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Childhood abuse and neglect are differentially related to perceived discrimination and structural change in empathy-related circuitry

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Behavioral studies indicate that adverse childhood experiences (ACE) are associated with altered empathic responding, but the neural mechanisms underlying this relationship remain unclear. Given the significance of empathy in contexts marred by historical conflict and systemic inequality, work on these mechanisms is particularly important in such contexts. The current study extends previous work by (1) examining associations of different dimensions of ACE with volumetric change in empathy-related circuitry, (2) distinguishing between trait and state empathy, and (3) including perceived discrimination as an additional psychosocial stressor. Thirty-nine healthy South African adults from the general population (M_{age} = 40.6 years) underwent 3 T MRI. FreeSurfer v6.0 was used to extract predefined volumes subserving empathy. Results showed that childhood abuse and perceived discrimination were associated with reduced state empathic concern, whereas childhood neglect was associated with reduced trait cognitive empathy. Childhood abuse was furthermore associated with volumetric increases in frontolimbic (hippocampus, anterior cingulate cortex (ACC)) and neocortical (superior frontal and temporal) regions subserving affective and cognitive empathy, and uniquely mediated the relationship between ACC volume and perceived discrimination. The association of ACE with altered empathic responding may thus be underpinned by specific circuitry reflective of adversity type, with childhood abuse contributing to heightened responsivity to socioemotional cues.

Keywords Adverse childhood experiences, Perceived discrimination, Empathy, Structural MRI, Childhood abuse, Childhood neglect

The social environment in which development occurs has a profound impact on the neural architecture underpinning socioemotional responding throughout life. Notably, adverse childhood experiences (ACE) are associated with enduring changes in brain structure and function in circuits that facilitate stress responsivity and emotion regulation[1–3]. While our understanding of the neural impact of perceived discrimination, or chronic unjust social treatment, lags behind this rich literature on ACE, initial evidence suggests that even subtle forms of discrimination are comparable to other psychosocial stressors[4,5]. Given the importance of empathy in a country like South Africa, which is marred by historical oppression and its enduring unequal legacies, it is important to gain insight into how ACE, discrimination, and the structural circuits underpinning empathic responding are interrelated.

Empathy is defined variously, but most conceptualizations emphasize two complementary, yet dissociable pathways to connect with others' emotional states[6]. The first pathway represents an embodied affective sharing

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process involving the anterior cingulate cortex (ACC), anterior insula, and amygdala[7,8]. By contrast, the second pathway represents a more effortful, cognitive process that also engages memory and other self-reflective processes to gauge complex mental states[9–11]. The latter typically recruits the mentalizing system, which involves cortical midline (medial prefrontal cortex (PFC) extending to precuneus) and temporoparietal (superior temporal gyrus, supramarginal gyrus (SMG), and temporoparietal junction (TPJ)) structures[12,13]. Encountering another's suffering can trigger feelings of personal distress or empathic concern through one or both of these pathways[14,15]. Empathic concern is sometimes described as the motivational aspect of empathy, and differs from affective empathy in that it involves prosocial feelings of warmth and care to improve another's wellbeing[10]. Recent neuroscientific research links these motivations to areas processing reward and affiliation, including the ventromedial prefrontal cortex and ventral striatum[16,17].

Most neural inferences regarding empathy have been gleaned from task-based functional activation studies, so that the above-mentioned affective and cognitive empathy pathways reflect momentary or state responses. Indeed, the neural systems subserving affect sharing and mentalizing commonly coactivate in response to complex social cues[18,19]. However, individual differences in dispositional empathy have been associated with functional[20–22], and increasingly also with neuroanatomical[23–28], variation in similar empathy pathways. While it cannot be assumed that functional activity is necessarily supported by corresponding variation in structural anatomy, there is growing support for experience-dependent plastic change in brain structures that influence social behavior[29,30]. Structural MRI research can thus complement interpretation of highly variable task-based approaches and predict higher-order human cognition and behavior[31,32].

ACE represents childhood exposure to the presence of stressful inputs (abuse), or absence of expectable inputs (neglect), which may precipitate an array of socioemotional issues in later life[33]. Although not restricted to families with low socioeconomic status (SES)[34], ACE tend to be strongly associated with income inequality[35], and is more prevalent in low- and middle-income countries, such as South Africa[36]. In fact, the prevailing systemic inequalities and poverty that is bound to South Africa's tragic history of racialized separation continue to shape not only the macro-level contours of the nation, but also the micro-level fabric of individual experiences[37].

While the lasting sequelae of ACE depend on various developmental and contextual factors, some behavioral studies point to altered empathic responding as one important consequence[38–41]. This may be because maturation of the processes that underlie one's capacity to empathize, such as emotion regulation and mental representation, are reliant on a nurturing environment during development[42,43]. Recent evidence underscores the importance of distinguishing between different dimensions of ACE, however, as these may influence learning in distinct ways and thus impact empathic responding differentially[44,45]. For example, because children exposed to threat (e.g., physical or emotional abuse) need to identify environmental dangers timeously, they may be prone to atypical emotion processing, such as generalizing fear responses also to non-threatening stimuli[46,47]. By contrast, children exposed to deprivation (e.g., physical or emotional neglect) may be at greater risk for developing language and executive function deficits through the absence of rich cognitive stimulation[48,49]. Consequently, threat exposure may be associated more strongly with changes in affective empathy, whereas deprivation may impact executive calculations involved in cognitive empathy.

ACE is often conceptualized as cumulative stress[50], and so brain areas with high densities of glucocorticoid receptors, such as the hippocampus and amygdala, are particularly affected in the long run[51–54]. A dimensional approach articulates a more nuanced understanding of how various neural mechanisms are impacted as a function of the kind of adversity experienced, however[55]. Accordingly, childhood abuse would differentially impact neural structure and function of medial frontolimbic circuitry involved in emotional learning and regulation, including the hippocampus, amygdala, ACC, and orbitofrontal cortex (OFC)[49,56,57]. These areas form part of the paralimbic "salience network", which responds to events of personal importance[58]. By comparison, childhood neglect would be more associated with volume reduction in higher-order association cortex involved in processing complex social and cognitive inputs, including the lateral and medial PFC, parietal cortex, and superior temporal cortex[45,49]. These areas coordinate responses across multiple sensory modalities and may be particularly vulnerable to the long-term effects of early neglect because of their protracted developmental trajectory[3,59,60].

A history of ACE may also confer greater risk for perceived discrimination as psychosocial stressor, although the mechanisms of this relationship remain largely understudied[61]. Perceived discrimination, rather than more objective measures of severe discrimination, is often employed in this literature and refers to the individual's subjective evaluation that routine unfair treatment is directed towards them[62,63]. Some argue that traumatic events might confer greater vulnerability to subsequent stressors through changes in underlying neurobiological systems[51,64]. Consequently, the individual is sensitized to respond to negative events with heightened intensity through greater perceptions of being a target of unfair treatment, or stronger evaluations of the events' threat to one's well-being[65]. Alternatively, traumatic events may trigger a proliferation of discriminatory experiences when marginalised individuals come into contact with biased systemic processes, for example, health, legal, and/or welfare systems[65]. These mechanisms require more examination and likely vary depending on both complex social norms and beliefs and the characteristics of the specific individual or group experiencing discrimination[66].

Chronic exposure to discrimination, whether subtle/ambiguous or overt, is typically experienced as stressful[67,68]. Indeed, substantial research documents that perceived discrimination has a pervasive impact on physical and mental well-being across the lifespan[63,66,69,70], and this perceived discrimination confers risk independently from that of ACE[71]. Only a few studies have explored the neurobiological effects of perceived discrimination, with initial neuroimaging evidence suggestive of functional alterations in activation and connectivity of the amygdala and ACC[72–74]. Cumulative effects of perceived discrimination might thus resemble morphological changes associated with childhood abuse, rather than neglect, where abuse is underpinned by altered salience attribution and greater susceptibility to stress.

Study aims

This research employed MRI to examine whether ACE and perceived discrimination are associated with structural changes in areas consistently implicated in affective and cognitive empathy in a diverse sample of healthy South African adults. We thus sought evidence of structural change in the absence of predefined psychiatric illness. Because existing research consistently implicates three focal areas in both ACE and empathic responding, our regions of interest (ROI) included: (1) subcortical structures involved in salience detection and memory (amygdala, hippocampus)[51,53], (2) frontolimbic circuitry involved in affective empathy (insula, ACC, OFC)[7,8], and (3) association cortex involved in cognitive empathy (medial PFC, superior temporal and parietal regions)[12,13].

We extended previous work on ACE and empathy in three ways: First, we examined how different dimensions of ACE (abuse versus neglect) associate with empathy and its neural substrates. Second, we distinguished between trait and state empathy, given that individual difference measures often show only weak correspondence to dynamic or situational empathy responses[75]. Finally, we included perceived everyday discrimination as additional psychosocial stressor in all analyses. The study was guided by the following hypotheses:

First, given that ACE has consistently been associated with greater perceived discrimination in adults[61,65], we expected these constructs to be positively associated. Moreover, because the neural mechanisms implicated in childhood abuse and perceived discrimination both involve altered emotional reactivity and salience attribution[72], we anticipated a stronger association between perceived discrimination and childhood abuse than neglect.

Second, we expected greater exposure to ACE and perceived discrimination to be associated with decreased trait[38] and state[39] empathy. Specifically, because of the association of childhood abuse with atypical emotional processing, we anticipated greater disruptions in state empathic concern with this measure[46]. By contrast, we expected childhood neglect to be more strongly associated with cognitive deficits reflected by alterations in trait cognitive empathy[45].

Third, we expected greater exposure to ACE and perceived discrimination to be associated with volumetric changes in ROIs underpinning empathic responding, regardless of SES. Specifically, we anticipated childhood abuse and perceived discrimination to be associated with morphological changes in areas subserving salience detection and affective empathy (amygdala, hippocampus, insula, OFC, and ACC), while we expected childhood neglect to be associated with reduced volumes in areas subserving cognitive empathy (medial PFC, superior temporal gyrus, and SMG). We further explored whether ACE helped explain the relationship between volumetric change in any ROI and perceived discrimination through mediation analysis, controlling for SES, age, and sex.

Methods

Participants

Thirty-nine healthy adults, recruited through local newspaper advertisements, completed all study procedures (21 female, M_{age} = 40.64 years, SD_{age} = 5.03, 19 identified as Black African, 20 identified as White). All participants were South African citizens and obtained Grade 12 as a minimum level of education (Education: M = 15.90 years, SD = 2.88). Participants were further without previously diagnosed neurological, cardiovascular, or psychiatric disorders, and none were clinically depressed, as assessed by the Beck Depression Inventory[76]. We computed an estimate of socioeconomic status (SES) using Hollingshead's scores for occupation and education[77]. Post-hoc power analysis using G*Power 3.1[78] indicated that we achieved $\beta > 0.85$ based on the brain-behavior effects in this sample.

All participants provided informed consent. The study was approved by the University of Cape Town's Human Research Ethics Committee and all procedures were carried out according to these guidelines.

Questionnaire measures

Adverse childhood experiences (ACE)

We used the 25-item Childhood Trauma Questionnaire Short-Form (CTQ-SF) to assess the severity of maltreatment "while growing up"[79]. This retrospective measure records the frequency of experienced *emotional abuse* "People in my family said hurtful and insulting things to me", *physical abuse* "I was punished with a belt, board, cord, or some other hard object", *sexual abuse* "Someone molested me", *emotional neglect* "My family was a source of strength and support" (reverse-coded), and *physical neglect* "I had to wear dirty clothes", ranging from 1 (*Never True*) to 5 (*Very Often True*). It is used extensively in peer-reviewed research and has good validity across clinical and nonclinical populations, including in the South African context[2,80].

We created separate indices of abuse and neglect: High intercorrelations between emotional and physical abuse, and between emotional and physical neglect, supported a CTQ_{Abuse} ($r_{39(2\text{-}tailed)} = 0.65$, $p < 0.001$) and $CTQ_{Neglect}$ ($r_{39(2\text{-}tailed)} = 0.74$, $p < 0.001$) index. Consistent with the initial factor structure,[79] sexual abuse was only moderately associated with the abuse subscales (rs = 0.39, ps = 0.013), and unrelated to the neglect subscales (rs < 0.22, ps > 0.18). Moreover, some evidence supports sexual abuse as trigger of distinct psychobiological pathways[33,81,82]. We therefore kept it as a separate index. Exploratory factor analysis confirmed this 3-factor structure (see Fig. 1 and Supplementary Material).

Perceived discrimination

We used the 9-item Everyday Discrimination Scale (EDS) to assess routine experiences of prejudice or unfair treatment[62]. The scale asks respondents to rank the frequency of different forms of social mistreatment in their day-to-day lives, such as "You are treated with less respect than other people are" and "You are called names or insulted" from 1 (*Never*) to 6 (*Almost Everyday*), and has been shown to have good internal validity in the South

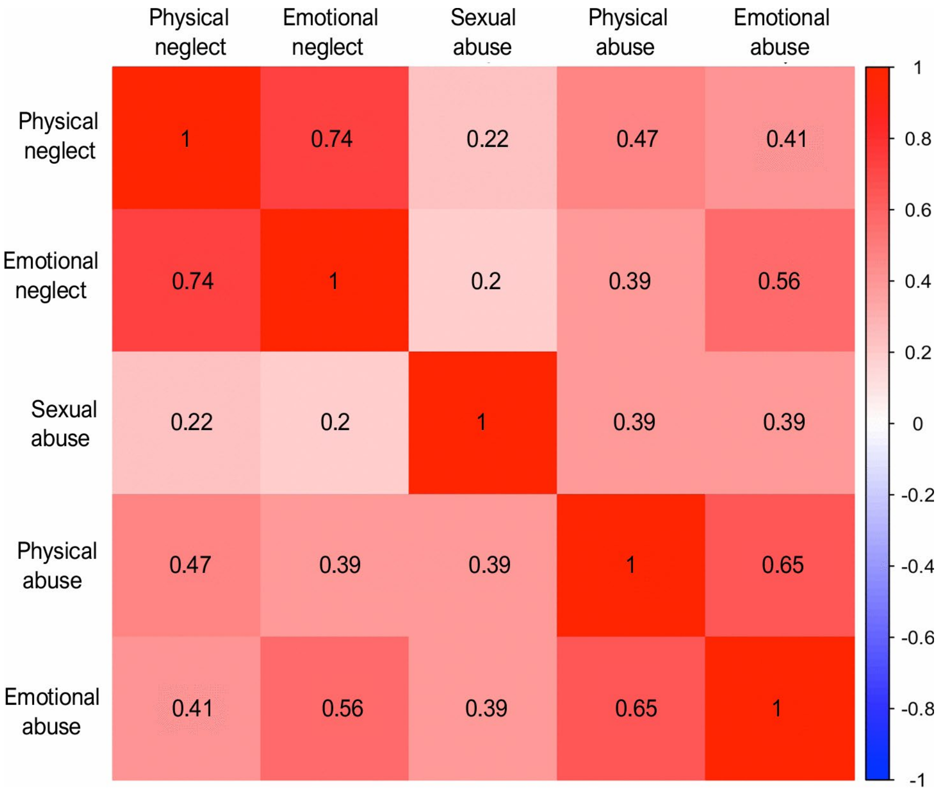

Fig. 1. Childhood Trauma Questionnaire Factor Structure. Exploratory factor analysis supported a 2-factor structure with emotional and physical abuse heavily loading onto one factor (CTQ_{Abuse}), and emotional and physical neglect loading onto a second ($CTQ_{Neglect}$). Because sexual abuse did not load strongly onto the abuse factor, it was retained as a separate measure.

African context[83]. Individuals experiencing frequent discrimination are given the opportunity to attribute their experiences to one/more aspect of their identity, such as race, gender, sexual orientation, or weight.

Trait empathy
We used the 31-item Questionnaire of Cognitive and Affective Empathy (QCAE) to derive trait empathy scores for each participant[84]. Cognitive empathy is assessed through the subscales *perspective taking* "I can easily tell if someone else wants to enter a conversation" and *online simulation* "I find it easy to put myself in somebody else's shoes"; whereas affective empathy is assessed through the subscales *emotional contagion* "People I am with have a strong influence on my mood", *proximal responsivity* "I often get emotionally involved with my friends' problems" and *peripheral responsivity* "I often get deeply involved with the feelings of a character in a film, play or novel" from 1 (*Strongly Disagree*) to 4 (*Strongly Agree*). The scale's cross-cultural validity has been demonstrated in various settings[85,86].

Procedure
An online screening survey assessed individuals' suitability to participate in an fMRI study seeking to better understand how the brain responds to others in distress. Exclusion criteria included any previous central nervous system insults, psychoactive medication, metal implants, and moderate depression (as assessed by a Beck Depression Inventory II score ≥ 20). Those who agreed to participate completed the questionnaire measures several weeks prior to MRI scanning during an information session. In the scanner, all participants first underwent a structural scan, followed by functional runs of video stimuli of people in distress. Specifically, participants watched (1) dynamic 2.2 s facial expressions of Black African and White people in physical pain (physical pain task), as well as (2) 6–9 s video clips of Black African and White people in emotional distress (social distress task). Details of stimuli employed in the functional component of the study are reported elsewhere[9]. Here we report on the structural data.

Post-scan state empathy ratings
Empathic concern in response to the physical pain and social distress tasks were assessed following the scan. Specifically, participants rated how sorry they felt for every individual from each task from 1 (*not at all*) to 9 (*extremely*), yielding estimates of empathy for physical pain (Task 1) and empathic concern for social distress (Task 2). We averaged state empathy ratings across Black African and White target individuals in each task.

MRI image acquisition and data analysis

MRI data were acquired on a 3-Tesla Allegra system (Siemens, Erlangen, Germany). The high-resolution anatomical scan was acquired with a T_1-weighted sequence (3D MPRAGE, TR/TE = 2530/6.5 ms).

Using FreeSurfer version 6.0 (https://surfer.nmr.mgh.harvard.edu), structural images were registered to standardized Talaraich space, intensity normalized, and skull stripped. Subcortical regions were then segmented, and the cerebral cortex parcellated according to the Desikan-Killiany (DK) atlas (see Figure S1)[87], after which regional and total brain volumes and regional cortical thickness and surface area were determined. Cortical thickness is calculated as the perpendicular distance between white and pial surfaces[88]. We inspected FreeSurfer outputs manually for any artefacts in cortical and subcortical segmentations, but no corrections were required.

To perform fewer statistical tests and reduce the Type-I error rate[89], we analyzed only hypothesis-driven ROI's. Subcortical volumes included the bilateral amygdala and hippocampus, and estimated total intracranial volume (TIV) was obtained via whole-brain segmentation. Cortical areas included the bilateral rostral ACC (rACC), insula, and medial OFC (affective empathy)[7,8]; and superior frontal gyrus, superior temporal gyrus, and SMG (the latter encapsulates the TPJ in the DK-atlas) (cognitive empathy)[12,13]. Although our analyses focused on extracted volumes, we also report analyses for surface area and cortical thickness in the Supplementary Material.

To examine volumetric associations between ROIs, ACE (CTQ_{Abuse} and $CTQ_{Neglect}$), and perceived discrimination, we performed zero-order correlations using the statistical analysis programming language R (https://www.r-project.org). We inspected 95% confidence intervals (CIs) derived through bootstrapping running 1000 iterations to help validate our findings given the sample size[90]. Because we were not predominantly interested in the effects of childhood sexual abuse, we report results for this measure in the Supplementary Material. We then also controlled for multiple comparisons using the Benjamini–Hochberg procedure and a false discovery rate (FDR) of 20%[91]. This threshold is often implemented in neuroimaging research where effect sizes tend to be modest to retain sufficient power to detect true effects[92,93]. Significant volumetric associations were further corroborated by examining the corresponding ROI surface area correlations, and were repeated controlling for Hollingshead SES, age, and sex.

Results

Behavioral data

Participant characteristics are presented in Table 1. As can be seen, we did not observe any sex differences in either demographics ($ps > 0.621$) or questionnaire measures ($ps > 0.084$). Associations between our primary variables of interest are presented in Table 2 and Fig. 2.

Consistent with our first hypothesis, ACE was significantly associated with greater perceived discrimination (CTQ_{Total}: $r_{39(2\text{-}tailed)} = 0.54$, $p < 0.001$). Specifically, childhood abuse was associated more strongly with perceived discrimination (CTQ_{Abuse}: $r_{39(2\text{-}tailed)} = 0.61$, $p < 0.001$), than childhood neglect was associated with perceived discrimination ($CTQ_{Neglect}$: $r_{39(2\text{-}tailed)} = 0.38$, $p = 0.016$), Steiger's $z = 1.74$, $p = 0.041$.

	Male (n = 18)	**Female (n = 21)**	**Test statistic**
	***M* (*SD*) or %**	***M* (*SD*) or %**	***t* or χ^2**
Demographics			
Age	40.83 (5.24)	40.48 (4.97)	0.21 ns
Years of education	16.00 (2.38)	15.81 (3.31)	0.20 ns
SES	45.06 (10.64)	43.65 (12.50)	0.37 ns
Black African (%)	44.44	52.38	0.24 ns
White (%)	55.56	47.62	
Questionnaire measures			
Depression (Beck-II)	10.06 (5.00)	10.76 (6.88)	0.37 ns
Childhood adversity (CTQ)	44.61 (16.51)	36.76 (9.13)	1.80 ns
None or minimal (%)	33.33	52.38	4.52 ns
Low (%)	38.89	42.86	
Moderate (%)	16.67	4.76	
Severe (%)	11.11	–	
Everyday Discrimination (EDS)	22.56 (5.77)	19.38 (8.12)	1.42 ns
Trait affective empathy (QCAE)	59.06 (7.45)	60.24 (7.53)	0.98 ns
Trait cognitive empathy (QCAE)	32.65 (6.16)	34.57 (5.83)	0.48 ns

Table 1. Participant characteristics. *Beck-II* Beck Depression Inventory-II, *CTQ* Childhood Trauma Questionnaire, *EDS* Everyday Discrimination Scale, *ns* not significant, *QCAE* Questionnaire of Cognitive and Affective Empathy, *SES* socioeconomic status using Hollingshead's scores.

Measures	1	2	3	4	5	6	7
1. Emotional and physical abuse (CTQ_{Abuse})[a]	1.00						
2. Emotional and physical neglect ($CTQ_{Neglect}$)[a]	**.54****	1.00					
3. Everyday Discrimination Scale (EDS)[b]	**.61*****	**.38***	1.00				
4. QCAE trait affective empathy[c]	.01	.12	.18	1.00			
5. QCAE trait cognitive empathy[d]	−.28	**−.34***	.11	.21	1.00		
6. State empathy for physical pain[e]	−.19	−.17	−.17	**.43****	.30	1.00	
7. State empathic concern for social distress[e]	**−.44****	−.09	**−.39***	−.04	−.08	.26	1.00
M	8.07	8.59	20.85	33.71	59.71	6.30	7.73
Range	5–16	5–17	9–46	19–44	43–72	2.5–9	4–9
SD	3.15	3.31	7.22	5.98	7.41	1.57	1.23

Table 2. Adverse childhood experiences, perceived discrimination, and empathy: variable intercorrelations (n = 39). Two-tailed Pearson's correlations were conducted. Significant values are in bold. *QCAE* Questionnaire of Cognitive and Affective Empathy. [a]Scores range from 5 (low) to 25 (high). [b]Scores range from 9 (low) to 54 (high). [c]Scores range from 12 (low) to 48 (high). [d]Scores range from 19 (low) to 76 (high). [e]Scores range from 1 (low) to 9 (high). $*p < .05$. $**p < .01$. $***p < .001$.

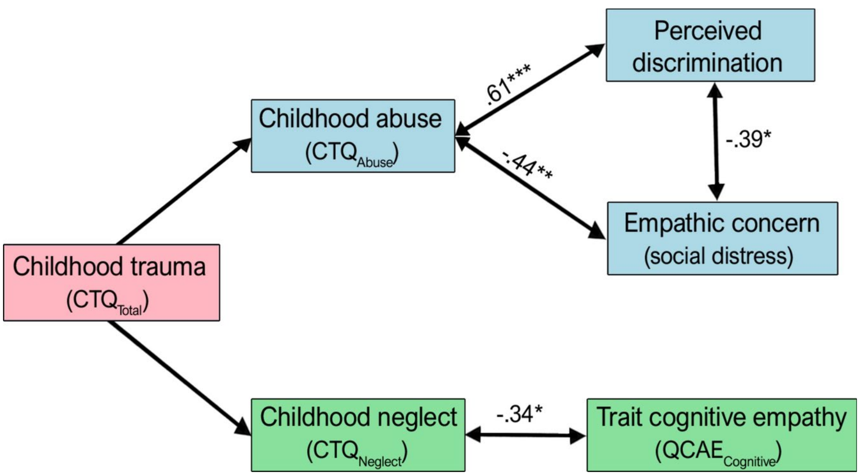

Fig. 2. Behavioral data: association between adverse childhood experiences (ACE), perceived discrimination, and empathy. Trait empathy was assessed with the Questionnaire of Cognitive and Affective Empathy (QCAE). Empathic concern represents state empathy in response to short video clips of individuals in emotional distress. Zero-order correlation coefficients are presented. *CTQ* Childhood trauma questionnaire. $*p < .05$. $**p < .01$. $***p < .001$.

Social adversity and trait empathy

As anticipated, greater childhood neglect ($CTQ_{Neglect}$: $r_{38(2\text{-tailed})} = -0.34$, $p = 0.037$), rather than abuse (CTQ_{Abuse}: $r_{38(2\text{-tailed})} = -0.28$, $p = 0.090$), was associated with reduced trait cognitive empathy. Neither index was associated with trait affective empathy ($rs < 0.12$, $ps > 0.481$).

Perceived discrimination was not associated with either trait cognitive or affective empathy ($rs < 0.18$, $ps > 0.280$).

Social adversity and state empathy

Here we examined associations between ACE, perceived discrimination, and participants' empathic concern ratings in response to individuals in physical pain (Task 1) and emotional distress (Task 2).

Neither childhood abuse nor neglect were associated with empathy for physical pain ($rs < -0.19$, $ps > 0.249$). However, greater childhood abuse (CTQ_{Abuse}: $r_{39(2\text{-tailed})} = -0.44$, $p = 0.005$), but not neglect ($CTQ_{Neglect}$: $r_{39(2\text{-tailed})} = -0.09$, $p = 0.591$), was significantly associated with reduced empathic concern for social distress. Perceived discrimination was also unrelated to empathy for physical pain (EDS: $r_{38(2\text{-tailed}} = -0.17$, $p = 0.301$), but significantly associated with reduced empathic concern for social distress (EDS: $r_{38(2\text{-tailed})} = -0.39$, $p = 0.015$).

Consistent with previous literature, trait and state empathy measures were unrelated, bar a significant association between empathy for physical pain and trait affective empathy ($r_{38(2\text{-tailed})} = 0.43$, $p < 0.007$).

Brain-behavior correlations

Here we examined ACE and perceived discrimination's association with volumetric change in empathy-related ROIs (see Table 3). Notably, childhood abuse, but not neglect ($ps > 0.080$), was significantly associated with several brain volumes that remained significant after controlling for age, sex, and Hollingshead SES. Childhood abuse's association with volumetric change in the L rACC and bilateral superior frontal and temporal gyri were further corroborated by corresponding surface area correlations ($rs > 0.37$, $ps < 0.019$). All surface area and thickness statistics are reported in Supplementary Material Table S5.

Total intracranial volume (TIV)

Because of TIV's high collinearity with sex ($r = 0.69$, $p < 0.001$), we did not include it as an additional covariate in our analyses. Indeed, inclusion rendered all volumetric associations with ACE and perceived discrimination nonsignificant ($ps > 0.081$), except that between the right hippocampus and childhood abuse ($r = 0.34$, $p = 0.023$). Of significance, however, is that TIV ($\beta s > 0.46$, $ps < 0.034$), rather than sex ($\beta s < 0.08$, $ps > 0.719$), significantly predicted childhood abuse and perceived discrimination in simultaneous regressions. TIV was also unrelated to participant race and SES ($ps > 0.248$). These findings suggest that childhood abuse and perceived discrimination may be associated with structural change that not only affects specific brain areas, but also overall brain volume (TIV). All TIV analyses are reported in the Supplementary Material Tables S3 and S4.

Subcortical structures

Greater childhood abuse was significantly associated with greater right hippocampal volume (CTQ_{Abuse}: $r_{39(2\text{-}tailed)} = 0.46$, $p = 0.004$). Neither ACE, nor perceived discrimination, was significantly associated with amygdala volume ($rs < 0.28$, $ps > 0.080$).

Affective empathy regions

Both childhood abuse and perceived discrimination were significantly associated with the left rACC volume (CTQ_{Abuse}: $r_{39(2\text{-}tailed)} = 0.38$, $p = 0.016$, EDS: $r_{39(2\text{-}tailed)} = 0.38$, $p = 0.016$) (Fig. 3). Neither ACE, nor perceived discrimination, was associated with medial OFC ($rs < 0.22$, $ps > 0.178$), or insula ($rs < 0.23$, $ps > 0.163$) volumes.

Cognitive empathy regions

Childhood abuse was significantly associated with greater bilateral superior frontal volumes (R: $r_{39(2\text{-}tailed)} = 0.36$, $p = 0.026$, L: $r_{39(2\text{-}tailed)} = 0.35$, $p = 0.028$), and with greater bilateral superior temporal volumes (R: $r_{39(2\text{-}tailed)} = 0.39$, $p = 0.016$, L: $r_{39(2\text{-}tailed)} = 0.45$, $p = 0.005$) (Fig. 3).

ROI volumes	Hem	CTQ_{Abuse}	$CTQ_{Neglect}$	EDS
Total intracranial volume (TIV)		**.43** [.18, .64]**	.21 [− .11, .48]	**.36* [.01, .67]**
Subcortical structures				
Hippocampus	R	**.46** [.24, .63]**[a]	.29 [− .00, .53]	.30 [.10, .48]
Hippocampus	L	.31 [.06, .54]	.20 [− .18, .48]	.14 [− .19, .42]
Amygdala	R	.24 [− .07, .50]	.00 [− .26, .29]	.13 [− .16, .42]
Amygdala	L	.24 [− .06, .48]	.24 [.00, .67]	.14 [− .16, .43]
Affective empathy regions				
rACC	R	.09 [− .26, .42]	.20 [− .29, .40]	.25 [.01, .46]
rACC	L	**.38* [.09, .61]**[b]	− .01 [.10, 60]	**.38* [.11, .64]**[b]
Medial OFC	R	.22 [− .04, .49]	− .05 [− .30, .24]	− .04 [− .32, .25]
Medial OFC	L	.22 [− .08, .50]	.20 [− .04, .44]	.18 [− .19, .56]
Insula	R	.26 [− .14, .56]	.20 [− .12, .59]	.11 [− .26, .50]
Insula	L	.18 [− .16, .48]	.08 [− .18, .49]	.08 [− .23, .45]
Cognitive empathy regions				
Superior frontal gyrus	R	**.36* [.07, .60]**	.03 [− .32, .35]	.15 [− .18, .47]
Superior frontal gyrus	L	**.35* [.10, .57]**[b]	.07 [− .27, .40]	.23 [− .09, .54]
Superior temporal gyrus	R	**.39* [.11, .64]**[b]	.11 [− .18, .39]	.03 [− .33, .39]
Superior temporal gyrus	L	**.45** [.15, .68]**[b]	.21 [− .21, .52]	.12 [− .16, .38]
Supramarginal gyrus	R	.26 [− .18, .62]	.26 [− .06, .55]	− .04 [− .43, .43]
Supramarginal gyrus	L	.03 [− .31, .35]	− .09 [− .40, .26]	− .22 [− .52, .18]

Table 3. Brain-behavior correlations: adverse childhood experiences, perceived discrimination, and empathy-related ROIs (n = 39). Two-tailed Pearson's correlations were conducted with 95% bootstrap confidence intervals (CI) in brackets[90]. Significant correlations surviving the Benjamini–Hochberg threshold for a 20% FDR are in bold. *CTQ* Childhood trauma questionnaire, *EDS* Everyday discrimination scale, *rACC* rostral anterior cingulate cortex, *OFC* orbitofrontal cortex. [a]An estimate that is significant at $p < .01$, controlling for Hollingshead SES, age, and sex. [b]An estimate that is significant at $p < .05$, controlling for Hollingshead SES, age, and sex. *$p < .05$. **$p < .01$.

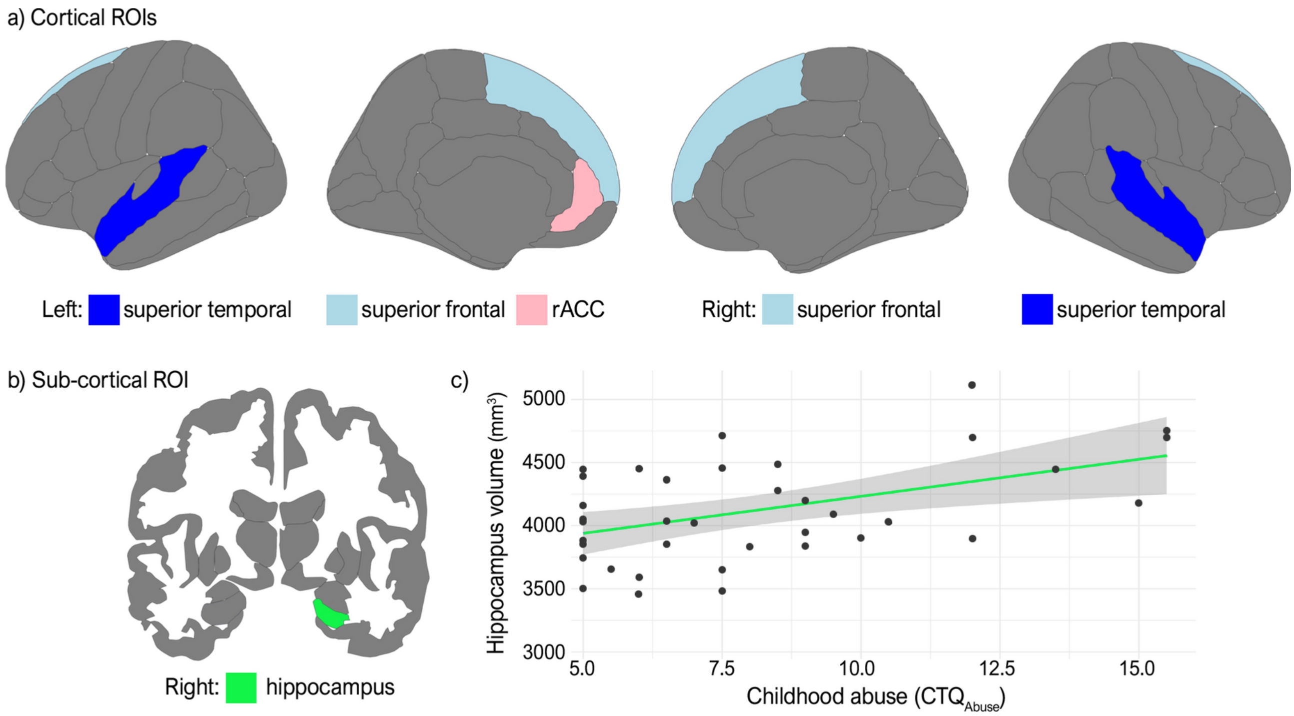

Fig. 3. Volumetric analysis: associations between childhood abuse, perceived discrimination, and empathy-related ROIs. (**a**, **b**) Childhood abuse (CTQ_{Abuse}) was associated with significantly greater volumes in frontolimbic affective (right hippocampus, left rACC) and cognitive (bilateral superior frontal gyri, bilateral superior temporal gyri) empathy regions. Perceived discrimination was associated with greater left rACC volume. (**c**) A scatter plot of the correlation between the right hippocampus volume and CTQ_{Abuse} ($r = 0.46$, $p = .004$). *rACC* rostral anterior cingulate cortex.

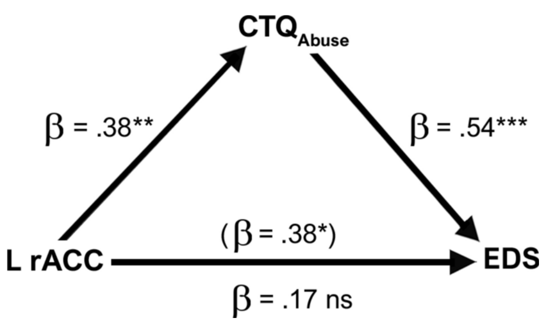

Fig. 4. Brain-behavior mediation analysis. Childhood abuse (CTQ_{Abuse}) fully mediated the association between the left rostral anterior cingulate cortex (rACC) volume and increased everyday discrimination (EDS) ($R^2 = .40$, $p < .001$). Coefficients presented are standardized linear β coefficients. $^{*}p < .05$. $^{**}p < .01$. $^{***}p < .001$.

Neither ACE, nor perceived discrimination, was significantly associated with supramarginal gyrus ($rs < 0.26$, $ps > 0.115$) volumes.

Exploratory mediation analysis

Given the robust associations between childhood abuse, perceived discrimination, and volumetric changes in the rACC, we conducted exploratory mediation analysis to determine whether childhood abuse partly explained this relationship. The model was specified with the left rACC as the independent variable, childhood abuse as the mediator variable, and perceived discrimination as the dependent variable (Fig. 4). Because we are not able to infer the directionality of these associations[94], the model tests whether childhood abuse represents a potential mechanism though which the left rACC and perceived discrimination are related.

Indeed, the positive association between perceived discrimination and the left rostral ACC ($B = 0.006$, $p = 0.016$, boot $SE = 0.002$, 95% CI [0.002, 0.010]) was rendered non-significant when childhood abuse was added as a mediator ($B = 1.25$, $p < 0.001$, boot $SE = 0.32$, 95% CI [0.60, 1.90]), indicating full mediation (Indirect effect: $B = 0.0032$, boot $SE = 0.0016$, 95% CI [0.0007, 0.0073]; Sobel test $Z = 2.38$, $p = 0.018$, 2-tailed). These effects remained unchanged after including age, sex, and Hollingshead SES in the model (Indirect effect: B = 0.0027, boot SE = 0.0019, 95% CI [0.0001, 0.0072]).

Discussion

The present study examined the association of ACE and perceived discrimination with volumetric changes in key areas subserving affective and cognitive empathy to identify neural mechanisms through which adverse social experiences may impact empathic responding. As anticipated, ACE and perceived discrimination were associated with reduced self-reported empathy, however, we observed an interesting dissociation. While childhood abuse and perceived discrimination were associated with reduced state empathic concern for social distress, childhood neglect was associated with reduced trait cognitive empathy. Childhood abuse was further associated significantly with greater volumes in frontolimbic affective (right hippocampus, left rACC) and cognitive (bilateral superior frontal gyri, bilateral superior temporal gyri) empathy regions, and uniquely mediated the relationship between the left rACC and subsequent perceived discrimination. These findings not only lend credence to the notion that ACE impact the neural circuitry involved in empathy, but also suggests the downstream psychobiological consequences of childhood abuse differentially impair affective empathy through increased susceptibility to negative socioemotional cues, such as everyday discrimination.

Our results confirm the close relationship between early adversity, particularly childhood abuse, and perceived discrimination in adulthood,[61] although this association cannot be interpreted causally. In a post-conflict country like South Africa, ACE and sustained discrimination often coexist in the context of poverty, socioeconomic inequality, and historical legacies of disconnect and disenfranchisement[5,95]. This interplay might be more complex, however, in that individuals who have experienced ACE may be more sensitive to social discrimination, and/or more articulate in labelling and describing such experiences as discriminatory[65]. We elaborate on such a sensitization mechanism below, which is supported by our current results.

Consistent with previous behavioral work[38–41], we found greater overall exposure to ACE to be associated with reduced trait and state empathy. Our dimensional approach further parcellated these findings, however. In agreement with the notion that childhood neglect has a depriving impact on processing complex social information, such as appraising one's own and others' emotional states[45,48], our neglect index was associated with reduced trait cognitive empathy. Individuals who have experienced significant emotional and/or physical neglect may therefore be compromised in developing the skills from which cognitive empathy arises, such as projection and theory of mind. By comparison, what appears to be impacted for those who suffered abuse as children, is the dynamic socio-affective capacity for empathic concern in response to others' misfortunes. Speculatively, the known association between abuse and dysregulated emotion might stimulate elevated personal distress in the face of others' suffering, which detracts from an other-oriented empathic concern response.

At the neural level, childhood abuse was positively associated with brain volumes in frontolimbic (right hippocampus, left rACC) and neocortical association areas (bilateral superior frontal and superior temporal gyri). Whilst being careful to not generalize the effects of ACE across brain regions, one framework to explain the directionality of our results may draw on insights from research on the amygdala. Early stress has been associated with morphological changes in stress-susceptible pyramidal cells in the amygdala, such as dendritic arborization, cell proliferation, and synaptic remodeling, resulting in increased volume and hyperactivity[52,96]. It is plausible that cortical ROIs, particularly those with protracted postnatal development, may respond to stress in a similar manner[3]. Accordingly, heightened social cognition may be necessary to identify environmental threats timeously, but does not necessarily contribute to greater empathy, as these capacities vary independently[10]. Indeed, in previous work from our group, enhanced activation in higher-order social information processing areas in response to complex social information was associated with greater social adversity and reduced compassion[4].

Consistent with the extant literature on ACE, the observed association between childhood abuse and hippocampal volume, particularly on the right, is one of our most robust findings[3]. While various studies found support for reduced hippocampal volume following ACE[53,60], there is also evidence for adversity-related hippocampal expansion linked to functional overuse[54,97,98]. Age at measurement, developmental timing, severity and type of adversity exposure, and psychopathology all potentially contribute to these inconclusive findings[99,100].

The well-established memory functions of the hippocampus have been shown to be invoked during both cognitive and affective empathic responding, facilitating appropriate emotional reactions through retrieval of personal memories and simulation of similar experiences[101–103]. However, heightened hippocampus activation in response to emotional or negative information has been observed in various populations with previous adversity[104,105]. Hippocampal expansion may thus be associated with greater encoding of negative information to enhance emotional learning and prepare the individual for subsequent stressful experiences[98]. Given that ACE in our sample was not associated with greater amygdala volume, these morphological changes might be considered adaptive, congruent with findings in other non-clinical samples[47,100].

The superior temporal and superior frontal (extending medially) gyri are regions crucially implicated in cognitive empathy. The superior temporal cortex is a hub for processing and interpreting various social stimuli, including perception of faces and bodily motion, evaluating goal-directed action, and understanding others' mental states[106,107]. By comparison, the dorsomedial PFC appears involved more in high-level representations, such as making judgements about a person's enduring personality traits[12,108]. While we expected childhood neglect to be associated with reduced volumes in these association cortices, we found evidence of their increased volumetric association with childhood abuse. Elevated activity in social information processing areas in adults who experienced ACE has previously been proposed to reflect strategies to compensate for deficits in emotional empathy by recruiting more effortful cognitive empathy[2,109,110]. Such responses might also reflect increased ruminations and representation of negative social cues[43,97]. While the early detection of threatening stimuli may be adaptive in the context of regular childhood abuse, it may detract from empathic concern when faced with others' distress. Childhood abuse may therefore affect the motivation and propensity, rather than the capacity, to empathize[111,112].

The left rACC was the only area that was positively associated with both childhood abuse and perceived discrimination. The ACC forms part of the paralimbic salience network, which directs attention to events (both internal and external) of personal or social importance[113]. Increased arousal when witnessing another in distress may thus be associated with more physiological signals to help interpret the target's emotional state or intention. Cumulative evidence suggests that social stressors, particularly those during development, may result in neural remodeling of ACC[74], however, with an over-active ACC corresponding to altered salience attribution and hypervigilance for environmental threats[72,114]. Given that ACE may increase vulnerability to subsequent stressors[115], and childhood abuse specifically interrupts developmentally appropriate emotional (fear) learning[46], it makes sense that our abuse index also partly explained the positive association between rACC volume and perceived discrimination. This association remained significant after accounting for age, sex, and SES, suggesting it was not driven by a particular demographic. Rather, childhood abuse might facilitate heightened vigilance or reactivity to emotionally salient inputs regardless of social status, which may prime individuals for increased susceptibility to everyday stressors such as subjective rejection or discrimination.

While our analyses focused on structural volumes, with corresponding surface area associations supporting these findings, the negative associations we observed between childhood abuse and cortical thickness in the superior frontal gyrus, and between perceived discrimination and cortical thickness in the left supramarginal gyrus, are consistent with previous research[116]. For example, greater trait cognitive empathy has been associated with increased thickness in superior frontal and lateral temporal cortices[26,30], whereas cortical thinning in several areas supporting mentalizing have been observed in clinical populations with impaired cognitive empathy[117–119]. We nonetheless cannot confirm any causal mechanisms from the present cross-sectional data.

Some matters merit consideration when interpreting the present results. The first relates to sample: we recruited a non-clinical, unmedicated sample from the general population, with average CTQ scores in the low to moderate range. While these characteristics may be regarded as a strength insofar as detecting resilience mechanisms in a sample with low vulnerability to developing psychiatric disorders[47,100], the observed structural associations may be more pronounced or qualitatively different in clinical populations with high exposure to ACE. The relatively small sample size further limits the generalizability of the results. While we compensated for this limitation through a theory-driven analysis and correcting for multiple comparisons, we employed a frequentist approach in our analysis to help align the present results with previous research. Future research may benefit from Bayesian approaches[120]. Nevertheless, previous structural neuroimaging studies on ACE often employ frequentist approaches with similarly-sized samples[60]. With respect to the lack of structural associations observed for childhood neglect, it may be that the early environment of the present participants, who were not institutionalized as children and who obtained Grade 12 education, buffered against significant deprivation effects.

Second, owing to the structural nature of this data, we cannot quantify effortful processing, nor reflect on how the regions are functionally connected or interact during empathic responding. While structural data contribute important information, several authors have noted the challenges involved in interpreting biologically ambiguous imaging results, where the direction of change is often hard to interpret[30,31,121]. We further note that the anatomical divisions afforded by the Desikan-Killiany atlas we employed involve regions larger than those typically reported in task-based functional studies of empathy[87]. Our results may thus be considered more conservative, potentially obscuring significant effects in smaller regions of interest (e.g., the TPJ). Our findings are nevertheless bolstered by converging results from cortical volume, surface area, and thickness measurements.

Third, because of the correlational nature of this study, we cannot deduce any causal relationships between ACE, perceived discrimination, and brain structure. Moreover, exposure age, duration, severity and type of adversity, and immediate appraisal of experiences are all continuous and dynamic variables that may influence these associations[54,122]. Future research should consider employing longitudinal designs with greater power so that causal relationships between ACE and empathy can be explored[123]. It is also relevant for future research to unravel the conditions that support increased sensitivity to discrimination versus actual instances of discrimination and how these relate to ACE. Finally, we note that the present functional inferences based on structural associations rely on reverse inference. Yet we feel reassured by the reduced state empathy we observed, which adds credence to our psychological interpretation of functional roles in selected regions.

Conclusion

Our findings underscore the importance of distinguishing between different dimensions of ACE. Childhood abuse corresponded to reduced state affective empathy, notwithstanding experience-dependent volumetric expansion in cognitive empathy areas, whereas childhood neglect corresponded to reduced trait cognitive empathy. Moreover, our mediation analysis provides a testable neural salience mechanism centered in the rACC, through which childhood abuse may be associated with greater perceived discrimination. Because of the selective disruption in affective empathy, training protocols specifically addressing socio-affective capacities in those who suffered extensive childhood abuse may be productive targets for intervention[10,14,44]. Treatment interventions may furthermore be adapted to incorporate discussions on perceived discrimination and to leverage coping strategies[68], given the close association between ACE and experienced discrimination. Finally, the context-dependent nature of adversity-related outcomes necessitates exploring such associations locally[65], where the intergenerational transmission of trauma may interact in complex ways with subsequent psychosocial stress[124]. A greater awareness of the neural underpinnings and implications of ACE and perceived discrimination, and the mechanisms that may either propagate or protect against negative outcomes, may ultimately assist efforts to strengthen empathic repair.

Data availability
The data that support the findings of this study are openly available at Open Science Framework, https://osf.io/5uw6z/.

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Author contributions

MMF, DS, MS, and JD designed the original research and protocol, while MMF and FW designed the protocol for the present structural analysis. TDS and HC analyzed all data under the supervision of MMF and FW. MMF wrote and prepared the main manuscript text and TDS and HC prepared the figures. DS, MS, and JD provided critical revisions. All authors approved the submitted version of the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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