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Abstract

Emerging research suggests that normative variation in parenting quality relates to children's brain development. However, although the young brain is presumed to be especially sensitive to environmental influence, to our knowledge only two studies have examined parenting quality with infants as it relates to indicators of brain development, and both were cross-sectional. This longitudinal study investigated whether different components of maternal sensitivity in infancy predicted the volume of two brain structures presumed to be particularly sensitive to early experience, namely the amygdala and the hippocampus. Three dimensions of sensitivity (Cooperation/Attunement, Positivity, Accessibility/Availability) were observed in 33 mother-infant dyads at 1 year of age and children underwent structural magnetic resonance imaging at age 10. Higher maternal accessibility/availability during mother-infant interactions was found to be predictive of smaller right amygdala volume, while greater maternal positivity was predictive of smaller bilateral hippocampal volumes. These longitudinal findings extend those of previous cross-sectional studies, and suggest that a multidimensional approach to maternal behavior could be a fruitful way to further advance research in this area, given that different facets of parenting might be differentially predictive of distinct aspects of neurodevelopment.

Mother-infant interaction and child brain morphology: A multidimensional approach to maternal sensitivity

It is now widely accepted that brain development is not only shaped by genetic factors, but also results from interactions between children and their environment (Belsky & de Haan, 2011; Fox, Levitt, Nelson, 2010; Stiles, 2009). Infancy may be particularly salient in this respect, as the brain is especially sensitive to environmental influences when it is undergoing rapid change (Casey, Giedd, & Thomas, 2000; Lupien, McEwen, Gunnar, & Heim, 2009), such as it is in infancy: the first year of life constitutes the period of greatest brain growth in normally developing children, with total brain volume reaching approximately 72% of its adult size at age 12 months (Knickmeyer et al., 2008). Environmental input during this period of accelerated growth might substantially influence the developing infant brain, and this could snowball into long-term consequences for children's neural development.

As one of the earliest, most intense, and most enduring experiences of childhood, the parent-child relationship lies at the heart of young children's environment and thus constitutes a prime candidate to account for environmentally-driven differences in children's brain maturation (Cicchetti, 2016; Lupien et al., 2011; Tottenham, 2014). Yet, Belsky and de Haan (2011) noted that nearly all research examining associations between children's brains and their caregiving experiences has focused on grossly inadequate caregiving (e.g., populations of institution-reared or maltreated children). Some progress has since been made in the investigation of the effects of normative variations in parenting quality on child brain development (e.g., Luby, Belden, Harms, Tillman, & Barch, 2016; Whittle et al., 2014), but this literature is still scarce, generally excludes infants, and is often based on retrospective data or self-reported parenting. Aiming to contribute to this emerging field, the current report focuses on what is perhaps the most widely used indicator of parenting quality toward infants: maternal sensitivity. In this 9-year prospective longitudinal study, we use an empirically-derived operationalization of maternal sensitivity to investigate whether different components of sensitivity as observed during mother-infant interactions predict the volume of two brain structures that are deemed sensitive to early experience, namely the amygdala and the hippocampus.

Caregiving and brain development in typically-developing children

Studies conducted with institutionalized or maltreated children (see Bick & Nelson, 2016; and Callaghan & Tottenham, 2016, for reviews) as well as animal research (Meaney, 2001) suggest that particular regions of the brain may be especially sensitive to caregiving influences, notably the hippocampus and amygdala (Tottenham & Sheridan, 2010). The hippocampus and amygdala are key components of the limbic system that are centrally implicated in basic socio-emotional functioning, in that they aid in learning about the emotional significance of the social environment (McDonald & Mott, 2017; Tottenham & Sheridan, 2010; Zheng et al., 2017). The amygdala plays a salient role in orienting to and processing emotionally significant information (Janak & Tye, 2015; Jin, Zelano, Gottfried, & Mohanty, 2015; Phelps & LeDoux, 2005). The hippocampus is central to learning and memory (O’Keefe & Nadel, 1978; Squire & Zola-Morgan, 1991) and consequently supports the retention of the emotional significance of events (Phelps, 2004), including those that relate to social interactions (Rubin, Watson, Duff, & Cohen, 2014). Importantly, both the amygdala and hippocampus develop rapidly during the first few years of life (Gilmore et al., 2012; Uematsu et al., 2012) and appear to be sensitive to early environmental influence (Tottenham & Sheridan, 2010).

Given that the hippocampus and amygdala play a key role in socio-emotional processing and responding early in life, they can be expected to be activated during, and thus influenced by, normative daily interactions between infants and their caregivers (Moutsiana et al., 2015). It is only very recently though that research has begun to investigate such claims among typically-developing children and to our knowledge only two studies, both cross-sectional, have investigated the relations between quality of parental care and brain morphology among infants (Rifkin-Graboi et al., 2015; Sethna et al., 2017). Both studies focused on the construct of maternal sensitivity, which consists of the accurate interpretation followed by prompt and appropriate response to the infant's signals (Ainsworth, Blehar, Waters, & Wall, 1978). A long history of empirical research shows that maternal sensitivity is predictive of child socio-emotional (Leerkes, Blankson, & O'Brien, 2009), cognitive (Tamis-LeMonda, Shannon, Cabrera, & Bradley, 2004), and biological functioning (Atkinson et al., 2013). Such associations could transit in part through an impact of sensitivity on infants' neural structures. In line with this, Sethna et al. (2017) reported a positive relation between maternal sensitivity during a face-to-face mother-infant interaction and concurrent overall subcortical gray matter volume (including the caudate, putamen, globus pallidus and thalamus) among 3 to 6 month-old infants. Somewhat contrasting with these findings, Rifkin-Graboi et al. (2015) observed that higher maternal sensitivity during a play session was related to *smaller* hippocampal volume among 6-month-olds, with similar but non-significant associations with the amygdala. These two studies suggest that there are links between maternal sensitivity and children's subcortical structures as early as infancy, but interpretation of these findings is constrained by the concurrent nature of the data. In a rare longitudinal study considering maternal sensitivity as an antecedent of child brain development, Kok et al. (2015) observed that higher sensitivity during play and problem-solving sequences across the preschool years (between 1 and 4 years of age) predicted larger total, but not regional, gray matter volume at age 8.

Two other studies are relevant to our aims. Although these studies did not assess maternal sensitivity, both examined another central indicator of the quality of early caregiving relationships, namely mother-infant attachment. Lyons-Ruth, Pechtel, Yoon, Anderson, and Teicher (2016) as well as Moutsiana et al. (2015) examined the quality of mother-infant attachment at 18 months as a predictor of hippocampal and amygdala volumes in adulthood. Both studies found that lower-quality mother-infant attachment predicted increased volume of the amygdala, and Lyons-Ruth et al. (2016) also reported a similar albeit non-significant trend with the hippocampus. Given that sensitivity is a well-documented predictor of attachment (De Wolff & Van IJzendoorn, 1997), these two studies provide indirect evidence for a potential role of maternal sensitivity in hippocampal and amygdala long-term structural development.

Overall, although studies are just beginning to emerge, there is preliminary support for the hypothesis that maternal sensitivity experienced during mother-infant interactions may contribute to shaping infants’ developing brains, notably the hippocampus and amygdala (although directionality of the links varies across studies). However, studies to date have used one global score of sensitivity to operationalize the quality of maternal care, though sensitivity is a rich and complex construct that encompasses a range of qualitatively distinct behaviors (De Wolff & Van IJzendoorn, 1997; Nievar & Becker, 2008). While understandable given the very young state of this literature, such a global approach to sensitivity may not be optimal in light of increasing consensus that sensitivity is a multi-componential construct, which can be fruitfully described by focusing on its different dimensions (Bernard, Meade, & Dozier, 2013; Leerkes, Gedaly, & Su, 2016; Mesman & Emmen, 2013). This raises the question of what exactly about sensitivity could play a role in infants’ subcortical brain development.

Deconstructing maternal sensitivity

With the goal of unpacking the construct of sensitivity by empirically deriving aspects of maternal behavior that constitute sensitivity, we submitted the items of the Maternal Behavior Q-Sort (MBQS; Pederson & Moran, 1995) to factor analysis (Bailey et al., 2017). The factor analysis yielded three factors: Cooperation/Attunement (mothers' ability to accurately interpret infants' cues and to adjust the interaction correspondingly; hereafter Cooperation); Positivity (maternal positive affect and attitude, describing mothers who show no overt signs of feeling overwhelmed or critical of the infant); and Accessibility/Availability (consistent attentiveness toward the infant, even when engaged in other tasks; hereafter Accessibility). We found that these dimensions differentially predicted child attachment security to mother (Bailey et al., 2017) and were predicted differently by family constellation (Bernier, Miljkovitch, Tarabulsy, Sirois, & Bailey, 2018). These dimensions have the advantage of being empirically-derived, strongly anchored in Ainsworth's original extensive descriptions of maternal sensitivity (Ainsworth, Bell, & Stayton, 1974), and congruent with both classic (De Wolff & Van IJzendoorn, 1997) and more recent meta-analyses on maternal sensitivity (Nievar & Becker, 2008).

In this preliminary investigation, we used the three behavioral dimensions of sensitivity (Cooperation, Positivity and Accessibility) along with an a priori regions-of-interest approach to examine whether specific aspects of maternal sensitivity during mother-infant home interactions, assessed at 1 year, were predictive of the volumes of the amygdala and hippocampus in late childhood. Based on the findings of Rifkin-Graboi et al. (2015), we expected that higher levels of at least some dimensions of maternal sensitivity would predict smaller hippocampal, and possibly amygdala, volume nine years later. Owing to the lack of previous research, no a priori hypotheses were made regarding the relative predictive power of different dimensions of sensitivity.

Method

Participants

Participants included in the present preliminary study (n = 33) were followed annually as part of an on-going larger longitudinal research project that documents the prospective associations between the early caregiving environment and several facets of child development (Bernier, Matte-Gagné, & Bouvette-Turcot, 2014). In the present study, we report on maternal sensitivity assessed around 1 year of age (*M* = 13.02 months, *SD* = 1.32, range = 11.0 – 16.5) and structural magnetic resonance imaging (MRI) data collected when children were 10-11 years of age (*M* = 10.59, *SD* = 0.46, range = 10.0 – 11.67 years). This study was conducted according to guidelines laid down in the Declaration of Helsinki, with written informed consent obtained from each child’s mother before any assessment. All procedures were approved by the Faculty of Arts and Sciences’ research ethics committee at the University of Montreal.

Families were recruited from random birth lists of the city of Montreal, Canada, provided by the Ministry of Health and Social Services. Inclusion criteria for participation were full-term pregnancy (i.e., at least 37 weeks of gestation) and the absence of any known physical or mental disability, severe developmental delay in the infant, acquired brain injury, and standard MRI counter-indications. For the current analyses, 64 families were invited to participate in structural MRI when children reached 10 years of age; these were the oldest children of the cohort, and the only ones who had reached the age of 10 at the time of data collection. To maintain a narrow age window for the MRI scan, younger children were not invited to participate. Among the 64 families invited, 39 (60.94%) agreed to participate. However, four of these children were not eligible due to security reasons (e.g., wearing braces); thus, 35 children underwent the MRI exam. These 35 families did not differ from those who declined (n = 25; 39.06%) or were not eligible in terms of family income, child sex, parental age, education, and ethnicity, as well as maternal sensitivity (all *p*s ≥ .21; see Table 1). Of the 35 children who took part in the MRI protocol, one was excluded from the analyses because of excessive head motion (which may bias volumetric estimates; Reuter et al., 2015) and one because of suspected neuropathology. Consequently, data from 33 children (20 girls and 13 boys) were used in the analyses. Group comparisons between families included in the analyses (*n* = 33) and those who declined or were not eligible (*n* = 29) revealed no significant differences.

Measures

Maternal sensitivity during mother-infant interactions. Maternal sensitivity was assessed at 1 year using the Maternal Behavior Q-Sort (MBQS; Pederson & Moran, 1995), a 90-item measure designed to assess the quality of maternal behavior during in-home mother-infant interactions. Home visits were modeled after the work of Pederson and Moran (1995), and aimed at challenging the mother's capacity to divide her attention between competing demands, thus reproducing the natural conditions of daily life when caring for an infant. Specifically, the home-visit protocol was designed to create a situation where maternal attention was being solicited by both the research tasks and the infant's demands, in order to produce an ecologically valid context in which the mother had to attend to ongoing activities while keeping track of her infant’s cues (Behrens, Parker, & Kulkofsky, 2014). Visits lasted 75 minutes on average and included a brief interview with the mother, research tasks with the infant, a 20-minute mother-infant free-play period, and a series of questionnaires that the mother was asked to complete while the infant was not kept busy by the research assistant. This procedure is considered to constitute the optimal use of the MBQS, given evidence for its ecological validity and predictive power (Booth, Macdonald, & Youssef, 2018; see Atkinson et al., 2000, for meta-analytic evidence).

Observations performed during these home visits were used to assess maternal sensitivity. A research assistant noted maternal behaviors throughout the visit and rated the MBQS immediately afterward, based on the entire observation period. To maximize the reliability of observations, research assistants attended a 2-day intensive training workshop, and then performed their first few home visits with a more experienced colleague, with whom they completed the MBQS assessment. When the junior home visitors were considered ready to rate maternal behavior, the first two or three independent visits were followed by a debriefing session with an experienced graduate student to review the salient elements of the visit before scoring the MBQS. The assistants then progressed to rating autonomously.

Each MBQS item describes a potential maternal behavior. Following each visit, the observer sorted the items into nine piles, ranging from very unlike to very similar to the observed mother's behaviors. Based on this sort, each item was assigned a score varying between 1 and 9, indicating the extent to which it resembled the mother's behavior during the visit. In the current study, we used the three MBQS dimensions derived by Bailey et al. (2017), namely: Cooperation ($\alpha = .90$; e.g., *Interactions revolve around baby's tempo and current state*), Positivity ($\alpha = .89$; e.g., *Is animated in social interactions with baby*), and Accessibility ($\alpha = .90$; e.g., *Monitors and responds to baby even when engaged in other activity such as cooking or having a conversation with visitor*). In this sample, the inter-correlations between these three dimensions were $r = .19$, $p = .295$ for Cooperation-Positivity; $r = .38$, $p = .033$ for Accessibility-Positivity; and $r = .61$, $p < .001$ for Accessibility-Cooperation.

The MBQS is one of the best validated observational sensitivity assessments and is often used to characterize the quality of maternal behavior toward infants (see Booth et al., 2018). It is significantly correlated with other measures of maternal behavior, such as the HOME Inventory and the Ainsworth scales (see Pederson & Moran, 1995), and shows good temporal stability (Behrens et al., 2014) and excellent predictive validity (Van IJzendoorn, Vereijken, Bakermans-Kranenburg, & Riksen-Walraven, 2004). Almost thirty percent (29.8%) of the visits were conducted by two research assistants who completed the MBQS independently. Agreement between the two raters' sort was very good, *ICC* = .87.

Mother-infant attachment. Attachment security was assessed at 15 months (*M* = 15.65 months, *SD* = 0.97, range = 14.5 – 18.0) using the Attachment Behavior Q-Sort (AQS; Waters, 1995) during a home visit similar to that used at 1 year to assess sensitivity. The AQS procedure is the same as for the MBQS, except that items and observations pertain to infant rather than maternal behavior. The psychometric properties of the AQS are well demonstrated by meta-analytic data (Van IJzendoorn et al., 2004). As explained in the analytic plan, we controlled for attachment in all main analyses so as to avoid overlap with previously published results on the same sample.

Structural magnetic resonance imaging

Neuroimaging data were collected using a 32-channel head coil on a Siemens 3 Tesla scanner (MAGNETOM Trio, Siemens, Erlangen, Germany). Structural data were acquired using a three-dimensional T1-weighted 4-echo magnetization-prepared rapid gradient-echo sequence (3D-T1-4echo-MPRAGE sagittal; repetition time (TR): 2530 ms; 4 echo times (TE): 1.64/3.5/5.36/7.22 ms; echo spacing ΔTE: 1.86 ms; flip angle: 7°; 176 slices; slice thickness: 1

mm; no gap; matrix: 256 × 256; field of view (FoV): 256 mm; in-plane resolution: 1 × 1 mm; duration: 363 sec). All images were visually inspected for artifacts and image quality.

Volumes of the hippocampus and amygdala (left and right hemispheres) were obtained using automated procedures in the Computational Anatomy Toolbox (CAT12; www.neuro.uni-jena.de/cat/) implemented in the SPM12 package (Statistical Parametric Mapping, Institute of Neurology, London, UK) running on MATLAB version R2016a (MathWorks, Inc., Natick, MA, USA). CAT12 enables the estimation of tissue volumes for different volume-based atlas maps in the native space before any spatial normalization. The Neuromorphometrics atlas (http://Neuromorphometrics.com), a label atlas based on manually segmented whole-brain parcellation, was used in the present study.

Analytic plan

Given the small sample size, we first carefully examined score distributions including univariate and multivariate outlying values to ensure that no result would be attributable to extreme scores. We then imputed maternal sensitivity scores that were missing for one child. Next, we examined the pattern of zero-order correlations between the three dimensions of maternal sensitivity and volumes of the amygdala and hippocampus. Left and right hemispheres were considered separately.

The main analyses consisted of multiple linear regression analyses in which the three dimensions of sensitivity were entered simultaneously (to account for their shared variance and avoid multiple analyses) as predictors of each region of interest: left amygdala, right amygdala, left hippocampus, right hippocampus. As per recommendations (e.g., Barnes et al., 2010), these analyses were adjusted for child age, sex, and total intracranial volume (TIV). Though pubertal status relates to brain volumes (Herting & Sowell, 2017), it was not retained as a covariate because of its strong relation to child sex ($r = .57$, $p = .001$). We chose child sex over puberty as a control because the former showed some marginal or significant relations with the volumetric outcomes (*p*s from .044 to .172), whereas the latter did not (*p*s from .541 to .827), thereby producing more conservative analyses. Given well-documented relations between maternal education and family income and child brain volumes (Jednoróg et al., 2012; Noble, Houston, Kan, & Sowell, 2012), education and income were also controlled for. Finally, we controlled for mother-child attachment security, which we previously investigated in relation to gray matter morphometry in a prior study with the same sample (Leblanc, Dégeilh, Daneault, Beauchamp, & Bernier, 2017). Although those prior analyses revealed no significant associations between attachment and amygdala or hippocampal volume, we controlled for attachment in the current analyses to ensure independent results. Indeed, given the reliable links between sensitivity and attachment (De Wolff & Van IJzendoorn, 1997), controlling for attachment allowed us to ascertain that any predictions would be specific to sensitivity rather than due to shared variance between sensitivity and attachment, hence ensuring the absence of overlap with our previous results. To summarize, child sex, age, and TIV, as well as maternal education, family income, and mother-child attachment were covaried in the main analyses. Although adjusting for several covariates is costly in terms of degrees of freedom, it safeguards against false positives that could result from uncontrolled third-variable effects; this may be especially important given the very young state of the literature on typical variations in parenting and children’s brain structure. Given that prior studies have found moderate to large effect sizes for the links between indices of parent-infant relationships and hippocampal and amygdala volumes after adjusting for covariates (Rifkin-Graboi et al., 2015), even across much longer time delays than in the current study (Lyons-Ruth et al., 2016; Moutsiana et al., 2015), we considered that the use of the chosen covariates would not compromise statistical power to an excessive degree and was appropriately stringent.

Results

Preliminary analyses

We first examined score distributions. All main study variables were normally distributed, except for the Cooperation dimension, for which kurtosis was at 4.07. This was due to one mother whose score was 3.54 standard deviations (*SD*) below the mean. Following Tabachnick and Fidell's (2013) recommendations for winsorizing, we substituted her score with the next lowest observed score for Cooperation ($Z = -1.97$), which brought kurtosis to 0.58, thus largely within the acceptable range. Note that this mother's child had brain volumetric scores that all fell well within one *SD* of the mean (*Z*s from .28 to .87). No other univariate outlying value was observed. We next checked for multivariate outliers by computing Mahalanobis distances for each outcome in turn; all obtained distances were largely below the corresponding χ^2 critical value, indicating the absence of multivariate outliers (Tabachnick & Fiddell, 2013).

Maternal sensitivity scores were missing for one child. In line with recommendations for best practices for handling missing data (Enders, 2010), multiple imputation was employed to estimate the missing values in SPSS 24.0. Ten imputations were used to maximize the precision of imputed data (Graham, 2009). To reach maximal accuracy, the imputations were performed based on the original 64 families using child sex and age at T1, as well as parental age and education at the time of recruitment as predictors in the imputation equation. Analyses were performed on each of the resulting 10 data sets, and pooled results are presented below. Note that results are almost identical when analyses are conducted without imputation on the 32 children with complete data.

Main analyses

Table 2 presents the zero-order correlations between the independent and dependent variables. Accessibility was significantly negatively associated with volume of the left hippocampus, right hippocampus, and right amygdala. In contrast, neither Cooperation nor Positivity showed statistically significant bivariate links to any of the volumetric outcomes – although relations with volumes of the left and right hippocampi were in the same direction as those involving Accessibility.

To tease apart shared and unique variance between the components of sensitivity while accounting for the covariates, we then ran hierarchical regression analyses predicting each brain volume in turn. Maternal education and family income, child sex, age, and TIV, as well as mother-child attachment security, were entered in a first block, followed by the three dimensions of sensitivity. Table 3 presents the results of these analyses. The first block explained between 34.9% and 45.7% of the variance in brain volumetric outcomes, mostly attributable to TIV. After accounting for this, the three dimensions of sensitivity together predicted a unique 18.6% of the variance ($p = .014$) in volume of the left hippocampus. This prediction was mostly due to Positivity, which negatively predicted left hippocampal volume ($\beta = -.54$, $p = .003$). Likewise, 21.6% of the variance ($p = .003$) in volume of the right hippocampus was uniquely predicted by maternal sensitivity dimensions, and this prediction was again mainly attributable to Positivity ($\beta = -.58$, $p < .001$).

Results were different when considering amygdala volumes. Volume of the left amygdala was not predicted by any aspect of sensitivity, which in fact explained only 1.5% of unique variance above the covariates. In contrast, volume of the right amygdala was significantly predicted by sensitivity dimensions (16.1%; $p = .030$); however, in this case this was due to the

Accessibility dimension, which was strongly predictive of a smaller right amygdala volume ($\beta = -.64$, $p < .001$).

To further investigate the value of the multidimensional approach to sensitivity, we also considered the overall maternal sensitivity score that can be derived from the MBQS – and is generally the only MBQS score used in studies. We submitted this score to regression analyses similar to those just described. The analyses revealed that after accounting for the covariates, overall sensitivity was not significantly predictive of any brain volumetric outcome (left hippocampus: $\beta = -.26$, $p = .289$; right hippocampus: $\beta = -.36$, $p = .105$; left amygdala: $\beta = -.08$, $p = .724$; right amygdala: $\beta = -.19$, $p = .449$).

Given that regression analyses are vulnerable to specific cases influencing the results in small samples, we computed Cook's distances for each of the above regression models (Tabachnick & Fiddell, 2013). These analyses revealed that no particular case was driving the results in any of the regressions.

Discussion

The young developing brain is presumed to be sensitive to environmental input (Lupien et al., 2009; Tottenham, 2014). Yet, only a handful of studies to date have examined parenting quality with infants in relation to indicators of brain development. Though scant, this literature is beginning to suggest that maternal sensitivity toward infants relates to their subcortical brain morphology (Rifkin-Graboi et al., 2015; Sethna et al., 2017). With the aims of adding to this slim body of work and providing some initial insight into specific aspects of parenting that may be worth considering in future larger-scale studies, this preliminary study used a small sample that was very well characterized in terms of quality of maternal caregiving behavior in infancy. Maternal sensitivity was assessed using a highly validated observational procedure conducted in the families' homes, carefully designed to elicit naturalistic patterns of interactions between mothers and their infants and thus provide ecologically valid assessment (Pederson & Moran, 1995 – see also Booth et al., 2018). The ensuing observations were used to derive three dimensions of sensitivity toward the infant: accessibility, positivity, and cooperation. The results revealed that after accounting for covariates and, importantly for our purposes, for the overlap between the different aspects of sensitivity, maternal accessibility was uniquely predictive of right amygdala volume, and maternal positivity was uniquely predictive of bilateral hippocampal volumes. Maternal cooperation showed no significant links to brain volumes.

Maternal accessibility and amygdala volume

Accessibility focuses on the consistency of mothers' psychological accessibility; mothers with high scores on this dimension are aware of their infant even when occupied with other activities. Such capacity to monitor the infant's whereabouts likely allows mothers to intervene quickly when their infant encounters a situation requiring adult help or reassurance (facing a large unknown animal in the park, startling over a loud noise, etc.). Thus, maternal accessibility may often shield infants from the highly distressing experience of fear or threat not followed by adult soothing. This may, in turn, protect their amygdala. Indeed, premature engagement and thus early functional and structural development of the amygdala are believed to ensue from exposure to caregiving deficiencies (Tottenham, 2012). Put simply, the hypothesis is that if an infant's mother reliably intervenes to protect the infant against perceived threats in the environment, the amygdala's threat-detection and stress-response functions are less often recruited (Callaghan & Tottenham, 2016; Lupien et al., 2011). In turn, less frequent use of these functions prevents the amygdala from excessive functional use and consequently, premature structural growth. In fact, although any conclusion regarding directionality of effects between caregiving and subcortical volumes remains elusive and may be age-dependent (Tottenham & Sheridan, 2010), the current results showing that higher maternal accessibility relates to *smaller* (right) amygdala volume are in line with the two longitudinal studies on infant attachment to date, which both found that lower-quality mother-infant attachment predicted increased volume of the amygdala (Lyons-Ruth et al., 2016; Moutsiana et al., 2015 – see also Rifkin-Graboi et al., 2015, for similar albeit non-significant results with sensitivity). Although this literature is just emerging, evidence to date therefore consistently suggests that in non-clinical, normative populations, higher-quality mother-infant interactions relate to smaller child amygdala volume. The current preliminary results also suggest that mothers' psychological availability to protect the infant against perceived threats in his or her environment may be key in this regard.

Findings with maternal accessibility were specific to the right amygdala. Lyons-Ruth et al. (2016) found that lower-quality attachment in infancy predicted larger left amygdala volume in adulthood, whereas Rifkin-Graboi et al. (2015) found that when controlling for maternal anxiety, sensitivity was related to right but not left amygdala volume in infants. Other relevant studies did not find laterality effects – thus, the parenting literature with normative populations is sparse to the extent of precluding any conclusions. In the current study, the lack of prediction of left amygdala volume was relatively striking, with the three dimensions of sensitivity together predicting a meager 1.5% of the variance, compared to 16.1% to 21.6% of the other volumetric outcomes. Given that the exact magnitude of estimates is unstable in small samples like this one, these differences may be less meaningful than they appear. Should, however, the current results be replicated in larger-scale studies, they may perhaps be interpretable in light of the amygdala's lateralized activation to certain types of stimuli: some studies have suggested that the left amygdala responds mostly to verbally-mediated and consciously processed stimuli, whereas the right amygdala responds mostly to ambiguous emotional stimuli, non-verbal stimuli, as well as when emotional stimuli are processed automatically (Costafreda, Brammer, David, & Fu, 2008; Gläscher & Adolphs, 2003; Phelps et al., 2001; Wang et al., 2017). Given that infants are non-verbal and that early parent-infant interactions are thought to be at least partly encoded at an automatic level (Johnson et al., 2010; Maier, Bernier, Pekrun, Zimmermann, & Grossmann, 2004), one might speculate that infants' right amygdala is perhaps often recruited in the process of their daily interactions with their mothers, and thus influenced by the nature and quality of these interactions. Moreover, it is suggested that right amygdala function could be linked to the autonomic arousal generated by rapidly processed emotional stimuli (Liu, Chen, Hsieh, & Chen, 2015). As maternal sensitivity is linked to children's autonomic responses during stressful situations (Conradt & Ablow, 2010), the association between maternal sensitivity and right, but not left, amygdala volume reported here might relate to the importance of maternal sensitivity for infants' early regulatory processes. That said, the exact nature of amygdala lateralization is a matter of debate (Fusar-Poli et al., 2009; Schneider et al., 2011; Sergerie, Chochol, & Armony, 2008). Accordingly, larger-scale studies, still quite rare in the parenting-MRI literature, are needed to test the robustness of apparent laterality effects and adjudicate between different interpretations.

Maternal positivity and hippocampal volume

Maternal positivity during interactions with the infant was uniquely predictive of bilateral hippocampal volume. The directionality of the findings, with more positivity predicting smaller hippocampal volume, is similar to that identified by Rifkin-Graboi et al. (2015) with concurrent overall maternal sensitivity. In a sample of low-SES, African-American children exposed to cocaine in utero, Rao et al. (2010) observed that greater maternal nurturance at age 4 (but not 8) predicted smaller hippocampus volume. Lyons-Ruth et al. (2016) also observed a sizeable (albeit not statistically significant; partial $r = .40$, $p = .125$) association between lower-quality mother-infant attachment and larger right hippocampal volume in adulthood. Overall, though, putative caregiving effects are often not found on the hippocampus (e.g., Moutsiana et al., 2015), and when found, their directionality varies greatly, possibly in relation to the developmental timing of assessments (see Rao et al., 2010; Tottenham & Sheridan, 2010).

Nevertheless, the current findings linking a more positive maternal attitude toward the infant to smaller bilateral hippocampal volume at age 10 were highly reliable over and above several important confounding factors. According to relational memory theory, the hippocampus is critically involved in the construction, updating, and reactivation of representations of relationships (Cohen & Eichenbaum, 1993; Eichenbaum & Cohen, 2001; see also Rubin et al., 2014). According to this model, the hippocampus enables to integrate different pieces of information, often distant in time or space, into coherent relational models such that how a person has acted toward the self in the past influences how he or she is expected to act in future interactions. These descriptions of the role of the hippocampus are reminiscent of the notion of “internal working models” (IWM) as described by attachment theorists. IWM consist of mental representations of the self and the caregiver, thought to be shaped by a variety of daily interactions with primary caregivers that are progressively integrated into a coherent view of the child-caregiver relationship (Bowlby, 1982). Once formed, these IWM help the child interpret and predict the caregiver’s behavior (Bretherton & Munholland, 2016). Thus, the link observed here between maternal sensitivity and hippocampal volume raises the intriguing possibility that the hippocampus might be a central element of the neural network subsuming IWM of parent-infant relationships, which stem from the infant’s cumulative experience of the caregiver’s sensitivity. One way to investigate this possibility would be to use experimental priming tasks to activate IWM (see e.g., Maier et al., 2004) in conjunction with functional MRI (Gee et al., 2014) to examine whether the hippocampus activates in response to the priming of IWM.

Hypotheses regarding why maternal positivity, in particular, would be involved in hippocampal development are admittedly speculative at this point. One possibility is that positivity is the MBQS dimension with the most overt emotional content. While accessibility and cooperation mostly describe what a mother does, positivity rather focuses on how she does it: it taps into mothers' positive attitude and delight in their infant, including mothers' warm and cheerful affect during interactions with the infant. One previous study found that maternal positive affect during mother-infant interactions, but not intrusiveness or sensitivity, predicted brain functional development across infancy, as assessed by EEG (Bernier, Calkins, & Bell, 2016), which also suggests the potential importance of the affective climate of mother-infant interactions for infant neural development. It is well demonstrated that the hippocampus acts in concert with the amygdala in the encoding and consolidation of memories of emotionally arousing events (McDonald & Mott, 2017; Phelps, 2004; Richardson, Strange, & Dolan, 2004). Hence, the current findings linking hippocampal volume to maternal positivity may suggest that the hippocampus is centrally involved in the neural process that allows for the emotional atmosphere of early mother-infant interactions to be gradually integrated into the infant's mental representation of that relationship. Undoubtedly, this explanation is tentative and in need of empirical research.

Maternal cooperation

The cooperation dimension showed no significant associations with any brain volumetric outcome. We previously reported cooperation to be the best predictor of mother-infant attachment assessed with the AQS (Bailey et al., 2017), which in turn, was found to be unrelated to hippocampal or amygdala volume in this sample (Leblanc et al., 2017; and current paper). It thus appears that in this sample, neither mother-infant attachment nor its best predictor, maternal cooperation, are significantly predictive of hippocampal or amygdala volume. This underscores the importance of a fine-grained approach to the parenting antecedents of child brain development: so little is currently known about the mechanisms underlying putative caregiving influences on neural development, that parenting dimensions that are central to children's socio-emotional functioning, such as maternal cooperation, may well differ from those that are implicated in their neural development.

Sensitivity as a multidimensional construct

A last potentially interesting aspect of the current results is that bivariate and multivariate analyses suggested fairly different conclusions regarding the relative salience of distinct aspects of maternal sensitivity. Though accessibility appeared, at the bivariate level, to be the most potent predictor of both amygdala and hippocampal volumes, the multivariate analyses revealed that the variance unique to maternal positivity was significantly predictive of hippocampal volume. Given that the magnitude of estimates is unstable in small samples like this one, caution needs to be exercised in interpreting the results observed here. Yet, the combined results of the bivariate and multivariate analyses do suggest that investigation of a single marker of parenting quality, because it does not allow to tease apart shared and unique variance between components of parenting, may mask meaningful specific predictions of children's brain structure, thereby leading to underestimation of the role of parental care in brain development. While suggested by this preliminary study, such specific predictive links will be more satisfactorily addressed by better-powered, larger-scale studies.

Limitations and conclusions

The results presented here must be interpreted in the context of some limitations. First, the longitudinal design, albeit an improvement over previous cross-sectional studies of sensitivity and infant brain volumes, was not cross-lagged, which precludes determination of directionality. The possibility of reverse causation, namely that smaller amygdala and hippocampal volumes were already present in these children in infancy, and may have predisposed their mothers to show greater positivity and accessibility toward them, cannot be excluded. In fact, given that developmental processes are transactional by nature (Sameroff, 2009), it is reasonable to expect that any caregiving-brain associations are probably the results of bidirectional influences. Although we did not assess sensitivity concurrent to the MRI scan, the addition of such concurrent measures would be a useful first step in delineating the direction of associations. The design also leaves open the possibility that shared genes between mother and infant may be partly responsible for the links observed. Indeed, hippocampal and amygdala volumes are moderately heritable (Swagerman, Brouwer, de Geus, Hulshoff Pol, & Boomsma, 2014 – though their developmental trajectories across childhood are largely due to environmental factors; Brouwer et al., 2017). Likewise, individual differences in parenting quality broadly defined are moderately heritable (Klahr & Burt, 2014). However, different components of parenting show different heritability estimates, and in particular, one study suggested that negative aspects of parenting were almost four times more heritable than positive aspects, which showed only modest heritability (Oliver, Trzaskowski, & Plomin, 2014). This suggests that genetic influences on maternal sensitivity, a positive aspect of parenting, could be modest. Indeed, behavior genetics studies have found that the variance in maternal sensitivity (Roisman & Fraley, 2008) as well as the shared variance between sensitivity and child behavioral outcomes

(Roisman & Fraley, 2012) was subject to small-to-negligible genetic contributions. Still, the possibility that shared genes between mother and infant could account for part of the associations observed here cannot be excluded. The small sample size, though it is the norm in studies of mother-infant relationship quality in relation to MRI data (N’s = 18, 59, 20, and 39 in Lyons-Ruth et al., 2016; Moutsiana et al., 2015; Rifkin-Graboi et al., 2015; and Sethna et al., 2017 respectively), reduced statistical power, with the consequence that only moderate to large effect sizes could be detected as significant. Overall, replication in larger independent samples is necessary to confirm the links reported in this preliminary small-scale study. Finally, we did not assess paternal sensitivity, although there is no theoretical reason to expect that fathering is less salient to brain development than mothering.

Despite these limitations, this longitudinal study corroborated the links between maternal sensitivity toward infants and subcortical brain volumes, which had only been observed in two cross-sectional studies thus far (Rifkin-Graboi et al., 2015; Sethna et al., 2017). The current study further suggested that a multidimensional approach to maternal (and paternal) behavior could be a fruitful way to advance the nascent research in this area, given that different facets of parenting could prove differentially predictive of distinct aspects of neurodevelopment. More broadly, the findings also add support to the idea that maternal sensitivity is made up of distinct components, not all of which are equally important for all infant outcomes (Bailey et al., 2017; Bernard et al., 2013; Leerkes et al., 2016; Mesman & Emmen, 2013). A multidimensional approach to normative parental care might allow for the identification of precise aspects of parenting toward infants that could be promoted so as to foster their optimal brain development.

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Table 1

Sociodemographic information and maternal sensitivity scores for children who underwent the magnetic resonance imaging (MRI) exam (N = 35) and those who declined (N = 25) or were not eligible (N = 4) to participate in the MRI protocol.

	Completed MRI *n* = 35	Declined or ineligible *n* = 29	Group comparisons
Parental age at recruitment			
Mothers	31.63 ± 5.05	32.02 ± 3.50	*t*(62) = -0.36; *p* = .73
Fathers	33.40 ± 5.29	34.07 ± 4.86	*t*(62) = -0.52; *p* = .60
Parental years of education			
Mothers	15.40 ± 2.23	15.26 ± 2.32	*t*(62) = 0.24; *p* = .81
Fathers	15.60 ± 1.94	14.97 ± 2.10	*t*(62) = 1.30; *p* = .21
Ethnicity			
Mothers	80.00	86.21	χ^2 (1) = 0.43; *p* = .51
Fathers	74.30	75.90	χ^2 (1) = 0.02; *p* = .89
Family income	74.29	79.31	χ^2 (1) = 0.22; *p* = .64
Child sex	60.00	44.83	χ^2 (1) = 1.47; *p* = .23
Cooperation/Attunement	7.26 ± 1.11	7.00 ± 1.51	*t*(62) = 0.77; *p* = .44
Positivity	7.66 ± 0.97	7.23 ± 1.63	*t*(62) = 1.27; *p* = .21
Accessibility/Availability	6.31 ± 1.36	5.98 ± 1.74	*t*(62) = 0.84; *p* = .40

Note. For ethnicity, family income, and child sex, values represent percentages of families with a Caucasian mother/father, an income above $60,000, and girls. For parental age, parental education, and maternal sensitivity, values represent mean ± standard deviation. Two children who underwent MRI were excluded from analyses; excluding them from the group comparisons did not change the results.

Table 2

Zero-order correlations between the three dimensions of sensitivity and brain volumes

	Brain volume			
Dimension of sensitivity	Left hippocampus	Right hippocampus	Left amygdala	Right amygdala
Cooperation/Attunement	-.23	-.22	-.17	.00
Positivity	-.26	-.28	-.06	-.09
Accessibility/Availability	-.43*	-.45**	-.28	-.39*

* *p* < .05. ** *p* < .01.

Table 3

Regression analyses predicting brain volumes from the three dimensions of sensitivity

	Predicted brain volume							
	Left hippocampus		Right hippocampus		Left amygdala		Right amygdala	
Predictors	β	Block R^2	β	Block R^2	β	Block R^2	β	Block R^2
Block 1	----	38.8%	----	45.7%	----	39.9%	----	34.9%
Maternal education	-.32^{t}		-.16		-.15		-.01	
Family income	.25		.13		.01		.05	
Child sex	-.04		-.01		-.08		-.01	
Child age	-.05		-.06		.12		.05	
TIV	.53**		.64***		.62***		.69***	
Child attachment	-.23		-.25^{t}		.13		-.01	
Block 2	----	18.6%	----	21.6%	----	1.5%	----	16.1%
Cooperation/Attunement	-.13		-.25		.03		.51^{t}	
Positivity	-.54**		-.58***		-.10		-.06	
Accessibility/Availability	.02		.07		-.11		-.64***	
Total model R^2	57.4%		67.3%		41.4%		51.0%	
F	5.49		7.86		2.67		4.47	
p	.001		.000		.030		.002	

Note. TIV: total intra-cranial volume.
$^{t}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$