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RESEARCH ARTICLE

Behavioral and neurostructural correlates of childhood physical violence victimization: Interaction with family functioning

Scott W. Delaney[1,2,3,4] | Andrea P. Cortes Hidalgo[2,5] | Tonya White[2,6] | Sebastien Haneuse[7] | Kerry J. Ressler[8] | Henning Tiemeier[1,2] | Laura D. Kubzansky[1,3]

[1]Department of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

[2]Department of Child and Adolescent Psychiatry, Erasmus University Medical Center, Rotterdam, The Netherlands

[3]Lee Kum Sheung Center for Health and Happiness, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

[4]Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

[5]The Generation R Study Group, Erasmus University Medical Center, Rotterdam, The Netherlands

[6]Department of Radiology and Nuclear Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands

[7]Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

[8]Department of Psychiatry, McLean Hospital, Harvard Medical School, Belmont, Massachusetts, USA

Correspondence
Scott W. Delaney, Department of Environmental Health, Harvard T.H. Chan School of Public Health, 665 Huntington Avenue, Building 1, Room 1301, Boston, MA 02115, USA.
Email: sdelaney@mail.harvard.edu

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Abstract

Violence victimization may cause child behavior problems and neurostructural differences associated with them. Healthy family environments may buffer these effects, but neural pathways explaining these associations remain inadequately understood. We used data from 3154 children ($\bar{x}_{age}$ = 10.1) to test whether healthy family functioning moderated possible associations between violence victimization, behavior problems, and amygdala volume (a threat-responsive brain region). Researchers collected data on childhood violence victimization, family functioning (McMaster Family Assessment Device, range 0–3, higher scores indicate healthier functioning), and behavior problems (Achenbach Child Behavior Checklist [CBCL] total problem score, range 0–117), and they scanned children with magnetic resonance imaging. We standardized amygdala volumes and fit confounder-adjusted models with "victimization × family functioning" interaction terms. Family functioning moderated associations between victimization, behavior problems, and amygdala volume. Among lower functioning families (functioning score = 1.0), victimization was associated with a 26.1 (95% confidence interval [CI]: 9.9, 42.4) unit higher CBCL behavior problem score, yet victimized children from higher functioning families (score = 3.0) exhibited no such association. Unexpectedly, victimization was associated with *higher* standardized amygdala volume among *lower* functioning families ($\hat{y}$ = 0.5; 95% CI: 0.1, 1.0) but *lower* volume among *higher* functioning families ($\hat{y}$ = −0.4; 95% CI: −0.7, −0.2). Thus,

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healthy family environments may mitigate some neurobehavioral effects of childhood victimization.

KEYWORDS
brain imaging, early experience, parental care, social, stress

1 | INTRODUCTION

Child behavior problems are associated with adverse outcomes later in life, including substance use disorder, suicide, and criminality (Bardone et al., 1998; Erskine et al., 2016; Wei et al., 2016). Physical violence victimization during childhood is associated with increased child behavior problems, particularly externalizing problems in boys and internalizing problems in girls (Lambert et al., 2021; Taylor et al., 2018). Prior research suggests that both supportive parenting relationships and healthy family functioning—that is, a family's ability to solve problems and support each other—may buffer the effects of violence on child behavior problems (Gorman-Smith et al., 2004; Ozer et al., 2017). However, neural pathways that may explain associations between violence victimization and behavior problems remain inadequately understood, as are neural pathways by which healthy family environments may buffer effects of violent experiences.

Prior research considering neural pathways relevant to these relations has focused on threat-responsive brain regions. In particular, several studies have investigated the amygdala because it is centrally involved in perceiving threatening stimuli, regulating the body's resulting stress hormone response, and in turn, generating a behavioral response to the stimuli (LeDoux, 2012; McLaughlin et al., 2019; Roozendaal et al., 2009). A number of these studies report that physically threatening experiences, including childhood violence victimization, are associated, on average, with lower preadolescent or adolescent amygdala structural volume between the ages of 6 and 17 (Delaney et al., 2021; Hanson et al., 2015; McLaughlin et al., 2016; Saxbe et al., 2018; Weissman et al., 2020). Other studies, however, found no such associations with participants in the same age range (Gold et al., 2016; King et al., 2019; Marusak et al., 2015; van Rooij et al., 2020). These conflicting findings may be due, in part, to an incomplete understanding of the cellular mechanisms that may underlie these findings. The neuronal effects of violence victimization—and of the biological stress response it may generate—on the amygdala are likely complex, heterogeneous, and sensitive to the presence or absence of stress-buffering resources (McEwen, 2012; McEwen et al., 2015; Roozendaal et al., 2009).

Early evidence suggests that a healthy family environment may serve as one such stress-buffering resource. For example, research suggests the presence of a supportive caregiver may dampen a child's neurobiological stress response to threatening situations by serving as a safety signal or cue indicating attachment security (Callaghan & Tottenham, 2016; Callaghan et al., 2019; Gunnar & Hostinar, 2015). A healthy family environment may also enhance the child's capacity to regulate emotions when caregivers model cognitive control and problem-solving skills (Brody et al., 2019; Morris et al., 2007). Both processes may separately or jointly alter the effects of stress on amygdala phenotype. Thus, in related research, Whittle et al. (2017) report that positive parenting practices moderated effects of childhood neighborhood disadvantage on amygdala structure, and Brody et al. (2019) found that supportive parenting moderated effects of childhood poverty on amygdala function (Brody et al., 2019; Whittle et al., 2017). These studies suggest that positive parenting—as one facet of a healthy family environment—may buffer effects of childhood stressors on amygdala structure and function. Similar studies investigating these effects on brain regions beyond the amygdala that are involved in behavioral responses to stressful stimuli have similarly demonstrated buffering by positive parenting (Brody et al., 2017; Holmes et al., 2018; Rakesh, Cropley, et al., 2021, 2021). However, these prior studies largely focus on parenting practices rather than broader measures of overall family functioning that may capture different characteristics within a complex family ecology (Delaney et al., 2022). Thus, whether other facets of a healthy family environment—including family functioning—similarly buffer effects of childhood violence victimization remains understudied.

Investigating interaction between childhood violence victimization and the family environment is complicated by the fact that while the majority of violence to which children are exposed is perpetrated by other children, some of it is perpetrated by parents in cases of physical abuse or child maltreatment (Finkelhor et al., 2015). In the latter cases, measures of the family environment may have a different interpretation than if the child were exposed to violence in the community. This challenge adds to limitations already inherent in most pediatric neuroimaging studies of childhood social exposures. For example, many such neuroimaging studies are limited by small, clinical samples of insufficient power to adequately assess statistical interaction. These samples can also differ widely on key sociodemographic characteristics—for example, parental education, income, occupation, and participant race/ethnicity (a proxy for racism exposure)—making cross-study comparisons difficult. In addition, many such studies incorporating behavioral outcomes rely upon a single reporter (usually the child's mother) for both exposure and outcome data, increasing the risk of common reporter method bias (Podsakoff et al., 2012).

Large population-based samples coupled with analytic methods from epidemiology may overcome many of these limitations. Population-based cohorts are more likely to include participants with a greater range in sociodemographic backgrounds and life experiences, including violence victimization not perpetrated by a parent.

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Moreover, such samples often enable multi-informant studies, in which one reporter provides exposure data, while a different reporter provides outcome data (Podsakoff et al., 2012).

Our study used data from the Generation R Study, a large, population-based birth cohort that has many of these characteristics, to explore whether a healthy family environment moderates relations between violence victimization, brain structure, and behavior problems. Study researchers collected data on preadolescent children's history of violence victimization (maternal report), family functioning (maternal report), and behavior problems (paternal and maternal report, separately). Researchers also scanned preadolescent children using magnetic resonance imaging (MRI). We hypothesized that childhood violence victimization (excluding parent-perpetrated child maltreatment or abuse) would be associated with (1) lower preadolescent amygdala volume and (2) more preadolescent behavior problems, and that (3) these associations would be attenuated when children had a positive family environment. Secondarily, we explored whether any association between violence victimization and higher behavior problems may be mediated by lower amygdala volume. We considered a spectrum of relevant potential confounders selected based on prior literature (Merikangas et al., 2017; Reiss, 2013; Tiesler & Heinrich, 2014; VanderWeele, 2019; Zhang et al., 2020). Because prior work has sometimes identified sex differences in similar associations, we also explored whether sex modified our associations of interest. Supporting Information S1 illustrates these hypothesized relations.

2 | MATERIALS AND METHODS

2.1 | Participants

We used data from the Generation R Study, a population-based birth cohort in Rotterdam, the Netherlands, seeking to identify factors affecting healthy child development (Kooijman et al., 2016). The study enrolled 9978 women during pregnancy or shortly after giving birth who were living in Rotterdam between 2002 and 2006. Researchers have collected data from children and their caregivers at multiple time points through the present after securing participants' informed consent. All consent forms and protocols were approved by the Medical Ethics Committee of Erasmus University Medical Center.

When children reached preadolescence (mean age: 10.1 years, range: 8.6–12.0), study scientists asked children's mothers whether their child had ever been victimized by violence, and children completed an MRI brain scan (Kooijman et al., 2016; White et al., 2018). Around the same time, mothers completed a postal questionnaire about their family's functioning, and both fathers and mothers separately completed a postal questionnaire about their child's behavior problems. This study included participants with violence victimization data and either child behavior data or a usable MRI scan. We excluded children exposed to cocaine or heroin in utero. When twins and triplets were enrolled, we excluded all but one randomly selected sibling to avoid potential problems with using correlated data ($n = 59$ removed). To maximize statistical power, we included participants in analyses of child behavior outcomes ($n = 3154$) or of amygdala volume ($n = 2905$) if they had relevant data on that particular outcome, even if they were missing data on the other one. Supporting Information S2.1 and S2.2 describe attrition from baseline and selection into our analytic samples, while Table 1 reports sociodemographic details of our analytic samples in further detail.

2.2 | Measures

2.2.1 | Violence victimization—Definition and validation

This study's measure of childhood violence victimization comes from an in-person interview of mothers that Generation R researchers designed using questions adapted from Kendler's Life Stress Interview and Brown and Harris' Life Event and Difficulty Schedule (White et al., 2018). When children reached preadolescence, trained Generation R study staff interviewed 5152 mothers about whether their child had ever experienced (yes/no) any of 24 stressful life events at any point in time during his or her childhood. Among these questions, researchers asked, "Has anyone ever used physical violence against your child, for example, beaten [him/her] up?" Importantly, interviewers were trained to clarify that the question was not meant to capture de minimis experiences of violence victimization, for example, rough play or playground skirmishes. Interviewers deemed responses from mothers unreliable if language barriers inhibited the mother's question comprehension. We excluded these participants ($n = 66$).

Of note, the interview did not ask about violence perpetrators. Understanding who perpetrated the violence is important because the buffering capacity of a healthy family environment may be less credible if parents victimized their children themselves. Additional data from Generation R provide evidence that our measure of non-parent-perpetrated violence victimization is valid and that parents were typically not the perpetrators of the violence against violence-exposed participants. These data, collected by Generation R researchers at different times in the participants' lives, include measures of exposure to harsh parenting tactics, corporal punishment, ongoing family conflict during childhood, and ongoing nonfamily conflict during childhood. Data on harsh parenting tactics were collected when participants were 3.0 years old from mothers and fathers separately using the Parent–Child Conflict Tactics Scale, a commonly used and well-validated instrument (Jansen et al., 2012; Straus et al., 1998). Later, when children were 8.1 years old, mothers answered survey questions from the Alabama Parenting Questionnaire, a valid and reliable measure of parenting practices (including corporal punishment), regarding how often either slapping or spanking "typically occurs in the home" (Essau et al., 2006; Shelton & Frick, 1996). Finally, in the same interview during preadolescence when Generation R researchers asked mothers about their child's violence victimization, the researchers also asked mothers separately about their child's lifetime exposure (yes/no) to ongoing conflict with (1) someone in the home or (2) someone outside the home.

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TABLE 1 Distribution of physical violence victimization and participant sociodemographic characteristics in primary analytic samples.

	Analytic sample			
	Amygdala volume		Behavior problems	
	Total	Violence exposed	Total	Violence exposed
	n (%)	*n* (%)	*n* (%)	*n* (%)
Total sample	2905 (100.0)	201 (6.9)	3154 (100.0)	190 (6.0)
Sex				
Female	1472 (51.0)	61 (4.2)	1607 (51.0)	56 (3.5)
Male	1433 (49.0)	140 (9.8)	1547 (49.0)	134 (8.7)
National origin/ethnicity				
European	1986 (69.6)	123 (6.2)	2541 (81.0)	149 (5.9)
Turkish	148 (5.2)	8 (5.4)	98 (3.1)	3 (3.1)
Moroccan	126 (4.4)	8 (6.4)	66 (2.1)	6 (9.1)
Surinamese	212 (7.4)	23 (10.9)	149 (4.8)	12 (8.1)
Other	381 (13.4)	31 (8.1)	283 (9.0)	20 (7.1)
Household education				
Less than high school	115 (4.2)	7 (6.1)	47 (1.6)	2 (4.3)
High school equivalent	946 (34.7)	87 (9.2)	867 (28.5)	70 (8.1)
More than high school	1665 (61.0)	91 (5.5)	2128 (70.0)	114 (5.4)
Household income				
€2200 per month or less	1441 (49.6)	125 (8.7)	1235 (39.0)	91 (7.4)
More than €2200 per month	1464 (50.4)	76 (5.2)	1919 (61.0)	99 (5.2)
Family functioning score, $\bar{x}(s)$	2.5 (0.5)	2.4 (0.4)	2.5 (0.4)	2.4 (0.5)
Family functioning score ≤2.0	339 (11.7)	28 (13.9)	344 (10.9)	32 (16.8)

Note: This table is based on observed values for each characteristic and does not account for missing data. Family functioning scores range from 0 to 3. Supporting Information S2.3 details additional family functioning scores and outcome measures by participant sociodemographic characteristics.

Supporting Information S3.1 and S3.2 include more details about these measures and when they were collected.

If parents were the primary perpetrators of violence against victimized children, one might expect the following when comparing victimized versus nonvictimized children: (1) harsh parenting and corporal punishment scores would be higher and (2) the odds ratio for having family conflict would be higher than for nonfamily conflict. We used two-sample *t*-tests to compare levels of harsh parenting and corporal punishment between violence-exposed versus violence-unexposed children. Mean maternal harsh parenting scores were similar: $\bar{x}_{\text{exposed}} = 0.51$ ($s = 0.04$), $\bar{x}_{\text{unexposed}} = 0.49$ ($s = 0.01$), $t = -0.66$, $p = .51$. Paternal harsh parenting and corporal punishment scores were similarly indistinguishable between violence-exposed versus violence-unexposed children (Supporting Information S2.4).

We also compared the odds of experiencing ongoing family conflict and ongoing nonfamily conflict among violence-exposed versus violence-unexposed children by directly calculating odds ratios from 2 × 2 tables of the number of violence-exposed and violence-unexposed participants reporting exposure to each type of conflict. The odds ratio for mothers reporting that their child experienced ongoing conflict *within* the family was substantially *lower* for victimized versus nonvictimized children than was the odds ratio of experiencing conflict with someone *outside* the family (Supporting Information S2.4). Taken together, our findings suggest our violence victimization measure does not primarily capture instances in which parents hit or shook their children, and that exposure to conflict with someone *outside* the family was more frequent than with someone *inside* the family for violence-exposed versus violence-unexposed children. These analyses suggest that parents were typically not the perpetrators of the violence captured by our primary measure of violence victimization.

2.2.2 | Family functioning

When children were mean 9.7 years old (range: 8.7–12.0), mothers completed via postal questionnaire the McMaster Family Assessment Device, General Functioning Subscale (Byles et al., 1988; Epstein et al., 1983; Wenniger et al., 1993). This is a 12-item self-report survey of established reliability and validity in Dutch and several other populations, in which mothers respond on a 4-point Likert scale to six positively framed and six negatively framed items (Boterhoven de Haan et al., 2015; Byles et al., 1988; Epstein et al., 1983; Wenniger et al., 1993). Representative questions include, "If there are problems, we can count on each other for support," and, "There are a lot of

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unpleasant and painful feelings in our family." We averaged responses to all items, reverse scoring where necessary, to derive a continuous family functioning score (range: 0–3, higher scores indicate better functioning). Cronbach's alpha in the analytic sample was strong (.90). We also constructed a binary family functioning measure (< or ≥2.0) drawing on a priori considerations of the scale's response options for use in a sensitivity analysis.

2.2.3 | Neuroimaging

Generation R researchers have previously described preadolescent MRI protocols (White et al., 2018). All scans were acquired on a 3T GE Discovery 750w scanner using a T_1-weighted sequence with 1 mm isotropic resolution. Researchers processed resulting images using FreeSurfer v6.0.0, which estimated left and right amygdala volumes (mm^3) and total intracranial volume for each participant. Study researchers visually inspected both FreeSurfer reconstructions and amygdala segmentations, and they removed poor-quality images. Thereafter, we excluded participants with left or right volumes over 4 standard deviations from the sample mean because such outlying values are either biological implausible or represent pathology or structural abnormality ($n = 21$ excluded). We summed hemisphere-specific volumes and then standardized them in our analytic sample.

2.2.4 | Child behavior problems

When participants were mean age 9.7 years (range: 8.6—12.4), fathers and mothers completed via postal questionnaire the Achenbach Child Behavior Checklist (CBCL/6-18), which asks how often children engage in 119 problematic behaviors on a 3-point frequency scale (Achenbach & Rescorla, 2001; Verhulst et al., 1988). Prior work demonstrates the items reliably load onto two broad subscales measuring externalizing and internalizing behaviors (Achenbach & Rescorla, 2001). We summed responses to create continuous scores for total behavior problems (119 items, possible range: 0—238), internalizing behavior problems (32 items, possible range: 0—64), and externalizing behavior problems (35 items, possible range: 0—70). Cronbach's alpha in our analytic sample was strong for all CBCL measures: total problems, .94; internalizing, .83; and externalizing, .88. We used paternal-report CBCL scores in our primary analyses to minimize the threat of common reporter method bias, but we also used maternal-report scores in sensitivity analyses.

2.2.5 | Covariates

Researchers retrieved sex from birth records along with birthdates, which we used to calculate age at MRI scan. Parents self-reported their national origin and ethnicity, used to categorize child "ethnicity" as European (non-Turkish), Turkish, Moroccan, Surinamese, and Other Ethnicity; household income during pregnancy (< or ≥€2200 per month); highest completed parental education level (less than high school equivalent; high school or intermediate vocational training; postsecondary or higher); parental history of psychosis (yes/no for each parent); maternal age at childbirth; maternal smoking during pregnancy (never; until pregnancy known; throughout pregnancy); and parental prenatal psychopathology symptoms (continuous sum scores for each parent from the 53-item Brief Symptom Inventory) (Derogatis & Melisaratos, 1983).

2.3 | Missing data

We imputed missing CBCL, family functioning, and covariate items (but not amygdala volume) using multiple imputation via chained equations to construct 50 imputed datasets, combining them using Rubin's Rules (Rubin, 1996). Supporting Information S4.1 details missing data and imputation models. To address possible bias from differences in sample composition for behavior, amygdala volume, and mediation models (described below), we used inverse probability of attrition weights (IPWs) in all analyses. When calculating the IPWs, we considered as lost to follow-up any participant enrolled at the Generation R baseline but excluded from the relevant analytic sample for any reason. Supporting Information S4.2 details IPW construction.

2.4 | Statistical analyses

To assess the association between violence victimization and paternal-report total behavior problems, we fit inverse probability (IP)-weighted, minimally adjusted ordinary least squares-estimated linear regression models adjusting for child age, sex, and ethnicity, and fully adjusted models incorporating all remaining covariates listed above. We also assessed whether the continuous family functioning score modifies those relations by fitting separate fully adjusted models including a violence victimization × family functioning interaction term. We used results from these models to calculate predicted effects of violence victimization at selected family functioning scores, which can aid interpretation of the model results. Next, we repeated this modeling strategy to assess relations with amygdala volume (in place of total behavior problems), except that all models of amygdala volume additionally adjusted for total intracranial volume (O'Brien et al., 2011).

In secondary analyses, we tested associations and moderation between violence victimization and paternal-report externalizing and internalizing behavior subscale scores using the same modeling strategy. We also repeated all behavioral analyses using maternal-report CBCL scores. Next, we considered potential effect modification by sex of relationships between violence victimization and our two primary outcomes, amygdala volume and total behavior problems. Finally, to explore whether amygdala volume may mediate the association between violence victimization and total problem behaviors, we used IP-weighted, fully adjusted bootstrapped regression models to estimate (1) the total effect of violence victimization on total behavior problems; (2) the direct (unmediated) effect; and (3) the indirect effect,

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that is, the effect explained by differences in amygdala volume (Valeri & VanderWeele, 2013). In a post hoc sensitivity analysis, we stratified these mediation models by binary (high/low) family functioning score to assess whether estimated indirect effects differed among high- versus low-functioning families. Supporting Information S4.3 describes these models further.

After modeling our data, we interpreted our results in a manner consistent with guidance provided by the American Statistical Association based on effect magnitudes, effect directions, and 95% confidence intervals (CIs) in lieu of binary indicators of statistical significance, though we provide *p*-values as an interpretive heuristic (Wasserstein & Lazar, 2016). For primary models, which assess four hypotheses (i.e., two related hypotheses for each of two outcomes, CBCL total problem score and amygdala volume), we do not adjust these *p*-values for multiple comparisons. We adopt the same approach for our two secondary outcomes (CBCL externalizing and CBCL internalizing scores).

3 | RESULTS

3.1 | Analytic sample characteristics

Analytic samples differed from the baseline cohort. In our analytic sample examining behavior problems, included versus excluded participants were more likely to be of European origin (81% vs. 51%), from higher versus lower income households (61% vs. 26%), and from higher versus lower educated parents (67% vs. 33%). Differences were similar (albeit of smaller magnitude) in the analytic sample examining amygdala volume. Supporting Information S2.2 provides more details.

Of 3154 participants in the analytic sample examining behavior problems, mothers reported 190 children exposed to violence (Table 1). Boys were more likely than girls to have been exposed (8.7% vs. 3.5%), as were children from lower versus higher educated parents (7.9% vs. 5.4%). We found similar patterns of exposure in our analytic sample examining amygdala volume (Table 1). In both analytic samples, family functioning scores were high (mean: 2.5, range: 0–3) and left skewed, that is, 89% of participants had scores of 2.0 or higher (Supporting Information S2.3).

3.2 | Violence victimization and behavior problems

In a fully adjusted model, violence victimization was associated with a 9.7 (95% CI: 3.9, 15.6) unit increase, on average, in total behavior problem score (Table 2; Supporting Information S5.1 reports minimally adjusted model results). For reference, this can be compared to the overall mean total behavior problem score in our sample, which was 17.3 (Supporting Information S2.3). As illustrated in Figure 1, Table 2, and Supporting Information S5.5, adding an interaction term to this model suggested family functioning (continuous score, range: 0–3) modified the association between violence victimization and total behavior problems. Specifically, victimization among the lowest functioning families (functioning score = 0) was associated with a 39.3 (95% CI: 12.6, 65.9) unit increase in total behavior problem score. However, this estimate decreased at a rate of 13.1 (95% CI: −23.8, −2.5) units per 1-unit increase in family functioning score, such that victimization among the highest functioning families (functioning score = 3) was not associated with any difference in total behavior problems (predicted effect = −0.16 units, 95% CI: −7.7, 7.4). Results using maternal-report CBCL scores were very similar and evinced the same overall pattern of interaction. See Supporting Information S5.2.

In secondary analyses, violence victimization was associated with higher scores for both internalizing ($\beta = 2.5$; 95% CI: 0.9, 4.0) and externalizing ($\beta = 2.9$; 95% CI: 0.8, 5.0) problems in fully adjusted models (Table 3). Adding a "victimization × family functioning score" interaction term to these models suggested family functioning modified the association between victimization and both externalizing behaviors ($\beta_{\text{victimization}} = 14.3$; 95% CI: 4.1, 24.4; $\beta_{\text{interaction}} = -5.1$; 95% CI: −9.1, −1.1) and internalizing behaviors ($\beta_{\text{victimization}} = 7.3$; 95% CI: −0.2, 14.8; $\beta_{\text{interaction}} = -2.2$; 95% CI: −5.1, −0.8), though evidence for associations with internalizing behaviors was weaker. See Table 3, Figure 2, and Supporting Information S5.6 for predicted effects of violence victimization at selected levels of family functioning. Finally, we found no evidence of effect modification by sex for any associations reported above.

3.3 | Violence victimization and amygdala volume

In a fully adjusted model, we found only some evidence suggesting a population-average association between violence victimization and lower standardized amygdala volume: $\beta = -0.10$ (95% CI: −0.24, 0.05). See Table 2. However, as Figure 3 and Supporting Information S5.7 illustrate, adding an interaction term to this model suggested family functioning modified the association between violence victimization and amygdala volume: $\beta_{\text{victimization}} = 1.0$ (95% CI: 0.3, 1.7), $\beta_{\text{interaction}} = -0.5$ (95% CI: −0.8, −0.2). In fact, violence-exposed (vs. violence-unexposed) children from the *lowest* functioning families demonstrated *higher* amygdala volume, while violence-exposed children from the *highest* functioning families demonstrated *lower* amygdala volume (Figure 3 and Table 2). Again, we found no evidence of effect modification by sex for these associations. Supporting Information S5.3 reports minimally adjusted model results.

3.4 | Exploratory mediation analyses

Despite evidence of associations between violence victimization and both amygdala volume and behavior problems, fully adjusted mediation models provided no evidence that amygdala volume lies on a mechanistic pathway between violence victimization and total behavior problems. Specifically, these models estimated the indirect effect, that is, the portion of the association between victimization and total behavior problems explained by differences in amygdala volume was essentially zero: $\beta_{\text{indirect effect}} = 0.1$ (95% CI: −0.3, 0.4). Findings were similar in models stratified by family functioning score (< or ≥2.0). Supporting Information S5.4 includes additional results.

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TABLE 2 Main effects and interaction estimates of the associations between childhood physical violence victimization and two outcomes in preadolescence: Standardized amygdala volume and total behavior problem score.

	Standardized amygdala volume			Paternal-report total behavior problem score		
	β	95% CI	*p*	*β*	95% CI	*p*
Main effect (no interaction)						
Violence victimization	−0.10	(−0.24, 0.05)	.18	9.71	(3.86, 15.55)	<.01
Interaction model						
Violence victimization	1.01	(0.30, 1.73)	<.01	39.27	(12.63, 65.92)	<.01
Violence victimization × Functioning	−0.48	(−0.78, −0.17)	<.01	−13.14	(−23.80, −2.49)	.02
Predicted effects of violence victimization at selected family functioning scores[a]						
Family functioning score	Est.	95% CI	*p*	Est.	95% CI	*p*
0.0 (lowest functioning)	1.01	(0.30, 1.73)	<.01	39.27	(12.63, 65.92)	<.01
1.0	0.54	(0.11, 0.96)	.01	26.13	(9.85, 42.42)	<.01
2.0	0.06	(−0.11, 0.22)	.49	12.99	(6.10, 19.88)	<.01
3.0 (highest functioning)	−0.42	(−0.67, −0.17)	<.01	−0.16	(−7.68, 7.37)	.97

Note: Main effect (no interaction) model beta coefficients are from fully adjusted models that do not additionally adjust for family functioning score. Interaction model beta coefficients are from fully adjusted models that include a main effect for continuous family functioning score as well as a "violence victimization × continuous family functioning score" interaction term. Models are fully adjusted and include covariates for child age at outcome assessment, sex, ethnicity, and in utero smoking exposure; parental highest household education, household income, history of psychosis, and psychopathology symptoms; and maternal age at child's birth. Amygdala volume models are additionally adjusted for intracranial volume. All estimates are weighted to reflect differential attrition from the baseline sample to the analysis samples; unweighted *n* for total behavior problems = 3154; unweighted *n* for amygdala volume = 2905. The continuous family functioning measure has a range of 0–3. Total behavior problems are measured by the paternal-report Achenbach Child Behavior Checklist (CBCL) total behavior problem score (range in sample 0–117). Results from models using maternal-report CBCL scores appear in Supporting Information S5.2. Amygdala volume is assessed as the standardized bilateral sum for each participant.

[a]These predicted effects—sometimes called "predicted marginal effects"—are derived from beta estimates from fully adjusted interaction models. They are the predicted "marginal effects" of physical violence experience on the given outcomes at selected family functioning scores. We present them here to aid interpretation of our interaction models.

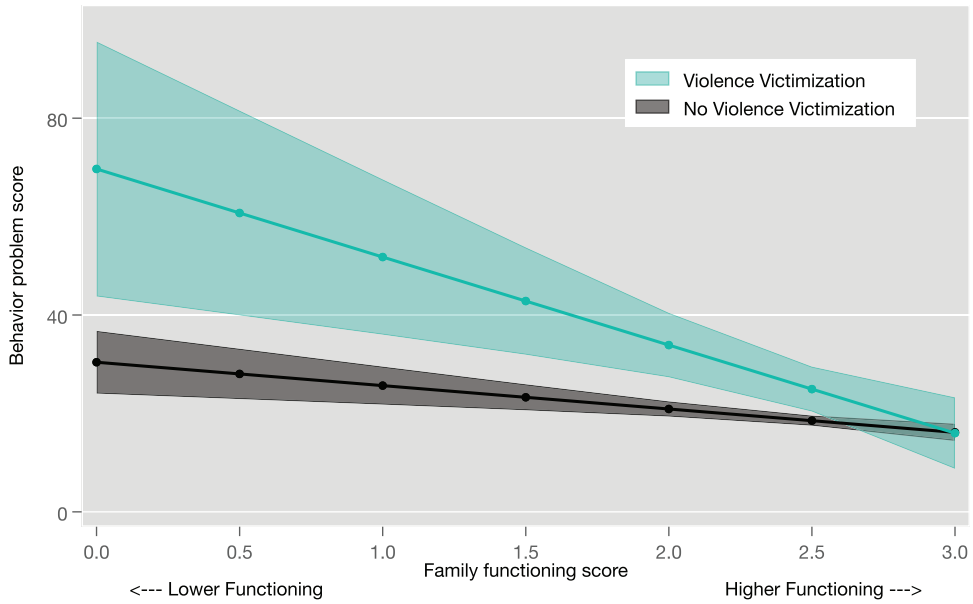

FIGURE 1 Estimated CBCL total behavior problem scores among both children exposed (i.e., victimized) and unexposed to physical violence victimization across the family functioning score range. Estimated values are from IP-weighted, fully adjusted models. Shaded regions are 95% confidence bands. CBCL, Child Behavior Checklist; IP, inverse probability.

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TABLE 3 Main effects and interaction estimates of the associations between childhood physical violence victimization and preadolescent behavior problem subtypes.

	Paternal-report externalizing behaviors			Paternal-report internalizing behaviors		
	β	95% CI	*p*	*β*	95% CI	*p*
Main effect (no interaction)						
Violence victimization	2.90	(0.83, 4.97)	.01	2.47	(0.92, 4.02)	<.01
Interaction model						
Violence victimization	14.31	(4.17, 24.44)	<.01	7.31	(−0.16, 14.78)	.06
Violence victimization × Functioning	−5.06	(−9.07, −1.05)	.01	−2.17	(−5.13, 0.78)	.15
Predicted effects of victimization at selected family functioning scores[a]						
	Externalizing behaviors			Internalizing behaviors		
Family functioning score	Est.	95% CI	*p*	Est.	95% CI	*p*
0.0 (lowest functioning)	14.31	(4.17, 24.44)	<.01	7.31	(−0.16, 14.78)	.06
1.0	9.25	(3.04, 15.46)	<.01	5.14	(0.55, 9.72)	.03
2.0	4.19	(1.64, 6.74)	<.01	2.96	(1.02, 4.91)	<.01
3.0 (highest functioning)	−0.86	(−3.44, 1.72)	.51	0.79	(−1.21, 2.80)	.44

Note: Main effect (no interaction) model beta coefficients are from fully adjusted models that do not additionally adjust for family functioning score. Interaction model beta coefficients are from fully adjusted models that include a main effect for continuous family functioning score as well as a "violence victimization × continuous family functioning score" interaction term. Models are fully adjusted and include covariates for child age at outcome assessment, sex, ethnicity, and in utero smoking exposure; parental highest household education, household income, history of psychosis, and psychopathology symptoms; and maternal age at child's birth. All estimates are weighted to reflect differential attrition from the baseline sample to the analysis samples; unweighted $n = 3154$. The continuous family functioning measure has a range of 0–3. Externalizing and internalizing behavior problems are measured by the paternal-report Achenbach Child Behavior Checklist; externalizing score range in sample was 0–48; internalizing score range in sample was 0–36.

[a]These predicted effects—sometimes called "predicted marginal effects"—are derived from beta estimates from fully adjusted interaction models. They are the predicted "marginal" effects of violence victimization on the given outcomes at selected family functioning scores. We present them here to aid interpretation of our interaction models.

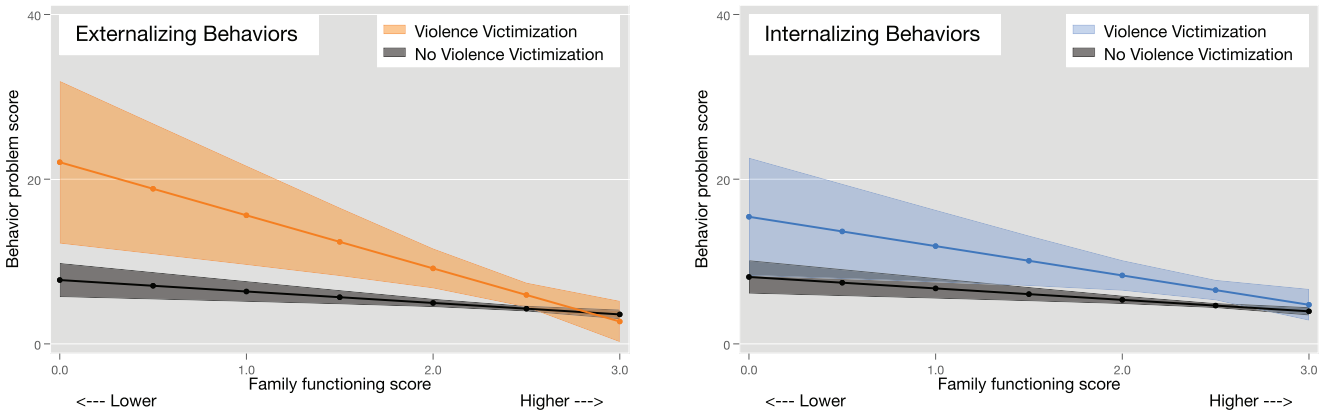

FIGURE 2 Estimated CBCL externalizing and internalizing behavior problem subscale scores among both children exposed (i.e., victimized) and unexposed to physical violence victimization across the family functioning score range. Estimated values are from IP-weighted, fully adjusted models. Shaded regions are 95% confidence bands. CBCL, Child Behavior Checklist; IP, inverse probability.

4 | DISCUSSION

Our study reports three main findings. First, violence victimization was associated with increased preadolescent behavior problems. Second, healthy family functioning modified the relationship between violence victimization and behavior problems. Third, healthy family functioning also modified the relationship between violence victimization and preadolescent amygdala volume. Specifically, violence victimization was associated with differences in amygdala volume, but the direction of those differences depended on the family environment and was not uniform for all exposed participants.

On *average*, our findings suggest that violence victimization may be associated with lower amygdala volume, though the main effect did not reach statistical significance at the $\alpha = .05$ level. However, this

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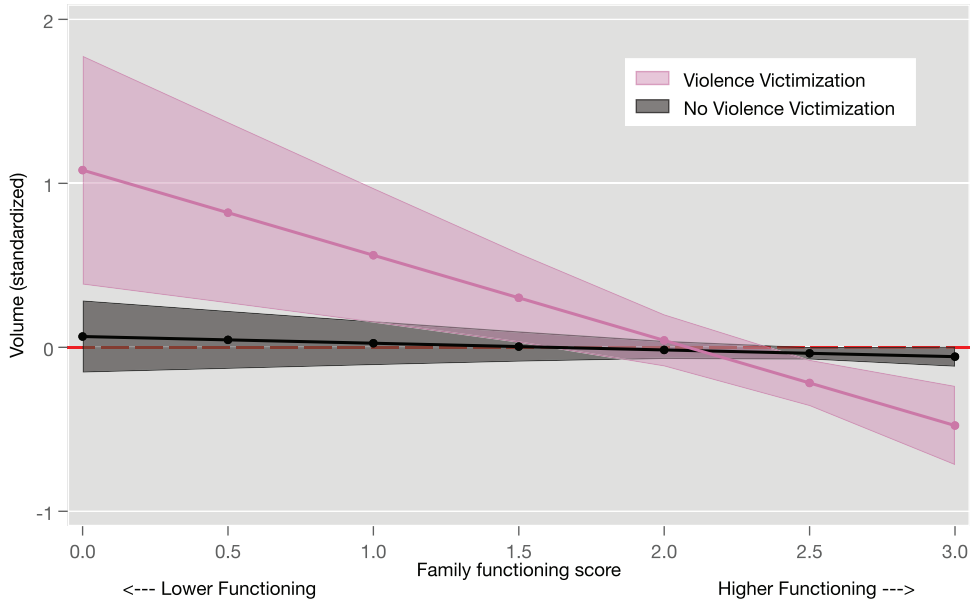

FIGURE 3 Estimated standardized amygdala volumes among both children exposed (i.e., victimized) and unexposed to physical violence victimization across the family functioning score range. Amygdala volume is standardized within the analytic sample: overall mean = 0.0, standard deviation = 1.0. Estimated values are from IP-weighted, fully adjusted models that are also adjusted for total intracranial volume. Shaded regions are 95% confidence bands. IP, inverse probability.

relation was not uniform across levels of family functioning. Rather, violence victimization was associated with *higher* amygdala volume among *lower* functioning families but *lower* volume among *higher* functioning families, and this interaction was statistically significant. Because more violence-exposed participants in our sample came from higher than from lower functioning families, the *average* effect of violence victimization on amygdala volume was negative, that is, suggestive of lower volume. Thus, the effect of violence victimization on preadolescent amygdala volume may depend on the presence or absence of stress-buffering contextual factors, and healthy versus unhealthy family environments may signal critically different contexts.

Our results are partially consistent with models of stressful experiences from prior literature that posit different neurobiological consequences depending on the severity and duration of stressor exposure. For example, Sapolsky (2015) and McEwen et al. (2015) suggest mild-to-moderate stress induces adaptive, possibly beneficial brain changes, while severe stress induces maladaptive, deleterious changes (McEwen et al., 2015; Sapolsky, 2015). Similarly, Shonkoff et al. (2009) differentiate "tolerable stress" (potentially deleterious stress buffered by supportive relationships) from "toxic stress" (extended exposure to unbuffered stressors), the latter of which they argue disrupts healthy brain development (Shonkoff et al., 2009). Applied here, violence victimization buffered by a healthy family environment may cause "tolerable" stress leading to decreased amygdala volume, while unbuffered violence exposure may cause "toxic" stress leading to increased amygdala volume. This is also consistent with findings from rodent models in which chronic stress causes increased dendritic spine density and arborization in the basolateral amygdala subregion, which may explain the increase in overall amygdala volume associated with unbuffered violence exposure (Mitra et al., 2005; Vyas et al., 2002).

At the same time, our results are also partially inconsistent with these models and with prior research reporting associations between child behavior problems and both lower and higher amygdala volume. Prior work has not clearly shown that lower amygdala volume is associated with "tolerable" stress and marks an adaptive response, or that higher amygdala volume is associated with "toxic" stress and marks a maladaptive response (Jones et al., 2019; Pardini et al., 2014; Rogers & De Brito, 2016; Schiffer et al., 2011; Thijssen et al., 2015). Moreover, we are aware of no research suggesting cellular mechanisms whereby "tolerable" stress would lead to lower amygdala volume. And insofar as rodent research suggests possible cellular mechanisms linking chronic or "toxic" stress to higher amygdala volume, such findings have generally not been replicated in humans. Instead, most neuroimaging studies in humans report violence victimization is associated with lower amygdala volume, but they do not assess buffering factors and thus do not differentiate between experiences of possible "tolerable" versus "toxic" stress (Delaney et al., 2021; McLaughlin et al., 2019; van Rooij et al., 2020). These studies also report mean estimates only and generally do not posit cellular mechanisms.

Notably, we found no evidence suggesting effects differed by sex. Prior studies suggest some sex-specific differences in behavioral and neurodevelopmental effects of trauma exposure, child maltreatment, or early life stress (Helpman et al., 2017; Herringa et al., 2013; Rakesh et al., 2023; Rakesh, Kelly, et al., 2021). Our results may differ for multiple reasons. For example, our study focuses narrowly on experiences of violence victimization that most likely occurred outside the home, while many prior studies assess somewhat different measures of stress, neglect, or abuse. Violent experiences in our population-based sample in Rotterdam may also be less acute, on average, than those experienced by children in clinical samples that were analyzed in many other

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studies. Future studies may further explore sex differences in these relationships using population-based samples.

We also found no evidence that amygdala volume mediated the relation between violence victimization and behavior problems. The amygdala is central to threat response, but other brain regions are involved in this process, too. Because our analyses do not account for these other regions, our exploratory mediation models may be insufficient to explain neurobiological mechanisms relating victimization to behavior problems. It is also possible that victimization in our population-based sample was less acute than in prior studies using clinical samples.

Our findings have implications for research, clinical practice, and policy. For behavior studies, our results suggest a healthy family environment may buffer a substantial proportion of these effects. And for neurodevelopmental studies, our findings suggest childhood violence victimization may be associated with differing effects depending on the family environmental context within which the violence occurs. Future research should either recruit participants from a broader range of socioeconomic backgrounds or assess carefully whether selection into the study limits the generalizability of the study's results. Separately, our findings also underscore the importance of clinical practices and policies designed to strengthen family functioning, particularly for children directly exposed to violence. High-functioning family environments may buffer a substantial portion of the health effects of early life adversity.

Our study has some limitations. It is effectively cross-sectional. Reverse causation could account for our results if children with more behavior problems were more likely to induce exposure to violence. Mothers reported their child's exposure to violence retrospectively, which can lead to recall bias, and we were unable to account for victimization frequency, severity, or timing. Relatedly, we do not have data on who perpetrated the violence against victimized children. If parents perpetrated the violence, the buffering capacity of family functioning may be diminished, though the totality of the evidence suggests parents were generally not the perpetrators of violence against their children. Because parents completed the CBCL questionnaires prior to the in-person maternal interviews, it is possible that some mothers may have reported violence victimization that occurred after the parents completed their CBCL behavioral assessments. In this case, our models would underestimate the association of victimization (vs. no victimization) with the behavioral outcomes, and results would be biased toward null values. Models of amygdala volume are not vulnerable to this bias because Generation R researchers collected MRI scans on the same day that they interviewed mothers about their child's violence victimization. Separately, despite adjusting for several potential confounders using prospectively collected data, residual and unmeasured confounding could affect our results. Finally, socially patterned attrition from the study may have induced selection bias, though our use of IPWs for attrition should partially mitigate this concern.

Our study also has several important strengths. Our design used interview-based exposure data and questionnaire-based family functioning data from mothers, objective MRI outcome data, and behavioral outcome data from fathers. This lowers the risk of common reporter method bias that can arise when the same reporter provides both exposure and outcome data (Podsakoff et al., 2012). Even where we used data from the same reporter, for example, from mothers for violence exposure and family functioning, the data were collected using different methods, thereby reducing the risk that answers to one instrument influenced responses to the other. Our sample was relatively large, population-based, and relatively diverse in childhood experiences, and it included children from both low- and high-functioning families. This increases the generalizability of the findings. Finally, the size of our sample increased our statistical power relative to smaller studies, an important consideration when modeling interactions.

5 | CONCLUSION

In a large, population-based neuroimaging birth cohort, better preadolescent family functioning substantially buffered the association between childhood violence victimization and child behavior problems. Family functioning also altered the association between violence victimization and amygdala volume. In turn, our results suggest a healthy family environment may blunt deleterious neurodevelopmental consequences of childhood violence victimization. Future studies of both brain development and behavior should consider interaction with social environmental exposures, and they should emphasize recruiting participants from a wider spectrum of childhood backgrounds and life experiences.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data subject to third party restrictions. Generation R data that support the findings of this study are available from Erasmus University Medical Center and the Principal Investigators of the Generation R Study. Restrictions apply to the availability of these data, which were used under license for this study. Data may be available from Dr. Henning Tiemeier with the permission of Erasmus University Medical Center investigators.

ORCID

Scott W. Delaney https://orcid.org/0000-0002-0813-018X

REFERENCES

Achenbach, T., & Rescorla, L. (2001). *Manual for the ASEBA school-age forms and profiles*. University of Vermont, Research Center for Children, Youth & Families.

Bardone, A. M., Moffitt, T. E., Caspi, A., Dickson, N., Stanton, W. R., & Silva, P. A. (1998). Adult physical health outcomes of adolescent girls with conduct disorder, depression, and anxiety. *Journal of the American Academy of Child & Adolescent Psychiatry*, *37*(6), 594–601. https://doi.org/10.1097/00004583-199806000-00009

Boterhoven de Haan, K. L., Hafekost, J., Lawrence, D., Sawyer, M. G., & Zubrick, S. R. (2015). Reliability and validity of a short version of the general functioning subscale of the McMaster Family Assessment Device. *Family Process*, *54*(1), 116–123. https://doi.org/10.1111/famp.12113

Brody, G. H., Gray, J. C., Yu, T., Barton, A. W., Beach, S. R. H., Galván, A., MacKillop, J., Windle, M., Chen, E., Miller, G. E., & Sweet, L. H. (2017). Protective prevention effects on the association of poverty with brain development. *JAMA Pediatrics*, *171*(1), 46–52. https://doi.org/10.1001/jamapediatrics.2016.2988

Brody, G. H., Yu, T., Nusslock, R., Barton, A. W., Miller, G. E., Chen, E., Holmes, C., McCormick, M., & Sweet, L. H. (2019). The protective effects of supportive parenting on the relationship between adolescent poverty and resting-state functional brain connectivity during adulthood. *Psychological Science*, *30*(7), 1040–1049. https://doi.org/10.1177/0956797619847989

Byles, J., Byrne, C., Boyle, M. H., & Offord, D. R. (1988). Ontario Child Health Study: Reliability and validity of the general functioning subscale of the McMaster Family Assessment Device. *Family Process*, *27*(1), 97–104. https://doi.org/10.1111/j.1545-5300.1988.00097.x

Callaghan, B., Gee, D. G., Gabard-Durnam, L., Telzer, E. H., Humphreys, K. L., Goff, B., Shapiro, M., Flannery, J., Lumian, D. S., Fareri, D. S., Caldera, C., & Tottenham, N. (2019). Decreased amygdala reactivity to parent cues protects against anxiety following early adversity: An examination across 3-years. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *4*(7), 664–671. https://doi.org/10.1016/j.bpsc.2019.02.001

Callaghan, B. L., & Tottenham, N. (2016). The neuro-environmental loop of plasticity: A cross-species analysis of parental effects on emotion circuitry development following typical and adverse caregiving. *Neuropsychopharmacology*, *41*(1), 163–176. https://doi.org/10.1038/npp.2015.204

Delaney, S. W., Cortes Hidalgo, A. P., White, T., Haneuse, S., Ressler, K. J., Tiemeier, H., & Kubzansky, L. D. (2021). Are all threats equal? Associations of childhood exposure to physical attack versus threatened violence with preadolescent brain structure. *Developmental Cognitive Neuroscience*, *52*, 101033. https://doi.org/10.1016/j.dcn.2021.101033

Delaney, S. W., Xerxa, Y., Muetzel, R. L., White, T., Haneuse, S., Ressler, K. J., Tiemeier, H., & Kubzansky, L. D. (2022). Long-term associations between early-life family functioning and preadolescent white matter microstructure. *Psychological Medicine*, *1–11–*. https://doi.org/10.1017/S0033291722001404

Derogatis, L. R., & Melisaratos, N. (1983). The Brief Symptom Inventory: An introductory report. *Psychological Medicine*, *13*(3), 595–605.

Epstein, N. B., Baldwin, L. M., & Bishop, D. S. (1983). The McMaster Family Assessment Device. *Journal of Marital and Family Therapy*, *9*(2), 171–180. https://doi.org/10.1111/j.1752-0606.1983.tb01497.x

Erskine, H. E., Norman, R. E., Ferrari, A. J., Chan, G. C. K., Copeland, W. E., Whiteford, H. A., & Scott, J. G. (2016). Long-term outcomes of attention-deficit/hyperactivity disorder and conduct disorder: A systematic review and meta-analysis. *Journal of the American Academy of Child & Adolescent Psychiatry*, *55*(10), 841–850. https://doi.org/10.1016/j.jaac.2016.06.016

Essau, C. A., Sasagawa, S., & Frick, P. J. (2006). Psychometric properties of the Alabama parenting questionnaire. *Journal of Child and Family Studies*, *15*(5), 595–614. https://doi.org/10.1007/s10826-006-9036-y

Finkelhor, D., Turner, H. A., Shattuck, A., & Hamby, S. L. (2015). Prevalence of childhood exposure to violence, crime, and abuse: Results from the national survey of children's exposure to violence. *JAMA Pediatrics*, *169*(8), 746–754. https://doi.org/10.1001/jamapediatrics.2015.0676

Gold, A. L., Sheridan, M. A., Peverill, M., Busso, D. S., Lambert, H. K., Alves, S., Pine, D. S., & McLaughlin, K. A. (2016). Childhood abuse and reduced cortical thickness in brain regions involved in emotional processing. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *57*(10), 1154–1164. https://doi.org/10.1111/jcpp.12630

Gorman-Smith, D., Henry, D. B., & Tolan, P. H. (2004). Exposure to community violence and violence perpetration: The protective effects of family functioning. *Journal of Clinical Child & Adolescent Psychology*, *33*(3), 439–449. https://doi.org/10.1207/s15374424jccp3303_2

Gunnar, M. R., & Hostinar, C. E. (2015). The social buffering of the hypothalamic–pituitary–adrenocortical axis in humans: Developmental and experiential determinants. *Social Neuroscience*, *10*(5), 479–488. https://doi.org/10.1080/17470919.2015.1070747

Hanson, J. L., Nacewicz, B. M., Sutterer, M. J., Cayo, A. A., Schaefer, S. M., Rudolph, K. D., Shirtcliff, E. A., Pollak, S. D., & Davidson, R. J. (2015). Behavioral problems after early life stress: Contributions of the hippocampus and amygdala. *Biological Psychiatry*, *77*(4), 314–323. https://doi.org/10.1016/j.biopsych.2014.04.020

Helpman, L., Zhu, X., Suarez-Jimenez, B., Lazarov, A., Monk, C., & Neria, Y. (2017). Sex differences in trauma-related psychopathology: A critical review of neuroimaging literature (2014-2017). *Current Psychiatry Reports*, *19*(12), 104. https://doi.org/10.1007/s11920-017-0854-y

Herringa, R. J., Birn, R. M., Ruttle, P. L., Burghy, C. A., Stodola, D. E., Davidson, R. J., & Essex, M. J. (2013). Childhood maltreatment is associated with altered fear circuitry and increased internalizing symptoms by late adolescence. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(47), 19119–19124. https://doi.org/10.1073/pnas.1310766110

Holmes, C. J., Barton, A. W., MacKillop, J., Galván, A., Owens, M. M., McCormick, M. J., Yu, T., Beach, S. R. H., Brody, G. H., & Sweet, L. H. (2018). Parenting and salience network connectivity among African Americans: A protective pathway for health-risk behaviors. *Biological Psychiatry*, *84*(5), 365–371. https://doi.org/10.1016/j.biopsych.2018.03.003

Jansen, P. W., Raat, H., Mackenbach, J. P., Hofman, A., Jaddoe, V. W. V., Bakermans-Kranenburg, M. J., IJzendoorn, M. H. V., Verhulst, F. C., & Tiemeier, H. (2012). Early determinants of maternal and paternal harsh discipline: The Generation R Study. *Family Relations*, *61*(2), 253–270. https://doi.org/10.1111/j.1741-3729.2011.00691.x

Jones, S. L., Dufoix, R., Laplante, D. P., Elgbeili, G., Patel, R., Chakravarty, M. M., King, S., & Pruessner, J. C. (2019). Larger amygdala volume mediates the association between prenatal maternal stress and higher levels of externalizing behaviors: Sex specific effects in project ice storm. *Frontiers in Human Neuroscience*, *13*, 144. https://doi.org/10.3389/fnhum.2019.00144

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King, L. S., Humphreys, K. L., Camacho, M. C., & Gotlib, I. H. (2019). A person-centered approach to the assessment of early life stress: Associations with the volume of stress-sensitive brain regions in early adolescence. *Development and Psychopathology*, *31*(2), 643–655. https://doi.org/10.1017/S0954579418000184

Kooijman, M. N., Kruithof, C. J., van Duijn, C. M., Duijts, L., Franco, O. H., van IJzendoorn, M. H., de Jongste, J. C., Klaver, C. C. W., van der Lugt, A., Mackenbach, J. P., Moll, H. A., Peeters, R. P., Raat, H., Rings, E. H. H. M., Rivadeneira, F., van der Schroeff, M. P., Steegers, E. A. P., Tiemeier, H., Uitterlinden, A. G., … Jaddoe, V. W. V. (2016). The Generation R Study: Design and cohort update 2017. *European Journal of Epidemiology*, *31*(12), 1243–1264. https://doi.org/10.1007/s10654-016-0224-9

Lambert, S. F., Tache, R. M., Liu, S. R., Nylund-Gibson, K., & Ialongo, N. S. (2021). Individual differences in patterns of community violence exposure and internalizing and externalizing behaviors. *Journal of Interpersonal Violence*, *36*(19–20), 9484–9506. https://doi.org/10.1177/0886260519867148

LeDoux, J. (2012). Rethinking the emotional brain. *Neuron*, *73*(4), 653–676. https://doi.org/10.1016/j.neuron.2012.02.004

Marusak, H. A., Furman, D. J., Kuruvadi, N., Shattuck, D. W., Joshi, S. H., Joshi, A. A., Etkin, A., & Thomason, M. E. (2015). Amygdala responses to salient social cues vary with oxytocin receptor genotype in youth. *Neuropsychologia*, *79*(Pt. A), 1–9. https://doi.org/10.1016/j.neuropsychologia.2015.10.015

McEwen, B. S. (2012). Brain on stress: How the social environment gets under the skin. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(Supplement 2), 17180–17185. https://doi.org/10.1073/pnas.1121254109

McEwen, B. S., Bowles, N. P., Gray, J. D., Hill, M. N., Hunter, R. G., Karatsoreos, I. N., & Nasca, C. (2015). Mechanisms of stress in the brain. *Nature Neuroscience*, *18*, 1353–1363. https://doi.org/10.1038/nn.4086

McLaughlin, K. A., Sheridan, M. A., Gold, A. L., Duys, A., Lambert, H. K., Peverill, M., Heleniak, C., Shechner, T., Wojcieszak, Z., & Pine, D. S. (2016). Maltreatment exposure, brain structure, and fear conditioning in children and adolescents. *Neuropsychopharmacology*, *41*(8), 1956–1964. https://doi.org/10.1038/npp.2015.365

McLaughlin, K. A., Weissman, D., & Bitrán, D. (2019). Childhood adversity and neural development: A systematic review. *Annual Review of Developmental Psychology*, *1*(1), 277–312. https://doi.org/10.1146/annurev-devpsych-121318-084950

Merikangas, A. K., Calkins, M. E., Bilker, W. B., Moore, T. M., Gur, R. C., & Gur, R. E. (2017). Parental age and offspring psychopathology in the Philadelphia Neurodevelopmental Cohort. *Journal of the American Academy of Child & Adolescent Psychiatry*, *56*(5), 391–400. https://doi.org/10.1016/j.jaac.2017.02.004

Mitra, R., Jadhav, S., McEwen, B. S., Vyas, A., & Chattarji, S. (2005). Stress duration modulates the spatiotemporal patterns of spine formation in the basolateral amygdala. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(26), 9371–9376. https://doi.org/10.1073/pnas.0504011102

Morris, A. S., Silk, J. S., Steinberg, L., Myers, S. S., & Robinson, L. R. (2007). The role of the family context in the development of emotion regulation. *Social Development*, *16*(2), 361–388. https://doi.org/10.1111/j.1467-9507.2007.00389.x

O'Brien, L. M., Ziegler, D. A., Deutsch, C. K., Frazier, J. A., Herbert, M. R., & Locascio, J. J. (2011). Statistical adjustments for brain size in volumetric neuroimaging studies: Some practical implications in methods. *Psychiatry Research*, *193*(2), 113–122. https://doi.org/10.1016/j.pscychresns.2011.01.007

Ozer, E. J., Lavi, I., Douglas, L., & Wolf, J. P. (2017). Protective factors for youth exposed to violence in their communities: A review of family, school, and community moderators. *Journal of Clinical Child & Adolescent Psychology*, *46*(3), 353–378. https://doi.org/10.1080/15374416.2015.1046178

Pardini, D. A., Raine, A., Erickson, K., & Loeber, R. (2014). Lower amygdala volume in men is associated with childhood aggression, early psychopathic traits, and future violence. *Biological Psychiatry*, *75*(1), 73–80. https://doi.org/10.1016/j.biopsych.2013.04.003

Podsakoff, P. M., MacKenzie, S. B., & Podsakoff, N. P. (2012). Sources of method bias in social science research and recommendations on how to control it. *Annual Review of Psychology*, *63*, 539–569. https://doi.org/10.1146/annurev-psych-120710-100452

Rakesh, D., Allen, N. B., & Whittle, S. (2023). Longitudinal changes in within-salience network functional connectivity mediate the relationship between childhood abuse and neglect, and mental health during adolescence. *Psychological Medicine*, *53*(4), 1552–1564. https://doi.org/10.1017/S0033291721003135

Rakesh, D., Cropley, V., Zalesky, A., Vijayakumar, N., Allen, N. B., & Whittle, S. (2021). Neighborhood disadvantage and longitudinal brain-predicted-age trajectory during adolescence. *Developmental Cognitive Neuroscience*, *51*, 101002. https://doi.org/10.1016/j.dcn.2021.101002

Rakesh, D., Kelly, C., Vijayakumar, N., Zalesky, A., Allen, N. B., & Whittle, S. (2021). Unraveling the consequences of childhood maltreatment: Deviations from typical functional neurodevelopment mediate the relationship between maltreatment history and depressive symptoms. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *6*(3), 329–342. https://doi.org/10.1016/j.bpsc.2020.09.016

Rakesh, D., Seguin, C., Zalesky, A., Cropley, V., & Whittle, S. (2021). Associations between neighborhood disadvantage, resting-state functional connectivity, and behavior in the adolescent brain cognitive development study: The moderating role of positive family and school environments. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *6*(9), 877–886. https://doi.org/10.1016/j.bpsc.2021.03.008

Reiss, F. (2013). Socioeconomic inequalities and mental health problems in children and adolescents: A systematic review. *Social Science & Medicine*, *90*, 24–31. https://doi.org/10.1016/j.socscimed.2013.04.026

Rogers, J. C., & De Brito, S. A. (2016). Cortical and subcortical gray matter volume in youths with conduct problems: A meta-analysis. *JAMA Psychiatry*, *73*(1), 64–72. https://doi.org/10.1001/jamapsychiatry.2015.2423

Roozendaal, B., McEwen, B. S., & Chattarji, S. (2009). Stress, memory and the amygdala. *Nature Reviews Neuroscience*, *10*(6), 423–433. https://doi.org/10.1038/nrn2651

Rubin, D. B. (1996). Multiple imputation after 18+ years. *Journal of the American Statistical Association*, *91*(434), 473–489. https://doi.org/10.2307/2291635

Sapolsky, R. M. (2015). Stress and the brain: Individual variability and the inverted-U. *Nature Neuroscience*, *18*, 13441346. https://doi.org/10.1038/nn.4109

Saxbe, D., Khoddam, H., Piero, L. D., Stoycos, S. A., Gimbel, S. I., Margolin, G., & Kaplan, J. T. (2018). Community violence exposure in early adolescence: Longitudinal associations with hippocampal and amygdala volume and resting state connectivity. *Developmental Science*, *21*(6), e12686. https://doi.org/10.1111/desc.12686

Schiffer, B., Müller, B. W., Scherbaum, N., Hodgins, S., Forsting, M., Wiltfang, J., Gizewski, E. R., & Leygraf, N. (2011). Disentangling structural brain alterations associated with violent behavior from those associated with substance use disorders. *Archives of General Psychiatry*, *68*(10), 1039–1049. https://doi.org/10.1001/archgenpsychiatry.2011.61

Shelton, K. K., & Frick, P. J. (1996). Assessment of parenting practices in families of elementary school-age children. *Journal of Clinical Child Psychology*, *25*(3), 317–329. https://doi.org/10.1207/s15374424jccp2503_8

Shonkoff, J. P., Boyce, W. T., & McEwen, B. S. (2009). Neuroscience, molecular biology, and the childhood roots of health disparities: Building a new framework for health promotion and disease prevention. *JAMA*, *301*(21), 2252–2259. https://doi.org/10.1001/jama.2009.754

Straus, M. A., Hamby, S. L., Finkelhor, D., Moore, D. W., & Runyan, D. (1998). Identification of child maltreatment with the Parent-Child Conflict Tactics Scales: Development and psychometric data for a national sample of

10982302, 2023, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/dev.22398 by Cochrane Netherlands, Wiley Online Library on [28/07/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

American parents. *Child Abuse & Neglect*, *22*(4), 249–270. https://doi.org/10.1016/S0145-2134(97)00174-9

Taylor, J. J., Grant, K. E., Zulauf, C. A., Fowler, P. J., Meyerson, D. A., & Irsheid, S. (2018). Exposure to community violence and the trajectory of internalizing and externalizing symptoms in a sample of low-income urban youth. *Journal of Clinical Child & Adolescent Psychology*, *47*(3), 421–435. https://doi.org/10.1080/15374416.2016.1152553

Thijssen, S., Ringoot, A. P., Wildeboer, A., Bakermans-Kranenburg, M. J., El Marroun, H., Hofman, A., Jaddoe, V. W. V., Verhulst, F. C., Tiemeier, H., van IJzendoorn, M. H., & White, T. (2015). Brain morphology of childhood aggressive behavior: A multi-informant study in school-age children. *Cognitive, Affective & Behavioral Neuroscience*, *15*(3), 564–577. https://doi.org/10.3758/s13415-015-0344-9

Tiesler, C. M. T., & Heinrich, J. (2014). Prenatal nicotine exposure and child behavioural problems. *European Child & Adolescent Psychiatry*, *23*(10), 913–929. https://doi.org/10.1007/s00787-014-0615-y

Valeri, L., & VanderWeele, T. J. (2013). Mediation analysis allowing for exposure–mediator interactions and causal interpretation: Theoretical assumptions and implementation with SAS and SPSS macros. *Psychological Methods*, *18*(2), 137–150. https://doi.org/10.1037/a0031034

VanderWeele, T. J. (2019). Principles of confounder selection. *European Journal of Epidemiology*, *34*(3), 211–219. https://doi.org/10.1007/s10654-019-00494-6

van Rooij, S. J. H., Smith, R. D., Stenson, A. F., Ely, T. D., Yang, X., Tottenham, N., Stevens, J. S., & Jovanovic, T. (2020). Increased activation of the fear neurocircuitry in children exposed to violence. *Depression and Anxiety*, *37*(4), 303–312. https://doi.org/10.1002/da.22994

Verhulst, F. C., Achenbach, T. M., Althaus, M., & Akkerhuis, G. W. (1988). A comparison of syndromes derived from the child behavior checklist for American and Dutch girls aged 6–11 and 12–16. *Journal of Child Psychology and Psychiatry*, *29*(6), 879–895. https://doi.org/10.1111/j.1469-7610.1988.tb00760.x

Vyas, A., Mitra, R., Shankaranarayana Rao, B. S., & Chattarji, S. (2002). Chronic stress induces contrasting patterns of dendritic remodeling in hippocampal and amygdaloid neurons. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *22*(15), 6810–6818. https://doi.org/10.1523/JNEUROSCI.22-15-06810.2002

Wasserstein, R. L., & Lazar, N. A. (2016). The ASA statement on p-values: Context, process, and purpose. *The American Statistician*, *70*(2), 129–133. https://doi.org/10.1080/00031305.2016.1154108

Wei, H.-T., Lan, W.-H., Hsu, J.-W., Bai, Y.-M., Huang, K.-L., Su, T.-P., Li, C.-T., Lin, W.-C., Chen, T.-J., & Chen, M.-H. (2016). Risk of suicide attempt among adolescents with conduct disorder: A longitudinal follow-up study. *The Journal of Pediatrics*, *177*, 292–296. https://doi.org/10.1016/j.jpeds.2016.06.057

Weissman, D. G., Lambert, H. K., Rodman, A. M., Peverill, M., Sheridan, M. A., & McLaughlin, K. A. (2020). Reduced hippocampal and amygdala volume as a mechanism underlying stress sensitization to depression following childhood trauma. *Depression and Anxiety*, *37*(9), 916–925. https://doi.org/10.1002/da.23062

Wenniger, W. F. M. D. B., Hageman, W. J. J. M., & Arrindell, W. A. (1993). Cross-national validity of dimensions of family functioning: First experiences with the Dutch version of the McMaster Family Assessment Device (FAD). *Personality and Individual Differences*, *14*(6), 769–781. https://doi.org/10.1016/0191-8869(93)90090-P

White, T., Muetzel, R. L., El Marroun, H., Blanken, L. M. E., Jansen, P., Bolhuis, K., Kocevska, D., Mous, S. E., Mulder, R., Jaddoe, V. W. V., van der Lugt, A., Verhulst, F. C., & Tiemeier, H. (2018). Paediatric population neuroimaging and the Generation R Study: The second wave. *European Journal of Epidemiology*, *33*(1), 99–125. https://doi.org/10.1007/s10654-017-0319-y

Whittle, S., Vijayakumar, N., Simmons, J. G., Dennison, M., Schwartz, O., Pantelis, C., Sheeber, L., Byrne, M. L., & Allen, N. B. (2017). Role of positive parenting in the association between neighborhood social disadvantage and brain development across adolescence. *JAMA Psychiatry*, *74*(8), 824–832. https://doi.org/10.1001/jamapsychiatry.2017.1558

Zhang, H., Lee, Z. X., White, T., & Qiu, A. (2020). Parental and social factors in relation to child psychopathology, behavior, and cognitive function. *Translational Psychiatry*, *10*, 80. https://doi.org/10.1038/s41398-020-0761-6

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10982302, 2023, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1002/dev.22398 by Cochrane Netherlands, Wiley Online Library on [28/07/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License