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Harsh Parenting and Child Brain Morphology: A Population-Based Study

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Abstract

Evidence suggests that maltreatment shapes the child's brain. Little is known, however, about how normal variation in parenting influences the child neurodevelopment. We examined whether harsh parenting is associated with the brain morphology in 2,410 children from a population-based cohort. Mothers *and* fathers independently reported harsh parenting at child age 3 years. Structural and diffusion-weighted brain morphological measures were acquired with MRI scans at age 10 years. We explored whether associations between parenting and brain morphology were explained by co-occurring adversities, and whether there was a joint effect of both parents' harsh parenting. Maternal harsh parenting was associated with smaller total gray ($\beta = -0.05$ (95%CI $= -0.08; -0.01$)), cerebral white matter and amygdala volumes ($\beta = -0.04$ (95%CI $= -0.07; 0$)). These associations were also observed with the combined harsh parenting measure and were robust to the adjustment for multiple confounding factors. Similar associations, although non-significant, were found between paternal parenting and these brain outcomes. Maternal and paternal harsh parenting were not associated with the hippocampus or the white matter microstructural metrics. We found a long-term association between harsh parenting and the global brain and amygdala volumes in preadolescents, suggesting that adverse rearing environments common in the general population are related to child brain morphology.

Keywords

hippocampus, discipline, parenting, brain morphology, magnetic resonance imaging

A growing body of research in clinical samples suggests that the exposure to early adverse caregiving is associated with child neurodevelopment. In particular, an effect of early-life maltreatment and traumatic events on the limbic morphology has been postulated. The amygdala and hippocampus are brain regions of interest in the context of adverse caregiving for several reasons. First, both structures undergo a period of rapid development in early childhood (Uematsu et al., 2012), and thus adverse caregiving environments coinciding with this developmental timing could influence the developmental trajectory (Tottenham & Sheridan, 2010). Second, as described by Tottenham and Sheridan (2010), the amygdala and hippocampus have a high density of cortisol receptors and therefore may be affected by variation in levels of this stress hormone. In fact, cortisol has been shown to influence the neurogenesis (Odaka et al., 2017), thus representing a pathway through which stressful environments could shape brain morphology. Finally, in addition to the biological relatedness between the limbic structures and the stress response, a functional relation exists. The amygdala plays a key role in the response to emotional stimuli (Bonnet et al., 2015) and fear conditioning (Milad & Quirk, 2012), whereas the hippocampus is involved in the memory encoding (Schiller et al., 2015) and the termination

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of the stress response (McEwen & Akil, 2020). Further, differential patterns of amygdala and hippocampal activation have been described among children exposed to threat (McLaughlin et al., 2019).

Based on animal and human studies, several potential mechanisms that link early life adversity with child brain development have been proposed. First, childhood trauma has been associated with the development of inflammation, and there is evidence supporting the influence of the immune system on brain morphology through an effect on the development of axons, synapses and the production of myelin (Danese & Lewis, 2017). Second, traumatic events have been related to oxidative stress in the central nervous system. Oxidative stress, defined as the excess of reactive oxygen species compared to the neutralizing antioxidant response, may lead to alterations in brain morphology, cause neuroinflammation and even generate neuronal death (Schiavone et al., 2013). Third, a disruption of the stress-response systems, including the hypothalamic-pituitary-adrenal (HPA) axis, has been suggested to explain the associations between adversities and brain differences (Wesarg et al., 2020). This latter mechanism likely occurs in parallel and in close relation with the previous two, and may exert an effect in the brain morphology through the secretion of catecholamines and glucocorticoids (Wesarg et al., 2020). As posited by the Allostatic Load Model, these different mechanisms may be activated in normal responses to stressful events, offering an adaptive and protective response (McEwen, 1998). However, when the exposure to stress is sustained, these mechanisms may be overstimulated and lead to a pathophysiological response (McEwen, 2001; McEwen & Akil, 2020). This maladaptive effect, termed "allostatic load" (McEwen & Akil, 2020), may generate neurotoxicity and volumetric reduction of multiple brain regions through processes such as neuronal damage, and dendritic remodeling (Kim et al., 2015; McEwen, 2001).

Overall, most research suggests that child exposure to adverse caregiving conditions is related to smaller volumes of the amygdala and hippocampus (see for a review: McLaughlin et al. (2019)). Also, associations between child maltreatment and smaller total brain, grey and white matter volumes have been described (McLaughlin et al., 2016; Teicher & Samson, 2016).

In comparison to the literature on extreme adverse caregiving, substantially less is known about the normative variation of harsh parenting. Whittle et al. (2009) described a cross-sectional relation between punishing maternal behaviors and *larger* amygdala and regional cortical volumes in 12-year-old children (N = 113). Maternal parenting was also assessed by Blankenship et al. (2019), who found that children exposed to negative parenting in early childhood had smaller volumes of the hippocampus tail at ages 5–10 years (N = 63). Few studies examined the association between adverse caregiving and white matter microstructure. One diffusion tensor imaging (DTI) study of 32 adults described a relation between parental verbal abuse and reduced fractional anisotropy (FA) of several white matter tracts, including the cingulum bundle (Choi et al., 2009). Additionally, childhood abuse was shown to be associated with reduced FA of the inferior fronto-occipital fasciculus in a sample of 63 youth (Lim et al., 2019).

Several aspects limit the comparability across studies. Whereas some assessed harsh parenting in early childhood, others measured it in pre-adolescence, and studies also differed in the brain outcomes examined. Moreover, most studies had a small-to-moderate sample size, and some oversampled participants with high risk for mental disorders (Blankenship et al., 2019; Whittle et al., 2009), limiting the generalizability of results.

Sex-specific associations have been described in relation to the brain vulnerability to environmental factors in early life. In particular, some maltreatment studies have reported greater brain morphological differences in males than in females, suggesting that some structures may be more susceptible to early-life stress in males (see for a review: Teicher and Samson (2016)). Thus, the sex-specificity of the association between parenting and child brain morphology should be considered.

A gap in the existing literature is the lack of research on paternal parenting, although evidence supports a role of fathers in offspring development. Both maternal and paternal sensitivity were associated with offspring brain differences in the present cohort (Kok et al., 2015). Additionally, an interaction effect has been described for maternal and paternal harsh parenting in relation to the offspring outcomes (Meunier et al., 2012; Wang et al., 2019). For example, children exposed to negative parenting by both parents have been shown to have the highest levels of emotional problems (Meunier et al., 2012). The primary aim of this study was to examine whether maternal and paternal harsh parenting behavior were associated with child brain morphology. In additional analyses, we addressed the relation between the combined maternal and paternal harsh parenting exposure and the child brain outcomes, and the interaction between both parental harsh parenting measures.

In 2,410 10-year-old children from the general population, we examined the relation between early-life harsh parenting and child brain morphology. Given that harsh parenting may be considered a chronic exposure to adverse caregiving conditions, we hypothesized parental harsh parenting would be associated with smaller amygdala and hippocampal volumes. We also examined the cortical thickness and the global brain volumes. Building on existing evidence, we expected to find an association between harsh parenting and smaller global brain volume measures. Further analyses with white matter microstructural metrics were performed with an exploratory approach given the scarcity of previous evidence. Also, we tested whether child sex modified the relation of harsh parenting with brain morphology.

Method

Participants

This study is part of the Generation R Study, a population-based cohort that follows the development of children in Rotterdam, the Netherlands (Kooijman et al., 2016). The design of the

cohort has been previously described in detail (Jaddoe et al., 2006). Briefly, pregnant women residing in the study area with a delivery date from April 2002 to January 2006 were eligible. They received information about the study from midwives and obstetricians and were contacted by study researchers for additional information (Jaddoe et al., 2006). In total, 9,778 mothers were enrolled (response rate of 61% at birth).

The cohort study includes families with various national origins (Dutch as the majority group). Mothers with higher socioeconomic status were more likely to participate. The aim of this ongoing cohort study is to identify environmental and genetic factors that influence children's growth, development and health. Thus, data on multiple child and parent characteristics, including biological and psychological factors, was collected. The study was approved by the Medical Ethical Committee of the Erasmus Medical Center and all participating parents gave informed consent.

Of the 4,974 children with information on maternal and/or paternal harsh parenting at age 3 years, 2,801 had neuroimaging data at age 10 years. For the analyses with structural MRI (magnetic resonance imaging), we excluded 521 children with poor image quality and nine with major incidental findings in the MRI scans. For the analyses with DTI metrics, we excluded 556 children with non-usable DTI data and eight children with major incidental findings. We also randomly excluded siblings to avoid bias due to paired data (N = 147). In total, 2,410 children were included in analyses (2,141 with structural MRI data and 2,108 with DTI data; Supplementary Figure 1).

Measures

Harsh parenting. Information on harsh parenting practices was collected when children were 3 years old using questionnaires based on the Parent-Child Conflict Tactics Scale (CTSPC) (Straus et al., 1998). Items on harsh punishment (e.g. spanking) originally included in the CTSPC were removed, as these practices may be considered illegal in the Netherlands and we had no mandate to follow-up on such practices. Additionally, one item that was not age-appropriate ("said you would kick child out of the house") was removed. Mothers and fathers independently reported the use of various harsh parenting practices in the preceding 2 weeks (see Supplemental Material), using a 6-point frequency scale (from *Never* to *More than four times*). In a previous study from this cohort, Jansen et al. (2012) described the selection of items for the harsh parenting measure. Briefly, an exploratory factor analysis on the 10 items included (using a 3-point frequency scale) showed a two-factor structure, and the six items of the first factor, with factor loadings >0.50, matched the construct and definition of harsh parenting (Jansen et al., 2012). We computed maternal and paternal harsh parenting scores by summing the scores on the six harsh parenting items (range = 0–30). The internal consistency of both maternal and paternal harsh parenting was low (Cronbach's α of 0.63 in the total sample, and in the study sample 0.60 for maternal harsh parenting, and of 0.58 for paternal harsh parenting), likely reflecting the small number of items in these scales. Importantly, the six items of the harsh parenting measure showed good model fit in both mothers (comparative fit index (CFI) = 0.970, Tucker-Lewis index (TLI) = 0.966, root mean square error of approximation (RMSEA) = 0.044) and fathers (CFI = 0.972, TLI = 0.965, RMSEA = 0.040) (Jansen et al., 2012). Several determinants and correlates of harsh parenting (e.g. socioeconomic status, family dysfunction, child behavioral problems) have been identified in the current cohort (Jansen et al., 2012; Mackenbach et al., 2014) supporting the validity of our harsh parenting measure.

Brain imaging

Acquisition. Magnetic resonance images were acquired at age 9–11 years using a 3-Tesla General Electric scanner (MR750w, Milwaukee, WI, US), with signal reception through an eight-channel head coil (White et al., 2018). T_1-weigthed images were collected with an Inversion Recovery Fast Spoiled Gradient Recalled sequence (TR = 8.77 ms, TE = 3.4 ms, TI = 600 ms, Flip angle = 10°, Field of View (FOV) = 220 × 220 mm, Acquisition matrix = 220 × 220, Slice thickness = 1 mm, Number of slices = 230, ARC acceleration factor = 2). The diffusion-weighted images were collected using an echo planar sequence with 3 b = 0 s/mm^2 volumes and 35 diffusion-weighted images (TR = 12.500 ms, TE = 72.8 ms, FOV = 240 × 240 mm, Acquisition matrix = 120 × 120, slice thickness = 2 mm, number of slices = 65, ARC acceleration factor = 2 and b = 900 s/mm^2).

Image processing. Images were processed with the FreeSurfer version 6.0 image suite (http://surfer.nmr.mgh.harvard.edu/), as previously described (Muetzel et al., 2019). In brief, we performed removal of non-brain tissue, voxel intensity normalization, volumetric segmentation and cortical reconstruction. Cortical thickness was estimated for each vertex as the distance between the grey/white matter boundary and the grey matter/cerebrospinal fluid boundary. Thickness maps were smoothed with a 10 mm full-width half-maximum Gaussian kernel. Image quality of the FreeSurfer reconstructions was assessed as described previously (Muetzel et al., 2019). Further details of the image quality control are described in the Supplement Material. We included the total grey and cerebral white matter volumes, amygdala and hippocampal volumes (averaged over both hemispheres) and cortical thickness vertex-wise data in analyses. The hemisphere-specific amygdala and hippocampus were examined in sensitivity analyses.

The DTI data was processed using the FMRIB Software library (FSL) (Jenkinson et al., 2012) and the Camino toolkit (Cook et al., 2006). We removed non-brain tissue and corrected the images for eddy-current artifacts and translations/rotations caused by head motion. The diffusion tensor was fitted and fully-automated probabilistic tractography was run, generating connectivity distributions for multiple white matter tracts. Average fractional anisotropy (FA) and mean diffusivity (MD) values were computed for each tract, weighted by the connectivity distributions, and global FA and MD metrics were derived from the metrics of multiple large fiber bundles with

confirmatory factor analysis (Muetzel et al., 2018). We used the global FA and MD factor scores. Detailed quality control of the brain images was performed and data rated as inadequate were excluded from analyses (see Supplemental Material).

Covariates. Potential confounders were selected based on previous studies (Kok et al., 2015; Whittle et al., 2016). Marital status, maternal ethnicity, prenatal smoking and alcohol consumption were self-reported with questionnaires during pregnancy. Information on child birth weight was collected from hospital registries and midwives. Maternal and paternal education were assessed prenatally and at age 3 years. Family income and parental depressive symptoms were self-reported at age 3 years. Maternal and paternal depressive symptoms were assessed with the depression subscale of the Brief Symptom Inventory (BSI) (Derogatis, 1993), a validated questionnaire that assesses psychiatric symptoms. The total intracranial volume was extracted from the structural imaging data (Additional information in the Supplemental Material).

Maternal alcohol drinking problems and marital problems were included in sensitivity analyses. Information on maternal alcohol consumption was collected by postal questionnaires when children were 5 years old. If mothers reported drinking any alcohol over the past 3 months, several follow-up questions were asked to examine the drinking pattern. We distinguished two problematic maternal alcohol drinking patterns: "regular drinking problems," defined as drinking more than one glass of alcohol a day on average (vs no alcohol consumption or consumption of one or fewer alcohol glasses per day), and "binge drinking," defined as drinking more than six glasses in 1 day more than once a month (vs drinking more than six glasses in 1 day less than once a month, or no consumption of more than six glasses in 1 day). Regarding marital problems, the primary caregiver (in most cases the mother) reported at child age 3 years whether problems in the couple relationship had occurred (yes/no) in the preceding 2 years.

Statistical Analyses

We examined whether the maternal and paternal harsh parenting scores were related to the regions of interest (ROIs, i.e. total grey and cerebral white matter volume, mean amygdala and hippocampal volumes; and global FA and MD) with linear regression. We controlled for confounders in two models. First, analyses were adjusted for total intracranial volume (in models with the amygdala and hippocampus), child age at the MRI scan, child sex, and maternal ethnicity. In a second model, we additionally controlled for birth weight, prenatal smoking and alcohol consumption, family income, maternal education, marital status and maternal depressive symptoms. Analyses with the paternal harsh parenting included paternal education and paternal depressive symptoms instead of the respective maternal covariates. Similar models were fitted to examine the association of parenting with cortical thickness at each cortical vertex (QdecR package, version 0.8.4, https://github.com/slamballais/QDECR) (Muetzel et al., 2019). We tested the interaction between child sex and (maternal and paternal) harsh parenting for the ROIs and followed-up significant results with sex-stratified analyses.

The eight analyses with the structural ROIs (four tests for each parent's harsh parenting) and the eight analyses of the interaction between child sex and harsh parenting (four tests for each parent's harsh parenting) were adjusted for multiple testing with the false discovery rate approach (FDR) (Benjamini & Hochberg, 1995). The vertex-wise analyses were adjusted for multiple testing using Gaussian Monte Carlo Simulations (Hagler et al., 2006) with a cluster-forming threshold (CFT) of $p = 0.001$ (Greve & Fischl, 2018) and a cluster-wise p-value (CWP) of $p < 0.025$ (Bonferroni-corrected for both hemispheres).

We performed several additional analyses, fully-adjusted for covariates (i.e. total intracranial volume (in amygdala and hippocampus analyses), child sex and age at the MRI scan, maternal ethnicity, birth weight, prenatal smoking and alcohol consumption, family income, maternal education, marital status and maternal depressive symptoms. In analyses with paternal harsh parenting, paternal education and depressive symptoms were included instead of the respective maternal covariates). First, as the amygdala and hippocampal volumes follow hemisphere-specific developmental trajectories (Uematsu et al., 2012), we examined left- and right-hemisphere measures in independent analyses. Second, we explored whether there was an interaction between maternal and paternal harsh parenting for the brain ROIs. Third, we explored the relation between the combined parental harsh parenting measure and child brain morphology. To this aim, we performed a principal component analysis (PCA), based on the original items of the harsh parenting maternal and paternal measures (six items per parent; missing values imputed with the median). Given that the purpose of this analysis was to combine maternal and paternal harsh parenting metrics in one measure, only the first component was extracted. The association between this combined parental harsh parenting measure and the child brain outcomes was examined with linear regression, fully adjusted for confounders (additionally, both maternal and paternal education and depression were included as covariates). Fourth, we examined whether our findings were explained by two other stressful experiences: maternal alcohol drinking problems, and marital problems. Parental alcohol abuse has been suggested to influence child psychological development (Raitasalo et al., 2019), and the likelihood of child maltreatment is higher in families where parents abuse alcohol (Dube et al., 2001). Similarly, family dysfunction has been associated with more parental harsh discipline (Jansen et al., 2012) and with offspring brain morphology (Xerxa, Delaney, et al., 2020). We further explored associations observed in the main analyses, by adjusting, first, for maternal regular drinking problems and binge drinking; and second, for marital problems.

All analyses were run with the statistical software R (version 3.6.1) (R Core Team, 2018). Estimates were standardized for ease of interpretation. Missing values in covariates (maximum missingness: Paternal depressive symptoms: 19.4%) were imputed with the Multivariate Imputations by Chained

Table 1. Baseline Characteristics.

	Mean (SD) or %*
Child characteristics	
Sex, % girls	50.7
Age at the MRI scan, years	10.1 (0.5)
Age at maternal harsh parenting measure, years (N = 2,358)	3.0 (0.1)
Parental characteristics	
Maternal characteristics	
Harsh parenting, maternal score, median (Q1, Q3) (N = 2,358)	2.0 (1.0, 4.0)
Education, %	
Low	37.1
Medium	28.3
High	34.6
Maternal Ethnicity	
Dutch	65.7
Non-Western	21.7
Non-Dutch Western	12.6
Marital status, % married or living together	91.4
Prenatal smoking, % never during pregnancy	79.8
Prenatal alcohol use, % never during pregnancy	34.7
Depression symptoms, BSI depression score, median (Q1, Q3)	0 (0, 0.17)
Paternal characteristics	
Harsh parenting, paternal score, median (Q1, Q3) (N = 1957)	1.0 (0.0, 3.0)
Education, %	
Low	39.4
Medium	24.0
High	36.6
Depression symptoms, BSI depression score, median (Q1, Q3)	0 (0, 0.01)

Note. Sample with available data for maternal and/or paternal harsh parenting and brain T1 and/or DTI MRI (N = 2410) *Otherwise indicated.

Equations (mice) package (version 3.6.0) (van Buuren & Groothuis-Oudshoorn, 2011) generating 20 imputed datasets. One participant with an outlying global MD score (>4 standard deviations below the mean) was excluded from the DTI analyses.

Non-response Analysis

Children in the analyses (N = 2,410) did not differ from children lost-to-follow-up (with harsh parenting data but no neuroimaging data, N = 2,173) in sex and maternal marital status. Children included in analyses were exposed to less harsh parenting by mothers and fathers than children with no imaging data (e.g. mean maternal harsh parenting: 2.88 vs 3.11, $p = 0.02$). Of the children in our study, 35% had highly-educated mothers whereas this was of 33% in those lost to follow-up (chi-square $p = 0.02$). Likewise, 66% of the children in our study sample had mothers with Dutch ethnicity, whereas this was of 63% in the lost-to-follow-up group ($p = 0.02$).

Results

Among the 2,410 children in analyses, 51% were girls. The correlation between maternal and paternal harsh parenting was moderate (Pearson's r = 0.36, p < 0.001, N = 1,905). The median (unstandardized) maternal harsh parenting score was the same for boys and girls (median = 2.0, IQR = 1.0, 4.0), whereas the median paternal harsh parenting score was 2.0 (IQR = 1.0, 3.0) for boys and 1.0 (IQR = 0, 3.0) for girls. Most mothers were married or living with a partner (91%) and 35% of mothers and 37% of fathers were highly educated (Table 1).

The exposure to maternal harsh parenting was associated with smaller total gray matter ($\beta = -0.07$ (95% confidence interval (95%CI) = −0.10; −0.03)) and cerebral white matter volumes ($\beta = -0.06$ (95%CI = −0.09; −0.02)) after adjusting for child age at the MRI scan, child sex, and maternal ethnicity. These associations remained after additionally accounting for birth weight, prenatal smoking and alcohol consumption, family income, maternal education, marital status and maternal depressive symptoms (total gray matter volume: $\beta = -0.05$ (95%CI = −0.08; −0.01)). Maternal harsh parenting was also related to smaller amygdala volumes ($\beta = -0.04$ (95%CI = −0.07; 0)), but not to hippocampal volumes. No association was found between maternal harsh parenting and global white matter microstructural metrics (Table 2).

Paternal harsh parenting had similar direction of effects as maternal harsh parenting for the associations with global brain volumes (e.g. cerebral white matter volume ($\beta = -0.03$ (95%CI = −0.07; 0.01)) and amygdala volume ($\beta = -0.03$ (95%CI = −0.07; 0.01)). However, these associations were not statistically significant. Similarly, no association was found between paternal harsh parenting and hippocampal volume or white matter microstructural metrics (Table 2).

After adjustment for multiple testing in the analyses with maternal and paternal harsh parenting and the brain structural regions of interest (eight tests), only the association between maternal harsh parenting and total gray matter volume survived (p-adjusted = 0.05). The associations of maternal parenting with cerebral white matter (p-adjusted = 0.09) and amygdala volumes (p-adjusted = 0.09) did not survive. No associations were found between maternal or paternal harsh parenting and vertex-wise cortical thickness.

We examined whether the relation between harsh parenting and the ROIs differed by child sex. However, no interaction effect was found between harsh parenting and the child sex for any of the brain outcomes examined (data not shown).

Next, we explored whether the associations between harsh parenting and amygdala and hippocampal volumes were hemisphere-specific. Maternal harsh parenting was consistently related to the left and right amygdala volumes (left: $\beta = -0.04$ (95%CI = −0.08; 0); right: $\beta = -0.03$ (95%CI = −0.07; 0)), although the analyses with the right amygdala were not statistically significant. We found similar estimates for the relation of paternal harsh parenting and the amygdala volumes (e.g. left: $\beta = -0.03$ (95%CI = −0.07; 0.01)), which did not reach significance. There was no association between each parent's harsh

Table 2. Harsh Parenting and the Child Brain Outcomes.

		Maternal Harsh Parenting					Paternal Harsh Parenting				
		Model 1		Model 2			Model 1		Model 2		
	N	β (95%CI)	P	β (95%CI)	P	N	β (95%CI)	P	β (95%CI)	P	
Brain Outcomes											
Global brain measures	2090					1754					
Total gray matter volume		−0.07 (−0.10; −0.03)	<0.001	−0.05 (−0.08; −0.01)	0.006		−0.03 (−0.07; 0.01)	0.152	−0.02 (−0.06; 0.02)	0.298	
Cerebral white matter volume		−0.06 (−0.09; -0.02)	0.003	−0.04 (−0.08; 0)	0.035		−0.03 (−0.07; 0.01)	0.100	−0.03 (−0.07; 0.01)	0.177	
Subcortical structures											
Amygdala volume		−0.04 (−0.07; 0)	0.043	−0.04 (−0.07; 0)	0.028		−0.02 (−0.06; 0.01)	0.226	−0.03 (−0.07; 0.01)	0.124	
Hippocampus volume		−0.02 (−0.06; 0.01)	0.200	−0.02 (−0.05; 0.02)	0.286		0 (−0.04; 0.04)	0.924	0 (−0.04; 0.03)	0.835	
Global DTI measures	2064					1720					
Global FA		−0.03 (−0.07; 0.01)	0.198	−0.02 (−0.07; 0.02)	0.275		0 (−0.05; 0.04)	0.898	−0.01 (−0.05; 0.04)	0.763	
Global MD		−0.01 (−0.05; 0.04)	0.758	−0.01 (−0.05; 0.04)	0.743		0.01 (−0.04; 0.05)	0.710	0.01 (−0.03; 0.06)	0.585	

Note. Associations between parental harsh parenting at age 3 years and child brain outcomes at age 10 years. Amygdala and hippocampal volumes averaged over both hemispheres. Model 1 is adjusted for: total ICV (total intracranial volume), child age at brain MRI scan, child sex and maternal ethnicity. Model 2 is additionally adjusted for birth weight, prenatal smoking and alcohol consumption, family income, maternal education, marital status and maternal depressive symptoms. In paternal harsh parenting analyses, paternal education and depressive symptoms are included instead of the maternal covariates. Global brain measures are not adjusted for total ICV. Estimates are standardized.

parenting and the hippocampal volumes (Supplementary Table 1).

To further explore the role of maternal and paternal harsh parenting in the relation with the child brain morphology, we performed two sensitivity analyses. First, we examined the interaction between maternal and paternal harsh parenting. We found no evidence for an interaction effect in relation to any of the brain outcomes examined (Table 3). Second, we modelled the joint effect of maternal and paternal harsh parenting, by performing a PCA based on the 12 items of the maternal and paternal harsh parenting reports. We extracted the first component, explaining 24% of the total variance, with an eigen value of 2.87. Factor loadings ranged from 0.31 to 0.57 for all items. We then examined the association between the harsh parenting factor score and the brain outcomes. Parental harsh parenting was related to smaller total gray matter volume ($\beta = -0.04$ (95%CI $= -0.07$; 0.00)) and amygdala volume ($\beta = -0.04$ (95%CI $= -0.07$; -0.01)) in analysis adjusted for all covariates. A suggestive, although non-significant association was observed between the parental harsh parenting measure and cerebral white matter volume (Supplementary Table 2). Considering the moderate correlation between maternal and paternal harsh parenting and the relatively low percentage of explained variance by the extracted principal component, we recommend caution in the interpretation of these results.

Finally, we explored whether our findings were explained by two potentially co-occurring stressors. We followed-up the associations of maternal harsh parenting with total gray matter, cerebral white matter and amygdala volumes, by adjusting for maternal alcohol drinking problems and for the presence of marital problems. However, neither of these factors even partly explained the associations between maternal harsh parenting and child brain morphology (Supplementary Table 3).

Discussion

In this population-based study, early-life maternal harsh parenting was associated with smaller total gray matter volumes in 10-year-old children. These results were robust to the adjustment for multiple confounding factors, and were not explained by the presence of other child stressful experiences. Similar associations were observed for the cerebral white matter and the amygdala volumes. However, these findings did not survive after adjustment for multiple testing. The associations between paternal harsh parenting and child brain morphology showed the same direction and largely similar effect sizes as maternal harsh parenting, but did not reach significance. Further, analyses with a joint parental harsh parenting measure showed results consistent with those of the separate maternal and paternal analyses: parental harsh parenting was associated with smaller global brain and amygdala volumes. Differences in the hippocampal volumes were not related to past harsh parenting exposure. Also, parental harsh parenting was not associated with regional cortical thickness or white matter microstructural metrics.

Table 3. Interaction Between Maternal and Paternal Harsh Parenting in Relation to Child Brain Morphology.

		Interaction Model					
		Maternal Harsh Parenting		Paternal Harsh Parenting		Interaction Maternal × Paternal Harsh Parenting	
	N	β (95%CI)	P	β (95%CI)	P	β (95%CI)	P
Brain Outcomes							
Global brain measures							
Total gray matter volume	1703	−0.04 (−0.08; 0.01)	0.104	−0.02 (−0.06; 0.02)	0.329	0 (−0.03; 0.03)	0.897
Cerebral white matter volume	1703	−0.03 (−0.08; 0.01)	0.188	−0.04 (−0.08; 0.01)	0.093	0.01 (−0.02; 0.04)	0.406
Subcortical structures							
Amygdala volume, average	1703	−0.03 (−0.07; 0.02)	0.234	−0.04 (−0.08; 0)	0.071	0 (−0.03; 0.03)	0.845
Hippocampus volume, average	1703	−0.03 (−0.07; 0.01)	0.182	−0.01 (−0.06; 0.03)	0.522	0.02 (−0.01; 0.05)	0.126
Global DTI measures							
Global FA	1677	−0.04 (−0.1; 0.01)	0.129	0 (−0.05; 0.06)	0.898	0.01 (−0.02; 0.04)	0.500
Global MD	1677	0.01 (−0.04; 0.07)	0.649	0 (−0.05; 0.05)	0.978	−0.01 (−0.04; 0.03)	0.730

Note. Predictors included: maternal and paternal harsh parenting, total ICV (total intracranial volume), child age at MRI scan, child sex, maternal ethnicity, birth weight, prenatal smoking and alcohol consumption, family income, maternal education, paternal education, marital status, maternal depressive symptoms, paternal depressive symptoms and **an interaction term between maternal and paternal harsh parenting**. Global brain measures are not adjusted for total ICV. Estimates are standardized.

Multiple studies have examined the brain morphology of children exposed to severe early-life adverse caregiving conditions and have consistently found that children who experienced adversity, such as maltreatment, have smaller global brain volumes than controls, with wide-spread differences observed in grey and white matter (Bick & Nelson, 2016; De Brito et al., 2013). In this large population-based cohort, we examined whether harsh parenting, which can be conceptualized along a continuum of parenting with maltreatment at the extreme end (Gershoff, 2002; Kim et al., 2010), was related to the child brain morphology. Interestingly, our results are in line with the existing maltreatment literature: harsh discipline was associated with smaller global brain volumes. Contrary to what we expected, harsh parenting was not related to child cortical thickness. Thinner cortices in specific regions, such as the prefrontal cortex, have been described by some studies of children exposed to severe caregiving adversity (McLaughlin et al., 2019). Yet, even though we observed global brain volumetric differences in relation to harsh parenting, no specific association with cortical thickness was found. Given the population-based design of our study, cortical thickness differences could be too subtle to be detected with our current sample size. It is also possible that the observed global differences are accounted for by differences in other components of grey matter rather than cortical thickness, such as the cortical surface area or the local gyrification (Kelly et al., 2013). Our findings add to the evidence linking harsh parenting with subsequent offspring behavioral problems (Jackson & Choi, 2018; Mackenbach et al., 2014), demonstrating a difference in child grey matter volumes. Research has shown that sustained exposure to stress can lead to allostatic load, and trigger pathophysiological reactions at the endocrine and molecular levels, among others (McEwen & Akil, 2020). Thus, the smaller grey matter volume could be related to neurotoxicity and dendritic remodeling, caused by a maladaptive stress response. Further studies are needed to better understand how brain morphology correlates at the local neuroanatomical level and how this corresponds to the association of parental harsh discipline with subsequent poor child outcomes.

The literature shows mixed results regarding the relation of early-life adverse caregiving with amygdala volume. Some research results suggest that the amygdala may be smaller in children exposed to severe adverse caregiving (McLaughlin et al., 2016), but larger amygdala volumes have also been described (Whittle et al., 2009). We report that harsh parenting was associated with smaller amygdala volumes, and this finding was consistently observed in the left and right hemisphere. Overall, it is difficult to compare findings across studies given the differences in age and measurements. For example, Whittle et al. (2009) examined the relation of mothers' punishing responses in reaction to adolescents' positive affective behavior with adolescents' brain morphology. Further, this parental behavior pattern was most probably related to the adolescents' neural circuitry of reward. In contrast, our study focused on parenting of 3-year-old children and examined the daily-life use of harsh discipline strategies, which are often seen as related to child maltreatment (Stith et al., 2009). Additionally, the age at the brain MRI assessment could influence the results, considering that the amygdala has a non-linear developmental trajectory plateauing in preadolescence (Uematsu et al., 2012). Importantly, our finding of a relation between harsh parenting and a smaller amygdala volume in children expands the existing evidence regarding adverse caregiving environments in the general population. Further, the experience of maltreatment has also been related to the functional connectivity between the amygdala and the prefrontal cortex, suggesting that early-life adversity could be related not only to the amygdala morphology, but also to its functional reactivity (Peverill et al., 2019).

It is well known that adverse experiences tend to co-occur (Felitti et al., 1998). Factors such as low SES (Roubinov & Boyce, 2017), alcohol drinking problems (Dube et al., 2001) and marital problems (Jansen et al., 2012) predict the use of harsh discipline strategies, and are related to child brain and psychological development (McDermott et al., 2019; Raitasalo et al., 2019; Xerxa, Rescorla, et al., 2020). Sensitivity analyses showed that our findings were not explained by these potentially co-occurring stressful factors. Rather, we hypothesize that harsh parenting represents a chronic stressor, that in the long term may alter the brain's developmental trajectory through a cascade of disruptions in the stress response system and in the physiological responses to external events (Evans et al., 2013). The prolonged exposure to stress has been suggested to alter neuronal morphology, the normative trajectory of neuronal proliferation, and synaptic plasticity (Kim et al., 2015).

Interestingly, mothers' and fathers' parenting were similarly related to the child brain outcomes, although the association of the father's parenting was attenuated. Differential parenting practices have been described for mothers and fathers (McKinney & Renk, 2008), yet, little is known regarding the relation of *paternal* parenting with the child brain morphology. Our study gives only a preliminary answer to this question. Given the smaller sample size of children with paternal parenting reports than maternal reports and the smaller effect sizes of the associations with the brain outcomes, it is possible that larger sample sizes are needed to observe a slightly subtler effect. The analyses with the joint parental harsh parenting measure supported a joint effect of maternal and paternal parenting, suggesting that the exposure to more harsh parenting from *both* parents is related to similar brain differences as those observed in the separate maternal and paternal analyses. Additionally, some researchers suggest that the harsh discipline of mothers and fathers could interact in relation to the offspring outcomes (Wang et al., 2019). However, we found no evidence for a maternal and paternal harsh parenting interaction effect in relation to the brain regions of interest. Also, some studies have described that boys may be more susceptible to poor parenting than girls (Spruijt et al., 2019), but we observed no interaction of maternal and paternal harsh parenting with child sex.

In this study, we found no association between parental harsh parenting and the hippocampal volumes. Although the literature is not very consistent, some studies have reported smaller hippocampal volumes in children exposed to early adversity (Bick & Nelson, 2016; McLaughlin et al., 2019). One study found that early-life negative parenting predicted smaller hippocampal tail volumes via cortisol reactivity, suggesting that stress reactivity may underlie the relation between parenting and offspring neurodevelopment (Blankenship et al., 2019). Moreover, extreme caregiving adversity has been related to deficits in memory (Bick & Nelson, 2016) and other hippocampal-related cognitive tasks (Edmiston & Blackford, 2013). Given that the hippocampus and amygdala have a period of rapid growth and development during early childhood (Uematsu et al., 2012), this may represent a period of critical vulnerability of these limbic structures to environmental effects. Thus, the lack of association between harsh parenting and the hippocampal volume in our study could simply reflect the fact that larger study samples of children from the general population are needed to detect small but possibly relevant hippocampal volumetric differences, and that these may be more apparent in children exposed to severe adverse caregiving conditions.

Similarly, we found no association between harsh parenting and the global white matter microstructural metrics in our exploratory analyses. While childhood abuse studies reported white matter microstructural differences in adults (Lim et al., 2019), further studies in children and in the general population are needed to understand the relation between caregiving adversity and child white matter microstructure.

Our findings must be interpreted considering some limitations. First, causality cannot be inferred. Future studies should include repeated parenting and neuroimaging measures, to examine the direction of effect. Second, harsh parenting measures were based on self-reports, which could be biased by social desirability. However, observational parenting assessments also have a tendency toward socially desirable behaviors, and other data collection methods, like child reports, are especially challenging when assessing harsh parenting in early childhood (Bennett et al., 2006). Third, children lost-to-follow-up less often had mothers with a Dutch national origin and high education than children included in our study. Moreover, the relatively high educational level of families in our cohort study and the low poverty rate in the Netherlands (Statistics Netherlands, 2019) may have limited the variation in our harsh parenting measure. Fourth, paternal harsh parenting data was less often available than maternal parenting. Although our sample is large compared to previous studies, and that there was an overall consistency of effect between both parents, larger population-based samples could be needed to capture subtle effects. Fifth, alcohol consumption was collected by postal questionnaires, which could have led to an underestimation of the amount of consumed alcohol.

Our findings in this population-based study suggest that early-life harsh parenting is related to smaller global brain and amygdala volumes in preadolescence. These results have public health relevance as these offer an extension of the evidence of child maltreatment studies, suggesting that adverse rearing environments common in the general population are related to child brain morphology.

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Supplemental Material

Supplemental material for this article is available online.

References

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society Series B (Methodological)*, *57*(1), 289–300. http://www.jstor.org/stable/2346101

Bennett, D. S., Sullivan, M. W., & Lewis, M. (2006). Relations of parental report and observation of parenting to maltreatment history. *Child Maltreatment*, *11*(1), 63–75. https://doi.org/10.1177/1077559505283589

Bick, J., & Nelson, C. A. (2016). Early adverse experiences and the developing brain. *Neuropsychopharmacology*, *41*(1), 177–196. https://doi.org/10.1038/npp.2015.252

Blankenship, S. L., Chad-Friedman, E., Riggins, T., & Dougherty, L. R. (2019). Early parenting predicts hippocampal subregion volume via stress reactivity in childhood. *Developmental Psychobiology*, *61*(1), 125–140. https://doi.org/10.1002/dev.21788

Bonnet, L., Comte, A., Tatu, L., Millot, J.-l., Moulin, T., & Medeiros de Bustos, E. (2015). The role of the amygdala in the perception of positive emotions: An "intensity detector". *Frontiers in Behavioral Neuroscience*, *9*(178). https://doi.org/10.3389/fnbeh.2015.00178

Choi, J., Jeong, B., Rohan, M. L., Polcari, A. M., & Teicher, M. H. (2009). Preliminary evidence for white matter tract abnormalities in young adults exposed to parental verbal abuse. *Biological Psychiatry*, *65*(3), 227–234. https://doi.org/10.1016/j.biopsych.2008.06.022

Cook, P. A., Bai, Y., Nedjati-Gilani, S., Seunarine, K. K., Hall, M. G., Parker, G. J., & Alexander, D. C. (2006). Camino: Open-source diffusion-MRI reconstruction and processing. In *14th Scientific Meeting of the International Society for Magnetic Resonance in Medicine*. https://cds.ismrm.org/ismrm-2006/files/02759.pdf

Danese, A., & Lewis, S. J. (2017). Psychoneuroimmunology of early-life stress: The hidden wounds of childhood trauma? *Neuropsychopharmacology*, *42*(1), 99–114. https://doi.org/10.1038/npp.2016.198

De Brito, S. A., Viding, E., Sebastian, C. L., Kelly, P. A., Mechelli, A., Maris, H., & McCrory, E. J. (2013). Reduced orbitofrontal and temporal grey matter in a community sample of maltreated children. *Journal of Child Psychology and Psychiatry*, *54*(1), 105–112. https://doi.org/10.1111/j.1469-7610.2012.02597.x

Derogatis, L. R. (1993). *Brief Symptom Inventory (BSI): Administration, scoring and procedures manual* (3rd ed.). National Computer Systems.

Dube, S. R., Anda, R. F., Felitti, V. J., Croft, J. B., Edwards, V. J., & Giles, W. H. (2001). Growing up with parental alcohol abuse: Exposure to childhood abuse, neglect, and household dysfunction. *Child Abuse & Neglect*, *25*(12), 1627–1640. https://doi.org/10.1016/S0145-2134(01)00293-9

Edmiston, E. K., & Blackford, J. U. (2013). Childhood maltreatment and response to novel face stimuli presented during functional magnetic resonance imaging in adults. *Psychiatry Research: Neuroimaging*, *212*(1), 36–42. https://doi.org/10.1016/j.pscychresns.2012.11.009

Evans, G. W., Li, D., & Sepanski Whipple, S. (2013). Cumulative risk and child development. *Psychological Bulletin*, *139*(6), 1342–1396. https://doi.org/10.1037/a0031808

Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., Koss, M. P., & Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*, *14*(4), 245–258. https://doi.org/10.1016/S0749-3797(98)00017-8

Gershoff, E. T. (2002). Corporal punishment by parents and associated child behaviors and experiences: A meta-analytic and theoretical review. *Psychological Bulletin*, *128*(4), 539–579. https://doi.org/10.1037/0033-2909.128.4.539

Greve, D. N., & Fischl, B. (2018). False positive rates in surface-based anatomical analysis. *Neuroimage*, *171*, 6–14. https://doi.org/10.1016/j.neuroimage.2017.12.072

Hagler, D. J., Saygin, A. P., & Sereno, M. I. (2006). Smoothing and cluster thresholding for cortical surface-based group analysis of fMRI data. *Neuroimage*, *33*(4), 1093–1103. https://doi.org/10.1016/j.neuroimage.2006.07.036

Jackson, A. P., & Choi, J. (2018). Parenting stress, harsh parenting, and children's behavior. *Journal of Family Medicine & Community Health*, *5*(3), 10.

Jaddoe, V. W. V., Mackenbach, J. P., Moll, H. A., Steegers, E. A. P., Tiemeier, H., Verhulst, F. C., Witteman, J. C. M., & Hofman, A. (2006). The Generation R Study: Design and cohort profile. *European Journal of Epidemiology*, *21*(6), 475. https://doi.org/10.1007/s10654-006-9022-0

Jansen, P. W., Raat, H., Mackenbach, J. P., Hofman, A., Jaddoe, V. W. V., Bakermans-Kranenburg, M. J., van IJzendoorn, M. H., 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

Jenkinson, M., Beckmann, C. F., Behrens, T. E. J., Woolrich, M. W., & Smith, S. M. (2012). FSL. *Neuroimage*, *62*(2), 782–790. https://doi.org/10.1016/j.neuroimage.2011.09.015

Kelly, P. A., Viding, E., Wallace, G. L., Schaer, M., De Brito, S. A., Robustelli, B., & McCrory, E. J. (2013). Cortical thickness, surface area, and gyrification abnormalities in children exposed to maltreatment: Neural markers of vulnerability? *Biological Psychiatry*, *74*(11), 845–852. https://doi.org/10.1016/j.biopsych.2013.06.020

Kim, E. J., Pellman, B., & Kim, J. J. (2015). Stress effects on the hippocampus: A critical review. *Learning & Memory*, *22*(9), 411–416. https://doi.org/10.1101/lm.037291.114

Kim, H. K., Pears, K. C., Fisher, P. A., Connelly, C. D., & Landsverk, J. A. (2010). Trajectories of maternal harsh parenting in the first 3 years of life. *Child Abuse & Neglect*, *34*(12), 897–906. https://doi.org/10.1016/j.chiabu.2010.06.002

Kok, R., Thijssen, S., Bakermans-Kranenburg, M. J., Jaddoe, V. W. V., Verhulst, F. C., White, T., van IJzendoorn, M. H., & Tiemeier, H. (2015). Normal variation in early parental sensitivity predicts child structural brain development. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*(10), 824–831. https://doi.org/10.1016/j.jaac.2015.07.009

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., Verhulst, F. C., Wolvius, E., Felix, J. F., … 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

Lim, L., Hart, H., Howells, H., Mehta, M. A., Simmons, A., Mirza, K., & Rubia, K. (2019). Altered white matter connectivity in young people exposed to childhood abuse: A tract-based spatial statistics (TBSS) and tractography study. *Journal of Psychiatry & Neuroscience*, *44*(4), E11. https://doi.org/10.1503/jpn.170241

Mackenbach, J. D., Ringoot, A. P., van der Ende, J., Verhulst, F. C., Jaddoe, V. W. V., Hofman, A., Jansen, P. W., & Tiemeier, H. W. (2014). Exploring the relation of harsh parental discipline with child emotional and behavioral problems by using multiple informants. The Generation R Study. *PLoS One*, *9*(8), e104793. https://doi.org/10.1371/journal.pone.0104793

McDermott, C. L., Seidlitz, J., Nadig, A., Liu, S., Clasen, L. S., Blumenthal, J. D., Reardon, P. K., Lalonde, F., Greenstein, D., Patel, R., Chakravarty, M. M., Lerch, J. P., & Raznahan, A. (2019). Longitudinally mapping childhood socioeconomic status associations with cortical and subcortical morphology. *The Journal of Neuroscience*, *39*(8), 1365–1373. https://doi.org/10.1523/jneurosci.1808-18.2018

McEwen, B. S. (1998). Stress, adaptation, and disease: Allostasis and allostatic load. *Annals of the New York Academy of Sciences*, *840*(1), 33–44. https://doi.org/10.1111/j.1749-6632.1998.tb09546.x

McEwen, B. S. (2001). Plasticity of the hippocampus: Adaptation to chronic stress and allostatic load. *Annals of the New York Academy of Sciences*, *933*(1), 265–277. https://doi.org/10.1111/j.1749-6632.2001.tb05830.x

McEwen, B. S., & Akil, H. (2020). Revisiting the stress concept: Implications for affective disorders. *The Journal of Neuroscience*, *40*(1), 12–21. https://doi.org/10.1523/jneurosci.0733-19.2019

McKinney, C., & Renk, K. (2008). Differential parenting between mothers and fathers: Implications for late adolescents. *Journal of Family Issues*, *29*(6), 806–827. https://doi.org/10.1177/0192513x07311222

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

Meunier, J. C., Bisceglia, R., & Jenkins, J. M. (2012). Differential parenting and children's behavioral problems: Curvilinear associations and mother–father combined effects. *Developmental Psychology*, *48*(4), 987–1002. https://doi.org/10.1037/a0026321

Milad, M. R., & Quirk, G. J. (2012). Fear extinction as a model for translational neuroscience: Ten years of progress. *Annual Review of Psychology*, *63*(1), 129–151. https://doi.org/10.1146/annurev.psych.121208.131631

Muetzel, R. L., Blanken, L. M. E., Ende, J. v. d., Marroun, H. E., Shaw, P., Sudre, G., Lugt, A. v. d., Jaddoe, V. W. V., Verhulst, F. C., Tiemeier, H., & White, T. (2018). Tracking brain development and dimensional psychiatric symptoms in children: A longitudinal population-based neuroimaging study. *American Journal of Psychiatry*, *175*(1), 54–62. https://doi.org/10.1176/appi.ajp.2017.16070813

Muetzel, R. L., Mulder, R. H., Lamballais, S., Cortes Hidalgo, A. P., Jansen, P., Güroğlu, B., Vernooiji, M. W., Hillegers, M., White, T., El Marroun, H., & Tiemeier, H. (2019). Frequent bullying involvement and brain morphology in children. *Frontiers in Psychiatry*, *10*(696). https://doi.org/10.3389/fpsyt.2019.00696

Odaka, H., Adachi, N., & Numakawa, T. (2017). Impact of glucocorticoid on neurogenesis. *Neural Regeneration Research*, *12*(7), 1028–1035. https://doi.org/10.4103/1673-5374.211174

Peverill, M., Sheridan, M. A., Busso, D. S., & McLaughlin, K. A. (2019). Atypical prefrontal–amygdala circuitry following childhood exposure to abuse: Links with adolescent psychopathology. *Child Maltreatment*, *24*(4), 411–423. https://doi.org/10.1177/1077559519852676

R Core Team. (2018). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing.

Raitasalo, K., Holmila, M., Jääskeläinen, M., & Santalahti, P. (2019). The effect of the severity of parental alcohol abuse on mental and behavioural disorders in children. *European Child & Adolescent Psychiatry*, *28*(7), 913–922. https://doi.org/10.1007/s00787-018-1253-6

Roubinov, D. S., & Boyce, W. T. (2017). Parenting and SES: Relative values or enduring principles? *Current Opinion in Psychology*, *15*, 162–167. https://doi.org/10.1016/j.copsyc.2017.03.001

Schiavone, S., Jaquet, V., Trabace, L., & Krause, K.-H. (2013). Severe life stress and oxidative stress in the brain: From animal models to human pathology. *Antioxidants & Redox Signaling*, *18*(12), 1475–1490. https://doi.org/10.1089/ars.2012.4720

Schiller, D., Eichenbaum, H., Buffalo, E. A., Davachi, L., Foster, D. J., Leutgeb, S., & Ranganath, C. (2015). Memory and space: Towards an understanding of the cognitive map. *The Journal of Neuroscience*, *35*(41), 13904–13911. https://doi.org/10.1523/jneurosci.2618-15.2015

Spruijt, A. M., Dekker, M. C., Ziermans, T. B., & Swaab, H. (2019). Linking parenting and social competence in school-aged boys and girls: Differential socialization, diathesis-stress, or differential susceptibility? *Frontiers in Psychology*, *9*(2789). https://doi.org/10.3389/fpsyg.2018.02789

Statistics Netherlands. (2019). *The Netherlands on the European scale 2019*. https://longreads.cbs.nl/european-scale-2019/

Stith, S. M., Liu, T., Davies, L. C., Boykin, E. L., Alder, M. C., Harris, J. M., Som, A., McPherson, M., & Dees, J. E. M. E. G. (2009). Risk factors in child maltreatment: A meta-analytic review of the literature. *Aggression and Violent Behavior*, *14*(1), 13–29. https://doi.org/10.1016/j.avb.2006.03.006

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

Teicher, M. H., & Samson, J. A. (2016). Annual research review: Enduring neurobiological effects of childhood abuse and neglect. *Journal of Child Psychology and Psychiatry*, *57*(3), 241–266. https://doi.org/10.1111/jcpp.12507

Tottenham, N., & Sheridan, M. (2010). A review of adversity, the amygdala and the hippocampus: a consideration of developmental timing. *Frontiers in Human Neuroscience*, *3*(68). https://doi.org/10.3389/neuro.09.068.2009

Uematsu, A., Matsui, M., Tanaka, C., Takahashi, T., Noguchi, K., Suzuki, M., & Nishijo, H. (2012). Developmental trajectories of amygdala and hippocampus from infancy to early adulthood in healthy individuals. *PLoS One*, *7*(10), e46970. https://doi.org/10.1371/journal.pone.0046970

van Buuren, S., & Groothuis-Oudshoorn, K. (2011). mice: Multivariate imputation by chained equations in R. *Journal of Statistical Software*, *45*(3), 67. https://doi.org/10.18637/jss.v045.i03

Wang, J., Shi, X., Yang, Y., Zou, H., Zhang, W., & Xu, Q. (2019). The joint effect of paternal and maternal parenting behaviors on school engagement among Chinese adolescents: The mediating role of mastery goal. *Frontiers in Psychology*, *10*(1587). https://doi.org/10.3389/fpsyg.2019.01587

Wesarg, C., Van Den Akker, A. L., Oei, N. Y. L., Hoeve, M., & Wiers, R. W. (2020). Identifying pathways from early adversity to psychopathology: A review on dysregulated HPA axis functioning and impaired self-regulation in early childhood. *European Journal of Developmental Psychology*, *17*(5), 1–20. https://doi.org/10.1080/17405629.2020.1748594

White, T. J. H., 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., Dennison, M., Schwartz, O., Simmons, J. G., Sheeber, L., & Allen, N. B. (2016). Observed measures of negative parenting predict brain development during adolescence. *PLoS One*, *11*(1), e0147774. https://doi.org/10.1371/journal.pone.0147774

Whittle, S., Yap, M. B. H., Yücel, M., Sheeber, L., Simmons, J. G., Pantelis, C., & Allen, N. B. (2009). Maternal responses to adolescent positive affect are associated with adolescents' reward neuroanatomy. *Social Cognitive and Affective Neuroscience*, *4*(3), 247–256. https://doi.org/10.1093/scan/nsp012

Xerxa, Y., Delaney, S. W., Rescorla, L. A., Hillegers, M. H. J., White, T., Verhulst, F. C., Muetzel, R. L., & Tiemeier, H. (2020). Association of poor family functioning from pregnancy onward with preadolescent behavior and subcortical brain development. *Journal of the American Medical Association Psychiatry*. https://doi.org/10.1001/jamapsychiatry.2020.2862

Xerxa, Y., Rescorla, L. A., Serdarevic, F., Van Ijzendorn, M. H., Jaddoe, V. W., Verhulst, F. C., Luijk, M. P. C. M., & Tiemeier, H. (2020). The complex role of parental separation in the association between family conflict and child problem behavior. *Journal of Clinical Child & Adolescent Psychology*, *49*(1), 79–93. https://doi.org/10.1080/15374416.2018.1520118