Normal Variation in Early Parental Sensitivity Predicts Child Structural Brain Development

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Objective: Early caregiving can have an impact on brain structure and function in children. The influence of extreme caregiving experiences has been demonstrated, but studies on the influence of normal variation in parenting quality are scarce. Moreover, no studies to date have included the role of both maternal and paternal sensitivity in child brain maturation. This study examined the prospective relation between mothers' and fathers' sensitive caregiving in early childhood and brain structure later in childhood.

Method: Participants were enrolled in a population-based prenatal cohort. For 191 families, maternal and paternal sensitivity was repeatedly observed when the child was between 1 year and 4 years of age. Head circumference was assessed at 6 weeks, and brain structure was assessed using magnetic resonance imaging (MRI) measurements at 8 years of age.

Results: Higher levels of parental sensitivity in early childhood were associated with larger total brain volume (adjusted $\beta = 0.15$, $p = .01$) and gray matter volume (adjusted $\beta = 0.16$, $p = .01$) at 8 years, controlling for infant head size. Higher levels of maternal sensitivity in early childhood were associated with a larger gray matter volume (adjusted $\beta = 0.13$, $p = .04$) at 8 years, independent of infant head circumference. Associations with maternal versus paternal sensitivity were not significantly different.

Conclusion: Normal variation in caregiving quality is related to markers of more optimal brain development in children. The results illustrate the important role of both mothers and fathers in child brain development.

Key Words: sensitivity, mother, father, brain structure, MRI

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Brain development reflects the interplay between genetic and environmental factors.[1] In the last decade, several longitudinal and intervention studies have provided evidence for caregiving influences on child structural and functional brain development.[2] These studies have mostly focused on heterogeneous samples with a high risk for abnormal development due to specific child or parenting characteristics. Studies on the relation between parental care and brain structure in more homogeneous population samples are scarce. Moreover, no studies on the influence of caregiving on child brain structure have used repeated measures of the quality of both maternal and paternal caregiving in early childhood. In the current study, the longitudinal relation of maternal and paternal caregiving with child brain structure is examined in a prospective population-based cohort (N = 191).

Studies of institutionalized care show that early deprivation is related to reductions in white and gray matter volume, reductions in the volume of the posterior corpus callosum and superior–posterior cerebellum, and larger amygdala volume compared to those in children adopted into foster care or healthy controls.[3-6] Moreover, longer exposure to deprivation appears to result in more atypical development.[3,6] Retrospective studies of exposure to childhood adversities, ranging from chronic family discord to child abuse, have demonstrated reductions in corpus callosum area, gray matter cerebellar and vermis volumes, and hippocampal volume.[7-9] Other studies of high-risk samples defined by preterm birth, socioeconomic deprivation, child depression, or maternal substance use show that more sensitive parental care is associated with greater cortical thickness and asymmetry in cortical thickness,[10] and with either smaller[11] or larger[12,13] hippocampal volumes. Moreover, an intervention to enhance maternal sensitivity resulted in greater white matter maturation and connectivity in preterm infants.[14] The results of these high-risk samples, however, may not be generalizable to the general population because of the relatively extreme caregiving experiences that these children were exposed to as well as the large number of potential confounders.

Research on normal variation in parental care and child brain structure in the general population is surprisingly scarce, considering the compelling evidence that early caregiving has a long-term impact on various aspects of child development. Sensitive parental care, characterized by prompt and adequate response to the child's signals and needs,[15] predicts a more secure attachment relationship,[16] higher levels of cognitive competence,[17,18] and fewer psychological problems.[19,20] The association between sensitivity and more favorable outcomes in children has been demonstrated for both mothers and fathers.[21] One possible

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mechanism driving the association between parental sensitivity and child development is the impact of sensitivity on brain structure.[2] In addition to genetics, environmental influences such as parenting are involved in experience-expectant and experience-dependent processes that can have an impact, for example, on the pruning and formation of synapses and thus affect brain structural development.[22] A recent study has demonstrated this mechanism in adolescents, showing that maternal sensitivity predicted reduced growth in the amygdala and greater thinning of the orbitofrontal cortex 4 years later.[23]

Our study is a unique contribution to the literature in several ways. First, we examined the relation between early parenting and child brain structure in a large and relatively homogeneous sample of healthy children (N = 191), thus extending previous results to nondisadvantaged families with fewer confounders. Second, we used repeated measures of observed parental sensitivity from 1 to 4 years of age to decrease measurement error in the estimated stability of parental sensitivity.[24] Third, we investigated the association of maternal and paternal sensitivity separately and explored whether differences exist in their respective influences on child brain structure. Fourth, we adjusted our analyses for head size at 6 weeks of age and thus accounted for a proxy of brain development immediately after birth and limited the risk of reversed causality. Finally, we examined total brain, white matter, and gray matter volume, and cortical thickness in addition to amygdala and hippocampus volumes to study the relation of parental sensitivity with child brain structure. This approach was chosen because previous studies did not justify testing more specific hypotheses. We expect that parental sensitivity is related to more optimal brain structure in childhood. We do not expect to find differences in the relation between maternal versus paternal sensitivity and child brain structure because both maternal and paternal sensitivity are related to more favorable child outcomes, and the quality of care may be more influential than whether it is provided by mother or father.

METHOD

The study was embedded within the Generation R Study, a prospective cohort investigating growth, development, and health from fetal life onward in Rotterdam, the Netherlands.[25] Detailed measurements were obtained in a subgroup of children of Dutch national origin, meaning that the children, their parents, and their grandparents were all born in the Netherlands, to reduce confounding and effect modification.[26] The study was approved by the Medical Ethics Committee of the Erasmus Medical Center. Written informed consent was obtained from all adult participants.

From 2009 until 2013, children 6 to 10 years old from the Generation R Study were invited to participate in a magnetic resonance imaging (MRI) component of the study.[27] Approximately 20% of the parents declined to participate. Exclusion criteria for the children were significant motor or sensory disorders, moderate-to-severe head trauma, neurological disorders, claustrophobia, and contraindications to MRI. A total of 246 children participated in the MRI measurement. For 220 children, obtained data were of sufficient quality. For 193 children, at least 1 measure of parental sensitivity was available. We excluded 1 twin pair, resulting in 191 parent–child dyads. In the final study sample of 191 parent–child dyads, sensitivity data were available in 188 mother–child and 161 father–child dyads.

A nonresponse analysis of the 55 parent–child dyads with insufficient data quality or missing data on parenting indicated that they did not differ in gender, parental educational level, hippocampal volume, or amygdala volume. Children excluded from the analyses had less sensitive mothers and smaller total brain, white matter, and gray matter volumes than children included in the analyses (all $p < .01$). Mothers excluded from the analyses were somewhat younger than included mothers ($p < .05$).

Measures

Brain Imaging: Infant Brain Structure. Two indicators of infant brain structure were used in the analyses as baseline measures: ventricular volume and head circumference. Postnatal cranial ultrasounds were performed at 6.6 weeks (SD = 1.7). To measure the ventricular system, the volume of the ventricular frontal horns, ventricular body, and trigone on both sides were quantified in milliliters. Further details about the ultrasound measurement of the ventricular system have been described elsewhere.[28,29] In addition, the fronto-occipital head circumference of the children was measured. Previous studies have shown that head circumference in infancy is a reasonable proxy for total brain volume.[30]

Child Brain Structure. Magnetic resonance imaging was performed when the children were approximately 8 years old (mean = 8.04 years, SD = 0.93 year). Children were familiarized with the MRI environment during a mock session. Images were acquired on a 3-Tesla scanner (750 Discovery, GE Healthcare, Milwaukee, WI) using an 8-channel head coil. Following a 3-planar localizing scan, a high-resolution T1 inversion recovery fast-spoiled gradient recalled sequence was acquired in the sagittal plane with the following parameters: TE = 4.24 milliseconds, T1 = 350 milliseconds, TR = 10.26 milliseconds, NEX = 1, flip angel = 16°, and resolution 0.9mm^3 isotropic.

Image Processing. Cortical reconstruction and volumetric segmentation was performed with the Freesurfer image analysis suite 5.1. The technical details of these procedures are described in prior publications.[31] Briefly, processing included intensity normalization, removal of nonbrain tissue, automated Talairach transformation into standard space, segmentation of the cortical and subcortical white and gray matter structures, tessellation of the gray–white matter boundary, automated topology correction, and surface deformation. Once the cortical models were complete, the images underwent surface inflation, registration to a spherical atlas, and parcellation of the cerebral cortex into units based on gyral and sulcal structure. Cortical thickness was calculated as the closest distance from the gray–white boundary to the gray–cerebrospinal fluid boundary at each vertex on the tessellated surface.[32] At the scan site and after processing through FreeSurfer, structural images and segmentation quality were rated. Images were excluded if initial T1 scans were judged to be unusable or poor, if images could not be processed by FreeSurfer, or if images had poor segmentation quality (n = 26). We excluded scans with unusable hippocampus or amygdala segmentation (n = 20) from the hippocampal and amygdala analyses, respectively. The following volume measurements were analyzed: total brain, gray matter, white matter, hippocampus (adjusted for total brain volume), and amygdala (adjusted for total brain volume). Volume measures were z standardized to facilitate interpretation.

Sensitivity. Parental sensitivity was observed when the children were 1, 3, and 4 years of age. At 1 year of age, child and primary caregiver (86% mothers) were observed in a 5-minute free play session and a 5-minute psychophysiological assessment (data not presented here) using the Ainsworth 9-point rating scales for sensitivity and cooperation.[15] An overall sensitivity score was created by