The impact of trauma: a focus on the neural correlates of intergenerational transmission of child maltreatment

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Chapter 3

The role of hippocampal volume in the intergenerational transmission of child abuse and neglect - a multigenerational neuroimaging study

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ABSTRACT

Background. Experienced childhood maltreatment has repeatedly been associated with reduced hippocampal volume and enhanced stress reactivity in the hippocampus across the lifespan. The hippocampus also seems to be involved in normative parenting behavior. However, it is unknown whether hippocampal volume alterations are associated with maltreating parenting behavior as well and hence, whether it might play a role in the intergenerational transmission of child maltreatment.

Methods. The current multi-generational family study, including 180 participants with a wide age range (8-70 years) from two generations (parents and their offspring) of 53 families, is the first to investigate the role of hippocampal volume in the intergenerational transmission of child abuse and neglect.

Results. We found associations between experienced child abuse and reduced hippocampal volume, only in men. That is, men who experienced more abuse during their childhood showed smaller bilateral hippocampal volume than men who experienced less childhood abuse, with more pronounced effects in the right hippocampus. No associations between hippocampal volume and perpetrated abuse or neglect were found.

Conclusion. No indications were found for a mediating role of hippocampal volume in the intergenerational transmission of childhood abuse or neglect. Our study highlights the importance to distinguish between different subtypes of maltreatment in research and clinical practice and to take gender effects into account when investigating the impact of child maltreatment.

Key words: child maltreatment, child abuse, child neglect, intergenerational transmission, hippocampal volume, gender.

INTRODUCTION

Child maltreatment is a globally prevalent problem that impairs normative development in biological, social and psychological domains and is associated with serious life-long consequences (e.g., Heim, Shugart, Craighead, & Nemeroff, 2010; McCrory, De Brito, & Viding, 2011; Dannlowski et al., 2012). Some of these adverse consequences are associated with interpersonal functioning, including later parenting behavior (e.g., Norman et al., 2012). That is, parents who experienced maltreatment during childhood have an increased risk of maltreating their own children (e.g., Madigan et al., 2019; Van IJzendoorn, Bakermans-Kranenburg, Coughlan, & Reijman, 2020). However, to date few mechanisms explaining the maltreatment cycle within families have been adequately tested and/or confirmed (Alink, Cyr, & Madigan, 2019). To help identify risk factors for maltreating parenting behavior and design effective preventive interventions, revealing the mechanisms that might play a role in the intergenerational transmission of child maltreatment (ITCM) is crucial. The current multi-generational family study, including 180 participants with a wide age range (8-70 years) from two generations (parents and their offspring) of 53 families, is the first to investigate the role of hippocampal volume in the intergenerational transmission of child abuse and neglect.

Research shows that our brain is particularly sensitive to stress during (early) childhood, probably because of the important neural changes during this period (Lupien, McEwen, Gunnar, Heim, 2009). Early life stress (including childhood abuse and neglect) can have a number of structural and functional neurobiological consequences in key regions of the limbic system, in particular the hippocampus (e.g., Teicher et al., 2003), which have been associated with the onset and severity of psychopathology following child maltreatment (McCrory et al., 2011). The hippocampus is known as one of the most plastic and stress sensitive structures of the human brain and plays an important role in learning and memory (Teicher et al., 2003, 2018; McEwen, 2010; Dannlowski et al, 2012; Whittle et al., 2016). Various psychiatric disorders are associated with alterations in hippocampal volume (Geuze, Vermetten, & Bremner, 2005). Experienced childhood maltreatment has been associated with reduced hippocampal volume (e.g., Riem, Alink, Out, Van IJzendoorn, & Bakermans-Kranenburg, 2015; Whittle et al., 2016; Teicher et al., 2018), both in maltreated individuals with (Thomaes et al., 2010) and without psychopathology (e.g., Dannlowski et al., 2012). These reductions in hippocampal volume are more often reported in adults who experienced child maltreatment than in maltreated children and adolescents (Teicher & Samson, 2016; Whittle et al., 2016). This might suggest a silent period between exposure to maltreatment and its effect on neural development, also referred to as the "sleeper effect" of trauma (Briere, 1992). Possibly, early life stress and repeated adverse events cause a gradual loss of hippocampal synapses over time (Carrion, Weems, & Reiss, 2007). However, some longitudinal studies do suggest that alterations in hippocampal development can already manifest just a few years after maltreatment experiences in children (e.g., Whittle et al., 2016) and may persist into adulthood, even in individuals without psychiatric disorders (Dannlowski et al., 2012). Hence, while there is evidence for an association between experienced child maltreatment and reduced hippocampal volume, findings regarding the exact mechanisms of this effect are mixed.

Furthermore, several other factors are important to take into account when examining the association between childhood maltreatment and hippocampal volume, such as laterality and gender. Findings regarding laterality are mixed. Some studies find effects only for the left or right hippocampus while other results show bilateral hippocampal volume alterations following maltreatment (for a review see Teicher & Samson, 2016). Gender is also an important factor, as the hippocampus seems to be more sensitive to stress in men than in women (e.g., Teicher & Samson, 2016; Whittle et al., 2016) even though the associations between PTSD and hippocampal volume seem to be driven by women (Logue et al., 2018). Mixed findings may be related to the potential protective effect of estrogen in women (McEwen, 2010). Estrogens modulate and mediate synapse and spine formation as well as neurogenesis in the hippocampus (Sheppard, Choleris, & Galea, 2019), and therefore stress may affect hippocampal development in men in particular (Teicher et al., 2018). Finally, type of maltreatment also seems important to take into account, as reduced hippocampal volume is found to be more strongly associated with experienced childhood abuse than with experienced childhood neglect (e.g., Hanson et al., 2015; Teicher & Samson, 2016). Moreover, gender-specific effects of abuse versus neglect on hippocampal volume are also described as one of the most important gender differences in the developing human brain (Teicher et al., 2018).

Alterations in the neural substrates associated with exposure to childhood maltreatment, such as the hippocampus, are likely to play a key role in social functioning via its impact on emotion processing and responding (Elzinga & Bremner, 2002; Hart & Rubia, 2012) and the control of aggression (Davidson, Putnam, & Larson, 2000). Hence, disruptions in these neural substrates in parents who experienced childhood maltreatment might make them more vulnerable to maltreatment of their own children. We therefore hypothesize that the hippocampus might be involved in one of the mechanisms underlying ITCM. To date, in spite of evidence for an association between experienced child maltreatment and reduced hippocampal volume, research on the neural correlates of maltreating parenting behavior is scarce (Van IJzendoorn et al., 2020). While neurobiological antecedents are suggested to play an important role as parental risk factors in the aetiology of child maltreatment, there are major gaps in knowledge regarding those neural antecedents of maltreatment. Functional imaging studies have demonstrated the involvement of the hippocampus in normative parenting behavior (Swain, Lorberbaum, Kose, & Strathearn, 2007). Context and memory processing regions, neural arousal and salience detection centers including the hippocampus support adequate parenting behaviors. For example, increased hippocampal activation was found while parents were exposed to the cry sounds of their own infant (Swain et al., 2004). Moreover, increased hippocampal activation was also found in mothers who were exposed to images of their own infant versus familiar and unknown infant facial images (Strathearn, 2002). However, to the best of our knowledge, little is known about the association between maltreating parenting behavior and hippocampal volume.

The current study is the first to examine the associations of (bilateral) hippocampal volume with both experienced childhood maltreatment and perpetrated maltreating behavior, enabling the investigation of the potential mediating role of hippocampal volume in ITCM. We used a multi-informant, multigenerational family design including 180 participants with a wide age range (8-70 years) from two generations of 53 families. We differentiated between effects of (experienced and perpetrated) abuse and neglect, as different types of maltreatment might be differentially associated with hippocampal volume (e.g., Hanson et al., 2015; Teicher & Samson, 2016). We also examined the role of gender and possible age effects on the association between hippocampal volume and experienced childhood maltreatment. We hypothesized that experienced childhood abuse and neglect are associated with reduced hippocampal volume, and that these effects are more pronounced in older participants who experienced child abuse. We also predicted to find a stronger association between experienced maltreatment and reduced hippocampal volume in men than in women. Furthermore, we hypothesized that reduced hippocampal volume is associated with perpetrated childhood maltreatment as well, and we examined whether hippocampal volume (partly) mediates ITCM.

METHOD

Participants

The current sample is a subsample from the larger 3 Generation (3G) parenting study, a three-generation family study on the intergenerational transmission of parenting styles, stress and emotion regulation (see also Van den Berg et al., 2018; Van den Berg, Tollenaar, Compier-de Block, Bakermans-Kranenburg, & Elzinga, 2019; Buisman et al., 2020). For this family study, participants were recruited via three other studies that included the assessment of caregiving experiences (Penninx et al., 2008; Scherpenzeel, 2011; Joosen, Mesman, Bakermans-Kranenburg, & Van IJzendoorn, 2013). Participants with an increased risk of experienced maltreatment were oversampled. Participants who had at least one child of 8 years or older were invited to participate in the 3G study. After their consent, their family members (parents, partners, offspring, adult siblings, nephews, nieces and in-laws) were invited to participate as well (total *n* = 395). All participants from the 3G study who participated in the fMRI part of the study were included for the current study. In total, we included 180 participants (*n* = 78 men and *n* = 102 women) from two generations (parents and their offspring) of 53 families. The mean age of the parents (*n* = 101; 45 men and 56 women) was 46.9 years (SD = 10.67, age range: 26.6-69.7 years) and the mean age of the offspring (*n* = 79; 33 male and 46 female) was 18.6 (SD = 7.75, age range: 8.0-40.1 years). See Supplement for more information on the relatedness, ethnicity and educational level of our participant sample.

Procedure

Written informed consent was obtained from all participants. We invited participants and their families to our lab at the Leiden University Medical Center (LUMC) for one or two days, depending on family composition. Participants with children visited the lab once with their family of origin and once with their nuclear family. During these laboratory visits, questionnaires and computer tasks were completed and saliva and hair samples were collected. Furthermore, participants did several interaction tasks together with their family members. If eligible, parents and their offspring were asked to participate in the MRI part of the 3G study. Imaging included several structural and functional scans. Results regarding the functional scans are reported elsewhere (Van den Berg et al., 2018, 2019). All offspring younger than 18 years were first familiarized with the MRI scanner using a mock scanner. The full protocol was conducted according to the principles expressed in the Declaration of Helsinki and approved by the Medical Ethics Committee of the LUMC (P11.134).

Measures

Childhood maltreatment

Experienced childhood abuse and neglect, perpetrated by mother and/or father, were assessed in all participants using adapted versions of the Conflict Tactics Scales (CTS; Straus, Hamby, Finkelhor, Moore, & Runyan, 1998) for emotional and physical abuse and physical neglect, which was supplemented with the emotional neglect scale from the Childhood Trauma Questionnaire (CTQ-SF; Bernstein et al., 2003; see also Buisman et al., 2020). All parents also filled out a CTS version in which they reported on their own perpetrated abusive and/or neglectful behaviors towards (each of) their child(ren). For experienced and perpetrated maltreatment separately, an overall Abuse score was comprised by averaging Emotional and Physical Abuse, and an overall Neglect score by averaging Emotional and Physical Neglect. Whenever possible, we combined information from multiple informants: offspring (experienced childhood maltreatment) and their parents (perpetrated child maltreatment; see Supplement). Because the distribution of the CTS data was skewed, scores were log-transformed (log10). Outliers (values more extreme than a standardized value of +/- 3.29), were winsorized to the most extreme value within the normal range plus or minus the difference between the two most extreme values within the normal range (*n* = 1 for experienced abuse and *n* = 1 for experienced neglect; Tabachnik & Fidell, 2001).

Covariates

Demographic information (age, gender, handedness and household social economic status (SES)) was assessed for all participants using questionnaires. Psychopathology symptoms were assessed based on three versions of Achenbach's screening questionnaires. For children younger than 12 years old, parents completed the Child Behavioral Checklist (CBCL; Achenbach, 1991). Participants aged 12-17 years filled out the Youth Self Report (YSR; Achenbach & Rescorla, 2001) and for participants from 17 years up the Adult Self Report (ASR; Achenbach & Rescorla, 2003) was used. A total psychopathology symptom score was calculated per questionnaire. Cronbach's alphas were good to excellent (.83-.97). To control for total intracranial volume (ICV), ICV was added as a covariate as well (see subsection 2.5 for more information on the MRI data analysis).

MRI data acquisition

High-resolution T1-weighted scans were acquired for all participants using a standard whole-head coil on a 3-T Philips Achieva scanner (Philips Medical Systems, Best, The Netherlands) in the LUMC. Foam inserts that surrounded the head were used to minimize head movement. Scan parameters were as follows: TR = 9.8 ms, TE = 4.6 ms, flip angle = 8°, 140 slices, voxel size = 0.875 x 0.875 x1.2 mm, FOV = 224×177×168 mm. All anatomical MRI scans were inspected by a neuroradiologist from the Radiology department of the LUMC. No anomalous findings were reported.

MRI data analysis

Cortical reconstruction and volumetric segmentation was performed using standard procedures in the FreeSurfer software (version 5.3.0), which is freely available (http://surfer.nmr.mgh.harvard.edu/). See Supplement for a short description of this process.

Subcortical segmentations of the hippocampus were visually inspected for accuracy according to standardized protocols designed to facilitate harmonized image analysis across multiple sites (http://enigma.ini.usc.edu/protocols/imaging-protocols/; see also e.g., Bas-Hoogendam et al., 2018). This quality control resulted in the exclusion of four participants. In addition, data of four other participants were excluded because the brain could not be reliably reconstructed from the T1-weighted scans using FreeSurfer. Volumes of the right and left hippocampi were checked for outliers (i.e., values with a standardized value of +/- 3.29) and winsorized when necessary (*n* = 1). Volumes of the left and right hippocampus (mm3) and total ICV (mm3) were included in the statistical analyses in SPSS (see below).

Multilevel analyses

Using SPSS 23, we employed three-level multilevel regression analyses to take the family structure of the data into account to examine whether experienced and perpetrated maltreatment was associated with hippocampal volume. Participants were nested within households (i.e., parents with their offspring) and households were nested within families (i.e., related households). Therefore, a model with three levels was specified, in which level 1 estimates variation at the participant level, level 2 captures variation among participants within the same households and level 3 models variation among families. Random intercept models were built sequentially. To test for random variation in the outcome variables at the different levels and compute the intraclass correlation coefficients (ICC) at the family and household level, we started with an empty (null) model without explanatory variables (see Table 1). Independent of ICC, multilevel analyses were consistently used to match the hierarchical structure of our data.

Table 1. Variance accounted for (ICCs) on household and family level.

	Hippocampus (bilateral)	Hippocampus (right)	Hippocampus (left)
Family level	.265	.241	.264
Household level	.002	.004	.012

Next, age, gender, handedness, ICV, socio-economic status (SES) and psychopathology were entered to the model as possible covariates. Because of the large age range in our study and because early adverse experience may yield different neurobiological manifestations in men and women (Teicher et al., 2003), age and gender were always included as covariates and factors in the final model. All other covariates were omitted when *p*-values exceeded .05. Separate models were run for experienced maltreatment (all participants: $n = 180$) and perpetrated maltreatment (parents only: $n = 101$). In Model 1 the main effects of abuse and neglect were added to examine the fixed effects of abuse and neglect. For experienced maltreatment a second model was tested in which the interaction effects of age x abuse, gender x abuse, age x neglect and gender x neglect were added. For the first multilevel regression analyses right- and left hippocampal volumes were combined. In case of significant results for bilateral hippocampal volume, we repeated our analyses for right- and left hippocampal volumes separately to examine possible effects of lateralization. All (continuous) predictor variables and covariates were centered. All independent and dependent variables were measured at the individual level (except SES, which was measured at the level of the household) and considered in the fixed part of the model. If both experienced and perpetrated maltreatment were found to be associated with hippocampal volume, mediation analyses were planned to examine the role of hippocampal volume in ITCM. However, this was not the case for the findings of this study.

RESULTS

Intergenerational transmission of childhood maltreatment

Characteristics of the sample (including maltreatment scores) are summarized in Table 2. Experienced abuse and neglect were strongly associated (r = .52, p < .001), and parental abusive and neglectful behavior were moderately associated (r = .38, p < .001). For all participants with offspring (n = 101 parents) regression analyses were conducted with experienced abuse and neglect as predictors and abusive and neglectful behavior as outcome measures separately to examine intergenerational transmission of childhood abuse and neglect in the current sample. Standardized regression coefficients are reported. Controlling for age, gender, household SES and psychopathology in the first block, experienced abuse (β = .50, t(94) = 4.68, p < .001) was a significant predictor of abusive behavior, whereas experienced neglect did not predict abusive behavior (β = -.14, t(94) = -1.24, p = .217) and none of the covariates were significant. Experienced neglect (β = .02, t(94) = 0.13, p = .897) and experienced abuse (β = -.04, t(94) = -0.32, p = .749) did not predict neglectful behavior. Psychopathology (β = .30, t(94) = 2.88, p = .005) was the only significant covariate for neglectful behavior.

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Table 2. Demographics and maltreatment scores (full sample n = 180).

Variables	Mean (SD)	Range
Age	34.50 (17.00)	8.00 - 69.67
Gender (*n:* men/women)	78/102	-
Handedness (*n*: left/right)	23/157	-
Abused[a]	1.62 (0.48)	1.00 - 4.50
Neglected[a]	1.83 (0.57)	1.00 - 5.00
Maltreated[a] (total)	1.73 (0.47)	1.02 - 4.75
Abusive[b] (n = 101)	1.46 (0.31)	1.00 - 2.53
Neglectful[b] (n = 101)	1.58 (0.33)	1.00 - 2.48
Maltreating[b] (total; n = 101)	1.52 (0.26)	1.00 - 2.22

[a]Combined experienced maltreatment scores by averaging parent and child reports as measured with the CTS. [b]Combined maltreating behavior scores by averaging parent and child reports as measured with the CTS.
Values of all included participants are presented (n = 180) unless otherwise specified.
Raw scores are presented.

Multilevel analyses: hippocampal volume and maltreatment

The ICC was .265 at the family level and .002 at the household level for bilateral hippocampal volume (see Table 1), indicating that hippocampal volumes within families (but not within households) are more similar compared to unrelated participants. Since right and left hippocampal volumes were significantly correlated (r = .72, p < .001), multilevel regression analyses were run using bilateral hippocampal volume to examine the associations with severity of experienced maltreatment (all participants: n = 180) and severity of perpetrated maltreating parenting behavior (participants with offspring: n = 101) separately. Only in case of significant findings, we repeated our analyses for right- and left hippocampal volumes separately. All multilevel regression analyses were run controlling for age, gender, handedness, ICV, SES and psychopathology. Unstandardized regression coefficients are reported.

Table 3. Multilevel models of hippocampal volume as related to experienced childhood abuse and neglect (n = 180).

Hippocampal volume									
	Bilateral			Right			Left		
	b	SE	*p*	*b*	SE	*p*	*b*	SE	*p*
Null model									
age	-13.93	3.83	.000**	-6.50	2.02	.002**	-8.05	2.35	.001**
gender (0=men)	591.69	124.58	.000**	284.33	66.14	.000**	315.01	76.84	.000**
handedness	256.83	195.05	.190	147.79	103.03	.153	141.39	119.77	.239
ICV	< 0.01	< 0.01	.209	< 0.01	< 0.01	.061	< 0.01	< 0.01	.459
SES	136.02	106.89	.205	37.15	55.32	.503	107.14	64.52	.099
PP	-445.94	328.16	.176	-117.14	172.86	.499	-352.61	201.11	.081
Model 1									
abused	-1269.33	732.47	.085	-633.22	383.86	.101	-606.54	450.20	.180
neglected	937.12	695.45	.180	569.92	366.14	.121	390.72	428.92	.364
	χ^2 (2) = 3.41		.182	χ^2 (2) = 3.57		.168	χ^2 (2) = 1.91		.385
Model 2									
abused*age	35.14	40.10	.382	15.73	21.15	.458	24.11	24.93	.335
neglected*age	-58.52	37.61	.122	-33.65	19.85	.092	-23.88	23.37	.308
	χ^2 (2) = 2.41		.300	χ^2 (2) = 2.79		.248	χ^2 (2) = 1.36		.506
Model 3									
abused*gender	-3091.66	1376.48	.026*	-1809.55	724.62	.013*	-261.36	861.69	.145
neglected*gender	118.93	1253.32	.925	97.89	660.99	.882	-43.79	785.53	.956
	χ^2 (2) = 6.64		.036*	χ^2 (2) = 8.03		.018*	χ^2 (2) = 3.08		.214

* $p < .05$; ** $p < .01$
ICV = intracranial volume; SES = social economic status; PP = psychopathology

Hippocampal volume: associations with experienced abuse and neglect

Results for the multilevel analyses with experienced abuse and neglect as predictors and bilateral hippocampal volume as outcome measure are shown in Table 3. Age (β = -13.93, SE = 3.83, $p < .001$; with smaller hippocampal volume in older participants) and gender (β = 591.69, SE = 124.58, $p < .001$; larger hippocampal volume in men compared to women) were the only significant covariates. In contrast to our expectations, no significant main effects were found for experienced abuse or neglect, nor significant interaction effects with age, on bilateral hippocampal volume (all $p > .08$). Results also showed no significant interaction between experienced neglect and gender on bilateral hippocampal volume ($\beta = 118.93$, SE = 1253.32, $t = 0.10$, $p = .925$). However, results did reveal a significant improvement of the model when the interaction between abuse and gender was added to the model (χ^2 (2) = 6.64, $p = .036$). The interaction term ($\beta = -3091.66$, SE = 1376.48, $t = -2.25$, $p = .026$) indicates that in men who experienced more childhood abuse bilateral hippocampal volumes were smaller than men who experienced less abuse, while for women bilateral hippocampal volume was not related to experienced abuse (see Figure 1).

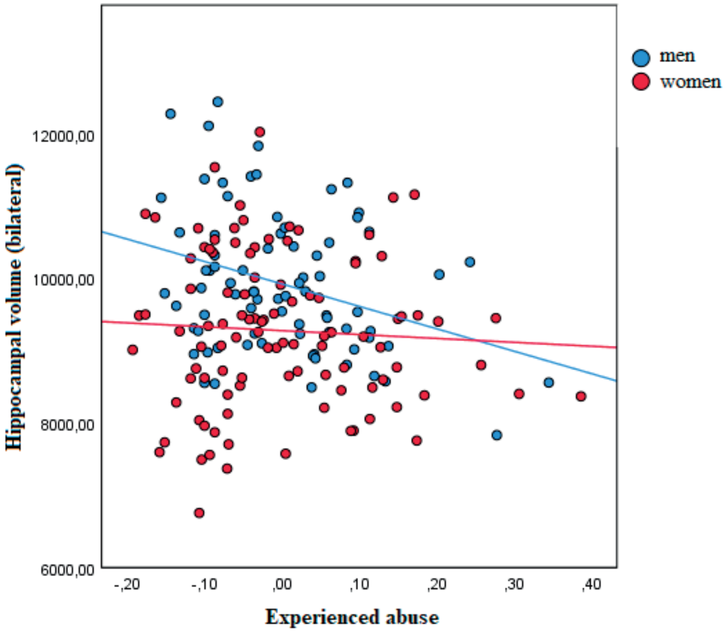

Figure 1. Visual representation of the significant interaction effect between experienced abuse and gender for bilateral hippocampal volume.

Additionally, we performed exploratory post-hoc analyses for right and left hippocampal volumes separately to examine possible lateralization effects (see Table 3). In the right hippocampus the same interaction effect between abuse and gender was found following the same interaction pattern ($\beta = -1809.55$, SE = 724.62, $t = -2.497$, $p = .013$) as was found for bilateral hippocampal volume. This was not the case for the left hippocampus ($\beta = -1261.36$, SE = 861.69, $t = -1.464$, $p = .145$).

Hippocampal volume: associations with abusive and neglectful behavior

Multilevel analyses were conducted for participants with offspring (n = 101) with abusive and neglectful behavior as predictors and bilateral hippocampal volume as outcome measure. Gender ($p < .001$) was again a significant covariate showing larger bilateral hippocampal volume in men compared to women, whereas age was not a significant covariate among participants with offspring. Results showed no significant main effects for abusive ($p = .836$) or neglectful behavior ($p = .704$) for bilateral hippocampal volume (see Table 4). Consequently, no mediation analyses on ITCM were conducted.

Table 4. Multilevel models of hippocampal volume as related to abusive and neglectful behavior (n = 101).

Bilateral hippocampal volume			
	b	SE	*p*
Null model			
age	-12.84	8.83	.149
gender	611.15	167.60	.001**
handedness	92.96	293.93	.753
ICV	< -0.01	< 0.01	.528
SES	209.72	139.49	.137
PP	-718.77	445.34	.110
Model 1			
abusive	-239.14	1155.66	.836
neglectful	-445.79	1170.51	.704
	χ^2 (2) = 0.28		.869

* $p < .05$; ** $p < .01$

ICV = intracranial volume; SES = social economic status; PP = psychopathology

DISCUSSION

The primary aim of the current study was to examine the potential role of hippocampal volume in ITCM using a multigenerational family study design. This design enabled us to differentiate between effects of (experienced and perpetrated) abuse and neglect. Moreover, we examined age and gender effects on the association between hippocampal volume and experienced childhood maltreatment.

Experienced abuse and neglect

Against our hypotheses, we found no associations between experienced childhood abuse or neglect and hippocampal volume in our total sample of participants. This is not in line with previous studies reporting reductions in hippocampal volume in maltreated individuals (e.g., Riem et al., 2015; Whittle et al., 2016; Teicher et al., 2018). However, we did find an interesting gender effect in this respect. Previous findings on gender differences in hippocampal volume have not always been consistent, which might be (partly) due to the use of different types of analyses or sample sizes (Perlaki et al., 2014). Our findings indicate that men who experienced more abuse during their childhood show smaller bilateral hippocampal volume than men who experienced less childhood abuse. These effects are particularly present in the right hippocampus. For women, experienced abuse or neglect were not related to hippocampal volume. This is in line with previous research showing that the male hippocampus is more sensitive to stress than the female hippocampus (e.g., Teicher & Samson, 2016; Whittle et al., 2016). Gender differences in the effects of experienced maltreatment on hippocampal volume may result in different neurocognitive and neuropsychological consequences (Teicher et al., 2018). These gender differences may be due to the potential protective effect of estrogen in women (McEwen, 2010) and dimorphic differences in developmental trajectory (Teicher et al., 2018). Childhood stress may affect hippocampal development in women by enhancing pubertal pruning, while it may lead to decreasing neurogenesis in men.

The finding that hippocampal volume in men was only associated with experienced abuse and not with experienced neglect is consistent with studies showing that specific types of maltreatment seem to selectively affect sensory systems and neural pathways that process stressful and traumatic incidents (Teicher & Samson, 2016). Our findings regarding the association between hippocampal volume and experienced abuse are consistent with previous studies showing reduced hippocampal volume to be more strongly associated with experienced childhood abuse than with experienced childhood neglect (e.g., Hanson et al., 2015; Teicher & Samson, 2016). However, those previous studies report their findings mostly in abused adults, whereas the current study demonstrates reduced hippocampal volume in abused men with a large age range.

Atypical hippocampal volume as a result of experienced child maltreatment might manifest as hippocampal asymmetry. Mixed findings regarding laterality in the literature are partly related to differences in sample characteristics such as age (Teicher & Samson, 2016). For example, greater right-sided than left-sided hippocampal effects are reported in adults with borderline personality disorder or without psychopathology. This highlights the importance of including participants with a large age range. In the current study a sample with a wide age range (8.0 to 69.7 years) was included which may help clarify the inconsistent findings regarding hippocampal volume in maltreated children and adolescents compared to adults (e.g., Edmiston et al., 2011). Since reductions in hippocampal volume are more often found in adults maltreated as children than in maltreated children and adolescents (Teicher & Samson, 2016; Whittle et al., 2016) we expected to find more pronounced effects of experienced maltreatment in older participants. In general, irrespective of maltreatment, we found smaller bilateral hippocampal volume in older participants in the current sample, even though in the older subsample of parents, age was not a significant predictor. This is in line with other studies showing loss of hippocampal volume into adulthood in the general population (e.g., Erickson et al., 2010). While estimates of age-related hippocampal volume loss vary widely across different studies, almost all report negative correlations between age and hippocampal volume (for a review see Van Petten, 2004). Importantly though, no interaction effects between experienced maltreatment and age were found in the current study. A within subject longitudinal design might further examine any age effects of the impact of experienced maltreatment, but our results suggest that the effect on hippocampal volume in men may be independent of age at measurement of the hippocampal volume.

Abusive and neglectful behavior

Even though some (functional) MRI studies have demonstrated the involvement of the hippocampus in parenting behavior in general (Swain et al., 2007), to date little is known about the role of hippocampal volume in maltreating parenting behavior. To the best of our knowledge the current study is the first to examine the association between abusive and neglectful behavior and hippocampal volume using a large multigenerational sample. Reduced hippocampal volume might play a role in the intergenerational transmission of maltreatment, because it has been associated with dysregulated responses to stress (Riem et al., 2015). Our findings provide indications that parental abusive or neglectful behavior is not associated with hippocampal volume. While alterations in specific regions of the human brain (including the hippocampus) following experienced childhood maltreatment have been consistently found across populations, linking such brain changes to brain function and future behavior seems to be more complex (e.g., Van den Berg, 2018, 2019). Even when it comes to memory, one of the most well-known functions of the hippocampus, mixed findings are reported regarding the size-function relationship of the hippocampus (e.g., Pohlack et al., 2014). For example, some studies report a surprisingly weak association between hippocampal size and episodic memory ability (e.g., Van Petten, 2004; Charlton, Barrick, Markus, & Morris, 2010). More research is needed to further understand the neural correlates of maltreating parenting behavior. An alternative explanation for our findings could be that the role of hippocampal volume in maltreating parents with a history of maltreatment is masked by compensatory changes in other brain regions (e.g., Van der Werff, Van den Berg, Pannekoek, Elzinga, & Van der Wee, 2013; Galinowski et al., 2015). This highlights the importance to also include other brain areas and their connectivity that might play a role in parenting behavior in future research, for example the corpus callosum, the anterior cingulate and the dorsolateral prefrontal cortex.

Intergenerational transmission of maltreatment

While we found smaller bilateral hippocampal volume in men who experienced more childhood abuse, parental abusive behavior was not associated with hippocampal volume. Hence, no indications were found for a role of hippocampal volume in ITCM in the current study.

On a behavioral level we observed intergenerational transmission of abuse, whereas intergenerational transmission of neglect was not found. This is in line with our findings regarding transmission of maltreatment in the total sample (*n* = 395) of the 3G Parenting study, where intergenerational transmission of abuse was consistently found independent of the informant (Buisman et al., 2020). The transmission of neglect was only found when analyses were based on the perspective of a single reporter. That is, self-reported experienced neglect predicted self-reported perpetrated neglect, but intergenerational transmission of neglect was not found using the current multi-informant approach where reports of different informants from each generation were combined. This calls the validity of the intergenerational transmission of neglect into question.

Limitations and recommendations for future studies

It is important to note that the majority of our participants reported about child maltreatment retrospectively. On the one hand, research shows that retrospective reports of maltreatment may be verifiable (Chu, Frey, Ganzel, & Matthews, 1999). On the other hand, a recent meta-analysis reports poor agreement between prospective and retrospective measures of childhood maltreatment (Baldwin, Reuben, Newbury, & Danese, 2019). Recall bias might have affected reports of childhood events in our study. A prospective study following three generations would be recommended, but practical possibilities to conduct such a study may be limited.

A few other limitations should also be taken into account when drawing conclusions based on our findings. Since not all participants were parents, we had less statistical power to examine the effects of perpetrated maltreatment than the effects of experienced maltreatment. Hence, the fact that we only found associations for experienced abuse and neglect and not for abusive and neglectful behavior may (partly) be due to differences in sample size. Another limitation of the current study is the lack of exact information on the age of exposure to the maltreatment experiences, although maltreatment tends to be chronic for many children (e.g., Gilbert et al., 2009). Future research should take this timing into account to examine possible sensitive exposure periods on hippocampal volume which might also be gender-specific (Teicher et al., 2018). Moreover, replication studies are warranted to determine the empirical robustness of our findings.

Conclusion

Our study highlights the importance to distinguish between different types of maltreatment and to take gender effects into account when investigating the associations between abuse and neglect and hippocampal volume. We found associations between experienced child abuse and reduced hippocampal volume in men. That is, men who experienced more abuse during their childhood show smaller bilateral hippocampal volume than men who experienced less childhood abuse, with more pronounced effects in the right hippocampus. No associations between hippocampal volume and perpetrated maltreatment (abuse or neglect) were found. Hence, we found no indications for a mediating role of hippocampal volume in ITCM.

The hippocampus is one of the most sensitive and plastic regions of the brain (McEwen, 2010). This plasticity might be functional to protect against permanent neural damage, but at the same time it may increase its vulnerability to stress. All the same, volume loss of the hippocampus as a result of childhood maltreatment points towards the need to examine effects of efforts to alleviate hippocampal volume reduction through psychotherapeutic or psychopharmacological interventions. For example, promising preliminary results show that mindfulness is associated with increased hippocampal volume and with improvement in hippocampal-dependent cognitive performance in maltreated young adults (Teicher & Samson, 2016). Further research into other neural mechanisms that might play a role in the intergenerational transmission of abuse and neglect is important for the design and implementation of effective preventive interventions.

CONFLICT OF INTEREST

None declared.

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SUPPLEMENT

Participants

The total sample of participants for the current study included six parent-child pairs with two parents and two children (*n* = 24), 13 pairs with two parents and one child (*n* = 39), 13 pairs with one parent and two children (*n* = 39), 17 pairs with one parent and one child (*n* = 34) and one pair with two children and three parents (two biological parents and a stepfather; *n* = 5). Additionally, 29 parents participated without their children and 10 children participated without their parents participating. The vast majority of all participants (96%) were Caucasian, five participants were of Latin-American descent and two of mixed descent. Elementary school or a short track of secondary school was completed by 27% of all participants, 33% held an advanced secondary school or vocational school diploma, 18% held a college or university degree and 7% a postgraduate diploma. 10% of all participants were still in elementary school. Education level of 5% was unknown, but most of these participants were under 17 years old.

Childhood maltreatment

For 123 out of 180 participants at least two informants (offspring and their parents) reported on maltreatment from the experienced and perpetrator perspective, respectively. In a similar vein, for 83 out of 101 parents at least two informants (parents and their children) reported on maltreating behavior.

MRI data analysis

The technical details of these procedures are described elsewhere (e.g., Fischl & Dale, 2000; Fischl et al., 2004a, 2004b; Jovicich et al., 2006; Reuter, Rosas, & Fischl, 2010). In short, this process includes motion correction, removal of non-brain tissue using a hybrid watershed/surface deformation procedure (Ségonne et al., 2004), automated Talairach transformation, segmentation of subcortical volumetric structures (Fischl et al., 2002; Fischl et al., 2004a), intensity normalization (Sled, Zijdenbos, & Evans, 1998), tessellation of the gray matter white matter boundary, automated topology correction (Fischl, Liu, & Dale, 2001; Ségonne, Pacheco, & Fischl, 2007), and surface deformation following intensity gradients to optimally place the gray/white and gray/cerebrospinal fluid borders at the location where the greatest shift in intensity defines the transition to the other tissue class (Dale & Sereno, 1993; Dale, Fischl, & Sereno, 1999; Fischl & Dale, 2000). Separate volumes of the right and left hippocampi (mm3) were generated for each participant. Additionally, total individual ICV (mm3) was extracted to use as a covariate in our analyses. Freesurfer morphometric procedures have been demonstrated to show good test-retest reliability across scanner manufacturers and across field strengths (Han et al., 2006; Reuter, Schmansky, Rosas, & Fischl, 2012).

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