356$, $p = .05$). The negative correlation between the left VS volume and cognitive reappraisal was marginally significant ($r = -0.334$, $p = .066$). No significant mediation model was found in the MDD group.

Discussion

This study is among the few to discover the associations between childhood maltreatment, and in later life brain structural differences, emotion-/reward-related processing and depressive symptoms. Our results suggested that cortical (i.e., cingulate cortex) and subcortical (i.e., striatum) morphological differences, coupled with their related difficulties in emotion regulation and hedonic capacity, could explain the association between early life adversity and future mental health problems of depression. These findings were consistent with our hypotheses and agreed with the theory of latent vulnerability (McCrory & Viding, 2015), highlighting the potential of emotion regulation and reward processing as candidate neurocognitive systems to be targeted at for maltreated individuals, offsetting their risk trajectories before psychiatric disorders emerge.

Regarding reward processing, we found increased ventral striatal volume associated with emotional abuse was related to diminished anticipatory pleasure, which further conveyed vulnerability to depression. Blunted striatal responses to rewards have been consistently found in individuals with exposure to early life stress (Teicher & Samson, 2016), and such alterations in neural reward circuits render individuals particularly vulnerable to depression (Romens et al., 2015). Complementary to these functional fMRI studies, our results provide support that maltreatment may not only contribute to maladaptive functions in reward circuits, but also lead to morphological differences in striatum. Enlarged volume and faster growth in the striatum are associated with oversensitivity to uncertain future threat and uncontrollable repetitive thoughts and actions (e.g., worrying, obsessing) in both healthy (Kim et al., 2017) and clinical populations such as individuals with autism (Langen et al., 2014) and anxiety disorders (Hilbert et al., 2015). It is thus possible that childhood maltreatment alters the development of striatum, which in turn shifts the approach-avoidance balance towards avoidance, making individuals hypersensitivity to threat and hyposensitivity to reward (Teicher & Samson, 2016). However, it should be noted that previous structural findings focusing on striatum are quite mixed, with only a limited number of studies reporting significant/nonsignificant increases in caudate and putamen volumes associated with maltreatment (Teicher & Samson, 2016). Whether maltreatment could have discernible influence on striatal structure thus needs more investigation.

Separating different components of hedonic capacity, anticipatory anhedonia, compared with consummatory anhedonia, was more strongly linked to childhood abuse. Previous studies have found that adolescents and young adults with maltreatment histories showed reduced activation in prefrontal and striatal regions during anticipation but not outcome/delivery phase in reward-related tasks (Dillon et al., 2009; Mehta et al., 2010; Romens et al., 2015). It is therefore possible that childhood maltreatment affects specific cognitive stages of reward processing. Maltreatment may disrupt the ability to anticipate pleasure and reduce goal-directed motivation, but not affect in-the-moment hedonic experiences to rewards (Fan et al., 2021).

As for emotion regulation, our study focused on a commonly studied adaptive strategy of cognitive reappraisal. It "changes the way a situation is construed so as to decrease its emotional impact" (Gross, 2002). Maltreatment-related structural differences in the cingulate cortex (i.e., increased thickness in the left MCC) were found to be associated with impaired cognitive reappraisal, and these alterations serially mediated the association between childhood maltreatment and depressive symptoms. Cognitive reappraisal involves large-scale networks in the lateral prefrontal regions and cingulate cortex during down-regulation of negative emotions (Morawetz et al., 2020). Individuals with mood disorders (Zilverstand et al., 2017) and those with maltreatment experiences (McCrory et al., 2017) both demonstrate altered activity/connectivity in these regions, suggesting their reduced regulatory capacity. Moreover, childhood maltreatment is associated with reliable structural alterations in prefrontal and cingulate cortex in individuals with and without psychopathology (Teicher & Samson, 2016), which is in line with our findings. Nonetheless, most previous research indicates attenuated structural measures (e.g., reduced volumes or thickness) in these regions (Teicher & Samson, 2016) rather than greater cortical morphometry observed in the current study. The underlying molecular mechanisms of increased cortical thickness related to maltreatment and impaired reappraisal remain unclear. We infer that greater cortical thickness in the cingulate cortex might reflect delayed or atypical cortical development due to insufficient synaptic pruning or altered myelination, which further embeds higher vulnerability to emotional and cognitive problems (Kirschner et al., 2022).

Among the five types of maltreatment examined, emotional abuse and neglect showed the strongest association with depressive symptoms, replicating previous meta-analytical findings (Infurna et al., 2016; Mandelli et al., 2015; Nelson et al., 2017). Further, only these two subtypes of emotional maltreatment were found to be correlated with significant brain structural alterations in this study. Compared with physical and sexual abuse, emotional forms of maltreatment have received less attention as they often leave scars invisible to others (Radell et al., 2021). However, many victims report that the hidden wounds of self-doubt, self-hatred and worthlessness are much deeper and last far longer than those from

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other types of abuse (Karakurt & Silver, 2013). Emotionally maltreated individuals are more likely to adopt negative perceptions of the self and the world, have difficulties in mood regulation, and habitually use less effective coping strategies such as avoidance and rumination (Radell et al., 2021). Moreover, neuroimaging findings reveal widespread abnormalities in fronto-limbic socioemotional networks associated with emotional maltreatment (Cassiers et al., 2018). All these behavioral and neural alterations are strongly related to depression. Therefore, it is important to identify victims of emotional maltreatment and provide them with targeted interventions prior to the development of psychiatric disorders.

In addition to the findings from non-clinical population, we also examined whether emotion and reward-related mediating effects existed in MDD adolescents. Compared with healthy individuals, patients with MDD showed higher levels of childhood maltreatment, and they reported fewer hedonic experiences and less frequent use of cognitive reappraisal. These significant group differences converged with previous studies suggesting that maltreatment exposure contributes to increased risk for depression (Kuzminskaite et al., 2021), and that reward processing and emotion regulation play a crucial role in the development and maintenance of depression (Aldao et al., 2010; Keren et al., 2018). However, due to our small sample size of clinical individuals, the significant associations between maltreatment, hedonic capacity, reappraisal and depression were not replicated, which was inconsistent with our hypothesis. We only found enlarged VS volume was correlated with reduced consummatory pleasure within the MDD group, suggesting the key role of striatum in reward processing regardless of diagnostic status. Another reason of the failure to replicate significant mediating effects in our MDD group might be due to the fact that we did not consider more proximal risk factors of depression such as recent stressful life events. According to the diathesis-stress model for MDD, it may not be the single effect of childhood adversity, but the complex interplay between this early environment risk and recent stressful events that affects brain structure and symptom severity in individuals with depression diagnosis (Ringwald et al., 2022). Given the hypothesis that exposure to maltreatment may represent a clinically distinct subtype of MDD characterized by early-onset, chronicity and treatment-resistance (Nelson et al., 2017), future studies can recruit larger samples of MDD patients and further explore whether and how maltreatment would interact with recent stressful life events, negatively influence neurocognitive systems and result in poorer clinical outcomes in major depression.

This study has several limitations. First, we only examined structural differences related to maltreatment but did not assess brain functional alterations. The morphometry of some subcortical regions including striatum is considered insensitive to the effects of early adversities; in contrast, childhood adversity may have a more discernible influence on function or connectivity than structure (Teicher & Samson, 2016). If this is true, functional imaging methods may be more suitable to detect robust differences following maltreatment. Second, only one adaptive strategy of cognitive reappraisal was examined because this is the only one emotion regulation strategy which is captured by both the ERQ and the CERQ. However, habitual use of maladaptive strategies like rumination and suppression is also supported as mediators in the relation between childhood adversity and psychopathology (Miu et al., 2022). Moreover, apart from emotion regulation and reward processing, other neurocognitive domains such as threat processing and executive functions could also be indicators of latent vulnerability. For example, maltreated children show threat hypervigilance as indexed by heightened neural response of the amygdala to threat stimuli, increasing the risk of anxiety and mood disorders in adolescence and adulthood (McCrory & Viding, 2015; McCrory et al., 2017). Therefore, it is important to more comprehensively explore possible linking path from childhood adversity to psychopathology. Third, our mediation model was based on cross-sectional questionnaire data and retrospective report of childhood maltreatment. Longitudinal design with more objective measures of maltreatment is required to elucidate the prospective associations between early traumatic events and future mental health problems. Fourth, the sample of this study had a relatively wide age range (12–26 years) encompassing adolescence and young adulthood, which may obscure the brain structural differences at different developmental stages. Finally, as mentioned earlier, limited sample size of the MDD group may prevent us from discovering significant mediating effects. It thus remains unknown whether the findings observed in healthy youth could generalize to clinical populations.

Despite the abovementioned limitations, our study provided evidence that childhood maltreatment was associated with depressive symptoms in adolescents and young adults. Such association was mediated by altered brain structures in the cingulate cortex and striatum, leading to impairments in emotion regulation and reward processing. These findings have important implications for psychological interventions in childhood adversity. For example, emotion regulation and hedonic capacity can be targeted in prevention programs using behavioral trainings (e.g., stress reappraisal interventions, Liu et al., 2019; anticipatory pleasure skills training, Favrod et al., 2010) as well as neurofeedback approaches (Lubianiker et al., 2022), reducing the risk of psychopathology in individuals with childhood maltreatment. Furthermore, our findings suggested the importance of considering different subtypes of childhood adversities and highlighted the prominent role of emotional maltreatment on the development of depression.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0954579423001591.

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Competing interests. None.

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