Manuscript Title

Bullying and Early Brain Development: A Longitudinal Structural Magnetic Resonance Imaging Study from Adolescence to Early Adulthood

Running Title

Bullying and Early Brain Development: An sMRI Study

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Data Availability

All the data are available from the authors upon reasonable request and with permissions of the IMAGEN consortia. https://github.com/imagen2/imagen_mri

Code Availability

https://github.com/mconnaug/Bullying_Brain_Development

Abstract

To explore this, we conducted the largest structural MRI analysis to date (n=2094, including 1009 females), across three time points from the IMAGEN study, tracking region-specific brain volume trajectories from adolescence to early adulthood using a data-driven approach. Generally, experienced bullying showed increased subcortical volumes in the putamen (β=0.12), caudate (β=0.06), accumbens (β=0.06), amygdala (β=0.07), hippocampus (β=0.06), paired with decreased cerebellar (β=-0.10), entorhinal, (β=-0.12), and insula (β=-0.11) volumes. Females exhibited more volumetric changes in emotional processing areas whereas males had more changes in motor and sensory regions. These findings point to widespread associations between bullying victimization and brain development, offering a potential neurobiological framework to explain the emotional and behavioral difficulties observed. Importantly, this study emphasizes the need for a sex-sensitive approach in future research and interventions related to bullying.

Introduction

Bullying victimization refers to an individual's experience of targeted aggressive behaviors, often done by peers, manifesting as physical, verbal, or relational aggression (1). During childhood and adolescence, especially when persistent and severe, bullying victimization has detrimental effects on mental health and cognitive functioning, with these adverse outcomes often continuing into adulthood (2, 3). This is particularly concerning because adolescence is a critical neurodevelopmental period, marked by extensive biological and psychological transformations (4). During this phase, significant brain growth and reorganization occur, making the developing brain especially vulnerable to stressors like bullying. Chronic exposure to stressors, such as bullying victimization, during this vulnerable period can lead to enduring changes in brain structure and function, potentially resulting in long-term mental health issues associated with bullying (5).

While cross-sectional structural MRI methods have effectively identified brain regions affected by bullying victimization (6), our understanding of its impact on brain development over time remains limited. Two longitudinal structural MRI studies have explored the effects of bullying victimization on brain development across two time points (7, 8). The first study, using data from the Adolescent Brain Cognitive Development (ABCD) dataset (9), focused on children aged 9 and 11 and found that chronic bullying victimization was associated with widespread changes in brain volume across multiple cortical and subcortical regions (7). Specifically, increased volumes were observed in the hippocampus, entorhinal cortex, superior parietal cortex, and fusiform gyrus, as well as larger surface areas in the frontal, parietal, and occipital cortices (7). In contrast, reductions in cortical thickness were noted in areas such as the entorhinal cortex, paracentral gyrus, pars orbitalis, superior parietal cortex, fusiform gyrus, and rostral middle frontal cortex (7). The second study, utilizing the IMAGEN project dataset (10), examined adolescents and found that chronic peer victimization was linked to steeper decreases in left putamen volume between the ages of 14 and 19 compared to non-victimized individuals (8). However, this study only examined nine brain structures bilaterally, leaving the broader impact of bullying victimization on brain development from adolescence into early adulthood remains uncertain.

Although limited, current MRI findings align with research suggesting that childhood bullying victimization is associated with stress-induced neuroendocrine reactivity, neuromodulation, and limbic system dysregulation, potentially driving widespread alterations in brain structure (11). The stress response evoked by bullying has been shown to lead to

overactivation of the limbic system, particularly the amygdala and hippocampus, potentially resulting in increased volume in these regions as the brain attempts to manage persistent stress (11). Conversely, prolonged exposure to stress hormones like cortisol can have neurotoxic effects on cortical regions, leading to reductions in cortical thickness and volume (11). This suggests that bullying victimization has widespread influences on childhood brain development, underpinned by a complex mix of adaptive and degenerative effects due to stress exposure. However, owing to limited whole-brain longitudinal MRI research mapping these structural changes over time, our understanding of the dynamic and long-term impacts of bullying victimization on brain development remains incomplete.

Several notable limitations in prior studies must be addressed to better understand the impact of bullying victimization on brain development. First, previous studies did not capture the intensity of the experienced stressor. Although bullying victimization is experienced by up to 30% of children and adolescents, the severity varies greatly (12). Some individuals experience severe, chronic bullying, while others encounter more sporadic or less intense incidents. An understanding of how different intensities of bullying influence brain development is needed. Second, the two-time-point design in previous longitudinal studies imposed a linear developmental trajectory. Brain structures do not develop linearly; rather, they follow quadratic patterns involving periods of rapid growth and subsequent stabilization (13). By not accounting for these non-linear developmental trajectories, previous studies may not have optimally mapped and tracked brain changes across critical developmental phases

Our study aims to measure the impact of bullying victimization on cortical and subcortical brain development using structural MRI data collected at three time points: ages 14, 19, and 22. This three-time-point longitudinal design allows us to capture region specific developmental changes, providing new insights into how chronic bullying victimization affects brain development during the transition from adolescence into early adulthood. Importantly, the severity of bullying victimization is assessed at each time point using the Olweus Bully/Victim Questionnaire (OB/VQ) (14), allowing for a comprehensive evaluation of its impact. We hypothesize that chronic bullying victimization is associated with widespread changes in brain development, particularly in regions related to emotion regulation and social processing. Specifically, we expect to find atypical volumetric changes characterized by decreased cortical and increased subcortical volume development across adolescence and early adulthood. Additionally, we conducted exploratory analyses to investigate potential sex differences in the impact of bullying on brain development, aiming to identify whether the effects of bullying victimization differ between males and females.

Materials and Methods

Participants

This study used data from the IMAGEN project, a European multicenter research initiative focusing on how different factors influence brain development and mental health in adolescents. For a comprehensive description of the IMAGEN project's methodology, refer to Schumann et al., 2010 (10). Participants were assessed at eight study sites in England, Ireland, France, and Germany. Data were first collected when the participants were aged 14, but subsequent follow-up assessments have taken place at ages 16, 19, and 22. The analysis in this study specifically looks at data collected when participants were 14, 19, and 22 years old. The data from the age of 16 were not included because MRI scans were not conducted at that age.

Written informed consent was obtained from participants and a parent/guardian before enrolment. The IMAGEN study was approved by local ethics research committees at each research site: King's College London, University of Nottingham, Trinity College Dublin, University of Heidelberg, Technische Universität Dresden, Commissariat à l'Energie Atomique et aux Energies Alternatives and University Medical Center. A detailed description of recruitment and assessment procedures, as well as general inclusion and exclusion criteria, has been published previously (10).

Bullying victimization

Bullying victimization was assessed using questions adapted from the revised Olweus Bully/Victim Questionnaire (OB/VQ) (14), previously employed in the international Health Behavior in School-Aged Children (HSBC) study. Four questions, scored on a 5-point Likert scale, measured the frequency of victimization over the past six months:

1. "I was bullied at school (a student/peer said or did nasty or unpleasant things to me)."
2. "I was called mean names, made fun of, or teased in a hurtful way by a student/peer."
3. "A student/peer left me out of things on purpose, excluded me from their group of friends, or completely ignored me."
4. "I was hit, kicked, pushed or shoved around, or locked indoors by a student/peer."

Responses ranged from 1 ("never") to 5 ("three or more times a week"). The four item scores were summed and standardized (z-scores) to yield bullying victimization scores at ages

14, 19, and 22, with higher scores reflecting greater self-reported victimization. The OB/VQ has demonstrated strong psychometric properties, with reliability estimates for the victimization items ranging from 0.83 to 0.88 (15, 16).

MRI Acquisition and Protocol

The MRI acquisition protocol for the IMAGEN project, detailed in Schumann et al. (2010) and available in the Standard Operating Procedures (https://imagen-europe.org/), was standardized across sites to ensure comparable data quality. High-resolution anatomical MRIs were obtained using a 3D T1-weighted magnetization prepared echo gradient sequence based on the Alzheimer's Disease Neuroimaging Initiative (ADNI) protocol. More details of the IMAGEN MRI acquisition and protocols are described in depth elsewhere (10). All MRI scans underwent a IMAGEN quality control procedure which included manually inspected and rated for artifacts, data quality issues, and excessive head motion (10). After quality control, 24 scans were removed, resulting in a final dataset of 4,561 structural scans.

All MRI images were processed using FreeSurfer's recon-all function (version 5.3.0) for full cortical reconstruction and brain segmentation (17, 18). The Desikan-Killiany-Tourville (DKT) atlas was used for brain parcellations, segmenting the cortex into 68 regions and subcortical structures into 20 regions of interest (19). Cortical and subcortical volumes were extracted for statistical analysis. Before statistical analyses, outliers were identified as any data points diverging by ±3 standard deviations from the data mean. In line with established statistical practice outliers were removed to minimize the effect of extreme values (20).

Statistical Analysis

To measure impact of bullying victimization score on brain development across adolescence and early adulthood, an established top-down mixed-effects model selection process was performed using the *lme4* package in R (version 1.1-27.1) (21). This approach begins with the most complex model, which includes all random and fixed effects, and systematically removes effects based on Akaike Information Criterion (AIC) and Log-Likelihood Ratio Test (LRT) to identify the optimal model for each brain volume. A more complex model was retained if it significantly improved model fit compared to a simpler model, indicated by both an AIC > 10 and LRT p-value < 0.05 (22-24).

Given prior evidence suggesting non-linear relationships between brain structure and age (13), both linear and quadratic models were tested to determine the optimal growth curve

for each brain structure (Table 1). Random effects were identified by comparing models with and without the random effect of slope. The random effect of intercept and slope was included if it significantly improved model fit. As recommended by Bayer et al. (2022), including scan location as a random effect accounted for individual variance in scan sites, a common issue in multicenter neuroimaging studies (25).

The fixed effects of interest (bullying victimization score and its interaction with age) were compared against null models containing only covariates (age, sex, pubertal status, socioeconomic status, and intracranial volume). If a fixed effects model significantly increased fit compared to the null model, it indicated a significant effect on brain volume. Maximum Likelihood (ML) was initially used to compare model fits, but the final optimal model was refitted using Restricted Maximum Likelihood (REML) for increased accuracy of parameter estimates. The covariance structure was set to "unstructured", which is the default covariance structure in R software. This structure imposes no restrictions on the covariance parameters, thus allowing the inclusion of variations in the slopes. To mitigate multiple comparison effects, a two-stage False Discovery Rate (FDR) correction was applied using the MuToss package (26) in R (version 4.1.1).

Sensitivity analyses assessed potential confounding effects from other negative life events using the Life Events Questionnaire. Optimal models were rerun with this additional variable, and post hoc two-stage FDR corrections were applied. For a brain region to be considered significant, the bullying victimization and/or bullying victimization-by-age terms had to remain significant with the additional variable of the Life Events Questionnaire and survive post hoc correction.

Exploratory analyses examined sex-specific differences in victimization and brain development by adding a bullying victimization-by-sex interaction term to the optimal models for significant brain regions. These models adjusted for age, sex, pubertal status, socioeconomic status, intracranial volume, and scan site. A two-stage FDR correction addressed multiple comparisons.

Table 1: Mixed models tested: limbic system structures in ADHD and controls.

Higher Order Models	
Linear Model	Bully victim score * age + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)
Quadratic Model	Bully victim score * age + age^2 + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)
Random Effects Models	
Linear RFX 1	Bully victim score * age + sex + SES + puberty + ICV + (1|subject) + (1|scan site)
Linear RFX 2	Bully victim score * age + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)
Quadratic RFX 1	Bully victim score * age + age^2 + sex + SES + puberty + ICV + (1|subject) + (1|scan site)
Quadratic RFX 2	Bully victim score * age + age^2 + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)
Fixed Effects Models	
Linear Null 1	age + sex + SES + puberty + ICV + (1|subject) + (1|scan site)
Linear Null 2	age + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)
Quadratic Null 1	Age + age^2 + sex + SES + puberty + ICV + (1|subject) + (1|scan site)
Quadratic Null 2	age + age^2 + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)
Linear FFX simple 1	Bully victim score + age + sex + SES + puberty + ICV + (1|subject) + (1|scan site)
Linear FFX simple 2	Bully victim score + age + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)
Quadratic FFX simple 1	Bully victim score + age + age^2 + sex + SES + puberty + ICV + (1|subject) + (1|scan site)
Quadratic FFX simple 2	Bully victim score + age + age^2 + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)
Linear FFX complex 1	Bully victim score * age + sex + SES + puberty + ICV + (1|subject) + (1|scan site)
Linear FFX complex 2	Bully victim score * age + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)
Quadratic FFX complex 1	Bully victim score * age + age^2 + sex + SES + puberty + ICV + (1|subject) + (1|scan site)
Quadratic FFX complex 2	Bully victim score * age + age^2 + sex + SES + puberty + ICV + (1 + age|subject) + (1|scan site)

Legend: RFX = random effects, FFX = fixed effects, ROI = regions of interest, ICV = intracranial volume, age = participant age from baseline (in months).

Results

Descriptive Statistics

Full details of the demographic and clinical characteristics of this study's population are provided in Table 2. Of the 4561 scans available, 44 scans were removed due to missing age and/or bully questionnaire (Time 1 = 12, Time 2 = 30, Time 3 = 2). The final sample

consisted of 4512 scans from 2094 subjects (female: 2171, male: 2341, age range: 13.23 – 25.11) across three timepoints.

Table 2: Demographics and Clinical Variables

Variable Name	Time 1	Time 2	Time 3
N	2052	1328	1132
Sex (female %)	1009 (49.17%)	632 (47.59%)	530 (46.81%)
Age	14.44 (0.39)	19.01 (0.78)	22.56 (0.65)
OB/VQ z-score (mean)	0.55 (0.901)	0.15 (0.434)	-1.19 (0.512)
SES (mean)	0.71 (1.09)	-	-
Pubertal Status (mean)	3.60 (0.71)	-	-
Number of Scans at IMAGEN Site			
London	251	168	153
Northampton	343	211	169
Dublin	192	122	116
Berlin	252	118	155
Hamburg	261	181	153
Mannheim	245	155	140
Paris	253	204	124
Dresden	255	169	122

Legend: The Olweus Bully/Victim Questionnaire (OB/VQ) is used to measure bullying victimization and bullying experiences. Pubertal status was assessed via self-report using the Pubertal Development Scale (PDS). Socioeconomic status (SES) was indexed using the family stresses subsection of the Development and Well-Being Assessment (DAWBA).

Impact of Bullying Victimization on Brain Development

Model Selection Procedure

Full details of the model selection fit statistics are provided in the appendices (eTables 1-5). In summary, introducing a quadratic fit significantly enhanced the model fit for fifty-two out of eighty-eight brain structures. Models incorporating both random effects of intercept and

slope were chosen for eighty-two structures. Among these, the complex model, which includes the bully victim score-by-age interaction term, was deemed appropriate for fifty-six structures. Meanwhile, the simple model was suitable for the remaining twenty-two structures. The selected optimal models derived from the top-down mixed model selection procedure are presented in eTable 6 in the supplemental material.

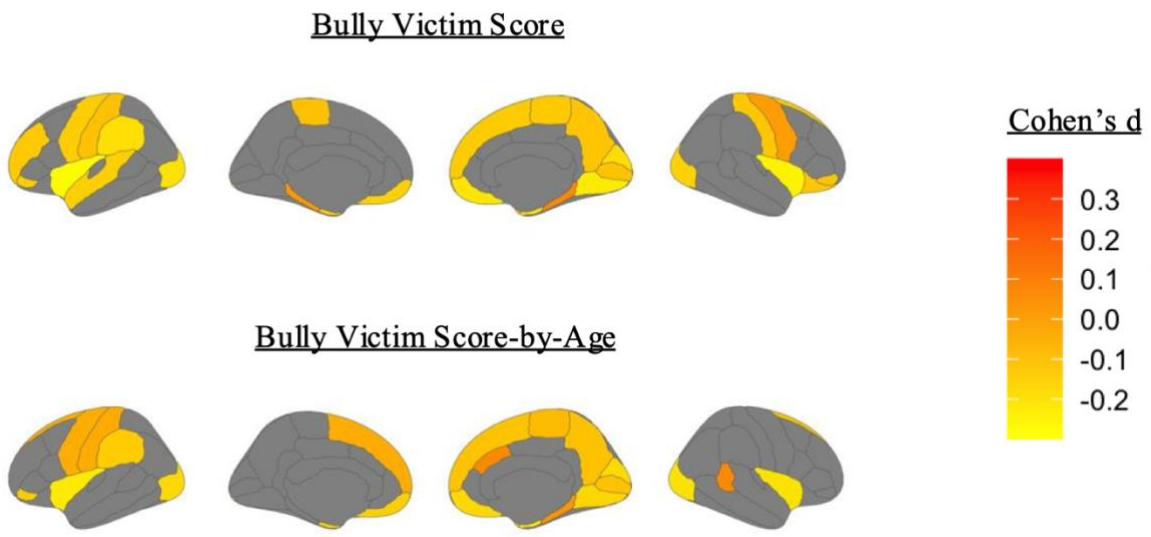
Optimal Model Results

The full results of the optimal models are presented in eTables 7-10 (supplemental material). Following post hoc and sensitivity analyses, significant effects of bullying victimization scores were observed on the volume development of 49 brain structures (eTable 11). Increased bullying victimization was associated with reduced brain volume in several regions, notably the frontal, parietal, occipital, temporal, and cerebellar areas. Specific reductions were observed in the left cerebellar cortex, bilateral insula, left pallidum, right lingual gyrus, left ventral diencephalon, right entorhinal cortex, and right medial orbitofrontal cortex, among others (Figure 1).

Conversely, increased bullying victimization was assoicated with increased volume in limbic and subcortical regions. Significant positive associations were found in the left and right caudate, left and right hippocampus, left and right amygdala, right and left accumbens area, and the left and right putamen (Figure 2). The developmental impact of bullying victimization on all brain volumes is detailed in eFigure 1 in the supplemental material.

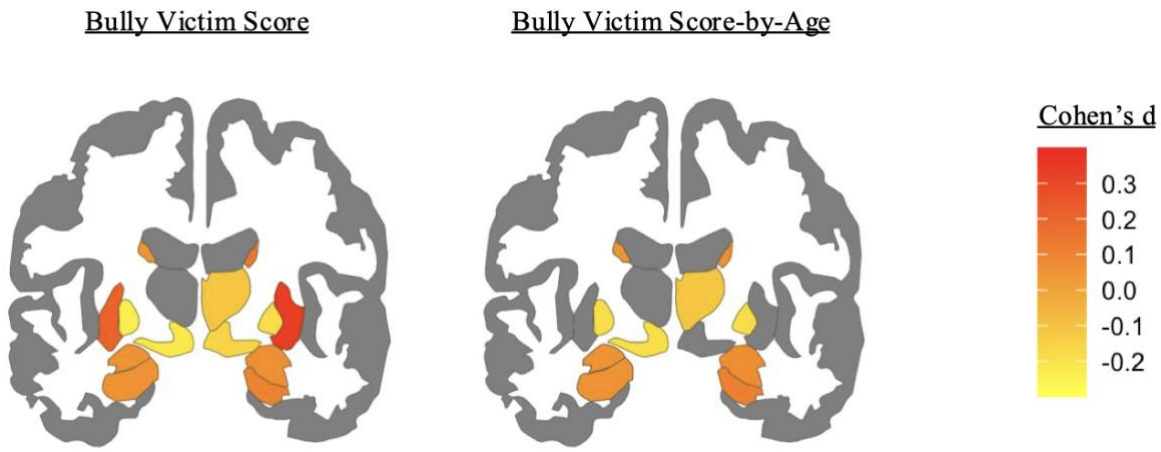
In summary, the general pattern indicates that increased bullying victimization is significantly associated with altered brain volume development from adolescence into adulthood. Specifically, it is associated with reduced volumes in the cerebellar, entorhinal, and insula regions, while leading to increased volumes in the limbic and subcortical areas.

Figure 1: Magnitude of Effect Sizes for Bullying victimization and Bullying victimization-by-Age on Cortical Brain Regions.



Legend: This figure displays the effect sizes (Cohen's d) for the association of bullying victimization and bullying victimization-by-age on cortical brain regions. The top row illustrates the effect sizes for the interaction term (Bully Score*Age), while the bottom row shows the effect sizes for the main effect of the Bully Score. The color scale represents Cohen's d values, indicating both positive and negative effect sizes, with warmer colors (red and orange) representing larger effect sizes. These visualizations highlight the cortical regions where bullying victimization and its interaction with age significantly influence cortical brain volume development.

Figure 2: Magnitude of Effect Sizes for Bullying victimization and Bullying victimization-by-Age on Subcortical Brain Regions.



Legend: This figure displays the effect sizes (Cohen's d) for the association of bullying victimization and bullying victimization-by-age on subcortical brain regions. The top bar graph illustrates the effect sizes for the interaction term (Bully Score*Age), while the bottom bar graph shows the effect sizes for the main effect

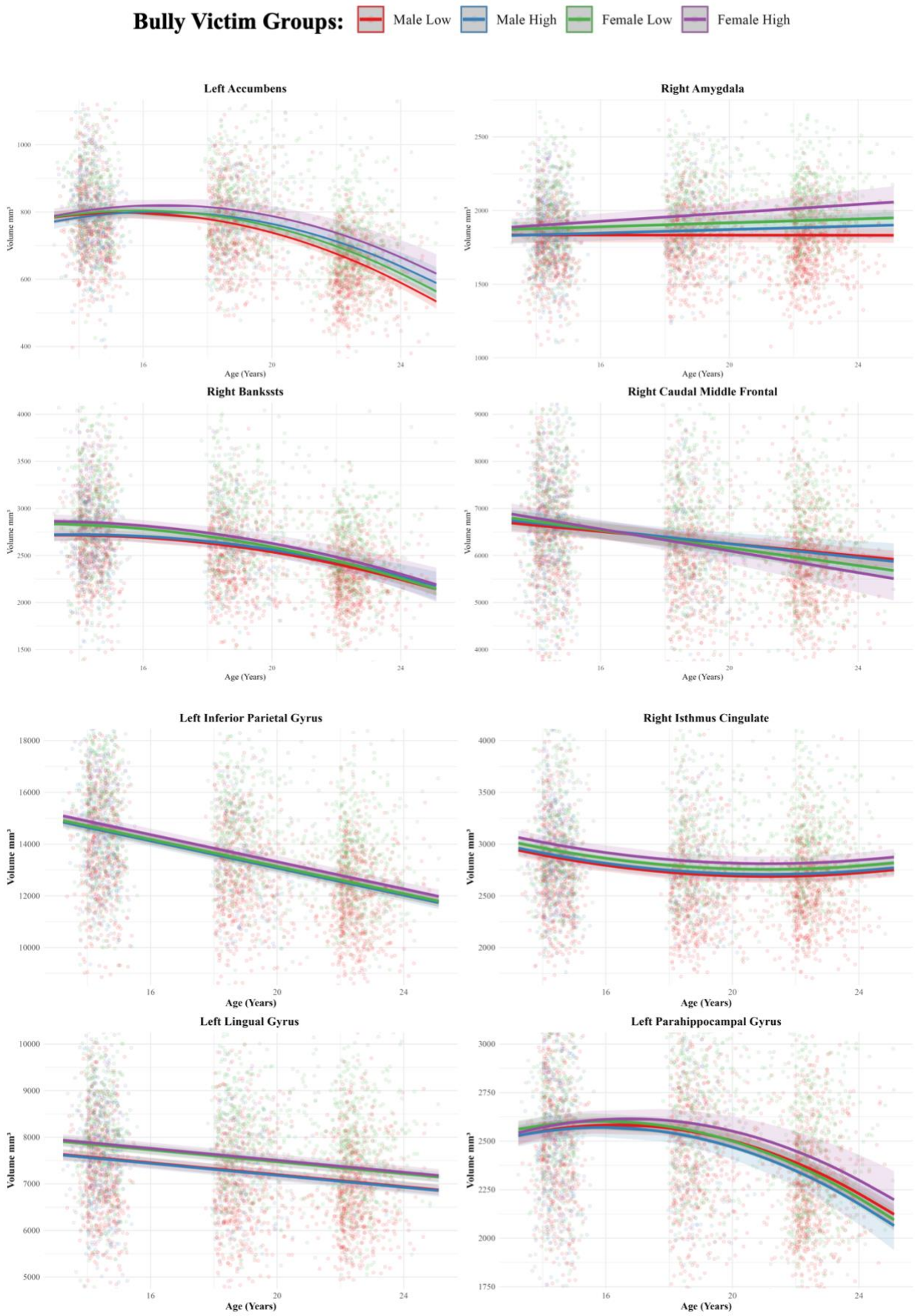
of the Bully Score. The color scale represents Cohen's d values, indicating both positive and negative effect sizes, with warmer colors (red and orange) representing larger effect sizes. These visualizations highlight the subcortical regions where bullying victimization and its interaction with age significantly influence brain volume development.

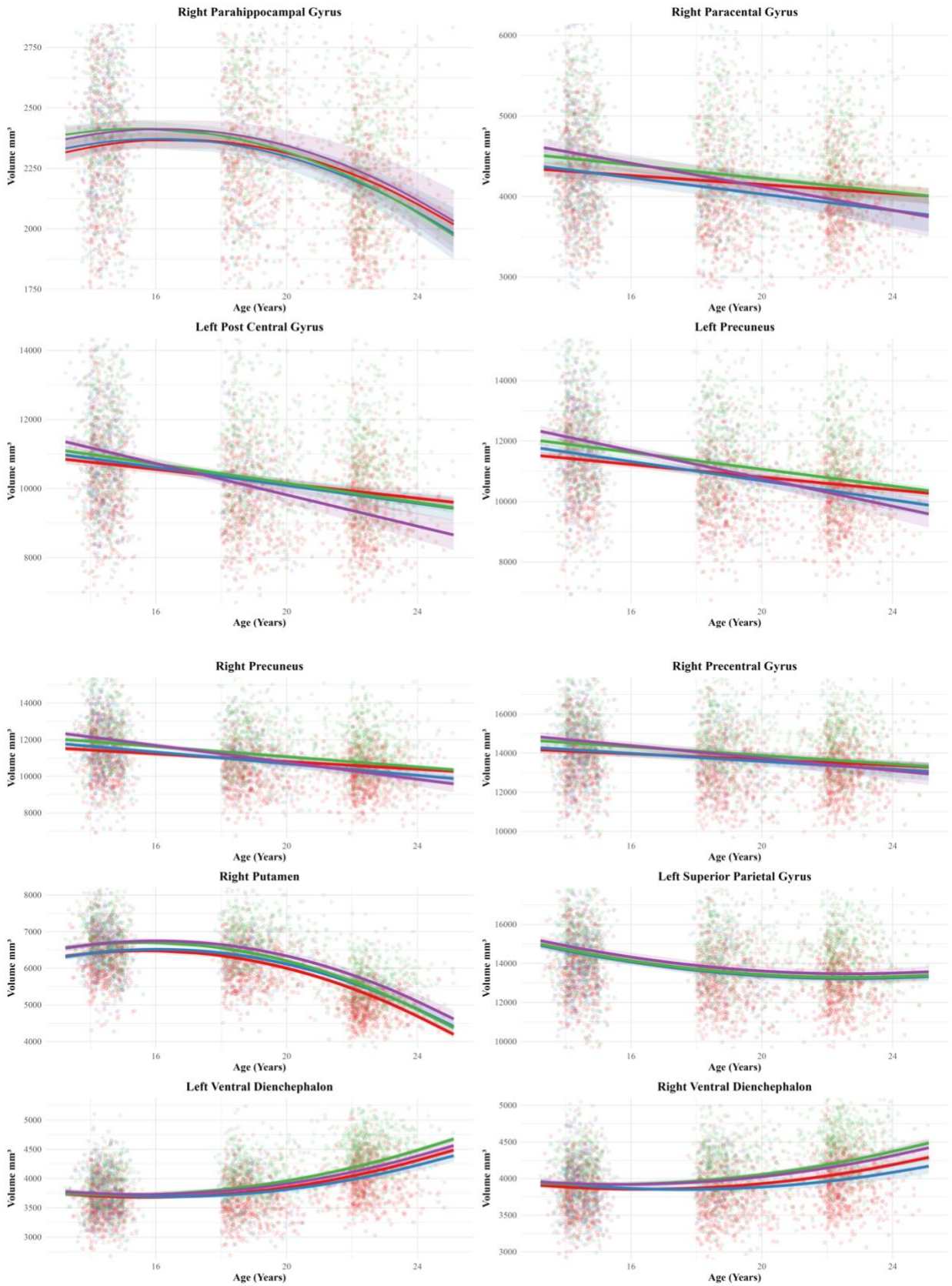
Sex Differences in the Impact of Bullying Victimization on Brain Development

Supplemental material eTables 12-15 summarize the fixed effects from the models assessing sex differences in the impact of bullying victimization on brain development across adolescence and early adulthood. Our statistical analyses revealed significant sex-specific associations between bullying victimization scores and volume development in several brain regions (Figure 3).

The analysis identified distinct sex-related differences in the associations between bullying victimization and brain development. Positive associations were found in the right ventral diencephalon and the left nucleus accumbens area, indicating that higher bullying victimization scores are linked to increased volume in these regions. Conversely, significant negative associations were observed in the right parahippocampal gyrus and the left inferior parietal gyrus, suggesting that higher bullying victimization scores are related to decreased volume in these areas. These results highlight the complex interplay between sex and bullying victimization, suggesting a potential differential impact on brain development during adolescence and early adulthood.

Figure 3: Sex Differences in the Impact of Peer Victimization on Brain Development.





Legend: The analysis had peer victimization as a sum score, but for visualization purposes, these scores were grouped into four categories. "Male Low" represents males in the lowest quartile of bullying victim scores, shown in red. "Male High" represents males in the highest quartile of bullying victim scores, shown in blue. "Female Low" represents

females in the lowest quartile of bullying victim scores, shown in dark green. "Female High" represents females in the highest quartile of bullying victim scores, shown in purple. “Bankssts” refers to the banks of the superior temporal sulcus. The shaded region around each line represents the 95% confidence interval for the predicted values.

Discussion

This study, the most extensive three-time-point longitudinal neuroimaging study of bullying to date, examined the association between chronic bullying victimization and brain development across adolescence and early adulthood. The principal findings are: 1) chronic bullying victimization is significantly associated with altered development of a wide range of cortical and subcortical brain structures during this period; and 2) there are notable sex-specific differences

The novelty of this study lies in capturing widespread non-linear developmental brain changes not observed in previous studies, highlighting that the neurodevelopmental impact of bullying victimization may be more widespread than previously reported (7, 8). Consistent with the well-documented trend that larger study samples tend to yield smaller effect sizes, the effect sizes reported in this study were slightly smaller than those in previous research (7). However, these findings are robust across variables such as sex, age, MRI scanner site, socioeconomic status, pubertal status, and other negative life events, suggesting that the observed brain differences may be uniquely attributed to bullying victimization.

Association Between Bully Bullying and Brain Development

Subcortical structures appear to be particularly sensitive to chronic bullying victimization, with significant volumetric increases observed in the structures of the basal ganglia, including the pallidum, caudate, putamen, and nucleus accumbens. These regions are integral to motor control, emotional regulation, and reward processing (27). The observed differences in the volumes of the caudate and putamen corroborate previous findings (8). Meanwhile, the discovery of increased volumes in the nucleus accumbens and pallidum represents novel contributions to the field.

Increased volumes in the pallidum, caudate, putamen, nucleus accumbens, and striatum were associated with heightened bullying victimization from adolescence into adulthood suggesting significant structural brain changes due to chronic social stress. Individuals experiencing high levels of bullying often face prolonged stress, which can lead to neuroplastic

changes as the brain attempts to adapt. Enlarged dorsal striatal structures (caudate and putamen), crucial for automatic/habitual responses and attention, may underlie the increased striatum-dependent ("habit") learning observed in bullied individuals (11). Specifically, bullied individuals often rely on habitual coping responses and behaviors that are linked to past threats, that may not be adaptive or appropriate in current, non-threatening contexts (11). This response inflexibility can cause social distress, making it difficult for these individuals to adapt to new social environments and maintain healthy relationships. Additionally, bullied individuals also display a striatal-dependent shift in memory processing, that is associated with cognitive inflexibility and anxiety, especially during adolescence (28). While striatal-dependent memory primarily involves the ventral striatum (nucleus accumbens) and various other cortical structures (11). The ventral striatum is particularly involved in negative emotional processes, with its hyperactivity linked with greater internalizing/externalizing symptoms among bully victimized adolescents (29). Thus, the enlarged ventral striatum may be associated with increased bias to striatal-dependent memory processing due to bullying victimization. Less is known about the involvement of the pallidum in bullying victimization; however, volumetric disruptions to this structure have been linked to depression, anxiety, and obsessive compulsive disorder (30-32). The pallidum is crucial for emotional regulation and processing through cortico-striato-thalamo-cortical (CSTC) circuits, with disruptions linked to altered cognitive regulation of emotion (30, 33). Therefore, increased pallidum volume may disrupt CSTC functioning, leading to heightened stress sensitivity and emotional dysregulation.

Another novel finding was the association between increased exposure to bullying and reduced ventral diencephalon volume. The ventral diencephalon, which includes structures such as the hypothalamus, plays a crucial role in regulating the neuroendocrine stress response (34). Reduced volume in this area may disrupt hormonal regulation, potentially impairing the body's ability to optimally manage stress (35, 36), which could contribute to the increased risk of anxiety, mood disturbances, and stress-related disorders seen in individuals affected by bullying victimization (37). These findings suggest that neuroendocrine functions could be an important area to explore further in interventions for those impacted by bullying.

Significant differences were also noted in the structures of the limbic system, particularly in the hippocampus and entorhinal cortex, and parahippocampal gyrus. Our findings of enlarged hippocampal and entorhinal cortical volumes are in-line with previous literature (7). However, our findings of enlarged amygdalae volumes were not replicated in previous research (7). This may be due to the methodological variations in prior research, specifically the use of binary bullied vs non-bullied groupings which does not capture the

severity of the experienced victimization. It is plausible that enlarged amygdala volume may reflect the heightened emotional reactivity often observed among individuals exposed to more severe chronic stress (38). Studies have shown that individuals subjected to victimization display heightened activity in response to emotionally charged stimuli, indicating greater sensitivity to stressors (39, 40). This heightened sensitivity can contribute to the development and maintenance of anxiety disorders, depression, and other psychological conditions frequently seen in victims of bullying (41, 42). Changes in the entorhinal cortex could reflect alterations in how spatial and contextual memories related to stressful experiences are processed (43). These adaptations may represent the brain's attempt to navigate and remember complex social landscapes under stress, potentially leading to enhanced recall of emotionally charged events (44). These adaptations might result in heightened sensitivity to social cues which can perpetuate stress responses, making victims more vulnerable to anxiety and depression (45).

Increased hippocampal volume among individuals exposed to chronic bullying may be explained by the brain's adaptive response to prolonged stress. It is plausible that chronic stress can lead to structural changes in the hippocampus, such as increased neurogenesis or dendritic branching with the heightened demand for processing and storing emotionally charged memories (45). These neuroplastic changes may underpin the negative emotional memory biases and increased false memory recall observed in individuals who have experienced bullying victimization (46). Specifically, violent and aggressive false memories have been shown to be positively associated with bullying victimization (46). This increased recall and processing of emotionally charged false memories could further explain the observed increase in hippocampal volume, reflecting the brain's adaptation to managing such intense and frequent emotional stimuli. Despite these promising findings, the mixed results regarding this structure necessitate further research to clarify its role in bullying victimization and to comprehend the long-term implications of these neuroplastic changes.

Alterations were also noted in various cortical areas across the frontal, temporal, parietal, and occipital lobes. In the frontal lobe, changes were observed in regions such as the medial orbitofrontal cortex, superior frontal gyrus, and frontal pole. Previous research has linked functional and structural alterations in these areas to bullying victimization, suggesting that victims may have difficulties in regulating emotions and making decisions under stress (6). Our findings support these previous studies, reinforcing the idea that bullying impacts critical areas involved in executive functioning (11).

The temporal regions, including the superior temporal gyrus, showed changes that could affect memory and emotional association. Studies have indicated that victims of bullying often exhibit altered temporal lobe structures, contributing to difficulties in processing and recalling emotionally charged memories (11). Our results are consistent with these findings, suggesting a common pathway through which bullying affects memory and emotional processing (11). Significant volume reductions were found in the insula, which are novel findings not previously reported in the literature. Prior research has highlighted significant differences in insula activity in the context of bullying victimization, but structural changes had not been documented until now (47). The insula is a deep cortical structure critical for emotional processing and interoceptive awareness (11). Alterations in this structure have been linked to heightened sensitivity to emotional stimuli and social rejection, a common feature of bullying victimization (11).

Alterations in the parietal and occipital lobes, such as the precuneus and cuneus, may influence how victims process and respond to visual and spatial cues (48). This can impact their social interactions and stress responses (11). Previous studies have found that these regions, when affected by bullying, can alter how individuals perceive and react to their environment, potentially leading to social withdrawal and heightened anxiety (11). Our findings align with these studies, suggesting that visual and spatial processing deficits may contribute to the social challenges faced by bullied individuals (11).

Globally, bullying victimization was negatively associated with total grey matter volume, suggesting a widespread impact on brain development. This finding is consistent with previous research that has documented reductions in grey matter volume following exposure to chronic stress and adversity (49). Grey matter comprises of neuronal cell bodies and dendrites, and alterations in its volume may reflect changes in neuronal density, synaptic connections, or cortical thickness (49). These disruptions, potentially influenced by stress-related neurobiological mechanisms, could contribute to deficits in attentional control and behavioral regulation (11). Given that total grey matter volume is linked to optimal information processing and supporting cognitive functions, its reduction may impair the brain's ability to regulate behavior and attention (49).

Our study identified a novel association between increased chronic bullying victimization and altered development of the cerebellum, characterized by reduced volume. While the cerebellum is primarily recognized for its critical role in the coordination and regulation of movements, it also plays a significant role in social and cognitive processes essential for effective social interactions (50). Poor motor skills, governed by cerebellar

function, have been identified as a strong predictor of being bullied (51). Individuals with less refined motor abilities may struggle with social coordination and physical activities, leading to difficulties in social integration. Thus, the cerebellum's developmental trajectory, potentially influenced by chronic stress, might exacerbate these motor and social coordination challenges, increasing vulnerability to bullying.

Beyond motor-related functions, the cerebellum is increasingly recognized for its role in higher-order and executive functions, including prediction, error-based learning, and emotional recognition (50). The cerebellum's involvement in prediction-based learning helps the brain anticipate and respond to various stimuli, playing a crucial role in how individuals process and interpret social cues (50). Cerebellar abnormalities may disrupt these predictive mechanisms, leading to difficulties in accurately interpreting social interactions (50). This impairment can underpin the negative emotional biases observed in bullied individuals, who often misinterpret neutral or ambiguous social cues as hostile, contributing to their interpersonal difficulties and increased risk for psychopathology (52).

To summarize the primary analysis, our findings suggest that chronic bullying victimization is associated with widespread cortical alterations affecting multiple cognitive and emotional processes. These structural changes support previous research and may underpin the various psychological and behavioral difficulties observed in bullying victims. Additionally, this study highlights a neurobiological basis for a vicious cycle in which bullying leads to increased social and emotional difficulties, which in turn may elevate the risk of continued victimization and its adverse effects on long-term mental health. This underscores the urgent need for early, targeted interventions to address these neurobiological impacts, helping to break the cycle of bullying and mitigate its long-term effects on mental health.

Sex-Specific Differences in Brain Volume Changes

Notably, sex differences in brain development were reported. In females, positive associations were observed in subcortical structures, specifically the ventral diencephalon, left nucleus accumbens, and right amygdala. These findings suggest that higher levels of bullying victimization are associated with increased volume in these regions in females compared to males. The increased volumes in areas such as the accumbens and amygdala, which are integral to emotional processing and stress responses, may reflect an adaptive neurobiological response to social stressors, potentially heightened by the more relational form of bullying often experienced by females (53). This form of bullying, which typically involves emotional

manipulation and exclusion, could lead to greater activation and subsequent changes in these brain regions, which are sensitive to social and emotional stimuli (54).

Conversely, negative associations were observed in several cortical structures among females, particularly in the parahippocampal gyrus, left inferior parietal region, right banks of the superior temporal sulcus. Research indicates that males tend to experience more physical bullying (55), which may lead to greater development in regions associated with sensorimotor processing and physical coordination. For instance, structures such as the right precentral gyrus, left and right postcentral gyrus, and right putamen, which are involved in motor control and sensory perception (56), are larger in bully victimized males. This could be a result of the repeated physical confrontations that bullied males face, which may stimulate growth in these areas. Similarly, the superior parietal and parahippocampal regions, which play a role in spatial orientation and motor planning (57, 58), are also larger in bully victimized males, likely reflecting their engagement in physical activities and the need for spatial awareness in these situations.

Overall, these results highlight the complexity of the brain's response to social stressors like bullying victimization, which is influenced by both biological sex and the type of bullying. Understanding these differences is crucial for developing sex-sensitive approaches that address the specific needs of young individuals facing bullying during critical developmental periods.

Limitations

Despite its comprehensiveness, this study has several limitations that warrant consideration. Bullying victimization is a complex construct influenced by numerous factors. Although this study controlled for variables such as negative life events, socioeconomic status, and pubertal hormones, it is impossible to account for all potential influences on brain development. Each child's developmental trajectory is shaped by a unique combination of genetic, environmental, and interpersonal factors. Consequently, while our findings offer insights into the impacts of bullying victimization, they represent only one aspect of the broader developmental context. Future studies should explore these complex interactions further and incorporate data that includes additional developmental influences.

Additionally, the onset of bullying victimization in our study was measured starting at age 14, meaning developmental changes occurring as a result of victimization before this age were not captured. This gap suggests that some early influences of bullying victimization on brain development might not be fully documented. Consequently, this study may not fully account for the onset of bullying victimization and may overlook brain changes that occur

before this age, potentially missing critical periods of brain development influenced by earlier victimization experiences. Future studies should aim to incorporate more extensive longitudinal data, enabling a more comprehensive assessment of how bullying victimization influences brain development over a broader age range.

Although the questionnaire included items that could capture aspects of cyberbullying, such as the response "I was called mean names, made fun of, or teased in a hurtful way by a student/bully," we did not specifically measure cyberbullying. Given the increasing prominence of cyberbullying, this may have led to an underestimation of bullying victimization in our sample. Future research should incorporate dedicated cyberbullying questionnaires, such as those developed by Aricak and colleagues (59), to achieve a more comprehensive understanding of bullying victimization and its impact on brain development.

Conclusion

This study represents the largest three-time-point longitudinal MRI research on bullying victimization, offering valuable insights into brain development from adolescence through early adulthood. The research highlights associations between chronic bullying and brain architecture, aligning with existing studies and identifying novel brain changes linked to bullying. Additionally, it observes sex-specific differences in the relationship between bullying victimization and brain development, providing important insights for developing preventative strategies and therapeutic interventions tailored to individuals affected by bullying. As our understanding of how chronic stressors influence brain development continues to evolve, longitudinal MRI research on bullying victimization holds significant potential to advance mental health and neurodevelopmental science and to inform future policy-making and clinical practices.

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